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Biosimilar Self-Administration as a Drug–Device–User System: A Conceptual Framework for Injection Mechanics, Handling Errors, and Delivered-Dose Consistency Across Presentation Changes

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ABSTRACT

Biosimilar switching is evaluated using pharmaceutical, analytical, pharmacokinetic, and clinical comparability, whereas the act of self-injection introduces a separate set of device-dependent and user-dependent conditions. To explain when presentation changes might alter administration consistency despite acceptable biosimilar comparability, and identify observations capable of testing that explanation. This nonempirical multilevel theory integrates published work on biosimilar switching, patient experience, simulated-use human factors, injection mechanics, tissue deposition, and subcutaneous absorption. Four noninterchangeable quantities are distinguished: nominal prepared dose, drug expelled from the delivery system, drug deposited into the intended tissue compartment, and resulting systemic exposure. Formulation properties condition mechanical resistance; device architecture and user action jointly influence initiation, contact, injection completion, and removal; tissue geometry and local transport subsequently condition absorption. The account predicts that apparently equivalent use-task results may coexist with different mechanical or deposition outcomes, and that observed exposure differences may occur despite equivalent expelled mass. These are discriminating hypotheses, not demonstrated biosimilar-specific causal effects. Product-matched mechanical, behavioral, deposition, and pharmacokinetic comparisons are needed before clinical meaning can be assigned. Presentation evaluation should specify which stage of delivery is measured and preserve competing explanations across drug, device, user, and tissue levels.

Key words: *Biosimilar self-administration, Drug–device combination product, Autoinjector usability, Injection force, Subcutaneous dose deposition, Pharmacokinetic bridging*

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INTRODUCTION

Evidence supporting therapeutic switching between a reference biologic and biosimilars, or among biosimilars, addresses comparability and the clinical consequences of product substitution. It is valuable for prescribing decisions, but does not measure every action by which a patient transfers drug from a particular injector to tissue. Cohen and Bodenmueller's synthesis of biosimilar-to-biosimilar switching illustrates the clinical evidence base and its therapeutic focus [1]. The administration problem therefore has its own estimand: the consistency of dose transfer when a product is used through a specified presentation by an intended population in a defined setting.

For self-injected biologics, the patient encounters a concrete interface: grip, cap removal, activation mechanism, needle shielding, contact force, audible or visible progress cues, and a hold interval. Product attributes may also shape experience. A review of adalimumab presentations discusses how formulation and device attributes

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contribute to reported injection experience [2]. Yet pain, preference, task completion, fluid leaving the needle, and systemic bioavailability answer different questions. A comfortable injector could be difficult to finish correctly; a mechanically complete injection could still create a tissue depot whose subsequent absorption varies for reasons unrelated to use error.

Switching practices also occur within clinical systems that influence expectations, training, information, and continuity of administration. International experience with adalimumab biosimilar switching supplies a relevant implementation context [3]. This article develops a nonempirical explanation for conditional relationships among pharmaceutical formulation, injection hardware, patient action, local tissue transport, and exposure. Its central test is whether changes attributed to user-interface performance remain distinguishable from formulation mechanics, tissue physiology, and measurement artifacts when those levels are independently observed. Therapeutic biosimilarity is not treated as proof of device-use equivalence, and theoretical pathways are not presented as validated clinical effects.

Biosimilar presentation changes as a pharmaceutical administration problem

A presentation change can preserve the active biologic's clinically comparable function while altering what a user handles. A pen and a prefilled syringe may differ in activation sequence, needle visibility, injection-force source, grip demands, and the feedback that signals completion. Within a product family, differences in excipients, concentration, injection volume, needle configuration, and device design may also affect comfort or administration mechanics. Such attributes warrant explicit product-by-presentation comparison; they cannot be assumed to co-vary or independently explain any patient-reported outcome.

In a Canadian survey comparing autoinjector experiences among people with rheumatoid arthritis and Crohn's disease, patient-reported preferences and usability perceptions offered evidence about acceptability of particular designs [4]. The survey does not establish expelled dose, injection depth, or systemic exposure. A separate UK cross-sectional survey found that information received before switching from reference adalimumab to a biosimilar was relevant to satisfaction [5]. Communication and expectation are therefore plausible contributors to patient experience that must be measured alongside device characteristics rather than incorrectly classified as mechanical failure.

