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SIG SPECIAL INTEREST GROUP | REPORT

Prefilled syringes in intensive care units and operating theaters

December 2023

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Foreword by the President

Patient safety lies at the heart of all representations made by the European Association of Hospital Pharmacists and its member associations. Its importance for hospital pharmacy practice has also been manifested in a dedicated section of the European Statements of Hospital Pharmacy that among other things emphasises that hospital pharmacists should help to decrease the risk of medication errors by disseminating evidence-based approaches to error reduction. Many different tools exist that can support this effort, for example ready-to-administer syringes and standardised drug concentrations.

Prefilled syringes can also support patient safety improvement as well as medication error and medicine waste reduction. Since their availability and viability in relation to the different levels of resources available to hospitals across Europe varies, the European Association of Hospital Pharmacists (EAHP) decided to investigate this topic further and created a Special Interest Group (SIG) on the Use of Prefilled Syringes in Intensive Care Units and Operating Theatres (financially supported by BD). This SIG was tasked with looking at the cost/benefits and viability of prefilled syringes in relation to the different levels of resources available to hospitals across Europe.

On behalf of EAHP, I would like to thank all SIG members for their valuable contributions and their engagement.

In addition, I want to convey my condolences to family, friends and colleagues of David Cousins who sadly passed away earlier this way and who contributed immensely to this report and other EAHP activities in the past.

András Süle
President of the European Association of Hospital Pharmacists

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Executive Summary

This report presents the findings of the Special Interest Group (SIG) on the Use of Prefilled Syringes in Intensive Care Units (ICU) and Operating Theatres set up by the European Association of Hospital Pharmacists (EAHP).

Background and aim

Preliminary data suggests that prefilled syringes (PFS) can ensure sterility and help reduce medication errors associated with dosing errors and related costs. The work of the SIG aimed at the development of a value framework for using multiple criteria decision analysis to support evidence-based implementation and purchasing.

Methods

To create the value framework for a multiple criteria decision analysis instrument that could support value-based purchasing and utilisation of PFS the SIG conducted a literature review and ran three surveys to gather feedback from professional associations, healthcare professionals and PFS manufacturers.

Results

The literature review demonstrated that in the preparation and administration of injectable medicines in operating theatres and ICUs, PFS are associated with reduced number of preparation steps and associated cognitive complexity, simpler use (no labelling needed on the point of care as already correctly labelled), reduced infection rates (reduced microbiological contamination), reduced drug, disposables and packaging wastage, reduced nursing time allocated to the preparation and administration of drugs, quicker to administer in an urgent crisis situation, reduced the likelihood of medication errors, reduced needlestick injuries and overall cost savings.

For the opinion questions included in the surveys there are high and good levels of overall agreement to half of the statements on the use of PFS among the healthcare professionals that participated Based on the results and their discussion, the SIG concluded that the availability of PFS differs widely in Europe.

Conclusion

The SIG considers that while there is evidence of much ongoing work on PFS there are several gaps ranging from the availability of information on PFS, studies supporting the use of PFS and communication by manufacturers about their PFS portfolios. Based on their discussions, the literature

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review, and the outcomes of the three surveys, the SIG members have developed the following recommendations:

- Researchers should publish more information and data concerning the use of PFS in Europe to better inform health professionals involved in their (potential) use. In particular, the waste reduction potential of PFS and their sustainability aspects have not yet been explored.
- PFS users should promote information on their benefits among healthcare professionals that are less aware of them.
- Healthcare professionals using PFS should be encouraged to conduct studies comparing the cost of using vials and syringes and clinical/nursing time over the cost of using PFS and clinical/nursing time, for a range of different medicines.
- Competent authorities must increase awareness about the availability of recommendations, which might help increase the provision of PFS.
- Manufacturers should regularly release information about the PFS that they market in Europe. This information must be made easily accessible to healthcare professionals.

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Background and Introduction

In the clinical setting where decisions are often made quickly or under stress (i.e. emergency department, ICUs, operating theatres, during urgent interventions), medication error rates preparing injectable drugs from vials and ampoules can be high. These errors can result from normal human factors and resource constraints and can lead to Adverse Drugs Events (ADEs). Data suggests, that ~6% of hospitalised patients experience preventable ADEs (Panagioti et al., 2019). ADEs can significantly increase hospital operating costs. In 2017, the World Health Organization (WHO) initiated the third Global Patient Safety Challenge tackling medication safety which aims at globally reducing the level of severe, avoidable harm related to medications by 50% over 5 years (Medication Without Harm, WHO, 2017). The activity of this Special Interest Group (SIG) aligns largely with the efforts of WHO.

Preliminary data suggest that PFS can ensure sterility and help reduce medication errors associated with mislabelling dosing errors and related costs. Additionally, research has indicated that secondary benefits of using PFS can include drug/disposables/packaging waste reduction and medication preparation time reduction by more than 50% (Subhi et al., 2016)

To ensure the effective, safe, and efficient delivery of care using injectable medicines, the European Association of Hospital Pharmacists (EAHP) has established a SIG focused on the viability of prefilled syringes in relation to the different levels of resources available to hospitals across Europe. The main aim of the SIG on the Use of PFS in ICU and Operating Theatres is the development of a value framework using multiple criteria decision analysis to support evidence-based implementation and purchasing.

The SIG's discussions focused on both pharmacy-prepared and industry-manufactured prefilled syringes that are filled and labelled before they reach the end user. The impact of the COVID-19 pandemic was also explored in the exchanges. In the absence of a suitable definition of PFS, the group aimed to develop its own.

Provisional data support the greater use of ready-to-use injectable medications in European hospitals to enable the following benefits:

- Complete removal of multiple human factor error steps in IV medicine preparation;
- Reduction in medication errors associated with their preparation in clinical areas;
- Reduction in medication errors associated with their administration in clinical areas;
- Better standardisation of infusion doses/concentration/final volumes;

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- Saving time that medical, nursing and operating department support staff take to prepare doses and enabling them to spend time on other important clinical tasks;
- Waste reduction due to expired and unused manually prepared infusions;
- Reduced infection risks (including contamination) and bloodstream infection rates associated with preparing infusions in clinical areas;
- Cost-effectiveness;
- Reduction of needlestick and broken ampoule glass injuries; and
- Reduction of staff stress and well-being improvement.

Terminology and definitions

The following terms and definitions were of relevance for the work of the SIG.

*A **medication error** is an unintended failure in the drug treatment process that leads to, or has the potential to lead to, harm to the patient. Mistakes in the prescribing, dispensing, storing, preparation and administration of a medicine are the most common preventable cause of undesired adverse events in medication practice and present a major public health burden. European Union (EU) legislation requires information on medication errors to be collected and reported through national pharmacovigilance systems. In addition, the European Medicines Agency (EMA) plays a coordinating role and has published a set of good practice guidance* (Medication errors, EMA).

It should be noted that a patient suffering serious harm because the dose of injectable medicines was not administered would not be included as an adverse drug event. Thus, the members of the SIG have decided to use the term "medication error" in a broader sense than an adverse drug event. Both errors of omission and commission are included since some of these errors have led to actual patient harm, while other errors may well have led to harm under different circumstances.

***Ready-to-administer (RTA**): An injectable medicine is Ready-to-administer when it requires no further dilution or reconstitution and is presented in the final container or device, ready for administration or connection to a needle or administration set. For example, an infusion in a bag with no additive required.*

***Ready-to-use (RTU):** An injectable medicine is Ready-to-use when it requires no further dilution or reconstitution before transfer to an administration device. For example, a liquid with an ampoule, of*

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the required concentration, that only needs to be drawn up into a syringe (Glossary of pharmaceuticals terms, WHO, 2016).

Prefilled syringe (PFS): *A ready-to-administer syringe that is filled and then labelled before it enters the final clinical area where it could be immediately administered without further manipulation.*

In relation to RTA, RTU and PFS, the SIG members have observed that some publications use them interchangeably although they have different meanings.

Point of care activation/reconstitution/transfer device. *Closed-system procedure for sterile medicinal products: a procedure whereby a sterile medicinal product is prepared by transferring sterile starting materials or solutions to a pre-sterilised sealed container, either directly or by using a sterile transfer device, and without exposing the solution to the external environment.* (Resolution CM/Res(2016)2 on good reconstitution practices in health care establishments for medicinal products for parenteral use, Council of Europe)

Multiple criteria decision analysis*: Multiple Criteria Decision Analysis (MCDA) is "an umbrella term to describe a collection of formal approaches, which seek to take explicit account of multiple criteria in helping individuals or groups explore decisions that matter." (Belton et al., 2002). MCDA is a way to assign numbers explicitly to the elements that are being considered implicitly. It can make the decision-making process more transparent and improve the consistency and legitimacy of decisions.*

European Statements of Hospital Pharmacy

In 2014, EAHP adopted the European Statements of Hospital Pharmacy that express commonly agreed objectives which every European health system should aim for in the delivery of hospital pharmacy services. The use of prefilled medicine syringes is linked to several Statements in the European Statements of Hospital Pharmacy cited verbatim, below:

Statement 4.2

All prescriptions should be reviewed and validated as soon as possible by a hospital pharmacist. Whenever the clinical situation allows, this review should take place prior to the supply and administration of medicines.

Statement 4.3

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Hospital pharmacists should have access to the patients' health record. Their clinical interventions should be documented in the patients' health record and analysed to inform quality improvement interventions.

Statement 4.5

Hospital pharmacists should promote seamless care by contributing to transfer of information about medicines whenever patients move between and within healthcare settings.

Statement 5.2.

Hospital pharmacists should ensure the development of appropriate quality assurance strategies for medicines use processes to detect errors and identify priorities for improvement.

Statement 5.3

Hospital pharmacists should ensure their hospitals seek review of their medicines use processes by an external quality assessment accreditation programme, and act on reports to improve the quality and safety of these processes.

Statement 5.4

Hospital pharmacists should ensure the reporting of adverse drug reactions and medication errors to regional or national pharmacovigilance programmes or patient safety programmes.

Statement 5.5

Hospital pharmacists should help to decrease the risk of medication errors by disseminating evidence-based approaches to error reduction including computerised decision support.

Statement 5.6

Hospital pharmacists should identify high-risk medicines and ensure appropriate procedures are implemented in procurement, prescribing, preparing, dispensing, administration and monitoring processes to minimise risk.

Existing Prefilled Syringe Recommendations

The SIG also identified recommendations from other groups – the Australian and New Zealand College of Anaesthetists (ANZCA), the Anaesthesia Patient Safety Foundation (APSF), the European Board of Anaesthesiology (EBA), the Institute for Safe Medication Practices (ISMP), the National Patient Safety Agency (NPSA) and the Royal Pharmaceutical Society (RPS) concerning PFS. These were issued between 2007 and 2022 and are summarised in the table below.

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Group	Year	Recommendation
NPSA	2007	*"For high-risk injectable products: Provide ready-to-administer products of standard strength."*(Promoting safer use of injectable medicines, NPSA, NHS
APSF	2010	*"Routine provider-prepared medications should be discontinued whenever possible."* *"Standardized pre-prepared medication kits by case type should be used whenever possible."* (APSF Medication Safety Conference 2010)
NPSA	2010	*"Consideration should be given to the supply and use of ready to administer infusion products, e.g. prefilled syringes of fast acting insulin 50 units in 50 mL sodium chloride 0.9%"*(Safer administration of insulin, NPSA, NHS, 2010)
EBA	2011	*"The EBA recommends that pre-filled syringes should be used wherever possible."* (Safe Medication Practice Recommendation, EBA, 2011)
RPS	2018	*"Medicines should be presented as prefilled syringes wherever possible."* (Professional guidance on the safe and secure handling of medicines, RPS, 2018)
ANZCA	2021	*"Consideration should be given to supplying selected drugs for intravenous use in prefilled and pre-labelled syringes rather than in ampoules."* (Guideline for the safe management and use of medications in anaesthesia, ANZCA, 2021)
ISMP	2022	*"Maximize the use of manufacturer-prepared, pharmacy-prepared, or commercially prepared (e.g., from a compounding pharmacy or outsourcing facility) syringes in the perioperative setting for adult, paediatric, and neonatal medication doses."*(Guidelines for Safe Medication Use in Perioperative and Procedural Settings, ISMP, 2022)

Table 1 *– Existing PFS recommendations collected and discussed by EAHP's SIG.*

Objectives

The SIG conducted a literature review on the use of PFS and other RTA products including patient safety, clinical time saving, wastage and cost-effectiveness. The literature review aimed at learning more about the current and future hospital use of PFS through the identification of available evidence to derive solid indications for the practical implementation of this approach and suggest areas to explore with future clinical studies.

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In addition, three surveys were prepared. One survey was targeting individuals and one was addressing associations. They covered the use of PFS focusing on the attitudes towards their use, capturing benefits and identifying the main obstacles of their implementation. The third survey aimed at manufacturers of PFS was distributed among industry representatives at EAHP's Congress in Lisbon in March 2023. Based on the results obtained from the literature review and the surveys the SIG prepared a value framework for PFS.

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Results

The following chapter summarises the results of the Literature Review, the Professional Association Survey on the Use of Prefilled Syringes in Hospitals, the Multi-professional Survey on the Use of Prefilled Syringes in Hospitals and the Survey on Prefilled Syringes in Intensive Care Units and Operating Theatres targeting Manufacturers.

Literature review

Background

WHO has identified unsafe medication practices and medication errors as leading causes of injury and avoidable harm in healthcare systems across the world with an estimated associated cost in the range of $42 billion annually. In connection with this, the WHO 3rd Global Patient Safety Challenge 'Medication Without Harm' was established and made medication error reduction the theme for the WHO World Patient Day 2022. (Medication Without Harm, WHO, Medication without harm, WFSA) It was also estimated that, in the United States, adverse events related to the administration of injectable medicines contribute to an increase from $2.7 to $5.1 billion in annual costs (Lahue et al., 2012).

Medication errors occur when weak medication systems and/or human factors take effect such as fatigue, poor environmental conditions, or staff shortages. These can all impact the preparation and administration of injectable drugs and result in severe harm to patients (Medication Without Harm, WHO). The highest error rates involve intravenously administered drugs (48%–81%) mainly related to the complexity of preparation and administration of these drugs (Westbrook et al., 2011). Their impact is particularly serious due to the immediate bioavailability of the IV-administered drugs, the narrow therapeutic window and the challenges involved in the reversal of systemic effects (Westbrook et al., 2011, Degnan et al., 2020).

The problem appears to be particularly frequent in clinical settings (e.g. emergency rooms, intensive care units, operating rooms, during emergency interventions), where there are many possible human factor error steps in medicine preparation and administration and decisions are made quickly or under stress.

The COVID-19-induced pandemic significantly impacted healthcare professionals, including pharmacists and nurses. The former found themselves facing particularly stressful factors such as

working extra hours to ensure a sufficient supply of medication to intensive care units and to mitigate drug shortages and disruptions in the supply chain. The latter faced the suffering and death of an extraordinary number of patients and the work overload caused by the shortage of personnel. Many of them were then asked to work in new unfamiliar clinical areas hurriedly set up to deal with the patient overload (Manzano et al., 2021). Furthermore, the contagious nature of the virus forced all healthcare personnel to operate wearing extra personal protective equipment (PPE) which undoubtedly limited movement, restricted vision, constrained communication, and reduced speed of action. It followed an increased risk of errors during the preparation and administration of drugs (Ludwin et al., 2021).

One of the methods proposed to reduce these errors is to use RTA product. RTA has been reported to play a significant role in increasing efficiency and saving nursing time (Guidance Transforming NHS pharmacy aseptic services in England, NHS, 2020), whilst reducing errors and potentially related patient harm (Lahue et al., 2012, Hertig et al., 2018, Adapa et al., 2012, Benhamou et al., 2016, Hansen et al., 2018).

The role of PFS, with specific reference to situations of heavy workload and high stress such as those experienced during the COVID-19 pandemic, has recently been reviewed by a systematic review of the literature (Malik et al., 2022). It emerged that the literature supporting this technology is made up of evidence of different types (observational studies, surveys, case reports and risk analyses) and that this evidence continues to evolve.

Materials and methods

A targeted literature review was performed to identify potential benefits offered by PFS. The literature review investigated the associated benefits and risks/additional harm, cost-effectiveness and potential barriers to the use of PFS.

Literature search

The literature search covered MEDLINE (via PubMed) database. The search strategy was built up as a combination of search strings related to prefilled syringes, allowing the capture of all relevant keywords and synonyms that may appear in the papers. The search syntax was built up from a combination of four sets of keywords:

- The first set was a general term for a prefilled syringe.
- The second set of keywords was added to cover the hits relevant to our topic but used different nomenclatures for prefilled syringes - "ready to use" and "ready to administer".

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- To specify these widely used terms, the third set of keywords comprising synonyms of medicine was added.
- As the aim of the research was to identify potential value attributes of prefilled syringes, the fourth set contained synonym keywords on benefits, assessment, cost-effectiveness and value. The fourth set also contained synonyms of safety and risk.

The literature search was limited to articles published from 1 January 1990 onward. The literature search was not limited to English language papers or specific study designs, however, papers without English or French abstracts were excluded. The literature search was conducted on 30 March 2022. The search strategy with the number of search hits can be found in Annex II.

Identification of relevant studies

Citation data and abstracts of all identified search hits were imported into a Microsoft Excel table to find and remove any duplicates and further processing as a merged database. Due to the overlap of coverage, search results were de-duplicated before literature screening. The screening was conducted in two steps:

1. Abstract and title screening of all identified records by two researchers independently, and
2. Full-text screening of potentially relevant articles by two researchers independently.

Disagreements between reviewers were assessed and resolved by discussion between reviewers. Group discussion was initiated in specific cases in order to meet consensus.

