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How are we handling protein drugs in hospitals? A human factors and systems engineering approach to compare two hospitals and suggest a best practice

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Abstract
Biopharmaceuticals are complex biological molecules that require careful storage and handling to ensure medication integrity. In this study, a work system analysis of real-world protein drug (PD) handling was performed with the following goals: identify main barriers and facilitators for successful adherence to accepted recommendations in PD handling, analyse differences in two organizations, and define a Best Current Practice in the real-life handling of PDs based on the results of the work system analysis. Observational study was held in two university hospitals in Spain and Sweden. Based on the Systems Engineering Initiative for Patient Safety (SEIPS) model, the tools chosen were: the PETT scan, in order to indicate the presence of barriers or facilitators for the PETT components (People, Environment, Tools, Tasks); the Tasks and tools matrices to construct a checklist to record direct observations during the real-life handling of biopharmaceuticals, and the Journey map to depict the work process. Observations were performed between March and November 2022. Each episode of direct observation included a single protein drug in some point of the supply chain and considered all the elements in the work system. Based on the results of the work system analysis and the literature review, the authors propose a list of items which could be assumed as Best Current Practice for PDs handling in hospitals. There were a total of 34 observations involving 19 PDs. Regarding People involved in the work process, there was a diversity of professionals with different previous training and knowledge, leading to an information gap. With respect to Environment, some structural and organizational differences between hospitals lead to risks related to the time exposure of PDs to room temperature and mechanical stress. Some differences also existed in the Tools and Tasks involved in the process, being especially relevant to the lack of compatibility information of PDs with new technologies, such as pneumatic tube system, robotic reconstitution, or closed-system transfer devices. Finally, 15 suggestions for best current practice are proposed. Main barriers found for compliance with accepted recommendations were related to the information gap detected in professionals involved in the handling of protein drugs, unmonitored temperature, and the lack of compatibility information of protein drugs with some new technologies. By applying a Human Factors and Systems Engineering Approach, the comparison of two European hospitals has led to a suggested list of Best Current Practices in the handling of protein drugs in a hospital.

Keywords: protein aggregation; chemical stability; monoclonal antibodies; hospital pharmacy; protein handling; human factor;

Introduction
Background
Biopharmaceuticals are complex biological molecules that require careful storage and handling to ensure medication integrity. It is recognized that biologicals are especially sensitive to mechanical stress and shaking, temperature and freeze-thaw cycles, in addition to light exposure [1]. Already in 2003, Crommelin *et al.* published a list of recommendations about the proper storage and handling of protein drugs throughout the supply chain from hospital pharmacy to patient [2].

During the last 20 years, the number of biopharmaceuticals has increased exponentially [3, 4], as well as the diversity of clinical conditions in which they are useful [5]. Several studies have been investigating the practices, instructions, and attitudes of health care providers regarding the handling of biologicals in hospitals. There is still significant variability in the handling practices and lack of guidelines in the hospital and outpatient clinics with risks that might affect protein drug quality; such as lack of visual inspection, vigorous agitation of vials or air bubbles, and foam formation [6, 7].

The main concern with the safety and efficacy of protein drugs (PDs) is related to the unwanted immunogenicity that can be caused by drug and patient-specific factors [8, 9]. Risks related to product quality factors can easily occur due to mishandling of biopharmaceuticals in the hospital supply chain [10].
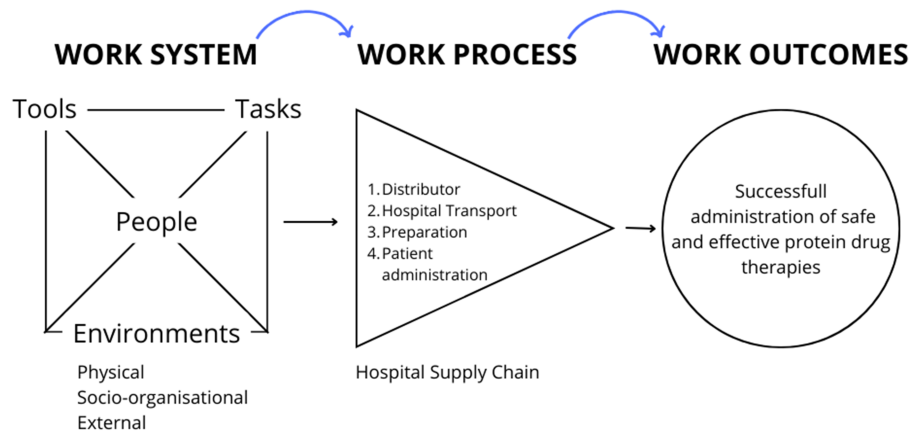
Figure 1 Systems Engineering Initiative for Patient Safety (SEIPS) model adapted from Holden *et al.*, 2021 [13].