The pharmaceutical question is not whether one presentation is globally superior. It is which product-dependent and context-dependent changes can alter specific steps of drug transfer. Consider three counterfactual comparisons: the same formulation operated through different devices; the same device design used with formulations of different mechanical properties; and the same product–device pairing used by groups differing in hand function or prior training. They isolate different causal candidates. None by itself establishes altered delivered dose; each requires measurements at the level where the putative effect occurs.

Current evidence on injection devices, handling, and self-administration

Human-factors studies provide direct observation of user behavior, but their outcomes are defined by their protocols. An investigation of autoinjector and prefilled-syringe use among people with generalized myasthenia gravis assessed acceptance and practical performance in the intended patient context [6]. Such evidence is especially pertinent where fatigue or hand function may influence self-administration; it is not a universal estimate for all biologics or diseases.

A study of SB4, an etanercept biosimilar, compared user-facing syringe and autoinjector presentations among people with rheumatoid arthritis [7]. It anchors device-specific usability questions in an actual biosimilar setting. Nevertheless, success in prescribed use steps should be distinguished from a direct mass-balance measurement of injection output. A device may be preferred because it is easier to hold even when preference cannot predict the amount transferred.

Comparative formative studies of changing autoinjector designs suggest that transition between user interfaces is feasible under studied conditions and identify tasks potentially sensitive to design differences [8]. Transferability depends on prior familiarity, the activation sequence, labeling, training, and the participants recruited. These studies can locate use risks but cannot infer how frequently a particular error occurs in routine care without representative field observation.

A 2026 comparative simulated-use study examined a biosimilar adalimumab autoinjector and its reference-product counterpart in patients with inflammatory conditions [9]. Critical-task success offers meaningful comparative evidence within the study's simulated setting. However, the observation cannot by itself determine

biologic depot mass or pharmacokinetic equivalence in living tissue. A separate simulated-use validation of an ustekinumab biosimilar autoinjector included patients, caregivers, and healthcare professionals [10]. Its multi-role design underscores that device performance is partly role-dependent, and that successful pad injection remains a surrogate for actual tissue delivery.

Formative and validation testing of a disposable prefilled injection device for corticotropin likewise illustrates the importance of identifying consequential user steps and interpreting error reports in the context of the tested interface [11]. Across these sources, the shared evidence is strongest for observable actions: cap removal, positioning, activation, contact maintenance, and task completion. It is less direct for hidden physical endpoints occurring after drug passes through the needle. The distinction motivates separate mechanical and biopharmaceutical measurements rather than extrapolation from favorable task scores.

Unresolved relationships between usability and pharmaceutical dose delivery

The first uncertainty is mechanical localization. In experimental work with shield-triggered autoinjectors, shield dimensions and applied force influenced needle insertion depth in porcine tissue [12]. The result concerns a defined device–tissue interaction, not a measured clinical failure rate in human biosimilar users. A person can perform the instructed push-on-skin action and still generate different tissue compression across device geometries. Conversely, an apparent variation in contact force may matter little once the relevant device or tissue response has saturated.

The second uncertainty concerns injectability. Mathematical modeling of prefilled syringes separates hydrodynamic resistance, friction, rheology, temperature, and tissue counterpressure [13]. In a related experimental investigation, plunger and needle attributes and human factors affected the measured resistance of prefilled systems [14]. Together these studies support evaluating an actual drug–container configuration against plausible user capability. They do not establish a universal force threshold above which patients will leave a dose incomplete.

Spring-driven systems introduce another dependency: injection duration is affected by liquid rheology and the device's energy-delivery characteristics. A study of a spring-driven autoinjector modeled the relation between shear-dependent fluid properties and injection time [15]. Slow or prolonged delivery may increase opportunity for early removal, but the frequency of that behavior cannot be inferred from the mechanics model. The behavioral connection is a hypothesis requiring synchronized observations of injection progress and human action.

Protein condition can produce a failure route distinct from user handling. Work on protein solutions in prefilled syringes describes a two-stage needle-clogging process with storage- and system-dependent determinants [16]. Such a mechanism could interrupt flow even when activation and hold behavior are appropriate. The converse also matters: a user error can alter delivered output despite unchanged formulation and an unobstructed needle. Experimental comparisons of viscosity and dosing materials further demonstrate that injectability depends on the tested needle and administration apparatus [17]. Neither force readings nor successful activation should substitute for expelled mass.