The process of literature selection and reason for exclusion were fully documented and a flow - diagram according to the PRISMA template was constructed. The exclusion criteria used during the literature screening were the following:

1. No English/French abstract is available, or no abstract is available.
2. Not related to prefilled syringes destined to be administered intravenously parenterally.
3. The article is not reporting original data (e.g., editorial, letter, comment, expert opinion, or review). The article is not a human study.
4. The article covers outpatients who self-administer PFS (not inpatients).
5. The article's scope excludes the possibility of assessment.
    a. Identification of the benefits and risks associated with the use of PFS.
    b. Investigation of the cost-effectiveness of PFS.

Data extraction

Data from included studies were extracted by the reviewers. A pilot, annotated, data extraction Microsoft Excel file was circulated to all reviewers. Data extraction was limited to findings relevant to the research topic. The following data were extracted from the included articles: study type; PFS characteristics; clinical setting and target population; type of intervention; and outcome data.

Findings

The search yielded 1804 records. After removing duplicates, 1803 records were screened by two independent researchers. As a result of the title and abstract screening, 1698 records were excluded. The number of records excluded with the associated exclusion criteria can be found in the PRISMA diagram in Annex II. After the full-text review of 105 papers, there were 30 studies processed for the systematic literature review. The full process of the literature review is illustrated in Annex II.

Findings on benefits and potential risks associated with prefilled syringes

All 30 studies were original research. They were categorised in the following manner:

- Country: most are from the US (10), 15 articles from European countries, 2 from Japan, 1 from New Zealand, 2 from Israel and, 1 from Canada
- Type of hospital: mainly university hospitals (12) or tertiary care specialized hospitals
- Setting: anaesthesia/intensive care units (5), surgical units (5), ophthalmology (4), radiology (3), emergency room (2), paediatric units (2), dermatology, oncology

The SIG investigated the terminology they used for the format. In most of the cases, the general terminology PFS was used (24 studies). RTU, RTA and premixed injections were used in 3, 2 and 1 articles respectively.

The majority of the PFS used in the studies were industry manufactured (16), but in some cases, hospital pharmacy-prepared/compounded PFS were used. Those contained the following actives: epinephrine, norepinephrine, atropine, morphine, and amiodarone.

The active ingredients used as a PFS in the selected studies were mainly medications used in anaesthesia and intensive care (epinephrine, norepinephrine, atropine, thiopental, amiodarone, dobutamine, ephedrine, lidocaine, morphine, fentanyl), saline prefilled syringes for venous catheter flushing, but also anti-VEGF medications (4 papers) used in ophthalmology as intravitreal injections and contrast agents (3 papers) coming more and more out in a format of a PFS.

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The objectives of the studies were to investigate an element of PFS usage (safety, efficiency, cost savings, etc.) in contrast to conventional preparation methods (self-filled syringes) by nurses or physicians.

The data extraction process identified the following attributes of PFS use:

Reduced microbiological contamination

Reduction of medication errors

Standardisation of preparations

Reduced wastage

Reduced staff time in clinical areas

Cost savings

These findings were considered and further discussed along with the attributes identified from the survey results during the development of the value framework for PFS.

Discussion

This literature review includes qualitative and quantitative analysis of the benefits and risks, cost-effectiveness and possible barriers to the use of PFS. Jacobs et al. conducted a pre-formulation and stability study for amiodarone RTU syringes (Jacobs et al., 2017). An RTU amiodarone product, prepared in a hospital pharmacy using cyclodextrins as a solubility enhancer, for intravenous application in an acute clinical setting is a feasible option from a chemical, physical and microbiological point of view.

Webster et al. conducted a prospective, randomized clinical evaluation of a new safety-orientated injectable drug administration system (PFS) in comparison with conventional methods (Webster et al., 2004). It was demonstrated that the new system was rated more favourably than conventional methods in terms of safety and usability and saved preparation time before and during anaesthesia. PFS also eliminate three known hazards for the patient, violation of sterile technique during the drawing up of a drug, drug error because of the mislabelling of a syringe under time pressure in the operating theatre and the persistent problem of the injection of minute glass shards which can contaminate the contents of ampoules upon opening.

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Yang Y et al. showed in the Human Factors Engineering Study of Medication Delivery observing practice in operating theatres that PFS were superior to self-filled syringes (SFS) simplifying the work processes with a reduced number of system vulnerabilities (Yang et al., 2016). One example of a high-risk system vulnerability in the SFS system was when a medication might need to be drawn up during surgery while completing other requests simultaneously. This system vulnerability adds 'cognitive complexity' during medication delivery but does not exist when using PFS. Bhavsar et al. evidenced that the use of intravitreal PFS reduces the risk of development of post-operative endophthalmitis and at the same time also reduces the use of prophylaxis with antibiotic, achieving both a reduction in the risk of infection and saving in terms of antibiotic therapy (Bhavsar et al., 2007). Ninomiya et al. carried out *in vitro* contamination study in order to compare the aseptic efficacy of industry-manufactured PFS with ampoules when used in a polluted environment (Ninomiya et al., 2001). It was concluded that the risk of contamination for PFS was significantly lower, thus rendering the use of PFS in environments with airborne contaminants, useful for preventing microbiological contamination of the medicine inside.

Buerke et al. investigated microbiological contamination and time efficiency of the use of automatic multidetector CT (MDCT) injectors with PFS (Buerke et al., 2010). The use of prefilled contrast syringes with single-use saline syringes is associated with the time-efficient assembly of injection systems and prevents microbiological contamination in clinical routine. The same authors evaluated three different injection systems (double-syringe contrast injector with disposable syringes, PFS, roller pump injector) with regard to microbiological contamination, time efficiency, and user handling (Buerke et al., 2011). Double-syringe injectors used with disposable or prefilled contrast agent syringes, as well as roller pump injectors, ensure hygienic conditions in the clinical routine. However, time efficiency and handling are aspects that favour PFS and roller pump systems. Melman et al.demonstrated that PFS' do not appear to be prone to the development of microbiological contamination for at least 2 weeks and the potency of the anaesthetic lidocaine is maintained (Melman et al., 1999).

Adapa et al. assessed in simulation studies the extent and frequency of dose errors and treatment delays made as a consequence of preparing drug infusions (of epinephrine and norepinephrine) at the bedside, compared to the use of PFS in a randomized, blind, controlled study (Adapa et al., 2012). It was demonstrated that PFS significantly reduced the likelihood of medication error and treatment delays. Moreira et al. conducted a prospective, block-randomized, crossover study to determine whether colour-coded PFS could decrease the time to delivery and dosing error in simulated Emergency Department (ED) paediatric resuscitations (Moreira et al., 2015). It was noted that the novel colour-coded PFS decreased the time to medication administration and significantly reduced critical dosing errors by the emergency physician and nurse teams during simulated paediatric ED

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resuscitations. Implementing systems that eliminate calculations during ED management of paediatric emergencies may reduce potentially harmful mistakes, therefore contributing to improved patient outcomes. In a similar study by Stevens et al., it was concluded that the novel colour-coded PFS also decreased time to medication administration and significantly reduced critical dosing errors by paramedics during simulated prehospital paediatric resuscitations (Stevens et al., 2015). This led to the conclusion that the implementation of standardised, mechanically, and visually simple systems that eliminate calculations during prehospital management of paediatric emergencies may facilitate appropriate patient care and contribute to improved outcomes.

The use of PFS, both industry-manufactured and pharmacy-prepared, in ophthalmology (anti-vascular endothelial growth factor (VEGF) such as bevacizumab, ranibizumab and aflibercept) reduce the risk of post-injection endophthalmitis (0.019% vs. 0.055%, $p<0.0001$) (Finkelstein et al., 2022). Blom et al. demonstrated that the relative risk of post-injection endophthalmitis following procedures utilising compounded versus clinician-withdrawn syringes was 0.55 (95% CI 0.17-1.79; $p=0.32$). In a large, multicentric, retrospective study the use of PFS during intravitreal injection of ranibizumab was associated with a reduced rate of culture-positive endophthalmitis (Blom et al., 2022). Syringes prefilled with sterile medication eliminate the transfer process from storage vial to syringe, which reduced the risk of microbiological contamination and may subsequently decrease the risk of infection (odds ratio 0.19; 95% confidence interval 0.045-0.82) (Storey et al., 2019). Moreover, Loewenstein et al. demonstrated that the use of PFS was associated with improved accuracy and precision (Loewenstein et al., 2019). These results argue a good case for the use of PFS for all drugs administered by intravitreal injection.

Vogl et al. conducted an observational study to evaluate the efficiency and safety of ioversol PFS compared with ioversol bottles in contrast-enhanced examinations (Vogl et al., 2012). Administration of ioversol for contrast-enhanced CT examinations is associated with a low incidence of adverse events and is generally safe and well tolerated. Ioversol PFS were associated with lower residual volumes and less potential reuse compared with bottles.

Larmené-Beld et al. compared the costs of production of ready-to-administer prefilled sterilized syringes by the pharmacy to the conventional preparation method (CPM) for intravenous medication by nurses in the clinical environment (Larmené-Beld et al., 2019). In this cost-minimisation study, costs related to the preparation of the medication, bacteraemia from contamination, adverse drug events because of preparation medication errors and wastage of syringes were taken into account. Three scenarios were compared:

1. all preparations as CPM (864,246 administrations per year);

2. all preparations as prefilled sterilized syringes; and,
3. 50% as prefilled sterilized syringes and 50% as CPM.

The first scenario found the highest annual costs at €14.0 million ($16.0 million) compared with the second scenario (€4.1 million, $4.7 million). The most realistic situation (third scenario) had an annual cost of €9.1 million and therefore found savings of €4.9 million ($5.6 million) compared with the first scenario. The use of prefilled sterilised syringes prepared in the hospital pharmacy yielded cost savings compared with the CPM on the ward in the Dutch hospital. Additionally, it was concluded that medications suitable to deliver as prefilled sterilized syringes should fulfil the following criteria: administered as a fixed-dose concentration, suitable for injection or infusion with a pump, and having a small volume (less than 50 mL).

Van der Linde et al. developed an economic model to measure, in a real-life setting, the benefits of using industry manufactured RTU preparations of dobutamine compared with conventional reconstituted admixtures (Admix) in cardiac surgery patients in terms of cost savings (Van der Linde et al., 2002). Nursing time was reduced by 32% in the RTU group compared with the Admix group. Material cost was also reduced and the overall cost savings in the RTU group amounted to a 60% reduction in the cost of the conventional Admix process ($p<0.001$). There was no difference between the RTU and Admix group in terms of safety and efficacy. However, a user satisfaction survey showed that medical staff especially welcomed improved ease of preparation and potential for prevention of errors and risks of handling. RTU forms have the potential to reduce the nursing time associated with the preparation and administration of intravenous admixtures and to enable overall cost savings.

Benhamou et al. conducted a budget impact analysis for industry manufactured PFS of atropine for anaesthesia care in French hospitals, considering wastage and medication errors (Benhamou et al., 2016). The systematic use of atropine PFS rather than atropine CMP yielded a net one-year budget saving of €5,255,304. Medication errors outweighed other cost factors relating to the use of atropine CMP (€9,425,448). Avoidance of wastage in the case of atropine CMP (prepared and unused) was a major source of savings (€1,167,323). It was concluded that atropine PFS is more expensive than atropine CMP, but its use would lead to significant cost savings, due to fewer medication errors and the absence of wastage.

Wazny et al. evaluated epoetin alfa drug costs in haemodialysis (HD) patients after a province-wide switch from multidose vials (MDV) to industry-manufactured PFS (Wazny et al., 2009). The average weekly dose calculated from drug costs was 13,282 units (MDV) versus 11,689 units (PFS). The average weekly costs were $195.71 (MDV) versus $183.23 (PFS). An estimated $12.48 per patient per week in

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savings ($518,519 annual savings across the Manitoba Renal Program). The switch from epoetin alfa MDV to epoetin alfa PFS realized cost savings and was likely a result of reduced drug wastage.

Murdoch et al. conducted a cost analysis study highlighting that thiopental PFS could reduce cost and wastage whilst improving safety (Murdoch et al., 2012). A financial saving could also be made while reducing wastage. Aseptic preparation removed the need for daily reconstitution, might avoid drug substitution errors, improved sterility and reduced the risk of tampering. In accordance with this study, Atcheson et al. reported also that there are large potential considerable savings due to the preventable waste of anaesthetic drugs (Atcheson et al., 2016).

Barbariol et al.measured the actual amount of drug wastage in the ORs and ICUs of a Regional Health Service and analysed the economic implications of this waste for the Health Service (Barbariol et al., 2021). Drug wastage was defined as drugs prepared in CPM syringes but not administered at all and discarded untouched, during 1-year period. Drug wastage varied from 7.8% to 85.7% of CPM-prepared syringes, with an overall mean wastage rate of 38%. The estimated yearly waste was 139,531 syringes, for a total estimated financial cost of €78,060 ($92,569), and an additional quantity of medical waste amounting to 4968 kg per year. Griffin et al.carried out an economic analysis of critical care nurse resourcing following the uptake of RTA noradrenaline for hypotensive shock in adults in critical care units (Griffin et al., 2022). It was seen that a ready-to-administer strategy would enable less noradrenaline wastage and more nursing time allocated to patient care.

Besides drugs, PFS containing saline can be used for flushing lines. Saliba et al. investigated the impact of flushing with prefilled saline syringes on the incidence of peripheral venous catheter failure (Saliba et al., 2020). It was concluded that the use of PFS for the flushing of peripheral venous catheters significantly reduced the incidence of their failure (57% vs 43.4%, $p<0.001$).

The review of the literature demonstrated that the use of PFS are associated with the following:

1. reduced number of preparation steps and associated cognitive complexity;
2. simpler use (no labelling needed on the point of care as already correctly labelled);
3. reduced infection (reduced microbiological contamination);
4. reduced drug, disposables and packaging wastage;
5. reduced nursing time allocated to the preparation and administration of drugs;
6. quicker to administer in an urgent crisis situation;
7. reduced the likelihood of medication errors;

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8. reduced needlestick injuries;
9. overall cost savings (although more money is spent to purchase PFS, the use of PFS led to significant cost savings).

Surveys

Three different surveys targeting professional associations, different healthcare professionals and manufacturers of PFS gathered data for the SIG.

Professional Association Survey on the Use of Prefilled Syringes in Hospitals

Survey design

A survey to understand the attitude of different healthcare (professional) associations towards PFS in hospitals was undertaken. It contained identification questions, collecting more information about the associations that participated, statements for ranking and a few questions on the usefulness of prefilled medicines syringes. In total associations had to answer 25 questions. The survey questions are annexed to this report (see Annex III).

Respondents

The survey was shared with professional associations (including hospital pharmacists, nurses and doctors) located in Europe by e-mail and via social media. The survey was answered by 17 associations. 80% of the participating organisations operated at the national level, while 20% represented European (umbrella) organisations. To ensure the possibility of contacting the responding associations, if needed, contact details of the responding person were collected. This information could be shared voluntarily by the responding person.

Survey findings

The first part of the survey focused on the completion of 13 different statements and gathered information on the future of prefilled syringes. 17 associations provided feedback to this section. When comparing the feedback of the professional associations with the responses of the individual healthcare professionals, the SIG concluded that the professional associations seem more positive towards PFS.

Statement 1: Prefilled medicine syringes save significant amounts of clinical (nurse/doctor) time in preparing infusion therapy for use in clinical areas.

The majority of responses either strongly agreed (65% (N=11/17)) with statement 1 or agreed (29% | N=5/17). One association had insufficient experience using PFS or has not seen sufficient information about their use to provide an opinion on this statement (6% | N=1/17).

Statement 2: Prefilled medicine syringes reduce medication errors.

The same majority of responses 94% (N=16/17) strongly agreed or agreed with statement 2. Also for the second statement, none of the respondents selected the options "disagree" or "strongly disagree". One respondent (6% | N=1/17) indicated again the lack of knowledge to rate this statement.

Statement 3: Prefilled medicine syringes reduce hospital-acquired infections.

One respondent (6%) disagreed that PFS reduce hospital-acquired infections, while two (12%) could not provide feedback due to the lack of knowledge to rate this statement. The remaining respondents either agreed (29% | N=5/17) or strongly agreed (53% | N=9/17) with the third statement.

Statement 4: Prefilled medicine syringes reduce the risk of needle stick injuries.

Over 70% of respondents either agreed (41% | N=7/17) or strongly agreed (29% | N=5/17) with statement 4. Three respondents (18%) disagreed with the fact that PFS reduce the risk of needle stick injuries, while two respondents (12%) could not rate the statement.

Statement 5: Prefilled medicine syringes reduce staff stress.

Staff stress reduction is seen by a majority of respondents as a positive effect of PFS with 53% (N=9/17) agreeing or strongly agreeing 29% (N=5/17) with statement 5. Similar to some of the previous statements, one respondent (6%) disagreed and two (12%) could not rate the statement.

Statement 6: Prefilled medicine syringes enable greater standardisation of infusion doses/ concentration/ final volumes.

For almost 90% of the respondents (agree (53% | N=9/17); strongly agree (35% | N=6/17)) PFS enable greater standardisation of infusion doses, concentration or final volumes. One respondent (6%)

strongly disagreed with the sixth statement, while another respondent (6%) reported not having sufficient knowledge to rank this statement.

Statement 7: Prefilled medicine syringes reduce the waste of syringes which are prepared and not used or later not required in the clinical area.

The majority of respondents either agreed (47% | N=8/17) or strongly agreed (41% | N=7/17) with statement 7. Similar to the previous statement, one respondent (6%) disagreed and one respondent (6%) could not rank the statement.

Statement 8: Prefilled medicine syringes cost significantly more to purchase than vials and syringes.

Around a quarter of respondents were not in agreement with the eighth statement and stated that they disagreed (18% | N=3/17) or strongly disagreed (6% | N=1/17) with it. More than half (agree (29% | N=5/17); strongly agree (29% | N=5/17)) indicated that PFS cost significantly more to purchase than vials and syringes. The remaining 18% (N=3/17) could not rank the statement.

