INSIGHTS INTO INDUSTRY PERSPECTIVES, PREFERENCES, AND DECISION-MAKING FACTORS ON LARGE-VOLUME SUBCUTANEOUS DRUG DELIVERY

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INTRODUCTION

Background

This survey study was conducted among experts in clinical development, medical affairs, and commercial roles within the pharmaceutical industry to examine perceptions, preferences, and decision-making factors concerning large-volume subcutaneous (SC) drug delivery. It challenges the conventional belief that SC delivery is limited to volumes of 2-3 mL without permeation enhancers (PEs) despite evidence suggesting otherwise. This misconception , partly driven by the limited volume capacity of traditional devices like autoinjectors and prefilled pens, as well as the precedent set by previously approved SC drugs, is precisely what our survey sought to fully elucidate.

The research investigates the intricacies of device format selection and the role of PEs in bioavailability (BA) for large-volume SC drug delivery. By analyzing responses regarding the prioritization of delivery attributes such as speed, ease of use, and patient and healthcare provider preferences, the study aims to clarify current decision-making. It also investigates motivations behind specific development paths and the role of historical device use in future development. In a field with limited public data, the findings are expected to inform a more nuanced approach to SC drug formulation and device selection, advocate for innovations that balance efficacy with patient comfort, and streamline care in pharmaceutical development.

Objectives

- Identify factors and biases influencing misconceptions about limited volume capacity in SC drugs without PEs
- Investigate factors shaping decision-making in SC drug development, including device selection and PE coformulation
- Understand implications of industry focus on expediting SC delivery time, including effects on patient and healthcare practitioner (HCP) experiences

METHODS

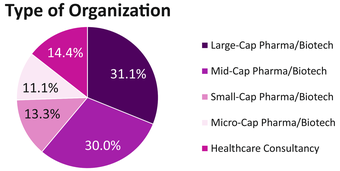
A blinded survey was conducted between 20 March and 4 April 2024, garnering 90 responses from experts in clinical development, medical affairs, and commercial development within the pharmaceutical industry with extensive experience working with SC drug products. The survey included multiple-choice and open-ended questions to capture data on current perceptions, preferences, and decision making factors concerning large volume SC drug delivery.

RESULTS

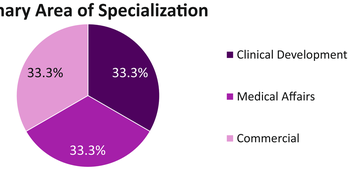
Survey Respondents: Professional Background

Characteristic	Respondents (n=90)
Geographic location, n (%)	
United States	50 (55.6)
Europe	38 (42.2)
Japan	1 (1.1)
Canada	1 (1.1)
Years of experience, mean (SD)	16.3 (8.5)
SC products worked on during career, mean (SD)	9.1 (12.2)
Current professional position, n (%)	
Executive Director or Director	26 (28.9)
Senior Director	25 (27.8)
Vice President	23 (25.6)
Senior Manager	10 (11.1)
Associate Director	4 (4.4)
Manager	2 (2.2)

Type of Organization

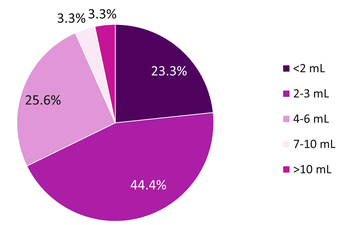


Primary Area of Specialization

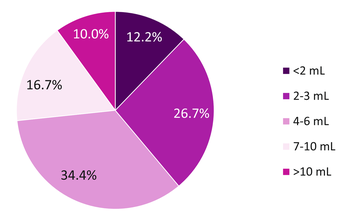


Survey Respondents: Knowledge of Large-Volume SC Drug Delivery

Perceived Maximum Drug Volume That Can Be Administered SC *as a Bolus* Without PE



Perceived Maximum Drug Volume That Can Be Administered SC *over Several Minutes* Without PE

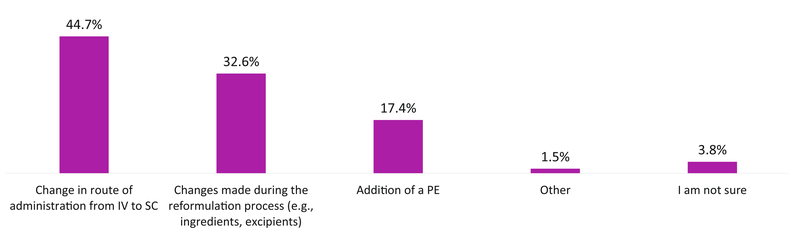


- Only 44% selected the range of 2-3 mL, which is widely considered to be the **maximum volume that can be delivered SC as a bolus without a PE** due to limitations with patient pain and drug leakage.[1]
- For both questions, respondents relied heavily on just **two sources for their knowledge of maximum SC volume limits:** 1) familiarity with commercialized products and 2) expert/colleague opinion.
- Only 10% selected >10 mL as the **maximum volume limit for SC administration over several minutes without PE.**
- This indicates a **lack of understanding** regarding the **difference between SC bolus and infusion.** It also highlights **limited awareness** of **approved large-volume SC drugs** without a PE, such as Hizentra®, Repatha®, Rystiggo®, Ultomiris® SC, and Empaveli®.