These uncertainties require endpoint-specific terminology. Nominal dose is the prepared labeled amount; expelled dose is the amount leaving the device under measured conditions; deposited dose is the amount reaching an identified tissue compartment; and systemic exposure is subsequently observed through pharmacokinetic measurements. Incomplete hold time, mechanical resistance, tissue compression, and absorption are possible contributors at different transitions, with no automatic equivalence between their measured signals. **Table 1** locates the principal variables at the point where they could affect transfer and identifies the inference that each observation alone cannot support.

Table 1. Distinct physical and behavioral comparisons needed to interpret biosimilar self-injection performance

Comparison unit	Supported source of variation	Directly observable endpoint	Inference that remains open	Proposed matched contrast
Formulated biologic in a filled container	Concentration- and shear-sensitive fluid resistance	Rheology and time-resolved force	Comparable viscosity does not ensure tissue deposition	Keep device geometry constant while varying tested formulation state
Prefilled syringe barrel–plunger–needle system	Friction, needle dimensions, and backpressure	Force–displacement trace and expelled mass	Mechanical effort does not identify individual task error	Pair component characterization with standardized user operation

Spring-driven autoinjector	Spring delivery profile and fluid rheology	Injection time and completion signal	Completion cue need not establish depot amount	Compare output mass against synchronized end-of-use actions
Shield-triggered device against skin	Shield contact area, normal force, tissue deformation	Contact force and insertion-depth measure	Experimental depth findings do not prove human tissue targeting	Repeat geometry comparison across controlled tissue conditions
Protein solution within needle pathway	Storage-dependent localized clog formation	Flow interruption and residual drug	Reduced flow does not necessarily imply early withdrawal	Pair post-use flow analysis with observation of user behavior
Intended self-administrator	Familiarity, grip function, sequence execution, hold duration	Critical-task observation and timed contact	Task success and satisfaction do not quantify expelled dose	Link participant-level actions to independently measured output

Note: Evidence-derived variation reflects distinct human-factors, syringe-mechanics and protein-flow investigations. Matched contrasts are proposed comparative tests, not results from a new experimental dataset.

Development of the drug–device–user systems framework

The theory begins at the boundary between device output and tissue delivery. High-speed synchrotron imaging has visualized subcutaneous depot development and subsequent fluid dispersion under experimental autoinjector conditions [18]. This makes deposition a separately observable event with a geometry and time course, instead of a quantity safely inferred from a click or an empty reservoir. Once fluid enters tissue, its dispersion depends on local physical conditions and is not simply a record of how well the interface was operated.

A mathematical account of monoclonal-antibody uptake highlights the role of initial lymphatics, injection conditions, and local transport in shaping subsequent absorption [19]. The same deposited mass may therefore yield exposure differences if tissue and molecular transport differ; a measured pharmacokinetic difference does not uniquely identify incomplete injection. Broader pharmacological synthesis of subcutaneous monoclonal-antibody administration addresses bioavailability, delivery, immunogenicity, and clinical-development considerations [20]. Those processes extend beyond the act of pressing a device and may be specific to a molecule, injection site, or patient.

A recent drug–device–container–tissue multiscale framework already describes physicochemical and mechanical connections from formulation through absorption [21]. The present contribution is deliberately narrower at the molecular end and more explicit at the human end: it introduces task execution as a time-varying influence on the mechanical boundary conditions of drug output and deposition. This is an extension for discriminating presentation-change effects, not a claim to have invented the molecule-to-absorption connection.

Operationally, a presentation state combines drug formulation and condition, container and injector geometry, spring or hand-generated driving force, and instructional interface. A use trajectory is a time-stamped sequence of patient actions, including preparation, activation, contact force, maintenance of contact, and withdrawal. A delivery trajectory is a corresponding set of measured changes in fluid flow, device residual mass, and tissue deposition. Administration consistency denotes reproducibility of a specified endpoint over repeated intended-use opportunities, conditional on the population and setting, without presuming identical pharmacokinetics.

These trajectories interact dynamically. More resistance may increase required hand force or injection time; unexpectedly prolonged operation may encourage early withdrawal; altered normal force can change tissue compression and insertion geometry. Successful completion can also occur despite high mechanical resistance when the user compensates appropriately. A measured discrepancy may instead originate from needle obstruction, physicochemical state, injection-site differences, or lymphatic uptake. These possibilities predict different combinations of critical-task observations, expelled mass, tissue deposition, and concentration–time behavior. None should be distinguished by a single undifferentiated 'injection success' score.