Statement 9: The total cost of using prefilled medicine syringes is not higher than the combined cost of vials and syringes and clinical/nursing time.

Answers to the ninth statement were mixed with one respondent (6%) strongly disagreeing, two (12%) disagreeing, eight (47%) agreeing and one (6%) strongly agreeing. 29% (N=5/17) could not rank this statement due to the lack of knowledge about the total costs of using PFS in comparison to the combined costs of vials and syringes and clinical/nursing time.

Statement 10: Prefilled medicine syringes have some disadvantages in use (other than cost) which prevents them being used in practice.

35% of respondents (N=6/17) agreed with this statement. 29% (N=5/17) disagreed, 12% (N=2/17) strongly disagreed and 24% (N=4/17) could not rank this statement that PFS have some disadvantages in use (other than cost) which prevent them from being used in practice.

What do you consider are the barriers for the adoption of prefilled medicine syringes in your hospital? Please select the 3 main barriers in your hospital.

Insufficient range of industry-manufactured PFS to meet our requirements (77% | N=13/17), the purchase price of industry-manufactured PFS (71% | N=12/17) and incompatibility with hospital syringe pumps and equipment (41% | N=7/17) were identified as the three main barriers for the introduction of PFS.

The two associations that selected the option 'other' highlighted the limited capacity of the hospital pharmacy and the lack of a clean area in the pharmacy department for the preparation of PFS as barriers.

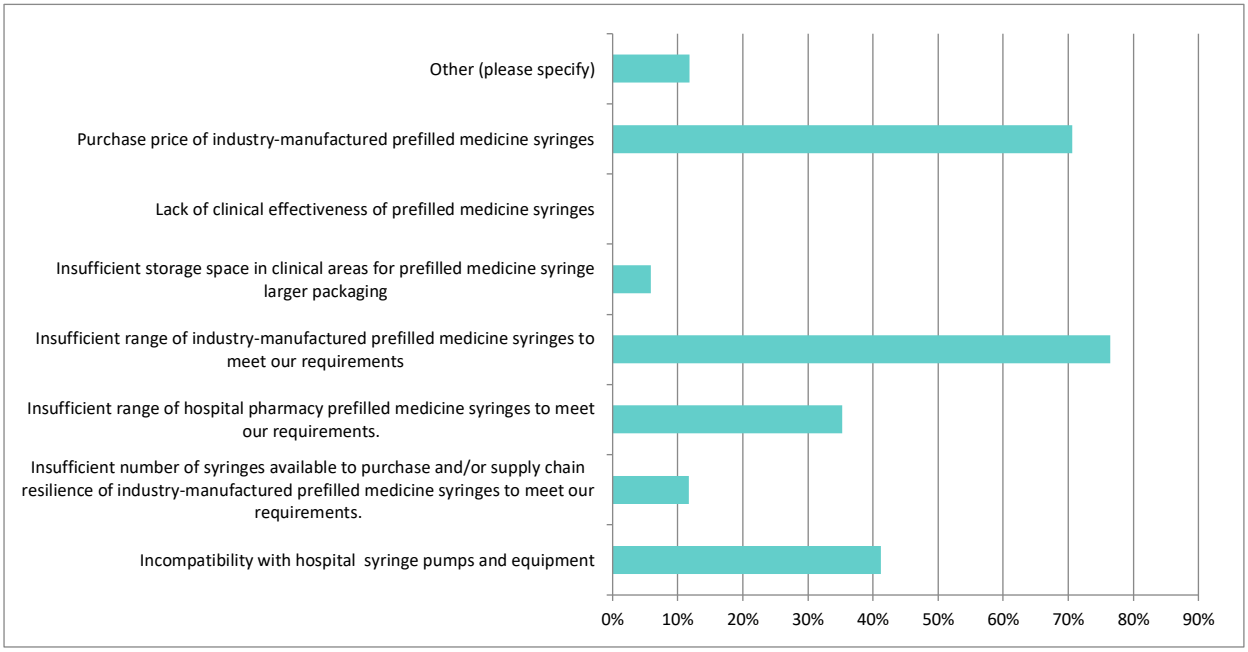

Figure 1 *– Percentage of responses by associations (N=17) for the question 'What do you consider are the barriers for the adoption of prefilled medicine syringes in your hospital?'.*

Statement 11: Industrially manufactured prefilled medicine syringes have advantages vs hospital pharmacy preparation (like quality, shelf life, etc.)

Over 80% of respondents agreed (71% (N=12/17)) or strongly agreed (12% (N=2/17)) with statement 11. One respondent (6%) indicated that industrially manufactured PFS do not have an advantage over those prepared in pharmacies, while two (12% (N=2/17)) could not rank this statement.

Statement 12: The use of prefilled medicine syringes has increased in the last two years.

Almost half of the respondents agreed (35% | N=6/17) or strongly agreed (12% | N=2/17) with statement 12, while 24% (N=4/17) disagreed that the use of PFS increased in the last two years. The remaining 5 respondents (29%| N=5/17) found it difficult to rank the use increase in the past two years.

How do you think will the use of prefilled medicine syringes change in the future?

For the overwhelming majority (94% | N=16/17) the use of PFS will increase in the future, while one respondent (6%) thought that it would decrease.

Statement 13: The main decision maker or makers for the introduction of prefilled medicine syringes in my hospital is/are.

For this statement, respondents could choose between hospital pharmacists, hospital management, managers of the intensive care unit (ICU) or anaesthesia, nurses and others. The main decision makers are hospital pharmacists (agree (42% | N=7/17); strongly agree (47% | N=8/17)) followed by ICU/ anaesthesia managers (agree (53% | N=9/17); strongly agree (24% | N=3/17)) and the hospital management (agree (31% | N=5/16); strongly agree (44% | N=7/16)). Nurses ranked fourth (agree (35% | N=6/17)); strongly agree (18% | N=3/17)). The option 'other' was ticked by nine respondents (disagree (11% | N=1/9); strongly disagree (11% | N=1/9); I don't know (78% | N=7/9)). One of them choose to mention the pharmacy and therapeutics committee as a specific decision maker that would fall into the category 'other'.

The second section of the survey inquired about the implementation of PFS, the existence of guidelines and the formulations that would be useful for participating organisations.

What was successful in convincing the decision maker or makers in your hospital to use prefilled medicine syringes?

Evidence showcasing that PFS reduce medication errors seems to be the most convincing argument for decision makers according to 65% (N=11/17) of respondents, followed by evidence on reduced risk of infection (41% | N=7/17) and business case showing return on investment and improved work-flow efficiency at any hospital (both 30% | N=5/17). The respondent that selected the option other (6%) stressed that the lack of resources, in particular of nurses, led to the introduction of PFS.

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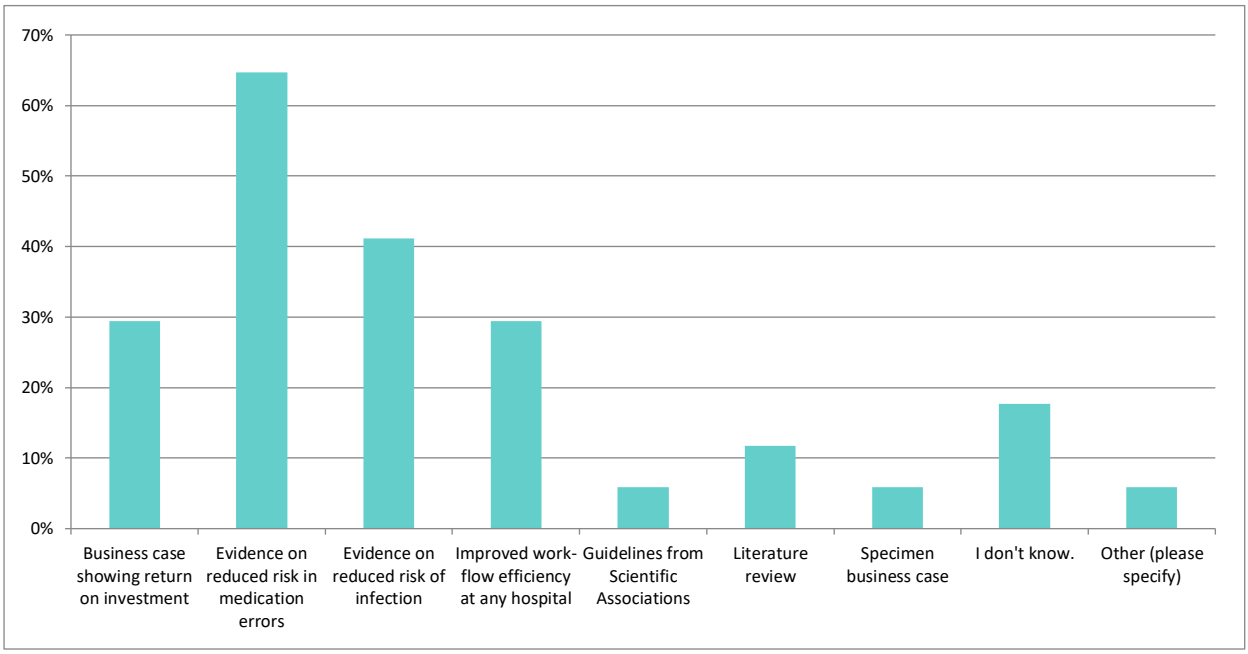

Figure 2 *– Percentage of responses by associations (N=17) for the question 'What was successful in convincing the decision maker or makers in your hospital to use prefilled medicine syringes?'.*

Are you aware of guidelines/recommendations on the use of prefilled medicine syringes or did you produce such guidelines/recommendations yourself?

Awareness is low since 69% (N=11/16) of participating associations had no knowledge of guidelines or recommendations on the use of PFS and 19% (N=3/16) did not know. The remaining 12% (N=2/16) specifically named the European Resolution on good reconstitution practices and SEDAR (Spanish Society of Anaesthesiology, Resuscitation and Pain Therapy) as guidelines/recommendations that existed for PFS (Resolution CM/Res(2016)2 on good reconstitution practices in health care establishments for medicinal products for parenteral use, Council of Europe).

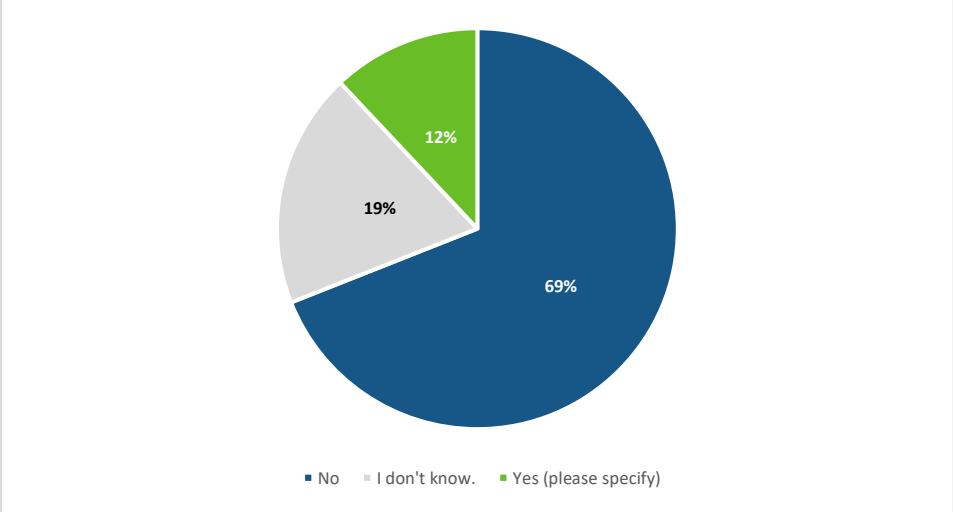

Figure 3 *– Percentage of responses by associations (N=16) for the question 'Are you aware of guidelines/recommendations on the use of prefilled medicine syringes or did you produce such guidelines/recommendations yourself?'.*

Please select, up to 5, active substances that you would like to have widely available as prefilled medicine syringe in hospitals for your members.

Feedback to the question on PFS that should be widely available varied greatly. Among the top 6 active substances, survey respondents included the following:

- Ephedrine (38% | N=6/16)
- Epinephrine/adrenaline (31% | N=5/16)
- Norepinephrine/noradrenaline (31% | N=5/16)
- Atropine (25% | N=4/16)
- Dobutamine (25% | N=4/16)
- Propofol (25% | N=4/16)

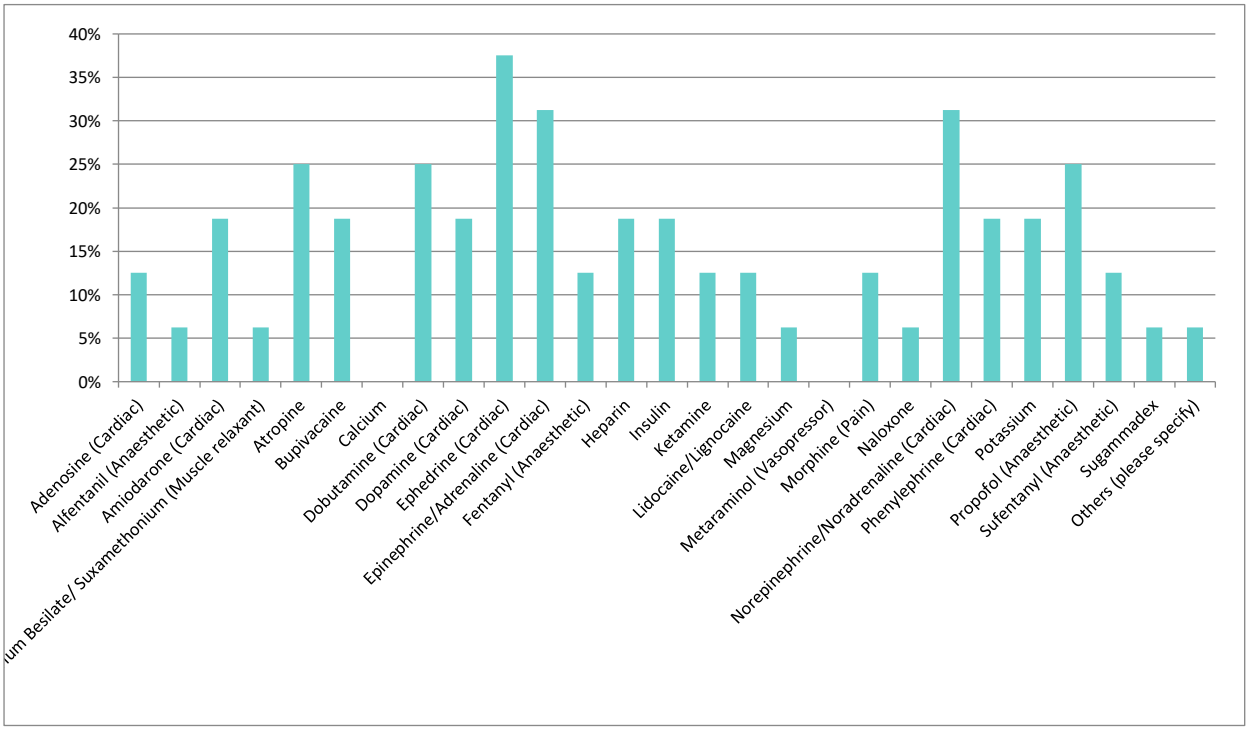

Figure 4 *– Percentage of responses by associations (N=16) for the question 'Please select, up to 5, active substances that you would like to have widely available as prefilled medicine syringe in hospitals for your members. The active substances are listed in alphabetical order.'.*

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For the 5 active substances that you would like to use as a prefilled medicine syringe, please add information on the concentration.

Six associations decided to provide feedback to this question, with five giving concrete examples while one highlighted that the needs differ from hospital to hospital. The choices varied and included amiodarone, atracurium, dobutamine, ephedrine heparin, insulin, morphine, naloxone, norepinephrine/noradrenaline, phenylephrine and propofol.

Multi-professional Survey on the Use of Prefilled Syringes in Hospitals

In addition to the survey for associations, the SIG also prepared a more detailed survey for individual healthcare professionals working across Europe. EAHP's member associations helped with the dissemination of this survey to hospital pharmacists. The dissemination among other professionals was performed by the SIG members. In addition, the survey was promoted via social media.

Survey design

The survey was designed to collect the views and opinions of a range of health professionals and managers on the current and future use of PFS. There was a total of 30 questions that needed to be answered by all respondents. Those working with PFS had to answer three additional questions and those not yet working with them had two additional questions. Also, hospital pharmacists were asked to provide feedback on four additional questions. The survey questions are annexed to this report (see Annex IV).

Respondents

The survey was available to anaesthesiologists, nurses (working in the operating room, ICU or general wards), pharmacists, hospital managers and others. There were 412 responses to the survey coming from more than 31 countries throughout Europe. The largest number of responses came from the United Kingdom (N=88), followed by Spain (N=78), Hungary (N=45) and Germany (N=31). Other countries with 10 to 20 responses were Italy (N=20), Turkey (N=20), the Netherlands (N=17), Austria (N=14), Switzerland (N=13), Portugal (N=11), France and Ireland (both with 10 responses).

Up to 42% of respondents (N=171/412) were hospital pharmacists and 35% (N=144/412) were anaesthesiologists. Nurses, mainly working in the operating room, represented 16% (N=68/412) of respondents. More than two-thirds of those professionals worked in either a teaching (29% | N=121/412) or specialised tertiary care hospital (39% | N=162/412) while 16% (N=65/412) of the respondents worked in a general non-teaching hospital. The remainder belonged to private hospitals, outpatient clinics, small community hospitals or other kind of facilities.

Most of the respondents belonged to a big or medium-big hospital, with > 1,000 inpatient beds or from 501 to 1,000 inpatient beds, (42% and 30%, respectively). Professionals from smaller hospitals (from 301 to 500 beds, or fewer than 300 beds) accounted only for 16% and 13%, respectively.