In this study, a work system analysis of real-world protein drug handling in two European hospitals was performed with the following goals: (i) to identify main barriers as well as facilitators for successful adherence to accepted recommendations in biopharmaceuticals handling, (ii) analyse differences in both organizations, and (iii) to define a Best Current Practice in the real-life handling of PDs based on the results of the work system analysis.

Methods

The two hospitals in this study were considered as two different organizations. They both are University hospitals (HCB in Barcelona, Spain and UAS in Uppsala, Sweden) with more than 700 beds including all main medical and surgical specialties. and attend patients with medical conditions that require biological therapies. This observational study is based on the Systems Engineering Initiative for Patient Safety (SEIPS) model that has previously been applied in healthcare to improve patient safety by comparing compliance data between hospitals [11]. The three major components of the SEIPS 101 model are shown in Fig. 1. Adapted to our study the components are: Work System (square), Work Process (triangle), and Work Outcomes (circle). The four elements of the Work System are: People, Environment, Tools, and Tasks (spelled 'PETT'). The Work Process refers to how work is done and the flow chart of the organization. The interactions between all these fields will provide the Work Outcomes: performance, quality, and patient safety [12]; in particular, for this study work outcome was considered as 'Successful administration of safe and effective protein drug therap*y*s'.

For this study, three SEIPS 101 tools were chosen: (i) the 'PETT scan', in order to indicate the presence of barriers or facilitators for the PETT components, (ii) the 'Tasks and tools matrices' to construct a checklist to record direct observations during the clinical practice handling of biopharmaceuticals along its supply chain at the hospitals. The checklist helped standardize the diverse elements for observation in both settings; and finally, (iii) the 'Journey map' to depict the work process [12, 13]. Based on the Journey map, further analyses regarding the people involved in the subprocesses, the environment, tools, and tasks regarding the compliance of evidence-based handling recommendations were done with the support of checklist audits [2]. Main risk

factors considered able to compromise biopharmaceuticals integrity were: (i) information gaps, (ii) long exposure to light or room temperature (RT), (iii) hits and mechanical shocks during transport, (iv) vigorous shaking, excessive foam formation, or the presence of air during preparation/administration, (v) consumables directly in contact with PDs during handling that may have negative effects, and (vi) incompatibility issues during administration.

Observations were performed from March to November 2022. Two pharmacists in each setting were responsible for the on-site interviews of users and data collection. An independent checklist was used for each step mentioned in the work process. All the checklists were developed in HCB by two pharmacists based on the stressors and risks found in literature. The languages used were Spanish (HCB) and English (UAS). The interviews included different stakeholders depending on each step of the process. Free comments from the participants related to the process in which they actively participated were all registered anonymously. Each episode of direct observation included a single protein drug in some point of the supply chain and considered all the elements in the work system.

Regarding the PETT-scan, and the 'People' component, it should be noted that no patients were interviewed during this study. When interviewing employees, focus was furthermore always on the drug product and no personal or sensitive data were included in the interviews. For this reason, only an internal ethical review of the study was performed by the researchers. Designing the study, focus on the 'Environment' elements such as 'temperature, light exposure, cleanroom conditions, etc., were considered in the checklist'. Studying the 'Tools' component, in the analysis we considered those tools and technology that directly affects biopharmaceuticals handling; for example, 'cars, vans, and containers used to transport biopharmaceuticals, information materials and guidelines, and compounding devices, such as closed system transfer devices (CSTD)'. Finally, the 'Tasks' component, focuses on the diversity of professionals that lead to a broad range of tasks including reception and classification of medicines, transport, preparation, verification, and administration. Pharmacists involved in the direct observation were responsible for carefully analysing these tasks and reporting every step of the process with the aid of checklists.