Physics-based autoinjector simulations combined with statistical optimization demonstrate how design variables may be explored without exposing patients to every parameter combination [22]. Simulation sensitivity remains conditional on imposed fluid, device, and tissue assumptions; it does not measure a patient's actual compensatory behavior or validate a biosimilar-specific dose effect. A scientifically discriminating test would first separate formulation and device changes, then observe user trajectories while independently quantifying mechanical output and, where ethically and technically feasible, deposition. Later exposure observations would test a subsequent

transition, with site and physiological differences controlled. **Figure 1** represents these linked levels and the alternative routes by which apparent failure or apparent equivalence can arise.

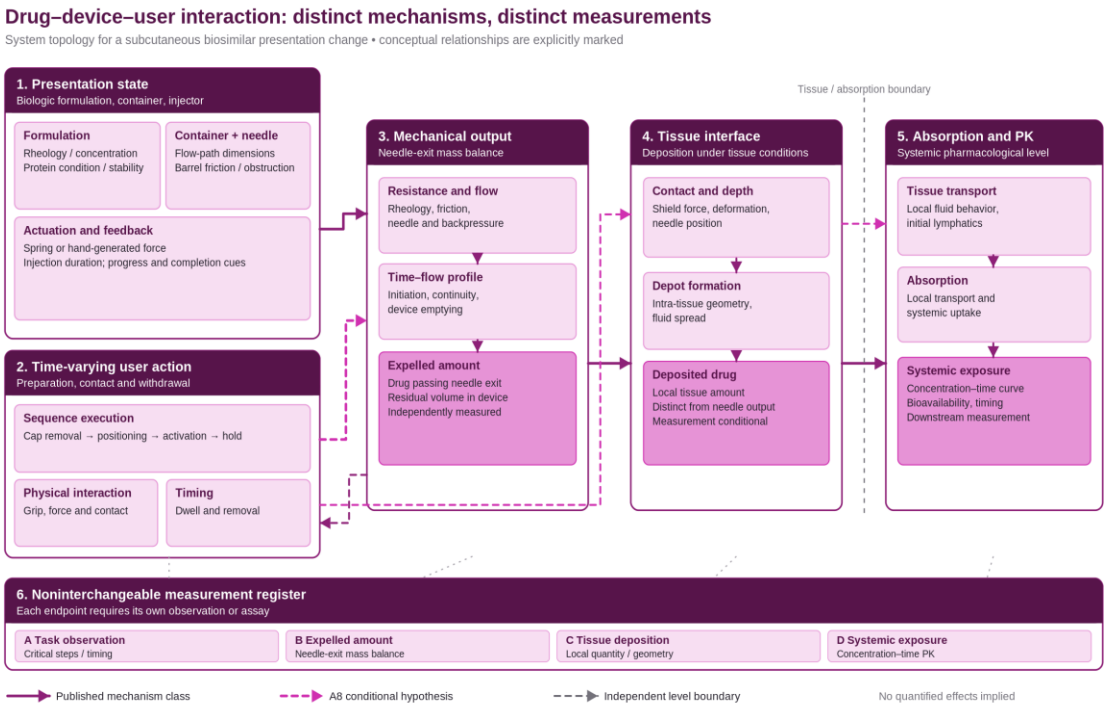


Figure 1. Administration consistency emerges from coupled use trajectories, mechanical output, and tissue transport across a presentation change

Caption/legend: The figure reads left to right, beginning with a formulation–container–device presentation and a parallel user-action trajectory. Solid arrows indicate empirically established *classes* of mechanical or transport interaction under cited experimental conditions; dashed arrows indicate A8-specific, still-untested links between use trajectories and measured drug transfer; paired arrows identify reciprocal feedback between operating resistance and compensatory user action. Separate measurement enclosures represent task observation, expelled mass, local deposition, and systemic exposure. The dotted tissue/absorption boundary and conditional alternative arrow mark how local physiology may modify exposure despite equivalent mechanical output. The figure does not assert a measured dose difference between any named biosimilar and reference product. SC, subcutaneous; PK, pharmacokinetics.

Alt text: Wide asymmetric conceptual map. A large left-hand region groups formulation state, container–needle, and injector actuation; an independent lower region contains timed user actions. Both regions converge through reciprocal and conditional links on a center-right mechanical-output region, which connects to local tissue deposition and then systemic PK exposure. Four measurement tags sit beneath successive levels. A dashed alternative arrow crosses the tissue/absorption boundary above the main output-to-depot-to-exposure path, indicating possible local physiological influences; a return link from device resistance to user dwell or withdrawal highlights behavioral adaptation. A dotted vertical boundary separates the deposition and absorption regions. Solid and dashed connectors have separate meanings and are explained in the legend.