Regarding the number of ICU beds in hospitals, only 12% of respondent hospitals had 100 or more ICU beds, and up to 25% of respondent hospitals had from 50 to 99 ICU beds. However, more than half of

respondents said that their hospitals had fewer than 50 ICU beds (32% with 20 to 50 and 27% of respondent hospitals had fewer than 20 beds)

The distribution of the number of operating theatres of respondent hospitals was wide. Only 9% of hospitals had the largest numbers of operating theatres (with 50 or more), whereas 19% of the respondents said that their hospitals had from 30 to 49 and up to 24% had from 15 to 29 operating theatres. Almost half of respondent hospitals (48%) had fewer than 15 operating theatres.

Survey findings – questions directed only to hospital pharmacists.

Hospital pharmacists that completed the survey were invited to provide feedback to four additional questions focused on "manufactured specials", their capacity and the barriers faced when preparing PFS.

Are hospitals permitted to purchase 'manufactured specials' from industry in your country?

Less than half of the hospital pharmacists that provided feedback to this question (40% |N=79/198) confirmed that their hospitals were allowed to purchase "manufactured specials" from industry in their countries, whereas 32% (N=63/198) were not. The remaining 28% (N=55/198) did not know the situation in their countries. These results mean that purchasing "manufactured specials" from industry is not an extended practice throughout Europe, except for Spain (N=9), the Netherlands (N=12) and Turkey (N=10) where "manufactured specials" seem to be used more widely than in the rest of the countries represented by the respondents.

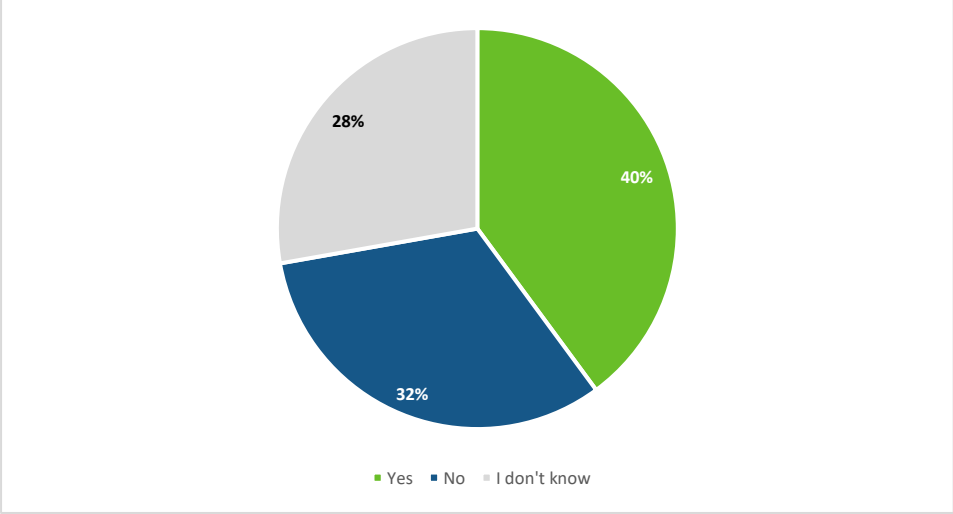

Figure 5 *- Percentage of responses by hospital pharmacists (N=198) for the question 'Are hospitals permitted to purchase 'manufactured specials' from industry in your country?'.*

Which industry-manufactured prefilled medicines syringes unlicensed "manufactured specials" are purchased and used in your hospital? Please provide information on the active substance, concentration and volume of the product that you are using as an unlicensed "manufactured specials"

There were only 63 respondents that could provide feedback to this question. Out of these, 32% (N=20/63) answered that they did not use unlicensed "manufactured specials". Among those who used them, the most common products were manufactured in different concentrations. The answers given sorted in alphabetical order by active substance included atropine, biperiden, chlorazine, dexamethasone, dexmedetomidine, epinephrine/adrenaline, ephedrine, magnesium sulphate, metoclopramide, morphine, norepinephrine/noradrenaline, phenylephrine, potassium, propofol, remifentanil and suxamethonium. There were also products for ocular use included in the answers: namely aflibercept, bevacizumab, cefuroxime and vancomycin.

Do hospital pharmacies have the capacity to prepare more prefilled medicines syringes?

Among the respondents to this question, 39% (N=77/198) considered that hospital pharmacies had the capacity to prepare more prefilled medicines syringes, whereas 51% (N=102/198) did not have additional capacity.

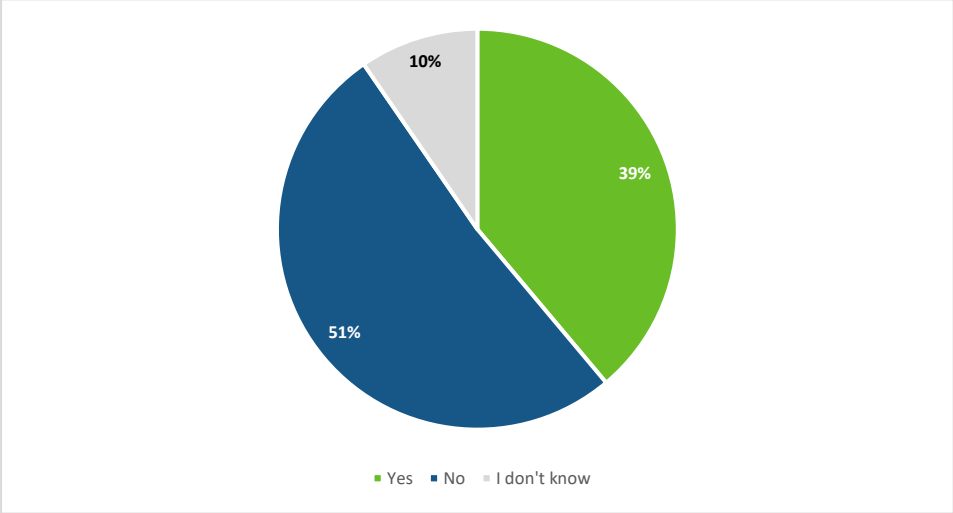

***Figure 6** - Percentage of responses by hospital pharmacists (N=198) for the question 'Do hospital pharmacies have the capacity to prepare more prefilled medicines syringes?'.*

What is the main barrier to hospital pharmacies preparing more prefilled medicines syringes?

There were 134 responses to this question. The most frequent barrier, according to the responses, was related to a lack of human resources or trained staff to assume the workload in the pharmacies. The costs to implement PFS preparation in the pharmacies were the second most frequent barrier, whereas regulation or lack of information regarding good manufacturing practice (GMP) was also considered in the top three barriers. Another barrier for hospital pharmacies was the lack of appropriate facilities to prepare PFS in hospital pharmacies. Finally, some considered that PFS were not a necessity in the hospital strategy, or that there was no PFS demand from hospital units.

Survey findings – opinion questions

Statement 1: Prefilled medicine syringes save significant amounts of clinical (nurse/doctor) time in preparing infusion therapy for use in clinical areas.

The majority of respondents (87% | N=360/412) either strongly agreed (57% | N=234/412) or agreed (31% N=126/412) with this statement. Out of the different professional groups surveyed, responses from nurses strongly agreed with this statement the most (78% | N=53/68). Only 29 respondents (7% | N=29/412) indicated that they had insufficient knowledge or experience to provide a response to this statement with hospital pharmacists selecting this option more often than the other professionals (9% | N=16/171). Only a handful of respondents were in disagreement with statement 1 with 4% (N=15/412) disagreeing and 2% (N=8/412) strongly disagreeing.

Statement 2: Prefilled medicine syringes reduce medication errors.

The same majority of responses (87% | N=360/412) strongly agreed (51% | N=212/412) or agreed (36% | N=148/412) with statement 2. Anaesthesiologists formed the group that was most supportive of the statement with 53% (N=76/144) sharing their strong agreement. Only 27 respondents (7%) indicated that they had insufficient knowledge or experience to provide a response to this statement. Hospital pharmacists were again the biggest group that selected this option (8% | N=14/171). The group in disagreement with statement 2 remained small with 4% (N=18/412) disagreeing and 2% (N=7/412) strongly disagreeing.

Statement 3: Prefilled medicine syringes reduce hospital-acquired infections.

Almost two-thirds of respondents agreed (38% | N=155/412) or strongly agreed (27% | N=113/412) that PFS reduce hospital-acquired infections, while 20% (N=83) could not provide feedback due to the lack of knowledge to rate this statement. Anaesthesiologists (25% | N=36/144) were the largest group that could not provide feedback due to insufficient knowledge. Responses from nurses strongly agreed with this statement the most (44% | N=30/68).

Statement 4: Prefilled medicine syringes reduce the risk of needle stick injuries.

Over 70% of respondents either agreed (39% | N=162/412) or strongly agreed (36% | N=150/412) with statement 4. Six respondents (1%) strongly disagreed with the fact that PFS reduce the risk of needle stick injuries. Similar to the previous statement, nurses responded most positively with 60% (N=41/68) strongly agreeing. Out of the 11% (N=44/412) that could not rate the statement, hospital pharmacists formed the group that ticked this option more often than the others with 19% (N= 32/171) not having sufficient knowledge to reply.

Statement 5: Prefilled medicine syringes reduce staff stress.

Staff stress reduction is seen by a majority of respondents as a positive effect of PFS with 44% (N=180/412) agreeing or strongly agreeing 38% (N=155/412) with statement 5. With over half of them strongly agreeing (54% | N=37/68) nurses were again the profession that supported this statement the most. The number of respondents that had insufficient knowledge or experience to provide a response to this statement decreased to 8% (N=33/412).

Statement 6: Prefilled medicine syringes enable greater standardisation of infusion doses/ concentration/ final volumes.

For almost 90% of the respondents (agree (42% | N=171/412); strongly agree (45% | N=186/412)) PFS enable greater standardisation of infusion doses, concentration or final volumes. The trend continued and nurses agreed strongest (62% | N=42/68) and that out of the 8% (N=25/412) that selected the option of having no sufficient experience or knowledge using PFS, hospital pharmacists formed the group that chose this option more frequently with 8% (N=14/171) ticking it.

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Statement 7: Prefilled medicine syringes reduce the waste of syringes which are prepared and not used or later not required in the clinical area.

The feedback to statement 7 remained similar to the previous one. Most respondents either agreed (39% | N=159/412) or strongly agreed (39% | N=161/412) that PFS reduce waste. The numbers of those in disagreement (12% | N=49/412) or strong disagreement (3% | N=13/412) remained low. Hospital pharmacists (11% | N=18/171) were again the leader among those that had insufficient knowledge or experience to provide a response to this statement (7% | N=30/412), while nurses remained those most supportive with 53% (N=36/68) in strong agreement.

Statement 8: Prefilled medicine syringes cost significantly more to purchase than vials and syringes.

Around half of the respondents were supportive of the eighth statement and stated that they agreed (31% | N=129/412) or strongly agreed (24% | N=97/412) with it. The group of those that could not rank the statement climbed to 30% (N=124/412). This time hospital pharmacists provided the most support with 30% (N=51/171) strongly agreeing, while nurses had a lack of sufficient knowledge (43% | N=29/68).

Statement 9: The total cost of using prefilled medicine syringes is not higher than the combined cost of vials and syringes and clinical/nursing time.

Answers to the ninth statement were mixed with most respondents (40% | N=163/412) not able to rank this statement due to the lack of knowledge about the total costs of using PFS in comparison to the combined costs of vials and syringes and clinical/nursing time. The support decreased to 37% with a quarter of respondents in agreement (26% | N=107/412) and 11% (N=45/412) indicating strong agreement. Nurses were the group that selected more often the response of not being able to rank the statement (43% | N=29/68).

Statement 10: Prefilled medicine syringes have some disadvantages in use (other than cost) which prevents them being used in practice.

For the first time, most respondents disagreed with a statement. Half of the respondents either disagreed (40% | N=163/412) or strongly disagreed (40% | N=163/412) that PFS have some disadvantages in use (other than cost) which prevent them from being used in practice.

Anaesthesiologists (15% | N=21/144) opposed the most. Less than one-third was in agreement with 27% (N=113/412) ticking the option 'agree' and 3% (N=13/412) selecting 'strongly agree'.

What do you consider are the barriers for the adoption of prefilled medicine syringes in your hospital? Please select the 3 main barriers in your hospital.

The purchase price of industry-manufactured prefilled medicine syringes (59% | N=245/412), the insufficient range of industry-manufactured PFS to meet our requirements (% | N=/412) and the insufficient number of syringes available to purchase and/or supply chain resilience of industry-manufactured prefilled medicine syringes to meet the requirements (% | N=/412) were identified as the three main barriers for the introduction of PFS.

Out of all respondents, 55 selected the option 'other'. Their feedback was very diverse. Comments that were shared by most ranged from capacity problems, not seeing any barriers, costs, medication errors due to similar-looking PFS to the short shelf-life of PFS. A few indicated that their hospitals do not have many PFS in use or are not open to change and thus are not considering the use of PFS.

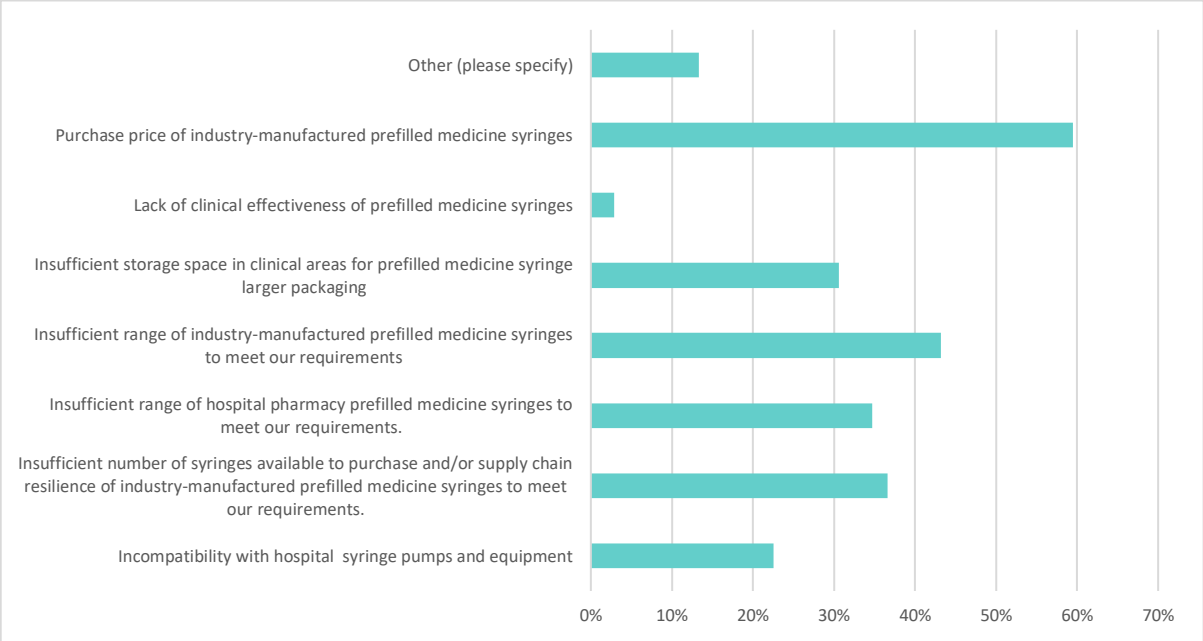

Figure 7 *– Percentage of responses (N=412) for the question 'What do you consider are the barriers for the adoption of prefilled medicine syringes in your hospital?'.*

Statement 11: Industrially manufactured prefilled medicine syringes have advantages vs hospital pharmacy preparation (like quality, shelf life, etc.)

Over half of the respondents agreed (39% (N=162/412)) or strongly agreed (17% (N=71/412)) with statement 11. Again, a quite sizable group (28% (N=114/412)) underlined their lack of knowledge to judge if industrially manufactured PFS have advantages over those prepared in a hospital pharmacy. The strongest agreement with this statement came from hospital pharmacists (23% (N=40/171)), while most nurses (43% (N=29/68)) could not rank this statement.

Statement 12: The use of prefilled medicine syringes has increased in the last two years.

For more than half of the healthcare professionals replying to this statement, the use of PFS increased in the past two years with 21% (N=86/412) strongly agreeing and 37% (N=152/412) agreeing to statement 12. Ninety respondents (22%) found it difficult to rank the use increase in the past two years.

How do you think will the use of prefilled medicine syringes change in the future?

For the overwhelming majority (96% | N=395/412) the use of PFS will increase in the future, while seventeen respondents (4%) thought that it would decrease.

Statement 13: The main decision maker or makers for the introduction of prefilled medicine syringes in my hospital is/are.

For this statement, respondents could choose between hospital pharmacists, hospital management, managers of the intensive care unit (ICU) or anaesthesia, nurses and others. The main decision makers are with 74% respectively hospital pharmacists (agree (38% | N=148/394); strongly agree (36% | N=142/394)) and hospital managers (agree (33% | N=130/391); strongly agree (41% | N=160/391)). ICU/ anaesthesia managers (agree (42% | N=164/388); strongly agree (29% | N=112/388)) ranked third, followed by nurses (agree (30% | N=108/366); strongly agree (11% | N=39/366)) and 'other' (agree (11% | N=17/154); strongly agree (8% | N=13/154)). Decision makers mentioned in the category 'other' were named by 25 respondents. They included for example the pharmacy commission, the drugs and therapeutics committee and national competent authorities like the Health Ministry or the Health Authority.

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What was successful in convincing the decision maker or makers in your hospital to use prefilled medicine syringes?

Evidence on reduced risk in medication errors seems to be the most convincing argument for decision makers according to 49% (N=201/412) of respondents, followed by improved work-flow efficiency at any hospital (36% | N=150/412) and business case showing return on investment (26% | N=107/412). The respondents that selected the option other (7% | N=30/412) stressed that the COVID-19 pandemic as well as cost and waste reduction played a role for their hospital to opt for PFS. Some respondents (N=11/412) also used the field other to underline that PFS are not yet used in their hospital.

