# Essential Drug Delivery Performance Characteristics for Devices Intended to Deliver Drugs and Biological Products

## Guidance for Industry

## *DRAFT GUIDANCE*

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# Essential Drug Delivery Performance Characteristics for Devices Intended to Deliver Drugs and Biological Products Guidance for Industry

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the FDA staff responsible for this guidance as listed on the title page.

## I. INTRODUCTION

This guidance addresses key aspects of drug delivery performance information for devices,[1] and combination products[2, 3] that include device constituent parts,[4] intended for delivery of a human drug, including a biological product[5, 6] (herein referred to as *drug delivery devices*). The guidance describes FDA's recommendations related to information that is essential for establishing and assessing drug delivery performance and focuses on recommendations for the information and data to submit in investigational, marketing, and post-market change applications.[7] This guidance also provides examples of such information for specific types of devices.

Device drug-delivery performance information is intended to demonstrate that the device drug-delivery function consistently performs as intended. FDA is providing recommendations for development and organization of this information and these data to improve the consistency of this information in applications and to facilitate transparency and predictability in development and regulatory review. Ultimately, these recommendations are intended to facilitate and streamline development and lifecycle management of drug delivery devices.

[1] The term *device* refers to a device as defined in section 201(h)(1) of the Federal Food, Drug, and Cosmetic (FD&C) Act (21 U.S.C. 321(h)(1)).
[2] See 21 CFR 3.2(e) for the definition of *combination product*.
[3] For the purpose of this guidance, the term *product* is used to refer to both stand-alone devices (i.e., not part of a combination product) and combination products.
[4] See 21 CFR 4.2 for the definition of *constituent part*. For the purpose of this guidance, the terms *device* and *device constituent part* are used interchangeably.
[5] The term *drug* refers to a drug as defined in section 201(g)(1) of the FD&C Act (21 U.S.C. 321(g)(1)), and includes biological products as defined in section 351(i) of the Public Health Service (PHS) Act (42 U.S.C. 262(i)).
[6] For the purpose of this guidance, the terms *drug* and *drug constituent part* are used interchangeably.
[7] For the purpose of this guidance, unless otherwise stated, the terms *applications* and *submissions* are used interchangeably and include, as applicable, initial, supplements to, and amendments to: investigational new drug applications (INDs), new drug applications (NDAs), abbreviated new drug applications (ANDAs), investigational device exemption (IDE) applications, premarket approval (PMA) applications, De Novo requests submitted under section 513(f)(2) of the FD&C Act, premarket notifications (510(k) submissions), and biologics license applications (BLAs), including BLAs submitted under section 351(k) of the PHS Act.

This guidance applies broadly to drug delivery devices. As appropriate, applicable consensus standards and other guidance(s) may be referenced in conjunction with this guidance.

This guidance does not address all of the data and information to be submitted in support of drug delivery devices (e.g., it does not address drug-device compatibility, biocompatibility, sterility, human factors, electrical safety, electromagnetic compatibility, radio frequency wireless technology, or cybersecurity). Applicants should refer to applicable regulations and guidance(s) for more information on what is required or recommended to be submitted to FDA in applications for such products.[8]

This guidance revises the draft guidance titled *Essential Drug Delivery Outputs for Devices Intended to Deliver Drugs and Biological Products* that issued in June 2024. The guidance is updated to clarify content on testing and controlling device drug-delivery performance and to align with the revised 21 CFR part 820 Quality Management System Regulation (QMSR).[9]

In general, FDA's guidance documents do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

## II. SCOPE

The focus of this guidance is the information and data developed and submitted to FDA regarding drug-delivery performance for devices regulated by CDRH and CBER and device constituent parts of CDER-led and CBER-led combination products[10] intended for delivery of a human drug, including a biological product.[11] Essential drug delivery device performance characteristics (EDDCs) are the key aspects of device drug-delivery that warrant development of and submission to FDA of performance information and data to ensure delivery of the intended drug dose to the intended delivery site. EDDCs demonstrate device drug-delivery performance at the system level that is dependent on the device design (see section IV for more information). Drug delivery includes successful product preparation[12] and the initiation, progression, and completion of dose delivery.

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[8] For additional guidance related to product development and postmarket product modifications, see the *FDA Guidance* webpage to search for an FDA guidance document or to browse FDA guidance documents by topic. Information on these considerations may be found in applicable guidances. For example, for more information regarding injector delivery devices, see the guidance for industry and FDA staff *Technical Considerations for Pen, Jet, and Related Injectors Intended for Use with Drugs and Biological Products* (June 2013). We update guidances periodically. For the most recent version of a guidance, check the FDA guidance webpage at https://www.fda.gov/regulatory-information/search-fda-guidance-documents.

[9] 89 FR 7496 (February 2, 2024). See footnote 13.

[10] CDER-led and CBER-led combination products refer to combination products for which CDER or CBER has primary jurisdiction (i.e., is the lead Center). For information regarding Center assignment, see the guidance for industry and FDA staff *Principles of Premarket Pathways for Combination Products* (January 2022).

[11] If an applicant has a question about whether the concepts in the guidance apply to a specific product, contact the applicable review division in the lead Center.

[12] See Appendices A and C for examples related to product preparation.

Examples of products that are within the scope of this guidance include syringes, injectors (e.g., autoinjector, on-body injector), infusion products (e.g., infusion pumps), nasal sprays, inhalers, nebulizers, and vaginal systems.

## III. BACKGROUND

Designing the drug delivery device to achieve its intended performance is necessary for marketing authorization and is part of the design and development process in the QMSR.[13] For purposes of this guidance, the EDDCs warrant design verification, design validation, control, and maintenance[14] to ensure that the device (1) functions as designed for its intended use, and (2) maintains its intended function, safety, and effectiveness throughout its lifecycle. To ensure the quality of the drug delivery function throughout the product lifecycle, data and information on EDDCs are developed and submitted for review to FDA as appropriate.[15, 16] For purposes of this guidance, in the context of an investigational or marketing application, the terminology used broadly relates to the submitted data and information and their associated scientific or technical justification (e.g., design verification and validation, control, and maintenance). Terminology used in this guidance is not intended to constrain how an applicant establishes their quality management system.

EDDC identification, control, and maintenance processes can also facilitate development by:

- Informing the determination of which data to submit in an investigational or marketing application to demonstrate the drug delivery performance;
- Ensuring the appropriate device design attributes and manufacturing process steps are evaluated during lifecycle changes; and
- Providing a basis for comparing device drug-delivery performance for bridging or leveraging data across products.[17]

[13] Design and development requirements are described in ISO 13485:2016(E) (hereinafter "ISO 13485"), *Medical devices – Quality management systems – Requirements for regulatory purposes,* Clause 7.3. The QMSR incorporates by reference ISO 13485 (21 CFR 820.7(b)). Updates to 21 CFR part 4 subpart A, *Current Good Manufacturing Practice Requirements for Combination Products* conform to the QMSR (see 21 CFR 4.4(b)(1); see also 4.4(f)(2) for incorporation by reference to ISO 13485). See 21 CFR 820.10(c) and 4.4(b)(1)(ii).

[14] The control strategy ensures the product consistently meets its EDDC specifications. Maintenance ensures that any changes to the product made during clinical development or post-market that could adversely impact the drug delivery performance are evaluated to help preserve the drug delivery function.

[15] Though design and development information can be reviewed on inspection, data and information on EDDCs submitted in an application typically do not cover all of the information documented and available for review as part of an establishment assessment or inspection to establish compliance with current good manufacturing practice (CGMP) and QMSR requirements, as applicable.