Based on the results of the work system analysis and the literature review, the authors propose a list of items which could be assumed as real-life handling Best Current Practice for PDs in hospitals.

Results

SEIPS models analysis

There were a total of 34 observations (20 in HCB and 14 in UAS), involving 19 PDs. Observers registered every deviation from general recommendations in each part of the supply chain.

'People' involved in the work process include carriers, porters, technicians, nurses, and pharmacists. They all do similar tasks in the two organizations. The main difference is that in the UAS, there are pharmacists in charge of the reconstitution and dilution of drugs at hospitalization wards, while in HCB this is always a nurse's responsibility. In HCB, technicians are also responsible for the unit dose distribution of drugs and automated dispensing cabinets refilling. In general, an 'information gap' was observed, since carriers, porters, many technicians, and some nurses did not know the nature of the product they were handling and the special precautions needed for proper preservation.

Related to 'Environment', some structural differences were observed: HCB is a compact main building serving also two external centres and UAS consists of separate buildings connected by underground corridors with one external centre. The longest travelling distances within the hospital is 400 metres inside the Barcelona building and 950 metres in Uppsala. On the other hand, HCB has different providers: pharmaceutical companies that delegate the transport to the hospital to different logistics companies. However, classification and storage are the responsibility of the hospital staff. UAS has only one medication distributor, responsible for the storage and transport of medicines. When medicines arrive, they are already classified according to storage conditions and destination within the hospital. At this point, observations addressed to the 'packaging and the time exposure of PDs to room temperature'. Logistic companies in Spain use validated refrigerated boxes or cool boxes monitored by data loggers, and KMB® boxes with monitored temperature in the case of Sweden [14]. There was no specific warning in the label about the nature of the drug, except for 'storage at 2–8°C'. Both organizations are confident that there is no 'risk of mechanical stress' during transport from the distributor to the pharmacy, but the truth is that there is no control or document that guarantees this fact.

The responsibility of the transport of PDs to external centres falls on the own hospital. UAS prepares some medicines for *Enköping* hospital (50 km away), while HCB provides daily PDs compounded in the cleanroom to two external centres, located less than 3 km away. They use cool boxes, but they are not validated; so, even though the distance is quite short, it was considered as a risk factor.

Some differences also existed in the 'Tools and Tasks' involved in the process. Following the hospital's reception, the medicines need to be transported to each correspondent ward. This internal transport in UAS is made by electric cars underground, and can take 40–120 minutes, where the PDs remain inside the KMB® validated boxes. Throughout the internal transport, different scenarios like 'hits and mechanical shocks' were reported by the observers. There is also a Pneumatic Tube System (PTS) available to distribute medicines to some wards, but it is not used for PDs; this was considered positively, since PTS should not be used in non-tested drugs, and current evidence related to the appropriateness of this kind of distribution for biopharmaceuticals is still not conclusive [15]. In HCB, the individual dosages are prepared for each patient and subsequently transported by medical mobile
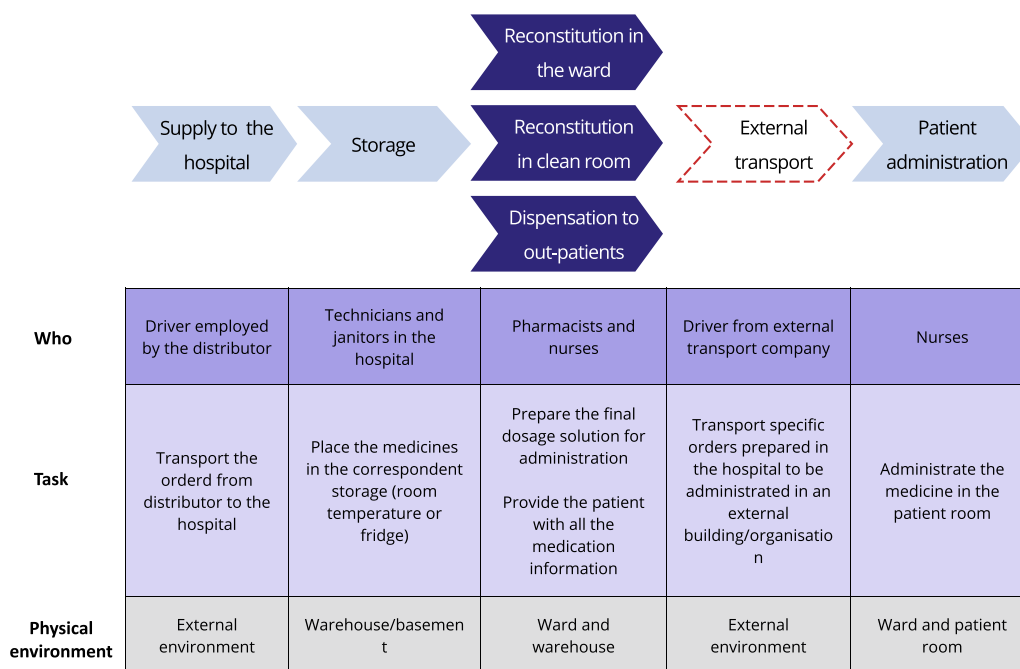
	Supply to the hospital	Storage	Reconstitution in clean room / Reconstitution in the ward / Dispensation to out-patients	External transport	Patient administration
Who	Driver employed by the distributor	Technicians and janitors in the hospital	Pharmacists and nurses	Driver from external transport company	Nurses
Task	Transport the orderd from distributor to the hospital	Place the medicines in the correspondent storage (room temperature or fridge)	Prepare the final dosage solution for administration / Provide the patient with all the medication information	Transport specific orders prepared in the hospital to be administrated in an external building/organisation	Administrate the medicine in the patient room
Physical environment	External environment	Warehouse/basement	Ward and warehouse	External environment	Ward and patient room