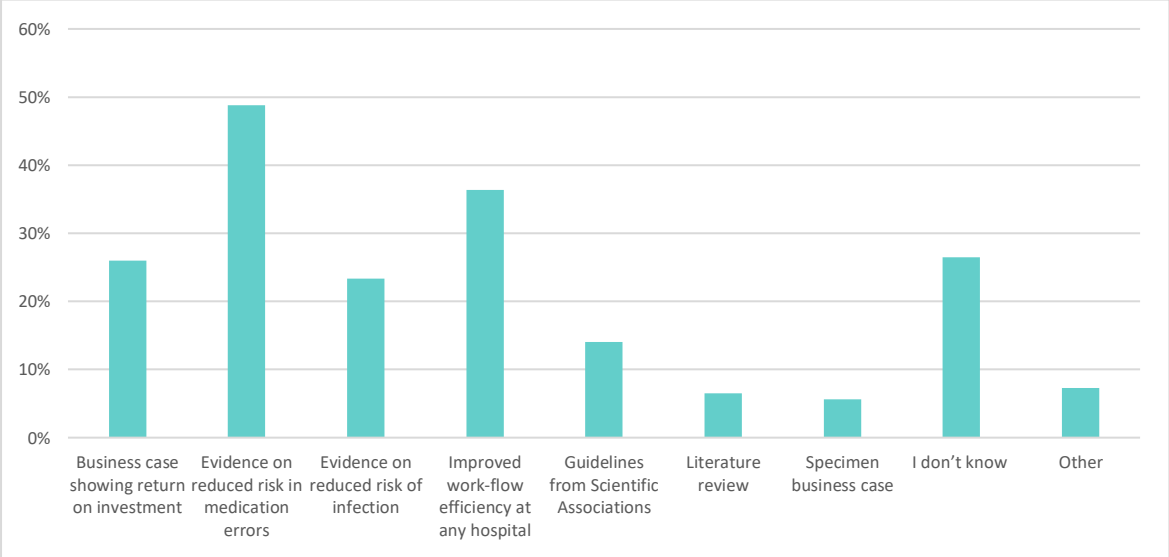

Figure 8 *– Percentage of responses (N=412) for the question 'What was successful in convincing the decision maker or makers in your hospital to use prefilled medicine syringes?'.*

Questions on the use of prefilled medicine syringes

Are prefilled syringes containing normal saline for flushing used in the area that you work in/ in the hospital you work in?

This question was answered by 401 respondents. 43% (N=172) use PFS containing normal saline for flushing, 48% (N=188) did not and 10% (N=41) did not know.

Are prefilled medicine syringes containing active substances used in the area that you work in/ in the hospital you work in?

In the case of PFS containing active substances, it is important to highlight that 72% of the respondents (N=290/401) used them in the area they work in or in their hospital and only 6% (N=23/401) did not know. This result is aligned with the recommendation of using medicinal products in a dosage form that is ready to be used or administered to a patient, especially in the case of parenteral administration. Comparing this and the previous question, it is interesting to see that 72% of respondents had PFS containing active substances but only 43% had syringes containing normal saline for flushing.

Is barcoding technology used at the point of administration to the patient in the area that you work in/ in the hospital you work in?

Barcoding at the point of administration is a strategy and a recommendation to improve patient safety. Nevertheless, only 13% of respondents (N=51/401) use this technology in their hospitals. Over two-thirds (73% |N=292/401) did not use this technology, while 14% (N=58/401) did not know. The system for barcoding most used was EPIC (23 respondents).

In your country, are there guidelines/recommendations on the use of prefilled medicine syringes?

This finding is tempered by 66% of health professionals (N=265/401) not having detailed knowledge of policies and national recommendations. This shows the need for education on patient safety and better diffusion of international recommendations to health professionals. 27% of the respondents (N=107/401) answered that they had no guidelines or recommendations on the use of prefilled medicine syringes. Only 7% of health professionals (N=29/401) identified some recommendations. Out of these, ten quoted national pharmacists' associations, others mentioned instructions on drug reconstitution (e.g. four quoted GMP), and two respectively referred to local policies, joints commission and HIQA (the Health Information and Quality Authority). The others mention ISMP (Institute for Safe Medication Practices), Safe Surgery, the European Board of Anaesthesiology and some specific articles on different drugs.

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Please select the active substance that you would like to use as a prefilled medicine syringe. Only 5 can be selected.

The question relating to the active substance that healthcare professionals would like to use as a PFS was a question for which respondents could select up to 5 active substances. Only 95 respondents selected active substance they would like to use. The top active substances (over 20%) that respondents would like to use in a pre-filled syringe were epinephrine/adrenaline (40% | N=38/95), propofol (35%| N=33/95), norepinephrine/noradrenaline (26%| N=25/95), atracurium besilate/ suxamethonium (24%| N=23/95), ephedrine (23%| N=22/95), fentanyl (23%| N=22/95), insulin (22%| N=21/95) and amiodarone (21%| N=20/95).

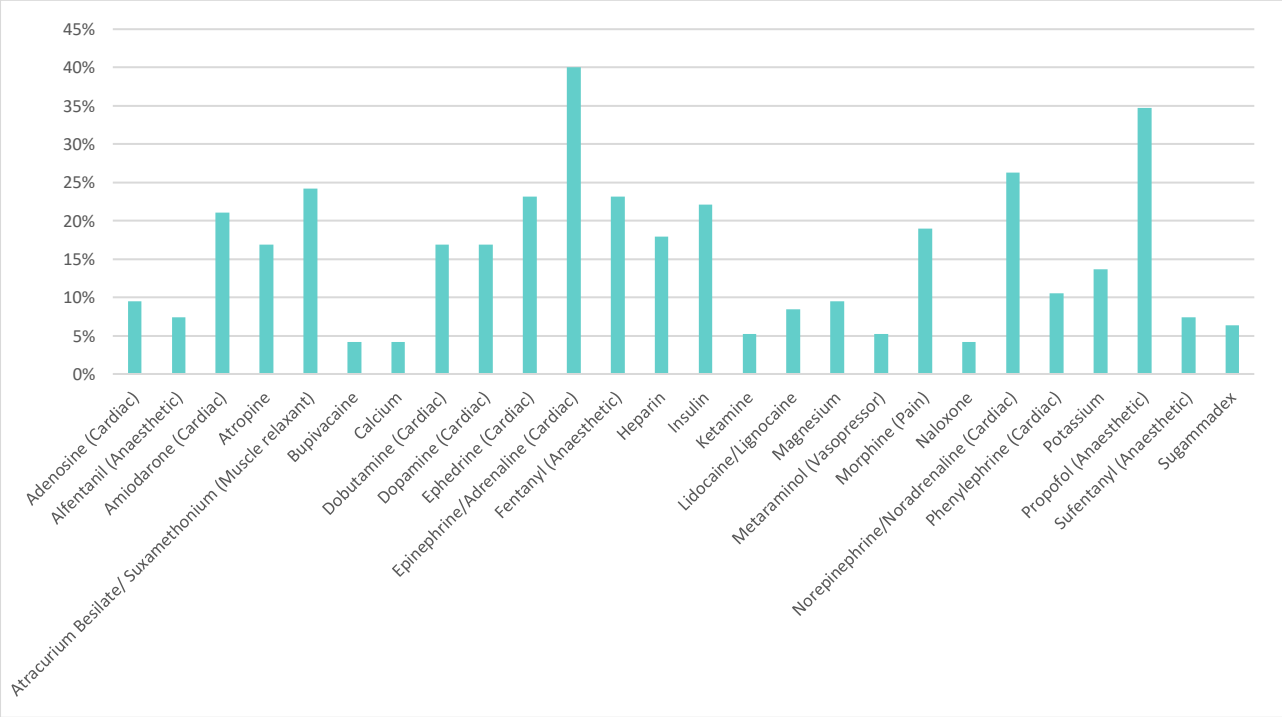

Figure 9 *– Percentage of responses (N=412) for the question 'Please select the active substance that you would like to use as a prefilled medicine syringe.'.*

For the 5 active substances that you would like to use as a prefilled medicine syringe, please add information on the concentration.

Fifty respondents mentioned a variety of concentrations that shows no standardization between hospitals (except insulin) and countries regarding the drugs used at the operating theatre. The concentrations and active substances mentioned by most included:

- Epinephrine/adrenaline 0.1mg/mL, 1 mg/mL, 1 mg/50 mL, 3 mg/50 mL, 4 mg/50 mL

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- Amiodarone 300 mg/20 mL, 600 mg/50 mL, 300 mg/10 mL, 900 mg/50 mL
- Ephedrine 3 mg/mL, 6 mg/mL, 1 mg/mL
- Fentanyl 2500 mcg/50 mL, 100 mcg/mL, 500 mcg/10 mL
- Insulin 50 I.U/50 mL
- Norepinephrine/noradrenaline 20 mcg/mL, 0.5 mg/mL, 8 mg/50 mL, 4 mg/50 mL, 0.1 mg/mL
- Propofol 1% and 2%
- Morphine 1 mg/mL, 2,5 mg/50 mL, 5 mg/50 mL, 10 mg/50mL, 20 mg/50 mL, 50 mg/50 mL
- Heparin 1500 IU, 2500 IU/50 mL, 5000 IU/50 mL, 10000 IU/50 mL, 5000 IU/1mL

Please select the active substances that are available in your hospital as a prefilled medicine syringe. Please indicate if these are industrially manufactured or prepared in the hospital. Only select those active substances that are used in your hospital.

The top active substances (over 20%) that respondents said were available as PFS included epinephrine/adrenaline (industrially manufactured 37% (N=90/243) | prepared in the hospital 14% (N=33/243)), atropine (industrially manufactured 40% (N=97/243) | prepared in the hospital 10% (N=25/243)), ephedrine (industrially manufactured 35% (N=86/243) | prepared in the hospital 11% (N=26/243)), insulin (industrially manufactured 25% (N=61/243) | prepared in the hospital 9% (N=23/243)), phenylephrine (industrially manufactured 22% (N=53/243) | prepared in the hospital 11% (N=27/243)), norepinephrine/noradrenaline (industrially manufactured 12% (N=29/243) | prepared in the hospital 17% (N=42/243)), heparin (industrially manufactured 18% (N=43/243) | prepared in the hospital 9% (N=21/243)), propofol (industrially manufactured 19% (N=46/243) | prepared in the hospital 5% (N=13/243)) and fentanyl (industrially manufactured 8% (N=20/243) | prepared in the hospital 12% (N=28/243)).

Please select 5 active substances that your hospital is not yet using and that you would like to use as a prefilled medicine syringe. Only 5 can be selected.

Regarding active substances wished as PFS, respondents were provided with the possibility to select one or up to five options. The top active substances (over 20%) that respondents would like to use as PFS and were not available in their hospitals were propofol (30% | N=73/243), fentanyl (23% |

N=56/243), morphine (22% | N=53/243), atropine (21% | N=52/243) and adrenaline/epinephrine (21% | N=52/243).

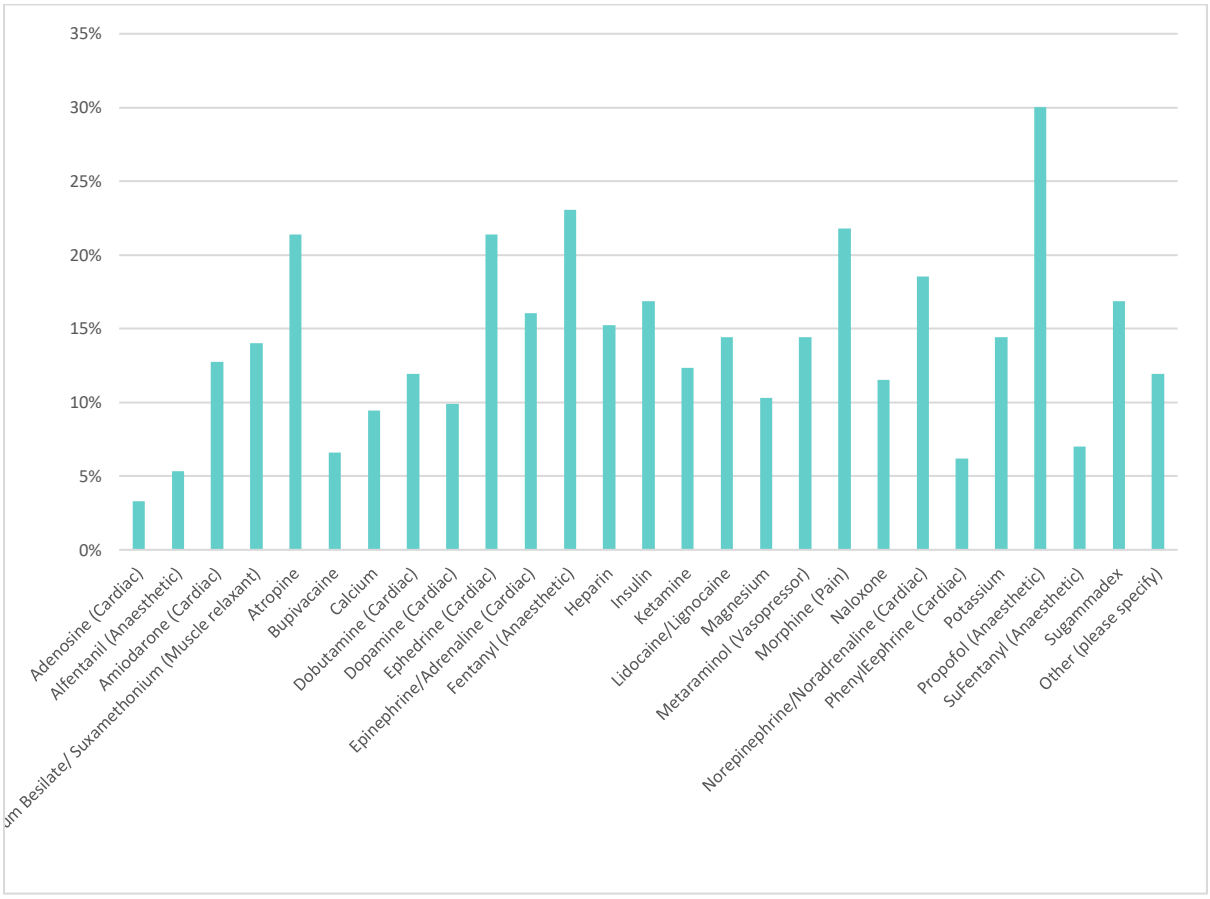

Figure 10 *– Percentage of responses (N=243) for the question 'Please select 5 active substances that your hospital is not yet using and that you would like to use as a prefilled medicine syringe.'.*

Looking at the professional groups, nurses and anaesthesiologists who were already using some PFS wished to have further active substances available as PFS for their clinical activity in theatre and intensive care. Both thought analgesics, such as fentanyl and morphine would be useful (possibly for infusions and use in patient-controlled analgesia (PCA) pumps), and propofol. Sugammadex (28% of anaesthesiologists | N=24/87) was suggested for theatre use. Heparin (29% | N=12/42) magnesium (26% | N=11/42) and potassium (24% | N=10/42) were further suggestions from nursing staff for intensive care use. These latter three will be likely to be used in 50 mL syringes for infusions, which are already available as industrially manufactured products in the UK.

For hospital pharmacists only propofol (29% | N=28/97) and the category 'other' (22% | N=21/97) reached over 20%. In relation to the latter, suggestions ranged from PFS for acute situations, like reanimation, to ceftriaxone and clonidine.

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When comparing the different professional groups that responded to the survey, it could be observed that the responses by hospital pharmacists were the most diverse, while for anaesthesiologists and nurses the top three responses were above or close to 30%. Looking at all three groups, the following preferences emerged:

Table 2 *– Top responses by anaesthesiologists (N=87), hospital pharmacists (N=97) and nurses (N=42) to the question 'Please select 5 active substances that your hospital is not yet using and that you would like to use as a prefilled medicine syringe.'.*

	Anaesthesiologists	Hospital pharmacists	Nurses
1.	Ephedrine (40% | N=35/87)	Propofol (29% | N=28/97)	Metaraminol (48% | N=20/42)
2.	Fentanyl (37% | N=32/87)	Atropine (19% | N=18/97)	Propofol (33% | N=14/42)
3.	Atropine & Morphine both (32% | N=28/87)	Potassium (18% | N=17/97)	Heparin (29% | N=12/42)

For the 5 active substances that you would like to use as a prefilled medicine syringe, please add information on the concentration.

Out of the respondents that answered this question 44% (N=107/243) mentioned the following concentrations regarding the top active substances:

- Propofol 10 mg/mL, 20 mg/mL
- Fentanyl 50 mcg/mL
- Morphine 1mg/mL, 5 mg/mL, 0.5 mg/mL, 1 mg/mL
- Atropine 0.1 mg/mL, 0.2 mg/mL, 0.5 mg/mL, 0.6 mg/mL
- Adrenaline/epinephrine 0.1 mg/mL, 1 mg/mL

It could be deduced that the concentrations for the top five active substances seem to have a greater consensus.

Survey on Prefilled Syringes in Intensive Care Units and Operating Theatres targeting Manufacturers

Survey design

Throughout its discussions, the SIG identified that there is a lack of awareness about the availability of manufactured PFS in Europe. To better understand which types of PFS are marketed, the SIG decided to launch a survey for manufacturers that was distributed at EAHP's Congress in March 2023. Manufacturers were asked 4 questions and given the opportunity to list the PFS that they were supplying. The survey questions are annexed to this report (see Annex V).

Respondents

The survey was shared with manufacturers that attended EAHP's Congress in March 2023. It was answered by seven manufacturers out of which two were supplying PFS in Europe.

Survey findings

The first question of the survey was used to determine if the manufacturer attending EAHP's Congress should answer the remaining questions of the survey. Only two out of the seven companies that participated confirmed that they were supplying PFS.

Please list the prefilled syringes that your company supplies.