[16] The data needed to support approval/clearance/authorization of a particular product depends on the application type under the applicable standard of review. For purposes of this guidance, the term "approval" or "approved" is used to refer to approval, licensure, clearance, or authorization, as applicable.

[17] For additional information on bridging data across combination products, see the draft guidance for industry *Bridging for Drug-Device and Biologic-Device Combination Products* (December 2019). When final, this guidance will represent FDA's current thinking on this topic.

Drug-device combination products may be more complex than their individual constituent parts because, in addition to the individual constituent parts, the interactions of the constituent parts also need to be assessed,[18] characterized, and controlled during product design, development, and production. The final rule *Current Good Manufacturing Practice Requirements for Combination Products*, codified at 21 CFR part 4 (CGMP requirements),[19] provided clarity regarding the applicability of CGMP requirements to combination products, along with a streamlined regulatory framework for demonstrating compliance with applicable requirements. Core requirements in the CGMP regulations provide for systems that ensure proper design, monitoring, and control of manufacturing processes and facilities.[20]

FDA acknowledges that ISO consensus standards and ICH[21] guidance include terms and concepts that may be related to EDDCs. To the extent that other terms cover information related to these characteristics, a sponsor may be able to leverage information used in the context of those terms to show that EDDCs are adequately addressed. For example, for certain combination products, FDA acknowledges that EDDC could be interpreted as analogous to "critical quality attribute" (CQA), which is described in the ICH guidance for industry *Q8(R2) Pharmaceutical Development* (November 2009) as "[a] physical, chemical, biological, or microbiological property or characteristic that should be within an appropriate limit, range, or distribution to ensure the desired product quality."[22] As appropriate for the type of drug delivery device (e.g., drug-eluting intravaginal ring), studies conducted to verify that the CQAs are met can also address verification related to drug delivery performance.[23] Applicants may be able to leverage CQA information to support EDDC identification, control, and maintenance processes.[24] When device drug delivery performance characteristics are amenable to verification through analytical methods (see section V), the chemistry, manufacturing, and controls (CMC) information may address the verification recommendations in this guidance. For medical devices, FDA recognizes several consensus standards that provide technical methods. For example, ISO 11608-1:2022, *Needle-based injection systems for medical use – Requirements and test methods* addresses "primary functions" and their associated test methods for certain device types. Although the standard's primary function definition identifies some of the functions identified as EDDCs in this guidance, primary functions and EDDCs do not necessarily align. However,

[18] For example, device and drug constituent part attributes may impact appropriate drug delivery.

[19] 78 FR 4307 (January 22, 2013); as amended 89 FR 7496 (February 2, 2024).

[20] See also the guidance for industry and FDA staff: *Current Good Manufacturing Practice Requirements for Combination Products* (January 2017) (part 4 CGMP guidance).

[21] ICH is The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use.

[22] See *ICH Q8(R2)* annex glossary at p. 18. In some instances, an applicant could expand CQAs to include EDDCs for a combination product.

[23] For additional discussion of the relationship of drug development and device development terms related to design control, see the part 4 CGMP guidance at section IV.A.2.

[24] "Established conditions" as described in the ICH guidance for industry *Q12 Technical and Regulatory Considerations for Pharmaceutical Product Lifecycle Management* (May 2021) and EDDCs are related, but their definitions and purposes do not directly align. For combination products, EDDCs and elements of the control strategy for an EDDC, as appropriate, could also be determined to be established conditions. See also the draft FDA guidance for industry *ICH Q12: Implementation Considerations for FDA-Regulated Products* (May 2021) (when final, this guidance will represent FDA's current thinking on this topic) and the ICH Q12 training materials, Module 8 Additional Examples and Practical Recommendations, page 45 (available at https://www.ich.org/page/quality-guidelines).

applicants may be able to leverage the ISO 11608-1:2022 information for the EDDCs when the test method is appropriate for the EDDC.

## IV. IDENTIFYING ESSENTIAL DRUG DELIVERY DEVICE PERFORMANCE CHARACTERISTICS

This section provides further description of EDDCs and a product-specific example of what is and is not an EDDC. The appendices in this guidance provide examples of potential EDDCs for different product types.[25]

EDDCs are based on product type (e.g., syringe, autoinjector, infusion pump) and product specifics. These characteristics warrant design verification, design validation, control, and maintenance, as appropriate, to demonstrate the drug delivery function performs as intended (i.e., delivery of the intended drug dose to the intended delivery site) throughout the product lifecycle.[26] Generally, EDDCs have specifications, including acceptance criteria that must be met to ensure that the product performs as intended. These specifications with acceptance criteria are generally included in the submission.[27] EDDCs are high-level characteristics that incorporate lower-level characteristics or product features. If the specification(s) for an EDDC is met, it should reflect that the specification(s) for the lower-level characteristic(s) related to that EDDC are also met. For EDDCs, the lower-level characteristics or product features alone do not ensure the intended drug delivery, and these data are generally not included in the submission for purposes of ensuring the EDDC performance.[28] In addition, although the design considers the user needs, the EDDCs are dependent on the functional design of the device (device design) and not on the user actions. The following illustrates what an EDDC is and is not.

- What is an EDDC? It is a drug delivery aspect that:
  - Is a high-level (i.e., system level) function that incorporates lower-level (i.e., component level) aspects, and
  - Depends on the functional device design.

- What is not an EDDC?
  - A component level aspect that is encompassed by a system level EDDC is not an EDDC.
  - A user dependent function is not an EDDC.

For example, for a prefilled syringe (PFS) that includes a needle and silicone oil as a lubricant:

- Glide force is an example of an EDDC.

[25] See Appendices A, B, and C.

[26] See 21 CFR 820.10(c) and 4.4(b)(1)(ii).

[27] For example, see the draft guidance for industry and FDA staff *Quality Management System Information for Certain Premarket Submission Reviews* (October 2025) (when final, this guidance will represent FDA's current thinking on this topic); and 21 CFR 314.50(d)(1)(ii)(a), 314.94(a)(9), and 601.2(a).

[28] For example, break loose and glide forces are EDDCs for a prefilled syringe. In contrast, for an autoinjector, injection time is an EDDC and break loose and glide forces are lower-level (i.e., component level) aspects that are already reflected in injection time.

- Silicone quantity and needle inner diameter are not EDDCs; rather, they are component level aspects already reflected in glide force.
- Injection depth is not an EDDC because it is dependent on the user.[29, 30]

This guidance provides potential examples of EDDCs for different product types. These are not automatically applicable to every product design, and sponsors should comprehensively evaluate their specific product to identify the appropriate EDDCs. For example, considerations to identify these characteristics include the proposed intended use and known product specifics (e.g., indications for use, population, condition and frequency of use, user requirements, route of administration, drug characteristics, dosage form, deliverable volume, performance expectations, etc.), as appropriate.

See Appendix A for a narrative illustration of identifying EDDCs for a PFS. Appendix B illustrates the distinction between EDDCs and other characteristics/features for an autoinjector. Appendix C provides examples of potential EDDCs for common drug delivery devices. The considerations in the appendices could be applied to product types that are not expressly illustrated in this guidance.

The following sections of the guidance provide recommendations regarding the data development for the design verification and validation, control, and maintenance of EDDCs.