Implications for biosimilar presentation evaluation and administration consistency

A changed presentation requires an evaluation question specified at the level of the changed component. Hu and colleagues' review of biological products bridging prefilled syringes with autoinjectors describes pharmacokinetic comparability as an established component of device-bridging evidence [23]. Such studies evaluate systemic drug exposure after administration under protocol-defined conditions. They do not independently identify whether a dose difference, if observed, originated with activation, incomplete emptying, local deposition, or subsequent absorption. Product comparability and delivery-presentation comparability consequently require separate, coordinated evidence streams.

This interpretive gap becomes salient when two presentations yield discordant concentration–time endpoints. Clinical pharmacology case examples show that noncomparable pharmacokinetics can arise during syringe–autoinjector bridging and require investigation rather than an automatic attribution to the device [24]. An informative investigation separates active-content or formulation differences, injection-site and administration procedures, device operation, assay variability, and physiologic absorption. The feasible causal contrast depends on which of these variables can be held constant and which remain changed together.

Two randomized phase 1 mirikizumab investigations compared an autoinjector and a prefilled syringe in healthy participants [25]. At the studied 200-mg dose, pharmacokinetic endpoints met the stated bioequivalence criteria. At 300 mg, exposure-area endpoints met those criteria while the confidence interval for peak concentration slightly crossed the prespecified upper limit. Mirikizumab is not a biosimilar experiment; these findings demonstrate why the endpoint, dose, and clinical context must be named before interpreting bridging. The increased peak is not evidence that a participant removed the device prematurely, nor proof of a formulation defect.

A second mirikizumab study found comparable systemic exposure for one 2-mL injection and two 1-mL injections of the same total dose in healthy volunteers under its specified study conditions [26]. It provides a useful counterexample to any universal proposition that changing injection volume or the number of injections must change systemic availability. The comparison does not identify depot geometry or prove that users in home settings would perform either regimen equally consistently.

Presentation-change assessment can therefore evaluate a pattern of independently observed endpoints. Reduced expelled mass with premature removal would support a use-associated transfer hypothesis; unchanged expelled mass with altered local deposition would shift attention toward insertion, tissue compression, or backflow; matched deposition accompanied by different exposure would require assessment of absorption and pharmacokinetic alternatives. These are proposed diagnostic patterns, not validated classifications. **Figure 2** separates those competing pathways and makes explicit why either a favorable task score or a deviating peak concentration is insufficient for causal attribution.