For this question manufacturers could list up to 5 active substances. Those mentioned included:

Active substance	Volume of syringe	Concentration	Shelf-life
Adrenaline	10mL	0,1mg/mL	2 years
Atropine	10mL	3mg	3 years
Atropine	Various	Various	3 years
Ephedrine	10mL	30mg	3 years
Epinephrine/adrenaline	10mL	3mg/mL	3 years
Epinephrine/adrenaline	10mL	1mg	2 years
Metaraminol	5mL	0,5mg/mL	3 years

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Active substance	Volume of syringe	Concentration	Shelf-life
Metaraminol	5mL	2,5mg	2 years
Phenylephrine	10mL	50mcg/mL	3years

Table 3 *– Prefilled syringes supplied by the manufacturers that responded to the survey.*

If your company supplies more than 5 different prefilled syringes, please provide information about the others below.

In addition to those PFS listed for the previous question, manufacturers that responded to the survey also indicated the availability of lidocaine (1% in 10mL) and suxamethonium (10mg/mL) as PFS.

Could EAHP share information on the prefilled syringes that you supply to its members?

Both respondents whose company makes available PFS agreed that the information included in the survey could be shared and thus replicated in the report of the SIG.

Discussion of survey results

For the opinion questions, there are high and good levels of overall agreement among the healthcare professionals that participated in the survey to six of the statements on the use of PFS. For the remaining statements, there is moderate and in one case poor agreement. As the level of agreement reduced, the number of healthcare professionals who could not rank the statement increased. This indicated that for half of the statements the health professionals who took part in the study had insufficient information and/or experience to provide any other response. Consequently, it would be necessary to provide further information and education on the use of PFS to healthcare professionals.

When comparing the feedback of the professional associations with the responses of the individual healthcare professionals, it could be observed that the professional associations seem more positive towards PFS than individual healthcare professionals.

Statements with high survey response agreement from healthcare professionals

There were a group of statements where the survey response overall agreement was very high (> 80%). These were those describing the following benefits of PFS:

- Saving significant amounts of clinical (nurse/doctor) time in preparing infusion therapy for use in clinical areas (Statement 1)
- Reducing medication errors (Statement 2)
- Reducing staff stress (Statement 5)
- Enable greater standardisation of infusion doses/ concentration/ final volumes (statement 6)

Nursing staff had the highest percentage of 'strong agreement' with these statements. Less than 10% of responses from all healthcare professionals indicated that they had insufficient knowledge or experience to provide a more detailed response. For statements 1, 2, and 6, hospital pharmacists provided a high percentage of responses that indicated that 'they did not know'. Sharing greater information on these benefits with hospital pharmacists may further increase agreement with these four key statements in future.

Statements with good survey response agreement from healthcare professionals

There were a group of statements where the survey response overall agreement was good (70%-80%). These were those describing the following benefits of PFS:

- Reduced needlestick injury (Statement 4)

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- Reduced waste (Statement 7)

Some 11% and 7% of responses indicated that they had insufficient knowledge or experience to provide a more detailed response. For these two statements, hospital pharmacists again provided the highest percentage of responses that indicated that 'they did not know'. It is the view of the SIG, that sharing greater information on these benefits with hospital pharmacists may further increase agreement with these two statements in future. Nursing staff once again had the highest percentage of 'strong agreement' responses to these statements.

Statements with moderate survey response agreement

There were a group of statements where the survey response agreement was moderate (50 – 70%). These were those describing the following attributes of PFS:

In order of agreement:

- Reduced hospital-acquired infection (65% overall agreement) (Statement 3)
- PFS have increased in the last two years (58% overall agreement) (Statement 12)
- Industrially manufactured PFS have advantages over hospital pharmacy preparation (like quality, shelf life, etc.) (56% overall agreement) (Statement 11)
- PFS cost significantly more to purchase than vials and syringes (55% overall agreement). (Statement 8)
- PFS have some disadvantages in use (other than cost) which prevents them from being used in practice. (50% overall agreement) (Statement 10)

There was less agreement and a higher percentage of 'do not know' responses to these statements. For instance, 25% of anaesthesiologists were not aware that PFS have the potential to reduce hospital-acquired infections. Some 30% of nurses did not know whether PFS cost significantly more to purchase than vials and syringes. More information/data concerning the use of PFS is required to better inform health professionals involved in their (potential) use.

The statement with poor survey response agreement.

There was one statement where the survey response agreement was poor.

- The total cost of using PFS is not higher than the combined cost of vials and syringes and clinical/nursing time (37% overall agreement) (Statement 9)

Some 40% of survey responses indicated that they have insufficient information or experience. This finding identifies an urgent need for studies comparing the cost of using vials and syringes and clinical/nursing time over the cost of using PFS and clinical/nursing time, for a range of medicines, to be shared widely across all the professional groups.

Availability of PFS

For nurses and anaesthesiologists, the three most frequently available industrially manufactured PFS were the same, i.e. epinephrine/adrenaline 67%, atropine 64%, and ephedrine 62%. Anaesthesiologists had phenylephrine 55%, propofol 39%, and metaraminol 37% available in pre-filled syringes particularly related to theatre use. For the nurses these were replaced by amiodarone 40%, calcium 33%, adenosine 33%, and insulin 26% reflecting the use of these drugs in intensive care units.

A supplementary question showed that 36% of PFS available drugs were pharmacy-prepared and 64% industrially manufactured. It is not clear if the pharmacies will have more capacity in the next years to prepare pre-filled syringes.

Pharmacy-prepared PFS seemed more commonly available to nursing staff and again the active substances available to them reflected their use in intensive care (e.g. noradrenaline, insulin, fentanyl, morphine, atracurium). In the case of anaesthesiologists, the most frequently used PFS were adrenaline/epinephrine, ephedrine and phenylephrine reflecting the use of these drugs in theatre rooms and the need to have these active substances prefilled (either industrially or pharmacy-prepared).

Three of the top 5 active substances wished for by healthcare professionals, were in the top five active substances that were already available:

- Epinephrine/adrenaline (51%: 37% industrially manufactured, 14% pharmacy prepared),
- Ephedrine (46%: 35% industrially manufactured, 11% pharmacy prepared)
- Insulin (35%: 25% industrially manufactured, 9% pharmacy prepared).

Interestingly, one of the top substances available as PFS (either industrially manufactured or pharmacy-prepared) was among those that should be made available as PFS (adrenaline/epinephrine). Based on the results and their discussion, the SIG would like to emphasise that the availability of PFS differs widely in Europe. To improve information flow about PFS manufacturers should make available a list of PFS that they have on the European market.

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Value Framework for Multiple Criteria Decision Analysis

Different components need to be considered by decision-makers in hospitals when introducing PFS or adding new active substances of PFS to the hospital formulary. A multiple criteria decision analysis (MCDA) helps to facilitate the processes of considering multiple criteria or objectives in order to rank between alternatives or choose the best available option.

The framework developed by the SIG serves as a core tool for building a MCDA instrument to support value-based purchasing and utilisation of PFS.

Development of the MCDA elements

Potential benefits offered by PFS were collected through a targeted literature review and expert surveys conducted with associations and individual healthcare professionals. The results were allocated into different domains. The list of domains and their applicability were discussed during a virtual meeting of the SIG members working in anaesthesiology and intensive care as well as hospital/clinical pharmacy. They also scored the domains.

Value attributes defined by capturing potential benefits associated to PFS in the literature review data extraction process.

The literature review working group developed a data extraction spreadsheet to standardise data collection. Data were recorded on general study characteristics, information regarding the PFS investigated and value attributions evaluated in the studies. After removing duplications and synonyms the following value attributes were defined.

Microbiological contamination

Different studies analysed the microbiological contamination of PFS. They concluded that the risk of contamination for PFS was significantly lower (Ninomiya et al., 2001, Buerke et al., 2010, Buerke et al., 2011, Storey et al., 2019). It was also demonstrated by one study that PFS do not appear to be prone to the development of microbiological contamination for at least two weeks (Melman et al., 1999). Patients can suffer serious consequences (e.g. bacteraemia) due to contamination. Studies have shown that these could be lowered significantly by PFS (Larmené-Beld et al., 2019). The incidence of bacteraemia due to contamination amounts to 1 to 3% regarding literature data.

Medication error reduction

Medication errors occur frequently in the process of reconstituting or administering parenteral medications. Because ADEs resulting from medication errors can be severe, prevention is highly

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important in areas where high-risk drugs are used in stressful environments like in critical care or operating theatres. There is evidence that the rate of medication errors is reduced when PFS are used (Adapa et al., 2012). In a randomized controlled trial, Adapa et al. investigated the extent and frequency of dose errors and treatment delays made as a consequence of preparing drug infusions at the bedside, rather than using pre-filled syringes. Medication errors were 17.0 times less likely when pre-filled syringes were used (95% CI 5.2-55.5), and infusions prepared by pharmacy and industry were significantly more likely to contain the expected concentration ($P<0.001$ for norepinephrine and $P=0.001$ for epinephrine).

Dosing accuracy

Standardised doses can be as much an advantage as a disadvantage of PFS, as it limits personalisation for patients. Due to this limitation, manufacturers should provide a sufficient range of standardised doses for their PFS, especially since dosing accuracy and dosing errors can be categorised as a type of medication error (Moreira et al., 2015).

Time of preparation

Staff time for the preparation of syringes is significant. This is an important factor to consider, as it takes away time from nurses or other clinical staff that could be used for patient care, which is especially crucial as the scarcity of staff is a general problem in healthcare globally (Buerke et al., 2011).

Wastage reduction

Reduction of drug wastage is another important benefit associated with the use of PFS. There is a considerable amount of wastage due to the short in-use stability of infusions/injections reconstituted in clinical areas, while it is a negligible factor for PFS (Barbariol et al, 2021). Another waste factor not explored by the literature that was reviewed nor the survey could be packaging waste reduction.

Cost savings

Cost savings associated with the use of PFS compared to conventional injectables were shown in 5 studies. Reduced overall costs stem from reduced medicinal waste, reduced number of medication errors and increased efficiency of preparing injectable medications (Benhamou et al., 2016).

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Value attributes defined by capturing potential benefits associated to PFS in the results of the Multi-professional Survey on the use of PFS in hospitals

The opinion questions were designed by the SIG to test specific assumptions that exist in relation to the use of PFS. The results of these questions support the inclusion of the following value attributes in the framework:

- Cost
- Availability of industry manufactured PFS across countries
- Availability of the industry manufactured prefilled syringes in sufficient dose ranges
- Standardisation of preparations
- Reduction of needle stick/sharp injuries
- Reduced clinical staff stress to prepare ready-to-administer injectables
- Reduction of time spent with preparation of injectable medications for staff in clinical areas
- Reduced wastage

Value attributes defined by capturing potential benefits associated to PFS based on the professional opinion of the SIG members

Neither the literature review nor the surveys conducted with healthcare professionals and associations were able to shed sufficient light on the reduction of cognitive complexity, the improved in-use stability and the quicker administration of injectable medicines in emergency cases. Similarly, the demand for the use of PFS as well as their compatibility with hospital syringe pumps and equipment were difficult to deduce from the investigation results. Consequently, the SIG members decided to include these attributes together with the pharmacy resources/facilities to prepare PFS as value attributes that are needed in an MCDA based on their professional experience and expertise.

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Domain	Value attribute for medicine PFS	Literature review (as number of references)	Survey of Professional Associations	Survey of Healthcare Professionals	Importance – SIG members
Safety	Reduced microbiological contamination	8 studies	82% responses 'agreed'	65% responses 'agreed'	83%
	Reduction of medication errors	4 studies	94% responses 'agreed'	87% responses 'agreed'	91%
	Improved in-use stability	/	Question not included in survey	Question not included in survey	68%
	Standardisation of preparations	4 studies	88% responses 'agreed'	87% responses agreed	79%
	Reduced needle stick injuries	/	70% responses 'agreed'	76% responses 'agreed'	62%
	Quicker administration of injectable medicines in emergency cases	/	Question not included in survey	Question not included in survey	95%
Efficiency	Reduced wastage	7 studies (referring to	88% responses 'agreed'	78% responses 'agreed'	72%

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		'medicine wastage' only)			
	Reduced staff time in clinical areas	8 studies	94% responses 'agreed'	87% responses agreed	82%
Cost	Increase purchase cost of PFS vs vials, and syringes	/	58% responses 'agreed'	55% responses agreed	74%
	Cost savings: No additional cost if the combined cost of vials and syringes and clinical/nursing time and reduced waste	8 studies	53% responses 'agreed'	37% responses agreed	61%
Clinical staff factors	Reduced clinical staff stress to prepare ready-to-administer injectables	/	82% responses 'agreed'	82% of responses 'agreed'	79%
	Demand for use of PFS	/	Question not included in survey	Question not included in survey	73%
Facilities	Increased storage space in clinical areas for PFS larger packaging	/	Question not included in survey	Question not included in survey	58%

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	Pharmacy resources/facilities to prepare doses – when it is applicable	/	Question not included in survey	39% of responses 'agreed'	71%
	Compatibility issues with hospital syringe pumps and equipment	/	Question not included in survey	Question not included in survey	69%
Availability	Availability of the industry manufactured PFS in sufficient dose ranges	/	Not measurable with the data collected by the survey	Not measurable with the data collected by the survey	71%
	Availability of industry manufactured PFS across countries in sufficient ranges	/	Not measurable with the data collected by the survey	Not measurable with the data collected by the survey	69%

Table 4 *– Framework developed by the SIG serving as a core tool for building a MCDA instrument to support value-based purchasing and utilisation of PFS.*

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Conclusion and recommendations

The SIG considers that while there is evidence of much ongoing work on PFS there are several gaps ranging from the availability of information on PFS, studies supporting the use of PFS and communication by manufacturers about their PFS portfolios. Based on their discussions, the literature review and the outcomes of the three surveys, the SIG members have developed the following recommendations:

- Researchers should publish more information and data concerning the use of PFS in Europe to better inform health professionals involved in their (potential) use. In particular, the waste reduction potential of PFS and their sustainability aspects have not yet been explored.
- PFS users should promote information on their benefits among healthcare professionals that are less aware of them.
- Healthcare professionals using PFS should be encouraged to conduct studies comparing the cost of using vials and syringes and clinical/nursing time over the cost of using PFS and clinical/nursing time, for a range of different medicines.
- Competent authorities must increase awareness about the availability of recommendations, which might help increase the provision of PFS.
- Manufacturers should regularly release information about the PFS that they market in Europe. This information must be made easily accessible to healthcare professionals.

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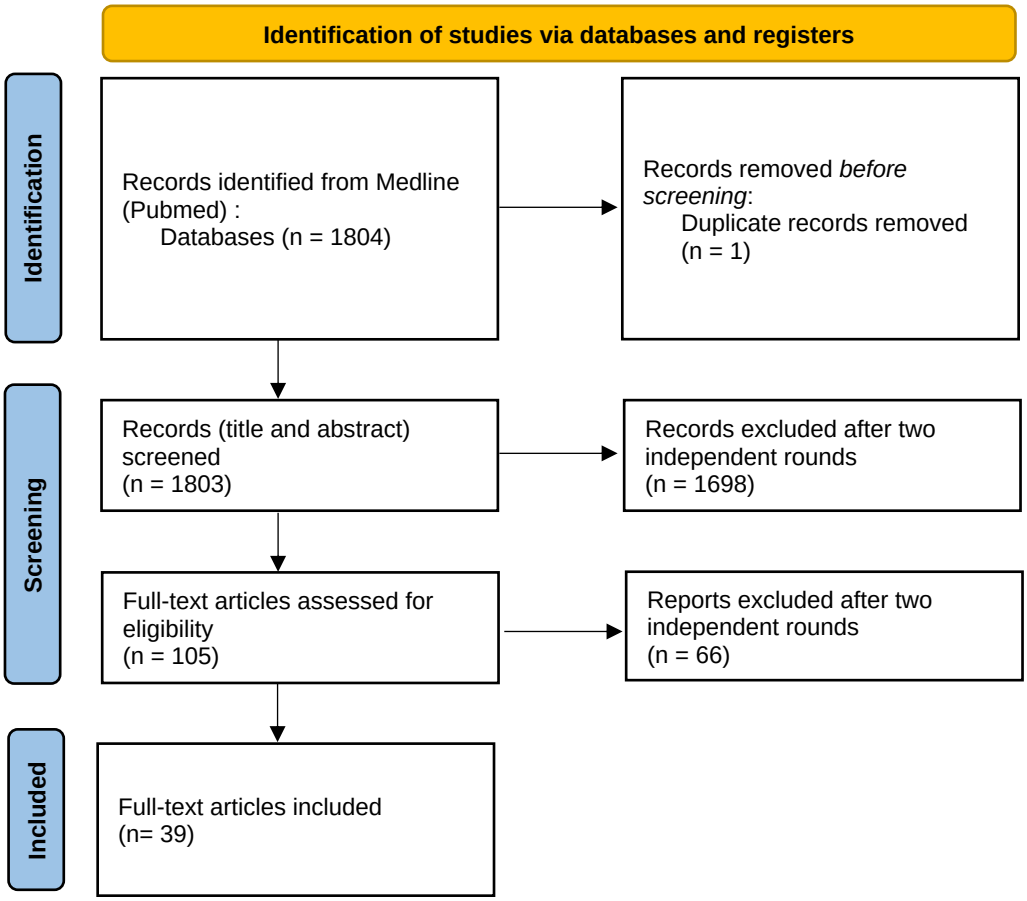
Annex I – SIG membership

Name	Role	Country
Luca Brazzi	Professor in Anesthesia and Intensive Care - Department of Surgical Sciencs - University of Turin (Italy) and representative of the European Society of Anaesthesiology and Intensive Care (ESAIC)	Italy
Zora Ćetković	PhD, Hospital Pharmacist at Procurement Department, University Clinical Centre of Serbia	Serbia
David Cousins	Independent Consultant in Safe Medication Practices	United Kingdom
Jose Luis Gomez	BD representative, VP PUBLIC POLICY & ADVOCACY EUROPE, MIDDLE EAST AND AFRICA en BD	Spain
Nóra Gyimesi *Chair of the SIG*	Chief pharmacist at Manninger Jenő Trauma Center, Budapest, Hungary	Hungary
Irene Krämer	Director of the Pharmacy Department, University Medical Centre & Professor of Clinical Pharmacy in the Faculty of Pharmacy Johannes Gutenberg-University, Mainz, Germany	Germany
Arif Özdemir	Pharmacist and Quality Director, Özel Giresun Ada Hastanesi	Turkey
Maarten Postma	Professor for Global Health Economics UMCG & RUG (Medical Sciences and Economics & Business) at the University of Groningen	The Netherlands
Almudena Ribed Sánchez	Hospital Pharmacist. Hospital General Universitario Gregorio Marañón, Madrid,	Spain
Alvaro Giménez Manzorro	Hospital Pharmacist. Hospital General Universitario Gregorio Marañón, Madrid,	Spain
Antonella Risoli	CTF Manager at the Hospital Pharmacy UOC, PO Annunciata, AO Cosenza	Italy
Camille Stampfli	Hospital Pharmacist at the Production Unit of the Pharmacy Service of the Lausanne University Hospital (Switzerland)	Switzerland
David Whitaker	Retired Anaesthesiologist and Chairman of the European Board of Anaesthesiology Safety Committee	United Kingdom

The work of this Special Interest Group (SIG) was financially supported by BD.