## V. VERIFYING AND VALIDATING EDDC SPECIFICATIONS

While design and development verification[31] and validation[32] activities are intended to address all device functions, the following recommendations are specific to EDDCs. Appropriate verification activities for EDDCs depend on the conditions (e.g., environmental conditions) to which the product will be exposed during production, shipping, storage, and preparation and the conditions associated with use. Examples of conditions that may impact performance include, but are not limited to, temperature, pressure, humidity, vibration and shock, and physical orientation. Also, during storage or shipping, a product may be exposed to more than one variation of a condition or sequence of conditions (e.g., ground by truck to air, ground by truck to boat, ground by rail to air to ground by truck). In addition to storage and shipping stressors, there are stressors associated with the use environments (e.g., health care facility, school, home, first response environment).

[29] Human factors validation is outside the scope of this guidance.

[30] In contrast, for an autoinjector, injection depth is an EDDC because it is dependent on device design and not on the user.

[31] ISO 13485 subclause 7.3.6 (21 CFR 820.10(c) and 4.4(b)(1)(ii)), see 21 CFR 820.7(b) and 4.4(f)(2) for incorporation by reference. Verification means "confirmation, through the provision of objective evidence [ ], that specified requirements [ ] have been fulfilled" (ISO 9000 subclause 3.8.12, see 21 CFR 820.7(a) for incorporation by reference).

[32] ISO 13485 subclause 7.3.7 (21 CFR 820.10(c) and 4.4(b)(1)(ii)), see 21 CFR 820.7(b) and 4.4(f)(2) for incorporation by reference. Validation means "confirmation, through the provision of objective evidence [ ], that the requirements [ ] for a specific intended use or application have been fulfilled" (ISO 9000 subclause 3.8.13, see 21 CFR 820.7(a) for incorporation by reference).

Further, although the specific tests (e.g., mechanical or analytical) are beyond the scope of this guidance, the testing may differ for active (e.g., autoinjector, metered dose inhaler) and passive (e.g., some implants, vaginal systems) drug delivery devices. As appropriate, the results of these tests can be leveraged as part of the verification information. See section VII for details on design verification and validation information included in applications.

It is important to establish specifications that are clinically meaningful and appropriate to meet user needs. In developing a specification, including the acceptance criteria, information to justify the EDDC specification might include:

- **Literature:** e.g., injection site and patient population information to support the needle length specification.

- **Anthropometric data:** e.g., data on grip strength from specific patient populations.

- **Simulated bench testing:** studies designed to evaluate whether the acceptance criteria fall within a range of what would be physiologically feasible for anticipated users in the intended patient population.[33]

### A. Design and Development Verification for EDDCs

Prior to initiation of any clinical studies (or any *in vivo* bioequivalence studies, as applicable) or commercial distribution, applicants verify the performance of the product as appropriate for the development stage. How applicants conduct design verification testing is dependent on device design, intended use, and applicable regulations, standards, and guidances. Design verification generally includes preconditioning and subsequent verification testing to confirm that the device drug-delivery function is maintained in accordance with the instructions for use. The following sections provide considerations when developing a design verification approach. If an applicant intends to use an alternative design verification approach, we recommend providing an explanation of and rationale for the alternative approach and requesting Agency feedback in a formal meeting or communication with FDA (see section VIII).

#### *1. Preconditioning*

During the product's lifecycle, the product can be exposed to multiple stressors prior to each use that may influence performance of the device drug-delivery function. Preconditioning is a method to simulate exposing the product to stressors prior to testing to which the product will likely be exposed (including worst case scenarios) during storage, shipping, and before each use (e.g., cleaning, reprocessing, storage (see section V.A.1.a), or repeat use, as applicable). Applicants should identify preconditions applicable to the specific product, and verification testing should assess the ability of the product to withstand those stressors. Applicants should identify preconditions based on the risk of the product design, research and development characterization testing, intended use, how the product will move from the manufacturer of the

[33] These simulated bench tests are different than human factors user validation studies.

final finished product[34] to the end user, and the conditions associated with use (see section V.A.1.c). For emergency-use products, because of the risk to the patient should the device fail, sequential preconditioning (i.e., applying preconditions in the appropriate sequence) is generally performed before the testing.[35] Sponsors should consider incorporating sequential preconditioning for other products when there is a serious risk to the patient if drug delivery is not achieved as intended and the device is sensitive to fluctuations in environmental conditions. In developing the preconditioning methods, applicants can leverage the test methods, acceptance criteria, and statistical analysis techniques from recognized standards.

a. Storage

Preconditions to simulate storage include, for example, specific temperatures, temperature fluctuations, pressure changes, and humidity. A product may be subjected to different storage conditions throughout the product lifecycle (e.g., conditions at the manufacturing facility, warehouse, health care facility, pharmacy, or home setting), and these should all be considered before verification testing.

b. Shipping

Preconditions to simulate shipping include, for example, vibration, shock, and pressure changes that may impact device drug-delivery performance. Some EDDCs (e.g., physical dimensions) would not be impacted by shipping and would not warrant preconditioning for shipping conditions. For the EDDCs that may be influenced by shipping conditions, shipping preconditioning representative of likely exposures (e.g., during shipping via air, ground by truck, ground by rail, boat) should occur before verification testing.

c. Conditions Associated with Use

Preconditions to simulate other stressors related to conditions associated with use may be warranted. These conditions are those associated with the product's labeling, including the instructions for use (e.g., retrieval from storage, set up, warm-up time, preparation of the product, repeat use, reprocessing, cleaning). Preconditioning should also consider all other devices that must be connected to or interface with the product to ensure drug delivery (e.g., other devices that are not part of the applicant's product).[36] Preconditioning to simulate conditions associated with use should be conducted in the order of steps as specified in the

[34] Final finished product is the product intended for marketing and submitted in the marketing application (i.e., final design and specifications). The terms *final finished product* and *to-be-marketed product* are intended to have the same meaning. For purposes of this guidance, the final finished product could be manufactured using the commercial process or a process that is representative of the commercial process (e.g., materials and methods of manufacture, process that is representative of that to be applied to full scale production of the commercial product). When using a representative process, it is recommended to identify and describe the differences and provide a justification of why the differences are acceptable for the information being provided at a given stage of product development.

[35] For additional information regarding preconditioning, see section V.4.a of the draft guidance for industry and FDA staff *Technical Considerations for Demonstrating Reliability of Emergency-Use Injectors Submitted under a BLA, NDA, or ANDA* (April 2020). When final, this guidance will represent FDA's current thinking on this topic.

[36] See ISO 13485 subclauses 7.3.6 and 7.3.7 (21 CFR 820.10(c) and 4.4(b)(1)(ii)), see 21 CFR 820.7(b) and 4.4(f)(2) for incorporation by reference.

instructions for use in the proposed labeling and, as appropriate for the other devices, should include the other connecting/interfacing devices needed for delivery. For drug delivery devices that are not addressed in a recognized consensus standard that includes preconditions or for which there may be preconditions in addition to those in a recognized consensus standard, sponsors should identify appropriate preconditions and develop methods for testing.

Additionally, depending on the device design and instructions for use, more than one preconditioning method may be needed to account for potential failure modes. For example, for infusion pumps, verification for flow rate accuracy should occur after preconditioning that accounts for any before-use and during-use instructions and all aspects of the infusion pump system, including accessories (e.g., infusion sets). Preconditions for the infusion pump and infusion pump accessories may be different. Therefore, the various preconditioning methods for the before-use and during-use steps should be applied as appropriate for the components of the infusion pump system and in accordance with the proposed labeling.