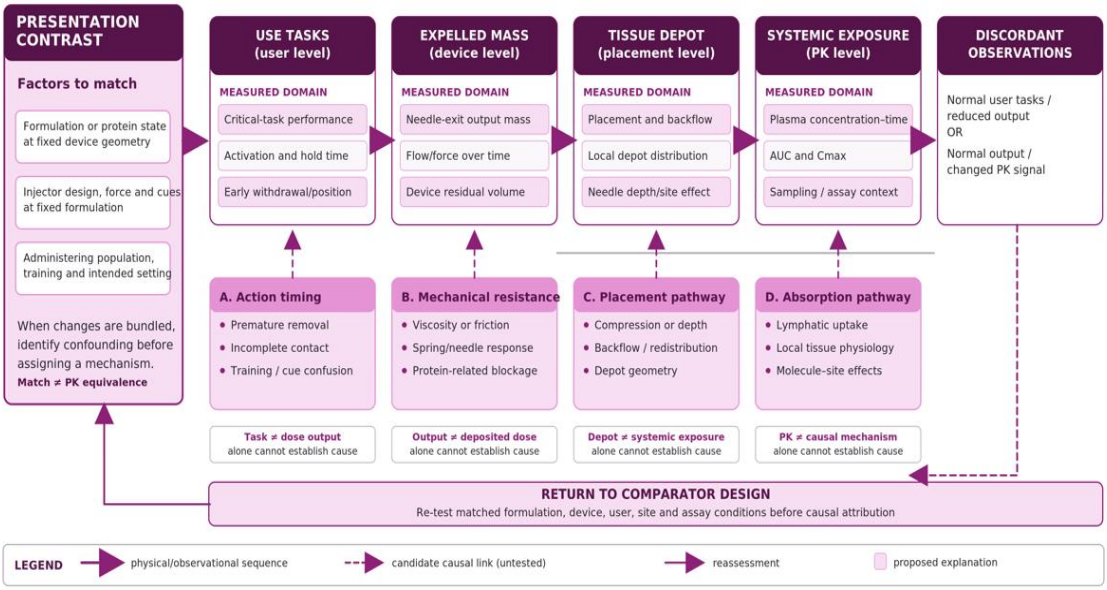


Figure 2. Distinguishing handling, mechanical transfer, tissue delivery, and absorption explanations for presentation-related observations

Caption/legend: This mechanism-discrimination map begins with a presentation comparison and branches according to independent observations of use tasks, expelled drug, local deposition, and pharmacokinetic exposure. Solid lines connect measured domains through known physical or biological process classes, while dashed lines specify conditional A8 hypotheses requiring joint tests. Restriction cards beneath each observed endpoint mark conclusions not licensed by that endpoint alone. A return loop from discordant evidence to comparator redesign indicates that mixed changes in formulation, interface, and injection site must be disentangled. Alternative pathways indicate mechanical obstruction, tissue placement/backflow, and local

absorption. Neither branch frequency nor clinical significance has been established for a particular biosimilar. AUC, area under the plasma concentration–time curve; Cmax, maximum observed plasma concentration; PK, pharmacokinetics.

Alt text: Landscape discrimination map with an irregular initial presentation-comparison block at left and four aligned measurement domains across the middle: user tasks, mass expelled at needle exit, drug placed in tissue, and systemic PK. Three nonidentical alternative-cause regions lie beneath these measurement domains, with dashed conditional paths to their candidate outcomes. A horizontal evidence-interpretation boundary separates measured domains from causal hypotheses. Restriction cards beneath each measurement domain identify causal conclusions unavailable from that observation alone. A long lower reassessment arrow returns from discordance at the right to the original comparator specification. Solid, dashed, and blocked connectors are labeled in a compact legend.

Evidence requirements for testing the proposed framework

High-concentration biologic formulations create interacting problems of protein condition, viscosity, injectability, and local bioperformance [27]. A valid test should therefore record the actual formulation state at use, device geometry and actuation conditions, and the human action trajectory. Product–device comparisons that change multiple factors together remain clinically relevant but cannot isolate a single mechanism. Where possible, matched-factor experiments should first characterize the effect of formulation within one injector and the effect of hardware within a stable formulation; patient comparisons then establish whether users modify those mechanical relationships.

Injection time is a measurable output with established modeling approaches, yet model assumptions and parameter estimation determine interpretability [28]. Force, duration, residual mass, and output kinetics should be recorded separately because a common total injection time can conceal differences in flow profile, start delay, or interruption. An end-of-dose cue is an interface event. Its relationship to actual reservoir emptying requires device-specific validation. Where a residual-drug mass can be weighed, standardized gravimetry supplies a more direct output measure than perceived completeness.

A staged discriminating study would begin with observed critical tasks under a declared training condition, using use scenarios appropriate to the intended population. Comparative biosimilar simulated-use work establishes the relevance of this observation level [9]. Each trial would pair a synchronized time record of contact, activation, dwell and removal with an independent measure of dose expelled. A selected subset could evaluate placement and backflow using ethically acceptable imaging or other validated methods; published visualization of depot behavior motivates this additional measurement tier [18]. Model-based extrapolation to living human tissue should remain explicitly unvalidated until confirmed.

Only after this separation should an exposure comparison be interpreted. The design would prespecify AUC and Cmax, injection site, dose, population, anti-drug antibody assessment when relevant, and analytic equivalence criteria. The device-bridging literature describes how such comparisons have been used [23]. The mirikizumab results warn against labeling all PK endpoints equivalent merely because total exposure is similar [25]. To challenge the A8 interaction hypothesis, a convincing negative result would show stable delivered mass and deposition across altered critical-task trajectories under adequately controlled conditions. Conversely, discrepant PK with matched deposition and no use difference would favor an absorption-related explanation.

Table 2 specifies which paired measurement and comparator would actually discriminate these proposed alternatives; it is a prospective evidence design, not a report of completed validation.