Annex II – Literature Review

PRISMA 2020 flow diagram for new systematic reviews which included searches of databases and registers only.



Objectives

The objective is to perform a targeted literature review on the use of prefilled syringes. The review will summarize the studies that performs a quantitative or qualitative analysis on the associated benefits and risks, cost-effectiveness, and potential barriers of the use of PFS. Narrative synthesis of review results will be provided, no meta-analysis will be performed. The results will provide input for developing an evaluation framework for PFS which is used for preparing an MCDA tool to support evidence-based decision making for the implementation of PFS.

Research questions

- RQ#1: What are the **benefits** and **possible barriers** of PFS use?
- RQ#2: What are the **risks/additional harm** arising from the use of PFS?
- RQ#3: Which **medications available** on the European market in PFS form?
- RQ#4: What are the **main areas** of PFS use?
- RQ#5: What factors are considered in the purchasing/implementation decision making process of PFS in European countries?
- RQ#6: Cost-effectiveness data on PFS

Scope of the review

Time scale: from 1990 to March 2022

Term: pharmacy-prepared and industry-manufactured PFS; PFS/PFSS/RTU/RTA/CIVA product / CIVAS (literature might not be using the same terminology for the same devices; another example would be compounding /prepared).

Site: Inpatient use only

Geographic limitations: no limitation

Language: English/French language abstracts

Sources: the literature search will be performed in the following databases: Medline (via PubMed) and Embase

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The search strategy is built up as a combination of search strings, allowing to capture of all relevant keywords and synonyms of prefilled syringes that may appear in the papers. Broad search strategy is used without keywords limiting hits on relevant data.

Search terms:

The search syntax is built up from a combination of four sets of keywords:

- The first set was a general term for prefilled syringe.
- The second set of keywords was added to cover the hits relevant to our topic, but used different nomenclatures for prefilled syringes - "ready to use" and "ready to administer".
- To specify these widely used terms, the third set of keywords comprising synonyms of medicine was added.
- As the aim of the research was to identify potential value attributes of prefilled syringes, the fourth set contained synonym keywords on benefits, assessment, cost-effectiveness and value. The fourth set also contained synonyms of safety and risk.

Literature search is limited to peer reviewed papers with English/French abstracts, published from 1990 until March 2022.

Search No.	Search type	Search	Date of search	Number of hits
Pubmed (Medline)				
#1	all fields search	((prefilled syringe) OR ((("ready to use") OR ("ready to administer")) AND (((((((drug) OR (medicin*)) OR (medicat*)) OR (pharmaceutical)) OR (product)) OR (device)) OR (injection)) OR (infusion)))) AND (((((((((benefit) OR (assessment)) OR (advantage)) OR (cost-effectiveness)) OR (cost-saving)) OR (evaluation))) OR (risk)) OR (safety))		

Search No.	Search type	Search	Date of search	Number of hits
#2	Applying language and publication date filters	Filters: from 1990 - 2022	30.03.2022	1804
EMBASE				
#1	all fields search	(prefilled AND syringe OR 'ready to use' OR 'ready to administer') AND (drug OR medicin* OR medicat* OR pharmaceutical OR product OR device OR injection OR infusion) AND (benefit OR assessment OR advantage OR 'cost effectiveness' OR 'cost saving' OR evaluation OR risk OR safety)	01.04.2022	1850

Screening

During the process of screening the search results duplicates will be removed (as overlap may exist between the databases), followed by title and abstract screening by two independent researchers.

The reasons for exclusion of papers will be the following (used in that order) :

1. **No English/French abstract is available, or no abstract is available.**
2. **Not related to prefilled syringes:**
   The articles discuss only other topics/devices than PFS. After the first round of screening, the criteria were refined to “Not related to prefilled syringes destined to be administered intravenously”. The term “intravenously” was discussed to be changed to “parenterally”.
3. **The article is not human study, editorial, letter, expert opinion, or review**.
4. **Article covers outpatients that self-use PFS and not inpatients**
5. **The article’s scope excludes the possibility of assessment**

a. identification of the benefits and risks associated with the use of PFS

b. investigation the cost-effectiveness of PFS

Any mismatches will be assessed and discussed between two researchers until a consensus is met. If not, the status of the publication will be further discussed between all members of the working group (n = 6) until a consensus is achieved.

To assess eligibility for inclusion in the review, potentially relevant articles will be evaluated in full text. Exclusive screening strategy will be used, studies that do not present relevant information on the benefits/risks or costs associated with the use of PFS will be excluded. Systematic literature reviews and meta-analysis studies will be included if they investigate the questions in scope. Articles which have reported PFS use but haven't included additional information on benefit/risk profile or data on costs or cost-effectiveness, will be excluded.

The process of literature selection and the number of excluded articles by reasons will be fully documented and presented in a PRISMA flow-diagram.

Data extraction

Data extraction from full text studies will be performed by members of the working group. The extracted data will be doublechecked by independent reviewers from a second working group. Potential conflicts between reviewers will be resolved by a consensus. A data extraction sheet will be developed together with a third working group.

Data extraction will be kept minimal to meet the deadline of the project. The focus will be on finding input data for developing a core evaluation framework for PFS.

Reporting

A narrative synthesis will be performed, quantitative analysis or meta-analysis of collected data is not in scope of this research. To provide timely input to the evaluation framework the results of the literature review will be summarized in a concise format.

Deliverables from literature review:

- List of relevant studies (MS Excel);
- List of excluded studies with reason for exclusion (MS Excel);
- Data extraction spreadsheet (MS Excel);
- Concise MS Word report that summarizes the key findings of the literature review and provides input for the development of the evaluation framework for PFS.

Results

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The number of hits through Medline (via PubMed) was 1804. After the removal of one duplicate, the number of hits from PubMed was 1803. The number of hits through Embase was 1850. After the removal of duplicates, the number of hits was 1057. After a quick evaluation, most of publications of interest were conference abstracts that lacked necessary data for further benefit/risk evaluations. Therefore, Embase database was discarded for the screening and only relevant studies were extracted.

The distribution of the task for screening through title and abstract is listed in the table below.

Number of publications	First round of screening	Second round of screening
1 – 300	CS	NG
301 – 600	ZC	AO
601 – 900	AR	CS
901 – 1200	AO	LB
1201 – 1500	LB	ZC
1501 – 1803	NG	AR

The results of the screening are summarised in the table below.

		First round of screening	Second round of screening	After consensus
Publication included		146 (8%)	141 (8%)	105 (6%)
Publication excluded		1647 (91%)	1659 (92%)	1698 (94)
	No English/French abstract is available	3	2	

Reason of exclusion	Not related to prefilled syringes (first round) Completed during the second round with "destined to be administered intravenously"	1383	1457	
	The article is not human study, editorial, letter, expert opinion or review	58	59	
	Article covers outpatients that self-use PFS and not inpatients (day surgery should be included)	152	107	
	The article's scope excludes the possibility of assessment (identification of the benefits and risks associated with the use of PFS, investigation the cost-effectiveness of PFS)	46	31	
	No reason specified		3	
Publication with no clear status		10	3	

Between the two rounds, there are 146 mismatched items (9%) concerning their status (included/excluded) and 370 (26%) concerning the reason of exclusion.

The distribution of the task for the full text assessment is listed in the table below.

Number of publications	First round of full-text review	Second round full-text review
1 – 9	CS	LB
10 – 17	DW	ARI
18 – 25	NG	AG

26 – 33	ZC	AO
34 – 41	DC	IK
42 – 49	LB	MP
50 – 57	IK	JG
58 – 65	AO	AR
66 – 73	ALR	ZC
74 – 81	MP	DC
82 – 89	AR	DW
90 – 97	AG	NG
98 – 105	JG	CS

The results of the full-text review are summarised in the table below.

		First round of full-text review	Second round of full-text review	After consensus
Publication included		47 (45%)	38 (36%)	39 (37%)
Publication excluded		58 (55%)	67 (64%)	66 (43%)
Reason of exclusion	No English/French abstract is available	8	9	
	Not related to prefilled syringes (first round) Completed during the second round with "destined to be administered intravenously"	6	11	

	The article is not human study, editorial, letter, expert opinion or review	14	7	
	Article covers outpatients that self-use PFS and not inpatients (day surgery should be included)	4	7	
	The article's scope excludes the possibility of assessment (identification of the benefits and risks associated with the use of PFS, investigation the cost-effectiveness of PFS)	25	29	
	No reason specified	1	4	
Publication with no clear status		0		

Between the two rounds, there are 29 mismatched items (28%) concerning their status (included/excluded).

Annex III – Professional Healthcare Associations Survey on the Use of Prefilled Syringes in Hospitals

Introduction

The European Association of Hospital Pharmacists (EAHP) has established a Special Interest Group (SIG) to gain more knowledge of the current and future use of prefilled medicines syringes (PFS) in hospitals.

A PFS is a presentation of one or more active medicines, at the required concentration and volume, in the final syringe and ready for parenteral administration to the patient. PFS are intended to reduce error and minimise the time taken to prepare parenteral medicine by staff in clinical areas. PFS are manufactured/prepared by pharmaceutical industry or hospital pharmacies.

Several additional benefits and some disadvantages have been reported for PFS. The SIG is preparing a comprehensive literature review on PFS.

Usage of PFS in hospitals in North America has been considerably larger than in Europe for many years. Recently the use of PFS in some European countries has increased.

This survey has been designed to collect the views and opinions of professional healthcare associations on the current and future use of PFS. We are only looking for one response from individual associations.
EAHP is also conducting a survey of individual healthcare professionals in European hospitals. You can access it HERE.

Your participation in completing this survey will assist the SIG with the preparation of a report for EAHP and other stakeholders to support the use of PFS in European hospitals.

The survey will approximately take 10 minutes to complete.

EAHP's SIG thanks the survey participants in advance for their participation in the survey.

Demographic questions

Please provide feedback to the demographic question.

1. What professional group(s) does your association represent?
   - Anaesthesiologists
   - Medical specialty physicians
   - Nurses working on the ward
   - Nurses working in the operating theatre
   - Nurse working in the ICU
   - Pharmacists
   - Other (please specify)

2. Name of your professional organisation

3. Type of association
   - National – representing 1 country
   - European/international

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4. Name of the individual completing the survey on behalf of the Association.

5. Job title of the individual completing the survey on behalf of the Association

6. Contact email address of the individual completing the survey on behalf of the Association

Opinion questions

Please rate the statements presented below on a scale from 1 (strongly disagree) to 4 (strongly agree).

7. Statement 1:
   Prefilled medicine syringes save significant amounts of clinical (nurse/doctor) time in preparing infusion therapy for use in clinical areas.
   - Strongly disagree
   - Disagree
   - Agree
   - Strongly agree
   - The Association membership have insufficient experience using prefilled syringes or have not seen sufficient information about their use to provide an opinion on this statement.

8. Statement 2:
   Prefilled medicine syringes reduce medication errors.
   - Strongly disagree
   - Disagree
   - Agree
   - Strongly agree
   - The Association membership have insufficient experience using prefilled syringes or have not seen sufficient information about their use to provide an opinion on this statement.

9. Statement 3:
   Prefilled medicine syringes reduce hospital acquired infections.
   - Strongly disagree
   - Disagree
   - Agree
   - Strongly agree
   - The Association membership have insufficient experience using prefilled syringes or have not seen sufficient information about their use to provide an opinion on this statement.

10. Statement 4:
    Prefilled medicine syringes reduce the risk of needle stick injuries.
    - Strongly disagree
    - Disagree
    - Agree
    - Strongly agree
    - The Association membership have insufficient experience using prefilled syringes or have not seen sufficient information about their use to provide an opinion on this statement.

11. Statement 5:
    Prefilled medicine syringes reduce staff stress.

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- Strongly disagree
- Disagree
- Agree
- Strongly agree
- The Association membership have insufficient experience using prefilled syringes or have not seen sufficient information about their use to provide an opinion on this statement.

12. Statement 6:
    Prefilled medicine syringes enable greater standardisation of infusion doses/ concentration/ final volumes.
    - Strongly disagree
    - Disagree
    - Agree
    - Strongly agree
    - The Association membership have insufficient experience using prefilled syringes or have not seen sufficient information about their use to provide an opinion on this statement.

13. Statement 7:
    Prefilled medicine syringes reduce the waste of syringes which are prepared and not used or later not required in the clinical area.
    - Strongly disagree
    - Disagree
    - Agree
    - Strongly agree
    - The Association membership have insufficient experience using prefilled syringes or have not seen sufficient information about their use to provide an opinion on this statement.

14. Statement 8:
    Prefilled medicine syringes cost significantly more to purchase than vials and syringes.
    - Strongly disagree
    - Disagree
    - Agree
    - Strongly agree
    - The Association membership have insufficient experience using prefilled syringes or have not seen sufficient information about their use to provide an opinion on this statement.

15. Statement 9:
    The total cost of using prefilled medicine syringes is not higher than the combined cost of vials and syringes and clinical/nursing time.
    - Strongly disagree
    - Disagree
    - Agree
    - Strongly agree
    - The Association membership have insufficient experience using prefilled syringes or have not seen sufficient information about their use to provide an opinion on this statement.

16. Statement 10:
    Prefilled medicine syringes have some disadvantages on use (other than cost) which prevents them being used in practice.
    - Strongly disagree
    - Disagree
    - Agree
    - Strongly agree
    - The Association membership have insufficient experience using prefilled syringes or have not seen sufficient information about their use to provide an opinion on this statement.

17. What do you consider are the barriers for the adoption of prefilled medicine syringes in your hospital? Please select the 3 main barriers in your hospital.
    - ☐ Incompatibility with hospital syringe pumps and equipment
    - ☐ Insufficient number of syringes available to purchase and/or supply chain resilience of industry-manufactured prefilled medicine syringes to meet our requirements
    - ☐ Insufficient range of **hospital pharmacy prefilled medicine syringes** to meet our requirements
    - ☐ Insufficient range of **industry-manufactured prefilled medicine syringes** to meet our requirements
    - ☐ Insufficient storage space in clinical areas for prefilled medicine syringe larger packaging
    - ☐ Lack of clinical effectiveness of prefilled medicine syringes
    - ☐ Purchase price of industry-manufactured prefilled medicine syringes
    - ☐ Other (please specify)

18. Statement 11:
    Industrially manufactured prefilled medicine syringes have advantages vs hospital pharmacy preparation (like quality, shelf life, etc.)
    - ○ Strongly disagree
    - ○ Disagree
    - ○ Agree
    - ○ Strongly agree
    - ○ The Association membership have insufficient experience using prefilled syringes or have not seen sufficient information about their use to provide an opinion on this statement.

19. Statement 12:
    The use of prefilled medicine syringes has increased in the last two years.
    - ○ Strongly disagree
    - ○ Disagree
    - ○ Agree
    - ○ Strongly agree
    - ○ The Association membership have insufficient experience using prefilled syringes or have not seen sufficient information about their use to provide an opinion on this statement.

20. How do you think will the use of prefilled medicine syringes change in the future?
    - ○ It will increase.
    - ○ It will decrease.

21. Statement 13:
    The main decision maker or makers for the introduction of prefilled medicine syringes in my hospital is/are:

	Strongly disagree	Disagree	Agree	Strongly agree	I don't know
Hospital pharmacists	☐	☐	☐	☐	☐
ICU/ Anaesthesia manager	☐	☐	☐	☐	☐
Nurses	☐	☐	☐	☐	☐
Hospital management (General/Finance)	☐	☐	☐	☐	☐
Other	☐	☐	☐	☐	☐

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If you selected 'other', please mention the other decision makers.

22. What was successful in convincing the decision maker or makers in your hospital to use prefilled medicine syringes?
    - ☐ Business case showing return on investment
    - ☐ Evidence on reduced risk in medication errors
    - ☐ Evidence on reduced risk of infection
    - ☐ Improved work-flow efficiency at any hospital
    - ☐ Guidelines from Scientific Associations
    - ☐ Literature review
    - ☐ Specimen business case
    - ☐ I don't know.
    - ☐ Other (please specify)

Questions on the use of prefilled medicine syringes

Please answer the questions to your best ability. Where needed please share additional information.