For reusable devices, preconditioning should simulate the worst-case number of repeat use and reprocessing cycles and should include cleaning and sterilization or disinfection methods identified in the proposed labeling.[37] For example, the labeling for some metered dose inhalers calls for periodic cleaning of the actuator to prevent orifice blockage. Additionally, labeling for metered dose inhaler and reusable nebulizer components often calls for periodic cleaning to prevent contamination and/or changes in electrostatic properties to minimize capture of small particles/droplets and any change in respirable drug.

*2. Design and Development Verification Testing*

Overall, the design and development verification assessment of EDDC specifications should occur after appropriate preconditioning. Depending on the product, the EDDC, and the specific types of preconditions, there may be different types of testing to demonstrate that an EDDC specification is met throughout the range of conditions and use environments described in the proposed labeling. This testing can include functional testing after preconditioning or it can be part of a design and development verification shelf-life testing program (see section V.A.2.b). For example, an applicant could follow a protocol for assessing the impact of shipping preconditions on a specific EDDC. When used to evaluate a product that has been fully preconditioned, the protocol should enable assessment of the impact of actual preconditions associated with use (e.g., repeat use following the instructions for use including any reprocessing steps) on the ability for an EDDC to meet its specification(s).

Regardless of the type of testing method, EDDC evaluation during design and development verification should address the applicable preconditions as described in section V.A.1. If preconditioning is omitted, the associated protocol should provide a rationale for the omission.

[37] Additional information regarding the reprocessing of medical devices can be found in the guidance for industry and FDA staff *Reprocessing Medical Devices in Health Care Settings: Validation Methods and Labeling* (March 2015).

a. Sampling considerations

Sampling plans for design and development verification testing should be risk-based, taking into consideration the indication for use, patient population, drug being delivered, context of use (e.g., immediate or emergency use versus chronic therapy, home versus clinical setting), and complexity of design and manufacturing. For example, a product with a higher risk profile would warrant a more robust sampling plan than a product with a lower risk profile. Sampling recommendations in recognized consensus standards could be used in developing sampling plans, as appropriate, based on product-specific risk considerations. A design verification testing protocol should include a statistical sampling plan. The plan should include justification for the number of lots to be tested, taking into consideration the potential impact of lot-to-lot variability, and acceptance criteria. The tested lots should be the final finished product.

b. Shelf-life and stability testing considerations

Design and development verification testing should include an evaluation of EDDCs that may change over time or have age-related failure modes. Data provided to support a proposed expiration date should demonstrate that EDDC specification(s) continues to be met. For a combination product, such data can be derived from design verification shelf-life testing,[38] stability testing,[39] or both for the final finished combination product. For a combination product, the final determination of the expiration date is based on a demonstration that the EDDC specification(s) and drug constituent part specifications continue to be met. EDDCs that would not change over time (e.g., physical dimensions such as needle length) would not generally warrant evaluation.

The testing to support a proposed expiration date should include consideration of the number of repeat uses of the product to deliver the drug and the potential impact of any associated cleaning and reprocessing cycles and interim storage between uses. This testing should consider and address the applicable preconditions as described in section V.A.1 and include a justification for any applicable preconditions omitted during the shelf-life or stability testing. This justification can include other testing information and, if so, should include an explanation as to how such testing information addresses or supports the omission of any identified precondition during shelf-life or stability testing.

For combination products, to support the proposed expiration date, verifying that certain EDDCs continue to meet specification(s) over time may be accomplished by relying on or leveraging drug stability testing results (e.g., for EDDCs for products subject to chemical degradation).[40] For EDDCs subject to physical or mechanical degradation, additional design and development verification shelf-life testing of the device drug-delivery function may be appropriate to support

[38] Shelf life is "the term or period during which a commodity remains suitable for the intended use" (FDA guidance *Shelf Life of Medical Devices* (April 1991)).

[39] Stability testing refers to a requirement for drugs and combination products addressed in 21 CFR 211.166 and 21 CFR 4.4, respectively.

[40] For EDDCs that are evaluated as part of stability testing, information and data as described in ICH Q1A(R2) *Stability Testing of New Drug Substances and Products* (November 2003) and related FDA stability guidances are appropriate to support the proposed expiration date.

expiration dating. Such design and development verification shelf-life testing should be conducted using the final finished product under real-time aging conditions. As appropriate, accelerated aging data can be used to establish the shelf life. When used, accelerated aging data must be confirmed by real-time aging data.[41]

### B. Design and Development Validation for EDDCs

In the context of EDDCs, the applicant must ensure that devices are capable of meeting the requirements for the specified application or intended use.[42] Design validation is performed on the final finished product to confirm that it meets the user's needs and intended uses.[43] This is typically performed after design verification has confirmed the product, including its EDDCs, meets its specifications. For devices for which the intended use requires that the medical device be connected to or interface with other medical devices, validation must confirm that the requirements are met when connected/interfaced.[44] The most appropriate validation method may depend on the application type, stage of development, product, and EDDC.[45]

For certain application types, approaches to validation may include:

- Clinical studies (and/or reliance on FDA's finding of safety/effectiveness for a reference listed drug (RLD) or reference product)
- Pharmacokinetic/pharmacodynamic (PK/PD) or bioequivalence/bioavailability studies
- Literature: e.g., published information relevant to the intended product in the intended clinical use with the intended patient population

When designing clinical studies that include device performance validation, the clinical protocol should include endpoints that are relevant to the EDDCs.

As an example, when developing an infusion pump that is submitted in an NDA, the product, and in particular the EDDC of flow rate, could be validated through effectiveness data, PK/PD data, and safety data (e.g., adverse events, occlusion rates, infusion site reactions) in appropriately designed clinical studies.

[41] See 21 CFR 4.4 generally and 4.4(b)(2)(vi).
[42] See footnote 32.
[43] Design validation shall be conducted on representative product, which includes initial production units, batches, or their equivalents (ISO 13485 subclause 7.3.7 (21 CFR 820.10(c), 4.4(b)(1)(ii)), and 4.4(a)), see 21 CFR 820.7(b) and 4.4(f)(2) for incorporation by reference.
[44] ISO 13485 subclause 7.3.7 (21 CFR 820.10(c) and 4.4(b)(1)(ii)), see 21 CFR 820.7(b) and 4.4(f)(2) for incorporation by reference.
[45] "As part of design and development validation, the organization shall perform clinical evaluations or performance evaluations of the medical device in accordance with applicable regulatory requirements" (ISO 13485 subclause 7.3.7 (21 CFR 820.10(c) and 4.4(b)(1)(ii))), see 21 CFR 820.7(b) and 4.4(f)(2) for incorporation by reference.

### *1. Additional Considerations for ANDA Submissions and for BLAs Submitted under Section 351(k) of the PHS Act for Combination Products*

For an ANDA submission or for a BLA submitted under section 351(k) of the PHS Act for a combination product, in addition to verification of the EDDC specifications, to support their validation, applicants may be able to rely on information about the RLD or reference product, respectively. For example, for an ANDA, applicants could provide a side-by-side comparison of EDDC specifications or EDDC testing results for the combination product against that for the RLD.