Table 2. Matched observations needed to adjudicate presentation-change explanations of delivered-dose variability

Discriminating comparison	Matched element	Independently measured contrast	Interpretation permitted	Unresolved condition
Formulation within fixed injector	Container, needle and actuation	Rheology, force profile, expelled mass	Detects formulation-sensitive mechanical response	Does not establish patient-use frequency
Injector with fixed formulation	Filled drug, intended dose, use environment	Activation timing, flow, residual mass	Detects device-sensitive transfer	May remain sensitive to operator adaptation
User trajectory for fixed presentation	Drug, injector and scripted opportunity	Critical tasks, dwell time, expelled mass	Tests action-to-output coupling	Simulation may not transfer to home use

Tissue interface under measured output	Expelled mass and injection site protocol	Insertion, backflow, local depot location	Tests transfer from needle to tissue	Depot assay or imaging may perturb conditions
Exposure after controlled deposition	Drug, site, dose and follow-up	AUC, Cmax and antibody response if relevant	Tests absorption/exposure alternatives	PK does not identify handling mechanism alone

Note: All comparisons are proposed and require prespecified measurement validity, reproducibility, and population applicability. No numeric effect or error threshold is inferred from existing publications.

Discussion, human-factor interactions, and future research

The theory's decisive claim is interaction, which is stronger than listing three causes. A new activation interface can change where users apply pressure and when they interpret a completion signal. An altered force–time profile may, in turn, affect the duration for which contact is sustained. Research on switching between autoinjector designs offers a starting point for identifying interface-sensitive tasks [8]. Syringe injectability studies show why that behavioral observation should be matched to physical resistance and component configuration [14]. Experimental confirmation would require a change in output conditional on the observed action, with a comparator capable of excluding purely mechanical failure.

A second explanation is local absorption. Models involving initial lymphatics show that exposure may vary after deposition, even without a change in the amount expelled [19]. Experience from PK-bridging discrepancies further cautions against treating an observed exposure difference as a reconstructed record of user action [24]. Future studies could combine upstream mechanical measurements with depot-site observations and later concentration–time data, explicitly allowing a null or inconsistent pathway. An interaction hypothesis gains credibility from surviving such rival explanations, not from maximizing the number of variables placed in a diagram.

A third explanation is perception and context. Patient preference between devices is an outcome with value in its own right [4]. Communication before biosimilar substitution may shape satisfaction and reported experience [5]. Neither observation establishes a dose-transfer error, although perceptions and training might plausibly affect subsequent technique. Longitudinal comparisons should assess skill acquisition, interruption of use, caregiver substitution, and repeated-injection variability, while maintaining separate measures of comfort, confidence, use tasks, drug output, and exposure. The critical research unit is the repeated drug–device–user event in a specified context, not the device considered in isolation.

Limitations and patient-specific applicability

The available sources span bench experiments, imaging, computational models, simulated-use studies, observational surveys, and healthy-volunteer pharmacokinetics. They do not constitute a completed dataset linking every level in the same biosimilar patient. Performance among people with generalized myasthenia gravis cannot be directly transferred to people with inflammatory bowel disease or rheumatoid arthritis [6]. Even within rheumatologic indications, a tested SB4 injector comparison represents its recruited users and device design [7]. Hand dexterity, fatigue, visual function, caregiver reliance, training history, and injection environment may change the effect of a presentation switch.

Mechanical generalization is similarly limited. Spring-driven flow varies with rheological and device parameters [15]. Protein-solution clogging depends on specific needle and storage conditions [16]. Such evidence identifies plausible failure routes, without establishing their prevalence during routine biosimilar use. At the biological level, subcutaneous antibody exposure depends on product and host characteristics [20]. Favorable comparisons of alternative mirikizumab injection volumes in healthy participants cannot establish comparable technique or clinical outcomes for other biologics or patient groups [26]. These restrictions are substantive: a theory that predicts universal dose disturbance after any presentation change would be contradicted by existing evidence.

CONCLUSION

Biosimilar self-administration can be evaluated as a coupled pharmaceutical, mechanical, human-use, and tissue-transport problem. Its core measurable states are the prepared dose, expelled amount, tissue placement, and systemic exposure, each with different comparators and uncertainty. A presentation change may perturb their relationships through device forces, user adaptation, or local biology, but neither therapeutic biosimilarity nor

favorable task performance determines every downstream endpoint. The proposed explanation remains unvalidated; its usefulness lies in specifying falsifiable, level-resolved comparisons that can distinguish handling problems from mechanical and absorption alternatives before attributing clinical significance.

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