

Optimising Clinical Trials for the Era of Self-Injectable Combination Products

Self administered injectable drug–device combination (DDC) products are entering a phase of accelerated therapeutic innovation. Demographic change, chronic disease trends and the push for patient centric care are converging to make self administration a practical imperative rather than a futuristic aspiration.

In the United States, the population aged over 50 years with at least one chronic disease is projected to increase by 99.5% from 71.5 million in 2020 to 142.7 million by 2050.¹ As Baby Boomers and Generation X age and live longer with multiple conditions, predictable demand is emerging for therapeutic modalities that reduce the burden on health systems while enabling patients to manage complex regimens at home. Established self administration paradigms in diabetes are now informing approaches for other patient populations and different diseases.

This shift is reflected in market dynamics. The global drug–device combination products market was valued at approximately 138 billion USD in 2023 and is expected to approach 252 billion USD by 2030,² corresponding to a compound annual growth rate of 9.0%. Within this trajectory, self administered injectable DDCs have become a keystone technology for upgrading drug delivery, improving adherence and ultimately optimising clinical outcomes. For sponsors, the logical extension of this trend is to incorporate self injectable DDCs early, at the clinical trial stage rather than only at commercialisation.

Clinical Trial Benefits of Self Injectable DDCs

Historically, single or multi use vials have been the default presentation for subcutaneous administration during preclinical and early phase trials because they offer flexibility in fill volume and dosing while developers focus on proof of concept, safety and dose finding. The growing emphasis on patient centricity and real world usability is now prompting a shift towards self-administered dosage forms, such as prefilled syringes, safety needle devices and autoinjectors.

Several biopharmaceutical companies are investing in device research and development to enhance functionality, expand compatibility with diverse molecules and introduce combination devices earlier in the development lifecycle. When integrated into clinical trials, these DDCs offer multiple advantages:

- Improved adherence and retention through self administration that reduces reliance on clinical visits and allows patients to manage dosing in their own environment.
- Greater dosage standardisation by means of prefilled presentations that deliver consistent doses and reduce human error inherent in manual preparation.
- Enhanced data integrity via devices capable of recording dosing events, including timestamps, to support pharmacokinetic and pharmacodynamic analyses.
- Closer alignment with real world use, since trials evaluate not only the pharmacology of the drug but also the performance, usability and risk profile of the device in realistic conditions.

For participants, well designed DDCs can reduce injection related anxiety, pain and procedural complexity, contributing to a more

positive trial experience and sustained engagement. For sponsors, early integration of combination products can de risk post approval use, facilitate evidence generation for regulators and payers, reduce cost and streamline the transition from trial to market.

Design and Human Factors: A Practical Challenges Checklist

The benefits of DDCs in trials are realised only when design, usability and safety are addressed systematically. Because these products are intended for patient self-administration rather than skilled medical use, human factors engineering is central to both clinical and commercial success.

Autoinjectors illustrate these considerations clearly. Ergonomically, they must be easy to grip, orient and activate across a broad demographic, including individuals with limited dexterity, reduced muscle strength, or visual impairment. Cognitive ergonomics are equally important; intuitive operation, simple two or three step procedures and clear visual, tactile and audible feedback help patients perform injections correctly and confidently.

Device–drug compatibility is another critical axis. Autoinjectors must accommodate formulation specific attributes such as viscosity, dose volume and required injection speed. High viscosity biologics, for example, demand sufficient mechanical force and robust drive systems to deliver the full dose reliably. Rigorous stability testing must demonstrate that device materials do not adversely interact with the formulation and that the combination maintains integrity over the intended shelf life.

Delivery speed should be optimised to balance patient comfort with pharmacological needs. Consistent with ISO 11608 5 expectations, the device must reliably deliver the intended dose, particularly for biologics where minor deviations can have clinically meaningful consequences. These ‘matchmaking’ efforts underscore that the ‘combination,’ in DDC is not rhetorical; drug and device must be developed as an integrated therapeutic system.

Equally, trial design must reflect participant diversity. Sponsors need to anticipate variations in age, comorbidities, prior experience with self injection and psychological barriers such as needle phobia. Training materials, instructions for use and support mechanisms should be adapted accordingly, without compromising the overriding priority of safety.

Safety features are fundamental in this context. Needle shields, automatic retraction mechanisms, and reliable locking systems are crucial to prevent accidental activation and needlestick injuries in populations that are not healthcare professionals. Designing for safe, error resistant use is therefore not an optional enhancement but a core requirement for trial implementation.

Regulatory and Risk Management Considerations

Regulatory pathways for self injectable DDCs are inherently more complex than for drug only products, but this complexity can ultimately facilitate smoother commercialisation once addressed early. Most self administered injectables will be classified as combination products, requiring integrated submissions that cover



both drug and device components and demonstrate compatibility between formulation and device materials.

Human factors and usability studies are central to regulatory evaluation. Sponsors must show, through realistic, scenario based testing, that lay users can safely and effectively self administer the product under expected conditions of use. This encompasses the complete user journey, including packaging, labeling, instructions for use and the step by step administration process.

Robust risk management frameworks are needed to identify, assess and mitigate issues spanning drug stability, device performance and potential interactions between components. Conducting human factors work early in the development cycle allows design modifications and process improvements before large pivotal studies are launched. Regulators increasingly regard human factors and usability engineering not as adjunct activities but as integral components of a complete DDC dossier.

Manufacturability, Supply Chain and Scale Up

Effective clinical use of DDCs must be planned with eventual commercialisation in mind. Sponsors need a realistic pathway from low volume clinical supply to potentially very high commercial volumes and this pathway must be reflected in early technical and sourcing decisions.

Key Considerations Include:

- Reliable supply of device components and assemblies, with contingency plans to mitigate disruptions that could delay trials or post approval supply.
- Strategic selection between customised autoinjectors and off the shelf platforms, balancing differentiation, technical fit, time to market and cost.
- Definition of initial and target volumes to guide investments in tooling, automation and validation, avoiding over or under engineering of manufacturing assets.

Cost-benefit analyses should be conducted during development rather than deferred to the commercial stage, recognising that clinical success may rapidly escalate volume needs. As production scales, alignment of efficacy, functionality, patient usability and cost effectiveness becomes essential to sustain both clinical and economic value.

Necessity and Opportunity in Trial Design

For sponsors deciding whether to integrate self administered injectable DDCs into clinical development, the case increasingly rests on necessity rather than optional innovation. The projected rise in chronic disease prevalence, combined with resource constraints in healthcare systems, will demand scalable, patient centric delivery models that can only be fully validated if studied under realistic conditions during trials.

Adopting DDCs in clinical studies does entail front loaded investment in device development, documentation, human factors work, manufacturing readiness and training for both site staff and participants. Yet these investments yield durable dividends in trial quality, regulatory robustness and post approval success. When thoughtfully designed and executed, incorporating self administered injectable DDCs into clinical trials transforms outsized challenges into equally substantial rewards for patients, sponsors and healthcare systems alike.

REFERENCES

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