If the comparison shows there are differences from the EDDC specifications or EDDC testing results for the RLD or reference product, then applicants may provide additional data to support that the specification is appropriate for an ANDA or BLA submitted under section 351(k) of the PHS Act, as applicable. For example, for the EDDC of activation force, if the specification or performance was different from the RLD or reference product, the applicant may provide data demonstrating the activation force is not too high such that the proposed combination product would not be therapeutically equivalent to, or biosimilar to or interchangeable with, as applicable, the RLD or reference product.[46]

FDA recognizes that in some instances applicants may not have certain information for comparison (e.g., if the RLD or reference product is discontinued or if the proposed combination product has different design features).[47] In such instances, the applicant should contact the Agency through a controlled correspondence or pre-ANDA meeting request, or following procedures described in the guidance for industry *Formal Meetings Between the FDA and Sponsors or Applicants of BsUFA Products* (July 2025), as appropriate, (see section VIII) with a proposal for how to validate the EDDCs.

### *2. Additional Considerations for Premarket Notifications [510(k)]*

For a 510(k), submitters compare the intended use (including indications for use) and the technological characteristics of their device, including EDDCs, to the predicate device. When there are differences in technological characteristics, which do not raise different questions of safety and effectiveness from the predicate device, FDA might request additional performance data, including clinical data as necessary, to assess whether the device is as safe and effective as the predicate device.[48]

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[46] Information on differences in the user interface between an ANDA and its RLD is beyond the scope of this guidance. For additional information on identifying and analyzing differences between a proposed generic combination product and the RLD, see the draft guidance for industry *Comparative Analyses and Related Comparative Use Human Factors Studies for a Drug-Device Combination Product Submitted in an ANDA* (January 2017). When final, this guidance will represent FDA's current thinking on this topic.

[47] Also see product specific guidances for generic drug development for testing information relevant to specific products (e.g., testing methodology, statistical sample sizes) available at https://www.fda.gov/drugs/guidances-drugs/product-specific-guidances-generic-drug-development.

[48] Applicants submitting 510(k)s for their devices should address the submission recommendations included in the guidance for industry and FDA staff *The 510(k) Program: Evaluating Substantial Equivalence in Premarket Notifications [510(k)]* (July 2014).

## VI. CONTROL STRATEGIES FOR EDDCS

A control strategy is used to ensure that each lot of the final finished product is manufactured to consistently meet its EDDC specification. For a given EDDC, an appropriate control strategy might consist of one or more types of control steps at different stages of the manufacturing process. Some control steps are performed earlier in the manufacturing process (e.g., upstream controls such as in-process controls, control of process parameters, control of incoming materials, and purchasing information). Other control steps are performed at the end of the manufacturing process (e.g., a downstream control such as lot release testing).

The control strategy should be based on product and process understanding in combination with risk management activities.[49] Product and process understanding can be drawn from sources such as development of the device design and manufacturing process, structural analysis, design and development verification testing, and prior knowledge from manufacture of similar devices. Risk assessments can include consideration of factors such as the intended user (e.g., healthcare provider, patient) and the context of use as well as the complexity of the EDDC (e.g., interdependencies at the component level) and the complexity and robustness of the manufacturing process. The result of the risk assessment is used to determine the need for risk controls; this information is further used to inform the type and extent of controls appropriate for each EDDC. The amount of information regarding the control strategy to include in an application should similarly be commensurate with the risks and associated impact.

Appropriate controls should be identified for each EDDC, considering the relevant features and manufacturing process steps, and the documentation used to support these controls should be identified. The control strategy can consist of one or more controls, implemented upstream, downstream, or both, as previously stated. When developing an upstream control strategy for an EDDC, it is important to consider the subsequent manufacturing process steps that can influence the EDDC and provide a justification describing why the proposed upstream control is adequate to ensure that the EDDC of the final finished product will meet its specification (i.e., after these process steps occur). For certain EDDCs, purchasing information or an incoming test/examination to confirm that the incoming product meets required specifications may be sufficient (e.g., for the length of a syringe and needle that cannot change over the expiration dating period). For other EDDCs, a singular downstream control (e.g., release testing) or a combination of upstream and downstream controls may be appropriate.

The description of the control strategy should include information to support why the control or combination of controls is considered to be adequate to ensure the EDDC will meet its specification(s). In the context of the manufacturing process, this information is submitted as part of the marketing application, submitted upon request, or available during facility inspection, depending on application type (see section VII.B). Depending on the EDDC and its proposed control(s), the supporting information might consist of risk analysis, engineering drawings, development work, supporting process knowledge, in-process data, batch analysis (i.e., testing the final finished product against the specification), or EDDC evaluation conducted as part of

[49] See, e.g., the ICH guidance for industry Q9(R1) *Quality Risk Management* (May 2023) and ISO 14971 Third Edition 2019-12 *Medical devices - Application of risk management to medical devices*.

stability testing (see section V.A.2.B). For more information, see regulations and guidance on specific application type submission requirements for manufacturing information. For products subject to premarket approval (e.g., under an ANDA, BLA, NDA, PMA), control strategy information is included in the application.[50] In contrast, 510(k) submissions generally do not include control strategy information as part of the 510(k) itself; however, information demonstrating control of the 510(k) device's manufacturing process must be available for FDA review during inspections.[51]

See Appendix D for an illustration of a control strategy for the final assembly of a syringe based autoinjector.

## VII. INFORMATION TO PROVIDE IN APPLICATIONS

This section describes the EDDC information and performance data included in investigational, marketing, and post-market change applications to demonstrate the device drug-delivery function.

### A. IND and IDE Applications

The data provided in IND[52] and IDE applications for drug delivery devices should reflect the development stage of the product. It is understood that for combination products, the drug delivery device could be introduced after the investigational drug development begins. We understand that the device design may evolve based on study results. The device drug-delivery data submitted in an IND or IDE application[53] should reflect the development process, and applicants should consider the device design, the drug being delivered, the patient population(s), study design, and risks to the study participants when determining the data to provide.

To support the first use of the device or device constituent part in a clinical study, it is important that applicants provide information demonstrating that the safety and performance of the device is adequate for the proposed investigation. Information from EDDC testing is provided to demonstrate that the device performs and the drug is delivered (dose and delivery site) as intended.

[50] Information on manufacturing controls must be included in such applications, see 21 CFR 314.50(d)(1)(ii), 314.94, 601.2(a), and 814.20(b)(4)(v).

[51] See section 704(a) of the FD&C Act. Such records must be made available for FDA review during an inspection conducted under section 704(a)(1) of the FD&C Act or when requested by FDA in advance of or in lieu of an inspection as described in section 704(a)(4) of the FD&C Act. See also 21 CFR part 820 and part 4 subpart A.

[52] Bio-INDs under 21 CFR 320.31 for ANDAs are out of scope of this guidance. A sponsor of a bio-IND under 21 CFR 320.31 with a drug delivery device may submit a controlled correspondence (see section VIII) with any questions regarding the applicability of the information described in this section. For additional information on bio-INDs, see Manual of Policies and Procedures 5210.5, *Review of Investigational New Drug Applications (Bio-INDs) by the Office of Generic Drugs* (Rev. 3, April 14, 2022).

[53] For combination products, see the guidance for industry and FDA staff *Principles of Premarket Pathways for Combination Products* for information on application types.

As development proceeds and the product design evolves, additional information may be needed to support the use of the final finished product in pivotal[54] clinical studies. As applicable, the submission should provide more comprehensive information that builds upon earlier safety information and study results, including information that applies to the device drug-delivery function. As product development continues, for any planned changes to the EDDC specifications, it may be possible to leverage the EDDC performance data from earlier clinical studies to help bridge between prototypes.