Figure 2 Journey map of the general supply chain of medicines in a hospital adapted from Holden *et al.*, 2021 [13]. Note that Step 4 "External transport" only applies to the minority of cases where there is a delivery outside the hospital.

carts/trolleys or manual transport by porters that can also take up to 180 minutes. The most relevant aspect is that while in UAS the PDs are stored in validated refrigerated boxes during internal transport, in HCB PDs are exposed to room temperature until they are stored in the ward. Refrigerators located at wards were usually monitored, such as the equipment located at the Pharmacy.

The preparation and reconstitution in the cleanroom (CR) must strictly follow specific guidelines and instructions, including GMP, national guidelines [16], and manufacturer instructions. Although some of the guidelines followed can differ, both hospitals have well-regulated procedures in the CR, leading to a similar way of working in both hospitals. The procedure can differ between manual or robot preparation, although both organizations use the same robotic compounding system [17]. Once the preparation is done, there is a visual check of particles and turbidity before it's placed in the refrigerator or to proper RT storage. Robotic compounding is applied to some liquid biopharmaceuticals, such as rituximab or bevacizumab. CSTD are not used to compound PDs in any of the two organizations' cleanrooms. Both items were positively weighed up in terms of PD handling, as the reconstitution process of biopharmaceuticals in robotic devices and the use of CSTD for this kind of molecules requires further research. The observers didn't report unusual foam or bubble formation at this point. Despite the work procedures in the cleanroom being clear and in agreement with data sheet instructions, a lack of specific guidelines was observed in other steps of the supply chain. Information at hospitalization wards is supported basically in the Computerized Physician Order Entry (CPOE) software and was considered scarce or insufficient relating to PDs in both hospitals. At day Hospitals in HCB, most of the existing information was provided by the manufacturer. Direct observations in HCB reported two episodes of excessive foam formation due to a rapid reconstitution. Furthermore, despite this information gap, during direct observations of PDs administration, no known incompatibility with other drugs or diluents was observed.

Sometimes there is no need to manipulate the drug before the administration and in that case, PDs are directly dispensed to patients for self-administration at home. Observers found a good level of information given to patients, but in general nurses didn't ask for feedback to guarantee the information has been properly understood. In HCB, most patients used cool boxes to transport PDs on their way home, but this wasn't the usual practice at UAS.

Considering the work process analysis, the supply chain of PDs included five subprocesses: supply of medicines to the hospital, storage and hospital internal transport, preparation and reconstitution, external transport to other organizations, and patient administration, as shown in the 'Journey map' (Fig 2). 'Barriers and facilitators' observed during the study related to these five subprocesses are described in Table 1.

