Handling of protein drug products and stability concerns

The first objective of this topic is to improve the understanding of real-world stressful drug product handling steps and their effects on protein product quality.

- All protein DPs are considered to be within the scope of the topic.
- All handling steps for preparation, transport and administration should be addressed:
  - Studying the effects of the handling steps on drug product quality is in the scope of the project.
  - Supplies that are used for handling of the protein pharmaceuticals are also to be investigated and evaluated. Evaluation of new technologies that are used to handle protein pharmaceuticals such as closed-system transfer devices are of interest;
  - Handling practices include the ones that are performed by healthcare professionals in hospital and compounding pharmacies and the ones in hands of patients. The understanding should be as thorough as possible and may be, obtained by the use of new technologies and digital tools that record details visually or by sensors of conditioning parameters during storage and administration processes, among other methods;
  - Routine handling procedures, i.e. the ones that are currently used as standard procedures for protein drug products in pharmacies and by patients should be addressed.
- These risks associated with the handling of protein DPs should be assessed and potential solutions developed;
- Mishandling cases with high level of likelihood or severe impacts should also be examined.

The second objective of this topic is to use this understanding for development of guidelines and operating processes to improve the DP robustness and pharma processes, and to develop more efficient training.

- Improving the in-use studies and other processes in development of protein pharmaceuticals is in the scope of the topic.
Innovative solutions that help ensuring the stability of DP during handling are welcome.

Improving the training materials and improving the handling culture are in the scope of the topic. Training aspects should cover training for professionals and patients.

Utilisation of technologic tools (video, webinar, online media and creative manuals) for development of novel training methods and materials is within the scope of the topic.

In the past two decades, protein pharmaceuticals have become the fastest growing class of therapeutics owing to their beneficial impacts on the treatment of severe and life-threatening conditions and diseases. Development and manufacturing of protein pharmaceuticals is, however, challenging and requires overcoming various manufacturing hurdles such as issues with the purity of the protein product. The safety and efficacy of protein pharmaceuticals depend on their purity. Impurities in marketed protein pharmaceuticals may be present due to limitations in manufacturing processes or may also be a result of degradation processes occurring not only during manufacturing, but also during long-term storage of the bulk drug substance and/or final drug product (DP). Impurities within therapeutic protein products can cause severe adverse drug reactions (ADRs) in patients, that may be acute, as is the case for infusion-induced anaphylaxis and pseudo-allergy responses, which may even result in patient death, or long-term like unwanted immunogenicity.

Physical aggregation and chemical degradation can occur throughout a protein product’s life history, and even modest environmental stresses can cause extensive damage. Development of effective upstream and downstream processes as well as robust formulations and filling processes are crucial for maintaining product quality, and hence, for the safety and efficacy of protein pharmaceuticals. The pharmaceutical industry has made great progress in improving bulk and DP manufacturing as well as storage and transportation conditions to minimise the level of degradation. However, there exists only low control over the many factors that may affect product quality after the protein pharmaceuticals are released and shipped. Routine handling or unintentional mishandling of therapeutic protein products may cause protein degradation that remains unnoticed but can potentially compromise the clinical safety and efficacy of the product. Storage of the DP outside the recommended condition ranges, use of incompatible supply and/or technology, careless handling of drug during preparation for administration and during delivery to patient are just a few examples of such (mis)handling. When it comes to handling of DP by patients, the social, cultural, logistical and environmental differences between different geographies and cultures can also impact the handling conditions.

There has been increasing expression of concern in the past decade regarding the significance of the post-production handling of protein pharmaceuticals. At the same time, studies revealed that the consequences of presence of impurities in DP can be severe. Potentially high likelihood and/or severity in consequences in combination
with the low level of control over the processes by the industry make these concerns a significant risk that needs to be addressed in a public-private partnership that includes all relevant stakeholders.

- Through this project, a better understanding of the handling procedures of protein DPs and associated stresses in hospitals and in the hands of patients will be obtained. The project will assess the risks associated with these handling steps and provide solutions to ensure high-quality delivery and administration of protein DP;
- The project will help participating pharmaceutical companies to improve their processes with regards to the development of more robust DPs that can withstand handling stresses;
- At the same time, access to the resulting improved methods to influence the handling culture can be used by both the private and public sectors in the interest of patients. Foremost amongst the expected impacts is the improved training for professionals and patient/caregivers to ensure the stability of protein DP. This will have global effects on the manufacturing side as well as the user side at pharmacies, hospitals and with patients, thus providing benefits to all healthcare stakeholders;
- Generation of knowledge in the area of stress-stability will help all the stakeholders involved and can be directly applied to the design of the processes and addressing important but challenging issues around the development of therapeutics and delivery to patients;

Overall, the project is expected to lead to improvements in the safety and efficacy of protein drug therapies.

**Last update:** 4 December 2019

**Permalink:** https://cordis.europa.eu/programme/id/H2020_IMI2-2020-20-06

European Union, 2023