For any required IDE and IND applications for drug delivery devices, requirements for submission content relevant to EDDCs include, but are not limited to, the following, respectively:

- A complete report of prior investigations of the device and a summary of certain sections of the investigational plan, or, in lieu of such a summary, the complete investigational plan;[55] a description of the methods and controls used for the manufacture of the device; risk analysis; and description of the device.[56]
- A brief summary of previous human experience with the product; an investigational plan; and information describing the composition, manufacture, and control of the product.[57]

As described above, depending on the application type, certain information on EDDCs is a required part of the application, while other information is recommended for submission. This section outlines considerations for this information that the applicant or submitter, depending on the context, is either required or recommended to "provide," "identify," "describe," or "compare," for example:[58]

(1) Device description documentation –

(a) Provide a description of the device design, including any novel features and functionalities, including engineering drawings or diagrams of the device with all

[54] For the purpose of this guidance, a pivotal study is a definitive study in which data are evaluated to establish the safety and effectiveness of the to-be-marketed product; this study is submitted in a marketing application to support its intended use. Other terms for such studies include key, critical, and major studies. See footnote 34 for a description of *to-be-marketed product.*

[55] We note that the sponsor shall submit to FDA the complete investigational plan and a complete report of prior investigations of the device if no IRB has reviewed them, if FDA has found an IRB's review inadequate, or if FDA requests them. 21 CFR 812.20(b)(2).

[56] See 21 CFR 812.20(b)(2) and (3), 812.25(c) and (d), and 21 CFR 812.27(a).

[57] See 21 CFR 312.23(a)(3)(ii), 312.23(a)(3)(iv), and 312.23(a)(7)(i).

[58] Master files may be useful tools to help preserve the trade secret information of a third party that is not known to the applicant. For more information on biologics, device, and drug master files, see CBER's Master Files for CBER-Regulated Products webpage (available at https://www.fda.gov/vaccines-blood-biologics/development-approval-process-cber/master-files-cber-regulated-products), CDRH's Device Master Files webpage (available at https://www.fda.gov/medical-devices/premarket-approval-pma/master-files), and CDER's Drug Master Files (DMF) webpage (available at https://www.fda.gov/drugs/forms-submission-requirements/drug-master-files-dmfs), respectively. See also the draft guidance for industry *Cross-Center Master Files: Where to Submit* (November 2025). When final, this guidance will represent FDA's current thinking on this topic.

dimensions labeled, descriptions of the individual device components, or any other available information to explain the device design.

(b) Describe the principles of operation of the device and how it functions throughout use.

(c) Describe any accessories or other devices labeled for use with the device.

(2) Device safety – Identify EDDCs that are necessary for patient safety during the study. For example, a device may cause harm if the dose accuracy performance is not adequate (e.g., by delivering a larger dose than intended). For safety-related EDDCs, provide verification data and, as appropriate, validation information to support that the EDDCs are appropriate for the intended user(s), prior to the start of a clinical study. See *Performance data* for data recommendations.

In the overall device risk analysis section, include EDDC-related risks.

(3) Performance data[59] – Include summary test results using established test methods for the device (e.g., recognized consensus standards, test methods discussed in FDA guidance) or complete verification test reports for unique or unrecognized test methods. Recommendations regarding the summaries and/or documentation can be found in the guidance for industry and FDA staff *Recommended Content and Format of Non-Clinical Bench Performance Testing Information in Premarket Submissions* (December 2019).

The following considerations apply when device performance validation includes use of a proposed clinical study:

- These clinical studies should be conducted with the final finished product.
- It is appropriate for the clinical study protocol to include endpoints relevant to the performance of the device (e.g., infusion rate, dose range, injection time). Where possible, to support provision of evaluable EDDC data, applicants should submit such protocols for Agency feedback on the EDDC validation endpoints in a formal meeting or communication with FDA (see section VIII).
- It is important that the clinical study protocol include safety endpoints that capture drug delivery device failures, malfunctions, and adverse events.[60]

[59] As discussed in the part 4 CGMP guidance, investigational combination products that include device constituent parts may be subject to design controls under 21 CFR 820.30. See the technical amendment to 21 CFR 812.1(a) amending the reference in 21 CFR 812.1(a) to now refer to 21 CFR 820.10(c) (*Design and development*), to align with the QMSR (90 FR 55980; December 4, 2025).

[60] Note that human factors considerations are outside the scope of this guidance; see section I.

### B. Marketing Applications

For marketing applications for devices and combination products, requirements for submission content relevant to EDDCs include, but are not limited to the following:

- A PMA must include a complete description of the device, each of the functional components or ingredients (as described in FDA regulations), and the methods used in, and the facilities and controls used for, the manufacture of the device; and information and results on nonclinical laboratory studies.[61]

- A 510(k) submission must include a description of the device, a statement indicating the device is similar to and/or different from other comparable products including data and information to support that statement, and as applicable, appropriate supporting data to show that the manufacturer has considered what consequences and effects any changes or modifications or new uses might have on the safety and effectiveness of the device.[62]

- A De Novo request must include a complete description of the device and information and results on nonclinical laboratory studies.[63]

- NDA, ANDA, and BLA applications must include a description of the product, data to show that the final finished product meets specifications, a description of the manufacturing processes and controls, and stability data.[64]

For products subject to premarket approval (e.g., under an ANDA, BLA, NDA, or PMA), as described above, manufacturing control strategy information is required to be included in the application. In contrast, 510(k) submissions generally do not include control strategy information as part of the 510(k) itself; however, information demonstrating control of the 510(k) device's manufacturing process as part of complying with applicable CGMP requirements[65] must be available for FDA review during inspection.[66]

As described above, depending on the application type, certain information on EDDCs is a required part of the application, while in other instances that same information is recommended for submission. This section outlines considerations for this information that the applicant or submitter, depending on the context, is either required or recommended to "provide," "include," "identify," "describe," or "compare," for example.[67]

(1) Device description documentation –

(a) Information in section VII.A, item #1

[61] See 21 CFR 814.20(b)(4)(i), (ii), and (v); 21 CFR 814.20(b)(6)(i).
[62] See 21 CFR 807.92(a)(4); 21 CFR 807.87(f) and (g).
[63] See 21 CFR 860.220(a)(6) and 21 CFR 860.220(a)(15)(i).
[64] See 21 CFR 314.50(d)(1), 314.94(a)(9), and 601.2(a).
[65] See 21 CFR part 820 and part 4 subpart A.
[66] See section 704(a) of the FD&C Act (21 U.S.C. 374(a)). Also see footnote 51.
[67] See footnote 58.

(b) When applicable, include a side-by-side comparison of the to-be-marketed device with any earlier versions utilized in the provided verification and validation testing, identifying any design and manufacturing changes.

(2) EDDC – Identify EDDC(s) for the drug delivery device

To facilitate submission and review of the EDDC information, provide a summary of the EDDC information included in the application in the device description documentation, referencing the performance data section and supportive information. For NDAs, BLAs, and ANDAs, if the EDDC performance relies on or leverages CQA and related information in the CMC sections, the summary should reference the relevant sections.[68]

(3) Performance data – Include test protocol(s), summary test report(s), and supporting data relevant to each EDDC for the final finished product.[69, 70] Applicants should use recognized consensus standards and FDA guidance to inform design and testing, as applicable. Include a justification to support how acceptance criteria for performance testing are clinically meaningful and appropriate to meet user needs. If changes are made after design verification or validation, include a discussion, along with supportive data, of either why the existing verification and/or validation data is still applicable or how the applicant verified and/or validated the changes.