23. Are you aware of guidelines/recommendations on the use of prefilled medicine syringes or did you produce such guidelines/recommendations yourself?
    - ○ No
    - ○ I don't know.
    - ○ Yes (please specify)

24. Please select, up to 5, active substances that you would like to have widely available as prefilled medicine syringe in hospitals for your members.
    The active substances are listed in alphabetical order.
    - ☐ Adenosine (Cardiac)
    - ☐ Alfentanil (Anaesthetic)
    - ☐ Amiodarone (Cardiac)
    - ☐ Atracurium Besilate/ Suxamethonium (Muscle relaxant) Atropine
    - ☐ Bupivacaine
    - ☐ Calcium
    - ☐ Dobutamine (Cardiac)
    - ☐ Dopamine (Cardiac)
    - ☐ Ephedrine (Cardiac)
    - ☐ Epinephrine/Adrenaline (Cardiac)
    - ☐ Fentanyl (Anaesthetic)
    - ☐ Heparin
    - ☐ Insulin
    - ☐ Ketamine
    - ☐ Lidocaine/Lignocaine
    - ☐ Magnesium
    - ☐ Metaraminol (Vasopressor)
    - ☐ Morphine (Pain)
    - ☐ Naloxone
    - ☐ Norepinephrine/Noradrenaline (Cardiac) PhenylEephrine (Cardiac)
    - ☐ Potassium

- ☐ Propofol (Anaesthetic)
- ☐ SuFentanyl (Anaesthetic)
- ☐ Sugammadex
- ☐ Others (please specify)

25. For the 5 active substances that you would like to use as a prefilled medicine syringe, please add information on the concentration.

Active substance 1
(Please indicate the name of the substance and your preferred concentration)

Active substance 2
(Please indicate the name of the substance and your preferred concentration)

Active substance 3
(Please indicate the name of the substance and your preferred concentration)

Active substance 4
(Please indicate the name of the substance and your preferred concentration)

Active substance 5
(Please indicate the name of the substance and your preferred concentration)

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Annex IV – Multi-professional Survey on the Use of Prefilled Syringes in Hospitals

Introduction

The European Association of Hospital Pharmacists (EAHP) has established a Special Interest Group (SIG) to gain more knowledge of the current and future use of prefilled medicines syringes (PFS) in hospitals.

A PFS is a presentation of one or more active medicines, at the required concentration and volume, in the final syringe and ready for parenteral administration to the patient. PFS are intended to reduce error and minimise the time taken to prepare parenteral medicine by staff in clinical areas. PFS are manufactured/prepared by pharmaceutical industry or hospital pharmacies.

Several additional benefits and some disadvantages have been reported for PFS. The SIG is preparing a comprehensive literature review on PFS.

Usage of PFS in hospitals in North America has been considerably larger than in Europe for many years. Recently the use of PFS in some European countries has increased.

This survey has been designed to collect the views and opinions of a range of health professionals and managers on the current and future use of PFS. Your participation in completing this survey will assist the SIG with the preparation of a report for EAHP and other stakeholders to support the use of PFS in European hospitals.

The survey will approximately take 10 to 15 minutes to complete.

EAHP's SIG thanks the survey participants in advance for their participation in the survey.

Demographic questions

1. In which country are you based?

- ○ Albania
- ○ Andorra
- ○ Armenia
- ○ Austria
- ○ Azerbaijan
- ○ Belgium
- ○ Bosnia and Herzegovina
- ○ Bulgaria
- ○ Croatia
- ○ Cyprus
- ○ Czech Republic
- ○ Denmark
- ○ Estonia
- ○ Finland
- ○ France
- ○ Georgia
- ○ Germany
- ○ Greece
- ○ Hungary
- ○ Iceland
- ○ Ireland
- ○ Italy
- ○ Latvia
- ○ Lichtenstein
- ○ Lithuania
- ○ Luxembourg
- ○ Malta
- ○ Monaco
- ○ Montenegro
- ○ North Macedonia
- ○ Norway
- ○ Poland
- ○ Portugal
- ○ Romania
- ○ Russia
- ○ Serbia
- ○ Slovakia
- ○ Slovenia
- ○ Spain
- ○ Sweden
- ○ Switzerland
- ○ The Netherlands
- ○ Türkiye
- ○ Ukraine
- ○ United Kingdom
- ○ Other (please specify)

2. What is your profession?
    - ○ Anaesthesiologist
    - ○ Hospital managers
    - ○ Medical specialty physician

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- Nurse working on the ward
- Nurse working in the operating theatre
- Nurse working in the ICU
- Pharmacist
- Other (please specify)

3. What type of hospital/clinic do you work in? Please tick the most appropriate option.
   - General non-teaching hospital
   - Outpatient clinic
   - Private hospital
   - Small community hospital
   - Teaching/university hospital
   - Specialised tertiary care hospital
   - Other (please specify)

4. How many inpatient beds does your hospital have?

   0 _____ over 3000

5. How many ICU beds does your hospital have?

   0 _____ over 300

6. How many operating theatres does your hospital have?

   0 _____ over 100

Pharmacy-specific questions

7. Are hospitals permitted to purchase 'manufactured specials' from industry in your country?
   - Yes
   - No
   - I don't know.

8. Which industry-manufactured prefilled medicines syringes unlicensed 'manufactured specials' are purchased and used in your hospital?

   Please provide information on the active substance, concentration and volume of the product that you are using as an unlicensed 'manufactured specials'.

9. Do hospital pharmacies have the capacity to prepare more prefilled medicines syringes?
   - Yes
   - No
   - I don't know.

10. What is the main barrier to hospital pharmacies preparing more prefilled medicines syringes?

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Opinion questions

Please rate the statements presented below on a scale from 1 (strongly disagree) to 4 (strongly agree).

11. Statement 1:
    Prefilled medicine syringes save significant amounts of clinical (nurse/doctor) time in preparing infusion therapy for use in clinical areas.
    - Strongly disagree
    - Disagree
    - Agree
    - Strongly agree
    - I have not sufficient experience using prefilled syringes or not seen sufficient information about their use to provide an opinion on this statement.

12. Statement 2:
    Prefilled medicine syringes reduce medication errors.
    - Strongly disagree
    - Disagree
    - Agree
    - Strongly agree
    - I have not sufficient experience using prefilled syringes or not seen sufficient information about their use to provide an opinion on this statement.

13. Statement 3:
    Prefilled medicine syringes reduce hospital acquired infections.
    - Strongly disagree
    - Disagree
    - Agree
    - Strongly agree
    - I have not sufficient experience using prefilled syringes or not seen sufficient information about their use to provide an opinion on this statement.

14. Statement 4:
    Prefilled medicine syringes reduce the risk of needle stick injuries.
    - Strongly disagree
    - Disagree
    - Agree
    - Strongly agree
    - I have not sufficient experience using prefilled syringes or not seen sufficient information about their use to provide an opinion on this statement

15. Statement 5:
    Prefilled medicine syringes reduce staff stress.
    - Strongly disagree
    - Disagree
    - Agree
    - Strongly agree
    - I have not sufficient experience using prefilled syringes or not seen sufficient information about their use to provide an opinion on this statement.

16. Statement 6:
    Prefilled medicine syringes enable greater standardisation of infusion doses/ concentration/ final

volumes.
- Strongly disagree
- Disagree
- Agree
- Strongly agree
- I have not sufficient experience using prefilled syringes or not seen sufficient information about their use to provide an opinion on this statement.

17. Statement 7:
Prefilled medicine syringes reduce the waste of syringes which are prepared and not used or later not required in the clinical area.
- Strongly disagree
- Disagree
- Agree
- Strongly agree
- I have not sufficient experience using prefilled syringes or not seen sufficient information about their use to provide an opinion on this statement.

18. Statement 8:
Prefilled medicine syringes cost significantly more to purchase than vials and syringes.
- Strongly disagree
- Disagree
- Agree
- Strongly agree
- I have not sufficient experience using prefilled syringes or not seen sufficient information about their use to provide an opinion on this statement.

19. Statement 9:
The total cost of using prefilled medicine syringes is not higher than the combined cost of vials and syringes and clinical/nursing time.
- Strongly disagree
- Disagree
- Agree
- Strongly agree
- I have not sufficient experience using prefilled syringes or not seen sufficient information about their use to provide an opinion on this statement.

20. Statement 10:
Prefilled medicine syringes have some disadvantages on use (other than cost) which prevents them being used in practice.
- Strongly disagree
- Disagree
- Agree
- Strongly agree
- I have not sufficient experience using prefilled syringes or not seen sufficient information about their use to provide an opinion on this statement.

21. What do you consider are the barriers for the adoption of prefilled medicine syringes in your hospital? Please select the **3 main barriers** in your hospital.
- ☐ Incompatibility with hospital syringe pumps and equipment
- ☐ Insufficient number of syringes available to purchase and/or supply chain resilience of industry-manufactured prefilled medicine syringes to meet our requirements
- ☐ Insufficient range of **hospital pharmacy prefilled medicine syringes** to meet our requirements
- ☐ Insufficient range of **industry-manufactured prefilled medicine syringes** to meet our requirements
- ☐ Insufficient storage space in clinical areas for prefilled medicine syringe larger packaging

- ☐ Lack of clinical effectiveness of prefilled medicine syringes
- ☐ Purchase price of industry-manufactured prefilled medicine syringes
- ☐ Other (please specify)

22. Statement 11:
Industrially manufactured prefilled medicine syringes have advantages vs hospital pharmacy preparation (like quality, shelf life, etc.)
    - Strongly disagree
    - Disagree
    - Agree
    - Strongly agree
    - I have not sufficient experience using prefilled syringes or not seen sufficient information about their use to provide an opinion on this statement.

23. Statement 12:
The use of prefilled medicine syringes has increased in the last two years.
    - Strongly disagree
    - Disagree
    - Agree
    - Strongly agree
    - I have not sufficient experience using prefilled syringes or not seen sufficient information about their use to provide an opinion on this statement.

24. How do you think will the use of prefilled medicine syringes change in the future?
    - It will increase.
    - It will decrease.

25. Statement 13:
The main decision maker or makers for the introduction of prefilled medicine syringes in my hospital is/are:

	Strongly disagree	Disagree	Agree	Strongly agree	I don't know
Hospital pharmacists	☐	☐	☐	☐	☐
ICU/ Anaesthesia manager	☐	☐	☐	☐	☐
Nurses	☐	☐	☐	☐	☐
Hospital management (General/Finance)	☐	☐	☐	☐	☐
Other	☐	☐	☐	☐	☐

If you selected 'other', please mention the other decision makers.

26. What was successful in convincing the decision maker or makers in your hospital to use prefilled medicine syringes?
    - ☐ Business case showing return on investment
    - ☐ Evidence on reduced risk in medication errors
    - ☐ Evidence on reduced risk of infection
    - ☐ Improved work-flow efficiency at any hospital

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- ☐ Guidelines from Scientific Associations
- ☐ Literature review
- ☐ Specimen business case
- ☐ I don't know.
- ☐ Other (please specify)

Questions on the use of prefilled medicine syringes

Please answer the questions to your best ability. Where needed please share additional information.

27. Are prefilled syringes containing normal saline for flushing used in the area that you work in/ in the hospital you work in?
    - ○ Yes
    - ○ No
    - ○ I don't know.

28. Are prefilled medicine syringes containing active substances used in the area that you work in/ in the hospital you work in?
    - ○ Yes
    - ○ No
    - ○ I don't know.

29. Is bar coding technology used at the point of administration to the patient in the area that you work in/ in the hospital you work in?
    - ○ No
    - ○ I don't know.
    - ○ Yes (please specify name of system you are using)

30. In your country, are there guidelines/recommendations on the use of prefilled medicine syringes?
    - ○ No
    - ○ I don't know.
    - ○ Yes (please specify)

Please select 5 active substances that you would like to use as a prefilled medicine syringe in your hospital and provide information on their concentration.

The active substances are listed in alphabetical order.

31. Please select the active substance that you would like to use as a prefilled medicine syringe.

    Only 5 can be selected.

    - ☐ Adenosine (Cardiac)
    - ☐ Alfentanil (Anaesthetic)
    - ☐ Amiodarone (Cardiac)
    - ☐ Atracurium Besilate/ Suxamethonium (Muscle relaxant) Atropine
    - ☐ Bupivacaine
    - ☐ Calcium

- ☐ Dobutamine (Cardiac)
- ☐ Dopamine (Cardiac)
- ☐ Ephedrine (Cardiac)
- ☐ Epinephrine/Adrenaline (Cardiac)
- ☐ Fentanyl (Anaesthetic)
- ☐ Heparin
- ☐ Insulin
- ☐ Ketamine
- ☐ Lidocaine/Lignocaine
- ☐ Magnesium
- ☐ Metaraminol (Vasopressor)
- ☐ Morphine (Pain)
- ☐ Naloxone
- ☐ Norepinephrine/Noradrenaline (Cardiac) PhenylEephrine (Cardiac)
- ☐ Potassium
- ☐ Propofol (Anaesthetic)
- ☐ SuFentanyl (Anaesthetic)
- ☐ Sugammadex
- ☐ Others (please specify)

32. For the 5 active substances that you would like to use as a prefilled medicine syringe, please add information on the concentration.

Active substance 1
(Please indicate the name of the substance and your preferred concentration)

Active substance 2
(Please indicate the name of the substance and your preferred concentration)

Active substance 3
(Please indicate the name of the substance and your preferred concentration)

Active substance 4
(Please indicate the name of the substance and your preferred concentration)

Active substance 5
(Please indicate the name of the substance and your preferred concentration)

33. Please select the active substances that are available in your hospital as a prefilled medicine syringe. Please indicate if these are industrially-manufactured or prepared in the hospital. Only select those active substances that are used in your hospital.

	I use an industrially-manufactured prefilled medicine syringe of this active substance	I use prefilled medicine syringe of this active substance that is prepared by my hospital pharmacy
Adenosine (Cardiac)	○	○

Alfentanil (Anaesthetic)	○	○
Amiodarone (Cardiac)	○	○
Atracurium Besilate/ Suxamethonium (Muscle relaxant)	○	○
Atropine	○	○
Bupivacaine	○	○
Calcium	○	○
Dobutamine (Cardiac)	○	○
Dopamine (Cardiac)	○	○
Ephedrine (Cardiac)	○	○
Epinephrine (Cardiac) /Adrenaline	○	○
Fentanyl (Anaesthetic)	○	○
Heparin	○	○
Insulin	○	○
Ketamine	○	○
Lidocaine/Lignocaine	○	○
Magnesium	○	○
Metaraminol (Vasopressor)	○	○
Morphine (Pain)	○	○
Naloxone	○	○
Norepinephrine/Noradrenaline (Cardiac)	○	○
PhenylEphrine (Cardiac)	○	○
Potassium	○	○
Propofol (Anaesthetic)	○	○
SuFentanyl (Anaesthetic)	○	○
Sugammadex	○	○
Other	○	○
Other	○	○
Other	○	○

If you selected 'other', please specify the active substance.

34. Please select 5 active substances that your hospital is not yet using and that you would like to use as a prefilled medicine syringe.

    Only 5 can be selected.

    - ☐ Adenosine (Cardiac)
    - ☐ Alfentanil (Anaesthetic)
    - ☐ Amiodarone (Cardiac)
    - ☐ Atracurium Besilate/ Suxamethonium (Muscle relaxant) Atropine
    - ☐ Bupivacaine
    - ☐ Calcium
    - ☐ Dobutamine (Cardiac)
    - ☐ Dopamine (Cardiac)
    - ☐ Ephedrine (Cardiac)
    - ☐ Epinephrine/Adrenaline (Cardiac)
    - ☐ Fentanyl (Anaesthetic)
    - ☐ Heparin
    - ☐ Insulin
    - ☐ Ketamine

- ☐ Lidocaine/Lignocaine
- ☐ Magnesium
- ☐ Metaraminol (Vasopressor)
- ☐ Morphine (Pain)
- ☐ Naloxone
- ☐ Norepinephrine/Noradrenaline (Cardiac) PhenylEephrine (Cardiac)
- ☐ Potassium
- ☐ Propofol (Anaesthetic)
- ☐ SuFentanyl (Anaesthetic)
- ☐ Sugammadex
- ☐ Others (please specify the active substance)

35. For the 5 active substances that you would like to use as a prefilled medicine syringe, please add information on the concentration.

Active substance 1
(Please indicate the name of the substance and your preferred concentration)

Active substance 2
(Please indicate the name of the substance and your preferred concentration)

Active substance 3
(Please indicate the name of the substance and your preferred concentration)

Active substance 4
(Please indicate the name of the substance and your preferred concentration)

Active substance 5
(Please indicate the name of the substance and your preferred concentration)

Annex V – Survey for Manufacturers of Prefilled syringes

The European Association of Hospital Pharmacists (EAHP) currently has a Special Interest Group (SIG) on the Use of Prefilled Syringes in Intensive Care Units and Operating Theatres. The SIG has identified that there is a lack of awareness about the availability of manufactured prefilled syringes in Europe.

In connection with this, the SIG would be very grateful if you could complete this short survey.

36. Does your company supply any injectable medicines in prefilled syringes?
    - Yes
    - No

37. Please list the prefilled syringes that your company supplies.

Name of medicine	
Volume of Syringe	
Concentration	
Shelf-life	

38. Please list the prefilled syringes that your company supplies.

Name of medicine	
Volume of Syringe	
Concentration	
Shelf-life	

39. Please list the prefilled syringes that your company supplies.

Name of medicine	
Volume of Syringe	
Concentration	
Shelf-life	

40. Please list the prefilled syringes that your company supplies.

Name of medicine	
Volume of Syringe	
Concentration	
Shelf-life	

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41. Please list the prefilled syringes that your company supplies.

Name of medicine	
Volume of Syringe	
Concentration	
Shelf-life	

42. If your company supplies more than 5 different prefilled syringes, please provide information about the others below.

43. Please provide contact details for further information on your companies prefilled syringes.

44. Could EAHP share information on the prefilled syringes that you supply to its members?
    - Yes
    - No

SPECIAL INTEREST GROUP | REPORT

Prefilled syringes in intensive care units and operating theaters

COVER DESIGN > www.biographia.it

REV. 0 12/2023

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