Best current practices proposal

Based on the work system analysis results and the barriers and facilitators identified, we suggest a hospital adapted Best Current Practice (BCP) approach to avoid drug mishandling and achieve best outcomes with PDs treatment. It is summarized in Table 2.

Discussion

Principal findings

In this study we applied a human factors and systems engineering approach to examine barriers and facilitators of compliance with the general recommendations of proper handling of biopharmaceuticals in two European hospitals.

The more the people involved, the more complex the work system is. In our case, we have different professionals and patients interacting and doing different tasks, and the information gap highlighted along the work process was, in our understanding, the main barrier to be overcome. It is especially critical in the case of nurses preparing and administering PD. Both organizations agree that pharmacists should be more proactive at this point providing information where it is needed; tools may be varied, such as infographics, posters, or other written information; or by adding specific information in the CPOE program.

Special mention deserves those PDs that are directly dispensed to patients and self-administered at home. Despite the SEIPS study showing in general a good level of information given to patients, the lack of knowledge about the storing and handling of drugs at home is at least worrying. Some authors have studied the storage conditions and range temperatures at patients' homes regarding more investigation and solutions for these common situations [18, 19].

May the location and structure of the hospital have an influence in PD handling? At this point, the SEIPS model pointed out that the organizational elements are more determinant than the environment. For example, waiting time at room temperature was generally longer in HCB even though the distances were longer in UAS because the logistic process has been well designed to preserve cold chain.

Strengths and limitations

The limitations faced along this study should be noted. The number of observations collected allowed us to get a general idea of the real-life problems handling PDs in a hospital, based on the judgement of the pharmacists in charge, but it is uncertain how many observations are needed to be reliable. The information concerning patients was provided from previous literature and from checklists performed during nurse administration, since no patients were interviewed. The reproducibility of the study is not representative since it only includes two hospitals in two different countries.

Despite its limitations, the study shows the daily life events during the handling of biopharmaceuticals from the hospital pharmacy to patients and it provides useful tools to evaluate these issues. The SEIPS model has been used by other authors to evaluate healthcare systems, but it is the first time, in our understanding, that it is applied in protein drug handling processes. Also, the BCP suggested can be applied in other hospital organizations leading to a closer standardized way of working with PDs in clinics. Even though it is mentioned that the reproducibility is a barrier, comparing two different hospitals in two different countries has helped both organizations to get and exchange new ideas and different ways of working.

Table 1. Barriers and facilitators (based on the PETT scan tool [13]).

	Barriers	Facilitators
Work systems factors	**Patient administration (hospital)**	
People: • Porters • Technicians • Pharmacists • Nurses	**General:** Technicians and porters doesn't know about protein drugs	
Environment: • Physical • Socio-organizational • External	**General:** No control on the truck movements and condition of the route	**General:** Cold preservation monitored and light protection Refrigerated truck
Tools	**General:** Lack of information about the medicines (more specific protein drugs)	
Tasks	**General:** Risk of mishandling the boxes during the unloading of the medicines from the truck to the warehouse/pharmacy.	
Work systems factors	**Storage and hospital internal transport**	
People: • Porters • Technicians • Pharmacists • Nurses	**General:** Technicians and porters do not know about protein drugs	
Environment: • Physical • Socio-organizational • External		**General:** Control of refrigerator temperature No exposure to light during the storage
Tools	**General:** Lack of information about the medicines (more specific protein drugs)	
Tasks	**UAS:** risk of dropping off the medicine boxes during the underground transport **HCB:** During the storage classification it can take between 15 and 30 min at RT	**UAS:** due to the fact that the boxes are validated during the storage classification in the hospital there is no exposure to RT
Work systems factors	**Preparation and reconstitution**	
People: • Porters • Technicians • Pharmacists • Nurses	**General:** Diversity of professionals involved (technician, nurse, pharmacists…); some of them are not trained in handling protein drugs	**General:** Pharmacists working in the CR know what a protein drug is
Environment: • Physical • Socio-organizational • External	**General:** Exposure to light and RT depends on the specification of each protein drug	**General:** CR adequately monitored
Tools	**General:** Lack of knowledge about the effect of CSTD or the robotic compounding in PD integrity.	**General:** In the CR the information and protocols for preparation reflects the recommendations from the technical sheet Technology, Equipment, and devices according to the nature of the drugs prepared.
Tasks	**General:** No robot reconstitution program for PDs Some bubble and foam are unavoidable	**General:** Smoothly swirl and homogenization during the manual preparation without shaking Visual particle check If there are particles or turbidity the final product is discarded No use of CSTD
Work systems factors	**Patient administration (hospital)**	
People: • Porters • Technicians • Pharmacists • Nurses	**General:** Diversity of professionals involved in the ward with different previous training and knowledge about protein drugs (nurse, pharmacists, porter)	
Environment: • Physical • Socio-organizational • External	**HCB:** up to 3 h at RT due to the internal distribution system **UAS:** exposure to light when it's taken out from the original package	**General:** Even though there is no continuous monitoring, the storage conditions in the ward room are well controlled. **UAS:** the cold chain is maintained in the ward No use of PTS for PDs **HCB:** original package or light protection bags—no exposure to light