For all EDDC(s), provide the following evaluations, when applicable as discussed in sections V and VI:

(a) Preconditioning – Provide documentation that demonstrates the device performance meets the specified EDDCs after preconditioning testing. See section V.A.1 for additional considerations.

(b) Stability/Shelf-life testing – Include endpoints in the final finished product stability and shelf-life testing program to verify that EDDCs that could change over time or that have age-related failure modes are maintained at expiry. See section V.A.2.b for additional considerations.

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[68] If the application includes proposed established conditions (ECs) for the device constituent part, and the EDDCs constitute a subset of the proposed ECs, we recommend referencing the EC-related sections of the application for the EDDC information. See the ICH guidance for industry *Q12 Technical and Regulatory Considerations for Pharmaceutical Product Lifecycle Management* and the draft FDA guidance for industry *ICH Q12: Implementation Considerations for FDA-Regulated Products* (when final, this guidance will represent FDA's current thinking on this topic).

[69] Recommendations regarding the summaries and/or documentation can be found in the guidance for industry and FDA staff *Recommended Content and Format of Non-Clinical Bench Performance Testing Information in Premarket Submissions*.

[70] See the following for how information can be provided: section 4 in the FDA Electronic Common Technical Document (eCTD) v4.0 TECHNICAL CONFORMANCE GUIDE Technical Specifications Document (June 2026). Also see the guidance for industry and FDA Staff *Electronic Submission Template for Medical Device 510(k) Submissions* (October 2023), guidance for industry and FDA Staff *Electronic Submission Template for Medical Device De Novo Requests* (August 2024), and the FDA webpage *PMA Application Contents* available at https://www.fda.gov/medical-devices/premarket-approval-pma/pma-application-contents.

(c) Control strategy – Provide a control strategy that ensures that the final finished product maintains its EDDC(s).[71] Include a summary of the controls implemented, including a justification describing how the controls are sufficient to assure the quality of the EDDC is achieved. In the control strategy description, include supporting evidence as justification for the control strategy. FDA might request additional specific documentation referenced in the control strategy during the review.[72] Applicants can consult with the appropriate product office for questions regarding control documentation to include in a submission.

See section VI for additional information on developing a control strategy.

(4) As appropriate for the application and device type, include the risk management plan and report which covers the EDDCs, including traceability to the risk analysis and how related performance data for the final finished product supports that a given risk is acceptable.

### C. Submissions for Post-Market Changes That May Impact EDDCs

When modifying the product design or manufacturing process of an approved product, applicants should evaluate whether there are any new EDDCs and verify and validate changes to drug delivery performance, as appropriate. Applicants should also perform an analysis of the impact of the change on the EDDC specifications of the approved product.

For post-market change submissions for devices and combination products, requirements for submission content relevant to EDDCs include, but are not limited to the following[73]:

- PMA, for changes requiring a submission/notice:[74] a supplement/notice must include identification of each change and the reason for each change (PMA supplements); must provide a full explanation of the basis for the changes (special PMA supplements); or must describe, in detail, the changes and summarize the data or information supporting the change (30-day notices).[75]

- 510(k) submission, for changes requiring a new 510(k):[76] a 510(k) must include a summary of how the technological characteristics of the device compare to a predicate device and what consequences and effects the difference(s) might have on the safety and effectiveness of the device.[77]

[71] See section VI for additional information.
[72] See Appendix D for an example of a control strategy for an EDDC where documentation to verify the control was either included (i.e., documentation from the applicant) or referenced (i.e., documentation from sources other than the applicant) in the submission.
[73] See footnote 8.
[74] See 21 CFR 814.39(a), (c), or (f).
[75] See 21 CFR 814.39(c)(1), 814.39(d)(1)(ii), 814.39(f).
[76] Changes to a previously cleared device may require the submission of a new 510(k). See the guidance for industry and FDA staff *Deciding When to Submit a 510(k) for a Change to an Existing Device* (October 2017).
[77] See, e.g., 21 CFR 807.92(a)(6), 21 CFR 807.87(f) and (g).

- NDA/BLA/ANDA, for changes requiring approval prior to distribution:[78] a supplement must include a detailed description of the proposed change; a description of the methods used and studies performed to assess the effects of the change; and the data derived from such studies.[79]

As described above, depending on the application type, certain information on EDDCs is a required part of the postapproval submission, while in other instances that same information is recommended for submission. This section outlines considerations for this information that the applicant or submitter, depending on the context, is either required or recommended to "provide," "include," "identify," or "describe," for example:

(1) Description of changes in comparison to the approved product

(2) Potential impact of the change to EDDCs

(3) Verification, validation, or both of potentially impacted EDDCs

To support the analysis of a design or manufacturing process change, provide a side-by-side comparison between the new design or new manufacturing process/site EDDC specification and the original device design or manufacturing process/site EDDC specification.

For the EDDC specifications that are unchanged, provide verification information, including stability and preconditioning (e.g., storage, shipping, conditions associated with use) information when applicable. If an applicant believes that the EDDC specification would not be impacted by preconditioning, then provide a scientific justification that the performance is not expected to shift outside the validated specifications over time or after preconditioning.

If the EDDC specifications are changing, provide new verification information (including stability and preconditioning information when applicable) and validation information for the new specification or a rationale for why the verification and validation information from the original application can be leveraged (e.g., tightening acceptance criteria for an EDDC specification).[80]

(4) Updated control strategy

To help ensure EDDC maintenance throughout the product lifecycle, include a re-evaluation of the control strategy to determine whether it is still applicable given the design changes, manufacturing changes, or both, including information to demonstrate that the control strategy is still effective.

[78] See 21 CFR 314.70(b), 314.97(a), and 601.12(b).

[79] See 21 CFR 314.70(b)(3), 314.97(a), and 601.12(b)(3).

[80] See the draft guidance for industry *Bridging for Drug-Device and Biologic-Device Combination Products*, which includes information on how to determine the type of bridging data that may be appropriate. When final, this guidance will represent FDA's current thinking on this topic.

Alternatively, if an applicant is making changes that necessitate a change to the control strategy, provide documentation for the changes made to the EDDC control strategy and information to demonstrate that the new strategy is as effective as the original control strategy.

## VIII. INTERACTION WITH FDA

During product development we strongly encourage applicants to begin developing and characterizing the EDDCs that will need to be controlled in the marketed product and to begin to develop a device control strategy for the product the applicant plans to market. We recommend applicants submit the proposed EDDCs and control strategy for Agency feedback. The EDDCs and control strategy could be discussed at multiple types of formal meetings or in other communications with FDA, depending on application type. These meetings should be used consistently with their intended purpose. Also, as appropriate for the type of submission and the combination product lead center, the meeting request information may vary.[81]

When seeking feedback on proposed EDDCs, the meeting background package should provide a clear description of the product and its drug delivery function. This may include figures, instructions for use, description of the intended user population, and context of use. The meeting background package should provide specific EDDC questions and may request the participation of an FDA office or staff with the appropriate expertise. If there are questions regarding the control of EDDCs, the control strategy proposal should be provided. These meetings would include discussion of the proposed control strategy and the proposed approach and timing of EDDC-related verification and validation activities (e.g., type of studies and completion in relation to pivotal clinical studies and marketing submissions). At a meeting type appropriate for the product, we recommend applicants request feedback on the identified EDDCs (and associated verification and validation activities) and approach to the control strategy that will be included in the marketing application. In addition, sponsors may request feedback on testing for other related characteristics during EDDC testing.