After reviewing a table of approved large-volume SC drugs (>3 mL), *55.6% changed their position* on the maximum deliverable SC drug volume, suggesting that most of the responses were due to misinformation or a lack of awareness.

20.0% did not change their minds even after reviewing these data, indicating potential bias.

Factors Contributing to Safety Benefits of SC vs. IV Drugs



- Most respondents recognize the safety benefits of SC drugs compared to IV, but confusion exists regarding PEs and their impact on safety.
- Although the safety benefits of adding PEs are not well-documented in the literature, **they are often conflated with the broader safety advantages of the overall IV-to-SC transition, leading to confusion within the industry.**

SC Drug Development

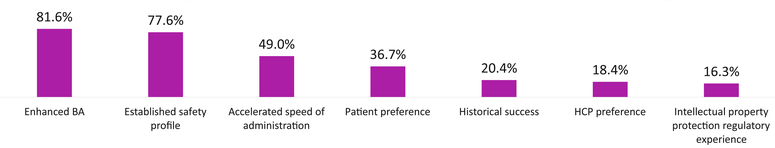
Most Important Attribute During Development of SC Drug Product		Most Important Attribute During Development of SC Drug Product *for Oncology Specifically*	
Attribute	**Mean (SD)** 1=Most Important, 7=Least Important	**Attribute**	**Mean (SD)** 1=Most Important, 7=Least Important
Device ease of use	1.9 (1.2)	Device ease of use	2.3 (1.4)
Patient preference	3.4 (1.9)	Optionality in site of care	3.3 (1.8)
Optionality in site of care	3.8 (1.7)	Patient preference	3.4 (1.9)
Speed of administration	4.3 (1.8)	Drug preparation complexity	3.8 (1.9)
HCP preference	4.4 (1.6)	HCP preference	4.6 (1.8)
Drug preparation complexity	4.8 (2.1)	Speed of administration	4.7 (1.8)
Nurse administration burden	5.6 (1.4)	Nurse administration burden	5.9 (1.4)

- The top 3 attributes in SC product development relate to patient experience: **device ease of use, optionality in the site of care,** and **patient preference**.
- Administration speed, typically associated with products with PEs, **ranks in the lower half of attributes**, reflecting a **paradigm shift in focus towards patient comfort and experience over speed**.
- The top attributes for SC oncology products are largely consistent with non-oncology products, with a slight shift toward in-clinic considerations such as drug preparation complexity.

81.1% reported that past use of an SC device format has a high or very high influence on the likelihood of using similar device formats in the future.

Permeation Enhancers

Participants Ranking Aspects of PE Coformulation in SC Drug Development as Valuable (3), Very Valuable (4), or Most Valuable (5) on 5-Point Value Ranking Scale



- There is a misconception about the effect of PEs on BA; **publicly available data do not show a consistent**, **clinically meaningful (>20%) improvement in BA** and a **significant portion of data is unpublished**.[1]
  - The BA benefits of rapid trafficking through the SC space to avoid lysosomal degradation are likely more pronounced in extremely large-volume applications. Consequently, the only publicly available data showing a significant improvement in BA with PEs beyond 20% is with SC immunoglobulin G (>50-100 mL delivered).
- In a similar survey (data not shown), nearly 35% of respondents (technical experts in coformulation with PEs) incorrectly reported that the average impact of PEs on BA was >20%. Therefore, the impact of PEs on BA and the magnitude of this impact are misunderstood.

CONCLUSIONS

- Most respondents were **misinformed about the maximum volume that can be administered SC without a PE**, in large part due to reliance on just two sources of information that reinforce this misunderstanding (i.e., familiarity with commercialized products and expert/colleague opinion).
  - More than half of the respondents **changed their stance after exposure to accurate information.**
- The focus on patient experience in large-volume SC product development is mainly driven by the goal of **improving treatment adherence**; however, the **previous use of a device format has an outsized influence on future device selection**, which could hinder the adoption of more suitable options.
- There is a **misconception that PEs significantly improve BA and safety** despite a lack of clinically meaningful data, but experts seem open to education on the true effects of PEs.
  - Over a third (36.7%) of respondents in the current survey were willing to adjust their stance upon viewing publicly available BA data on PEs, indicating that experts may be unaware of these data.

[1]Desai M, Kundu A, Hageman M, Lou H, Boisvert D. Monoclonal antibody and protein therapeutic formulations for subcutaneous delivery: high-concentration, low-volume vs. low-concentration, high-volume. MAbs. 2023 Jan-Dec;15(1):2285277.

Abbreviations: BA, bioavailability; HCP, healthcare practitioner; IV, intravenous; mL, milliliters; n, number of participants; PE, permeation enhancer; SC, subcutaneous; SD, standard deviation.

If you have questions about this poster, please email Mehul Desai at mdesai@enableinjections.com.

Prepared with writing and editorial assistance from Terri Levine, MSc, PhD, CMPP.

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