Table 1. (Continued)

Work systems factors	Barriers	Facilitators
	Patient administration (hospital)	
Tools	**General**: Lack of validated protocols (or insufficient information in CPOE) inside the ward/Day Hospital Scarce information about physico-chemical incompatibilities	
Tasks	**General**: Some bubbles and foam are unavoidable. Lack of smoothy homogenization in the ward or short waiting time until bubbles/foam disappear (some nurses HCB)	**General**: Visual particles check during the administration. Smoothly and gently swirl during the manual preparation without shaking (pharmacists, most nurses)
Work systems factors	**Patient administration (home)**	
People: • Porters • Technicians • Pharmacists • Nurses	**General**: Diversity of professionals involved in the ward with different previous training and knowledge about protein drugs (nurse, pharmacists) It's unpredictable and uncertain how the medicines are handled at patients' home	
Environment: • Physical • Socio-organizational • External	**General**: Transportation time from the hospital until home storage **HCB**: Refrigerators at wards in HCB are controlled, but most are not continuously monitored	**General**: Refrigerator temperature and storage well monitored
Tools	**UAS**: the organization does not generally provide a cool box to the patient	**General**: The patient is well informed about the storage and handling of the medication The indications given to the patient correlate to the manufacturer instructions **HCB**: the manufacturer can provide a cool box to the patient
Tasks	**General**: There is not always a verification that the patient has understood everything	
Work systems factors	**External transport**	
People: • Porters • Carriers • Technicians • Pharmacists • Nurses	**General**: The carrier does not know what a protein drug is	
Environment: • Physical • Socio-organizational • External	**General**: Route and traffic difficulties are unpredictable **HCB**: cool boxes not always validated **UAS**: long transport distances	**General**: The packaging to other organizations or building are validated cool boxes No exposure to light during the transport **HCB**: short transport distances
Tools	**General**: Lack of information about PDs given to the personnel involved in the transport	
Tasks		**General**: Avoid rough/brusque movements

General: similar observations found in both hospital organizations.
UAS: observation found in Uppsala University Hospital.
HCB: observation found in Hospital Clínic Barcelona.
RT: room temperature; CR: clean room; PD: protein drug; CPOE: Computerized Order Entry Software; CSTD: closed system transfer device; PTS: pneumatic tube system.

Interpretation within the context of the wider literature

Twenty years after Crommelin's publication [2], it seems that the risk factors that biopharmaceuticals are subjected in real-life handling are still significantly important and the window for improvement is wide. Our findings are not very different from the ones previously reported by Narhi *et al.* or Jiskoot *et al.*[6, 19]. Excessive room temperature exposure or vial shaking is still observed during drug handling. The implementation of in-use analytical methods in the near future could be extremely useful to highlight the real effect of these issues in drug quality [20, 21].

Implications for policy, practice, and research

On the other hand, what is certainly a challenge and a matter of future research is the use of new technologies, such as CSTD and compounding robots in the reconstitution of biopharmaceuticals [22]. For example, some hospitals use CSTD for the reconstitution of all drugs, proteins or not, even in the absence of compatibility information [23, 24]. Similarly, the PTS has been recently installed in different hospitals in Europe, even for chemotherapy transport [25]; however, the formation of subvisible particles and the possible adverse impact on the product quality is still a concern of consideration [26].

To enhance the relevance and impact of the present study, future research efforts could focus on expanding the discussion to explore the potential implementation of the study's findings across diverse hospital settings. A more in-depth exploration into the scalability of the proposed best practices would be beneficial, addressing how these practices can be effectively adapted to accommodate the distinct resources and infrastructures present in various healthcare environments.

Table 2. Suggestion of best current practice. The list is based on finding from using the SEIPS model and literature review (Ref 23,27,28).

Quality issue	Risk of mishandling	Best current practice
Information gap	Lack of knowledge of nurses involved in the preparation and administration of PDs	1. Design infographics or similar about the proper reconstitution and administration of PDs addressed to nurses in Day hospitals and wards. 2. Review instructions about reconstitution and dilution of specific biopharmaceuticals in the CPOE program. 3. Provide the patient with specific instructions for the correct handling and preservation of PDs at home, and guarantee its appropriate understanding.
Monitored temperature ranges	Excessive exposure to room temperature	4. Validation of the cool boxes used in the transport to external centres. 5. Implementation of validated cool boxes or a refrigerated drawer during internal transport from Pharmacy to the wards. 6. Promoting the use of cool boxes for the transport of PDs from the Pharmacy to home in ambulatory patients. 7. All the refrigerators in the hospital should have a monitored temperature track system and will need to be checked every specific time.
Monitored transport	Mechanical shock/hits	8. Full traceability of the hospital internal and external transport would be desirable.
Reconstitution procedures and handling materials	Excessive shaking; presence of air in the bag; use of devices with no evidence of compatibility with PDs	9. Consider to increase the waiting time after reconstitution in those drugs in which foam and bubble formation may be a problem. 10. Carefully remove or reduce as much as possible air head space in infusion bags. 11. Use a non-flicking technique and syringes with the minimal amount of silicone oil or silicone oil free syringes for ophthalmic use. 12. Robotic compounding: to develop and implement new sensitive programs including movements like swirling or no shaking would be desirable. 13. Until further research is available, the use of CSTD in PDs should be limited to those biopharmaceuticals considered hazardous drugs with documented compatibility information
Light exposure	Excessive exposure to light (especially daylight)	14. Provide a validated list in the wards of the protein drugs that must be protected from light.
Administration procedures	Risk of physico-chemical incompatibility in case of Y-administration	15. Due to lack of information, the use of simultaneous Y-site administration can only be done when supporting data are available. Otherwise, stopping infusions and flushing between with compatible solutions should be done. Also, the use of inline filter should be done according to supplier recommendations.

PD: protein drug; CPOE: Computerized Order Entry Software; CSTD: closed system transfer device.

Moreover, extending the observational study to encompass a broader spectrum of hospitals is recommended. Additionally, it is advisable to delve into the establishment of relevant policies and procedures within the work system. Addressing the gap among healthcare providers and workers through the governance of practices for the safe handling of biopharmaceuticals could significantly contribute to the overall efficacy of the proposed best practices. Investigating the impact of these policies on safety outcomes and adherence to best practices could be valuable for further exploration. By expanding the scope of the research in these ways, future investigations have the potential not only to strengthen the current study's conclusions but also to contribute significantly to a more thorough understanding of the complexities involved in biopharmaceuticals handling within hospitals worldwide. This, in turn, will enhance the practical implications and generalizability of the study's outcomes, giving more informed decision-making within the healthcare community.

Conclusions

Main barriers found for compliance with accepted recommendations were related to the information gap detected in professionals involved in the handling of protein drugs, unmonitored temperature, and the lack of compatibility information of biopharmaceuticals with some new technologies. By applying a Human Factors and Systems Engineering Approach, the comparison of two European hospitals has led to define a list of the Best Current Practices in the handling of protein drugs in a hospital, based on pharmacists' criteria, to implement in a future and improve the real-handling of biopharmaceuticals.

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Author contributions

Clàudia Sabaté-Martínez (Methodology, Investigation, Analysis, Writing),
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Ulla Elofsson (Supervision, Project administration),
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Conflict of interests:

The authors declare no conflict of interest.

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Data Availability Statement

The data underlying this article will be shared on reasonable request to the corresponding author. A copy of the checklist template has been attached as Supplementary material.

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