[81] For information on requesting FDA feedback, see the guidance for industry and FDA staff *Requesting FDA Feedback on Combination Products* (December 2020). For additional information on the process to request a meeting under user fee programs, see the guidance for industry *Formal Meetings Between the FDA and Sponsors or Applicants of BsUFA Products* and the guidance for industry *Formal Meetings Between the FDA and Sponsors or Applicants of PDUFA Products* (August 2026). For information on feedback and meetings related to devices, see the guidance for industry and FDA staff *Requests for Feedback and Meetings for Medical Device Submissions: The Q-Submission Program* (May 2025). ANDA applicants may submit a pre-ANDA meeting request or a controlled correspondence to obtain Agency feedback. See the guidances for industry *Formal Meetings Between FDA and ANDA Applicants of Complex Products Under GDUFA* (October 2022) and *Controlled Correspondence Related to Generic Drug Development* (March 2024). Also, for general development information, see the FDA guidance webpage at https://www.fda.gov/regulatory-information/search-fda-guidance-documents.

## APPENDIX A - ESSENTIAL DRUG DELIVERY DEVICE PERFORMANCE CHARACTERISTICS EXAMPLE – PREFILLED SYRINGE

In this hypothetical example, the applicant is developing a drug in a prefilled syringe (PFS) intended for subcutaneous injection that will be delivered by a health care provider (HCP) to a patient in a health care setting. The PFS is a glass barrel containing a 12mm prestaked needle. The labeling directs the HCP to administer the drug using the PFS at a 30-45 degree angle while pinching the skin. The PFS is also manufactured with a needle safety feature to mitigate the risk of accidental needle sticks. The device design requires the needle safety feature to be activated before completion of injection.

The below table shows characteristics/features considered during identification of the EDDCs for this hypothetical product.

| Characteristic/feature | EDDC (yes or no) and rationale |
|---|---|
| Deliverable volume | Yes. The volume of drug that can be delivered during injection is dependent on the device design and fill volume (independent of the user). |
| Needle safety feature activation force | Yes. It is dependent on the device design (independent of the user). |
| Glide force | Yes. It is necessary for the progression and completion of the dose. |
| Breakloose force | Yes. This force to initiate the injection is dependent on the device design (independent of the user). |
| Cap removal force | Yes. It is dependent on the design and manufacture of the cap and its interface to the nozzle PFS barrel tip. |
| Clarity of the barrel | No. It is not a drug delivery function. |
| Biocompatibility | No. It is not a drug delivery function. |
| Sterility | No. It is not a drug delivery function. |
| Color of plunger rod | No. It is not a drug delivery function. |
| Markings on the barrel | No. It is not a drug delivery function because the entire volume is injected. |
| Injection depth | No. The user controls the injection depth through the injection technique (i.e., injection depth is dependent on the user and independent of the device). |

## APPENDIX B – ESSENTIAL DRUG DELIVERY DEVICE PERFORMANCE CHARACTERISTICS EXAMPLE – AUTOINJECTOR

As an illustrative example of the distinction between essential drug delivery device performance characteristics (EDDCs) and other characteristics/features, the table below lists characteristics/features that were considered in identifying EDDCs for a hypothetical autoinjector. The hypothetical product is an autoinjector with a prefilled syringe (PFS) subassembly device constituent part that is also the primary container closure for the drug constituent part.[82]

| Characteristic/feature | EDDC (yes or no) and rationale |
|---|---|
| Dose accuracy | Yes. The automated dose delivery is necessary to ensure appropriate drug delivery. |
| PFS-fill volume/container content | No. It is a component level aspect because the fill volume influences but is already reflected in dose accuracy. |
| Biocompatibility | No. It is not a drug delivery function. |
| Container closure integrity | No. It is not a drug delivery function. |
| Packaging integrity | No. It is not a drug delivery function. |
| Extended needle length | Yes. It ensures the needle is at the right depth and is dependent on the device. |
| PFS-needle length | No. It is a component level aspect because it influences but is already reflected in the extended needle length function. |
| Needle inner diameter | No. It is a component level aspect because it influences but is already reflected in the injection time function. |
| Activation force | Yes. It initiates drug delivery and is dependent on the device, not the user. |
| Breakloose force | No. It is a component level aspect because it influences but is already reflected in the injection time function. |
| Glide force | No. It is a component level aspect because it influences but is already reflected in the injection time function. |
| Injection time | Yes. It ensures the drug is delivered to the intended space within the appropriate time and is dependent on the device, not the user. |
| Override force | No. It is not a drug delivery function because it is the force to overcome the needle safety mechanism, which is activated post drug delivery. |
| Drug visibility | No. It is not a drug delivery function because the drug appearance assessment is a user action. |
| Stopper height | No. It is not a drug delivery function because it is the depth that the stopper should be placed at in the syringe for compatibility with the autoinjector plunger rod, filling process, and to ensure the stopper does not come out. |

[82] It should be noted that the EDDC identification is distinct from CQA identification; however, some design aspects in the table may also be considered critical from a drug quality and manufacturing perspective. Refer to section III for further explanation regarding the relationship between EDDCs and CQAs.

| Characteristic/feature | EDDC (yes or no) and rationale |
|---|---|
| Needle pullout force | No. It is not a drug delivery function because it is specific to the device durability, ensuring the needle does not detach. |
| Audible feedback/clicks | Yes. It signals that the injection is complete and is dependent on the device. |
| Visual feedback | Yes. It signals that the injection is complete and is dependent on the device. |
| Cap removal force | Yes. Cap removal needs to be completed before the injection can be administered and it is dependent on the device. |
| Rigid needle shield removal force | No. It is a component level aspect because it influences, but is already reflected in, the cap removal force function. |

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## APPENDIX C – EXAMPLES OF POTENTIAL ESSENTIAL DRUG DELIVERY DEVICE PERFORMANCE CHARACTERISTICS BASED ON PRODUCT TYPE

The following tables provide examples of potential essential drug delivery device performance characteristics (EDDCs) for different product types. Note that the EDDCs for specific products may vary due to product specific differences (e.g., indications for use, population, condition and frequency of use, user requirements, route of administration, drug characteristics, dosage form, deliverable volume, performance expectations).

**Table 1: Prefilled Syringes**

| Delivery of intended dose | Delivery to the target site | Product preparation | Initiation of dose delivery | Dose delivery progression | Dose delivery completion |
|---|---|---|---|---|---|
| Deliverable volume | Needle length[83] | • Cap removal force<br>• Withdrawal force[84] | Breakloose force | Glide force | • Glide force<br>• Needle safety feature activation force[85] |

[83] If a device is designed such that needle length is validated to reach a specific delivery space or tissue independent of user technique (e.g., pinching, skin test bleb method), needle length is an EDDC.

[84] For some co-packaged combination products, an empty syringe or a diluent prefilled syringe is used to withdraw drug directly from a vial, or to reconstitute or mix a drug. The withdrawal force (a type of injection force) of this empty or prefilled syringe is an EDDC because it is necessary for the preparation of the drug for injection and the drug cannot be delivered to the patient unless preparation is successfully completed. If the empty or prefilled syringe used in preparation is also used to deliver the drug, breakloose force and glide force are EDDCs.

[85] If a device design requires the needle safety feature to be activated to complete drug delivery, needle safety feature activation force is an EDDC. Conversely, if a device design does not require the needle safety feature to be activated to complete drug delivery, then needle safety feature activation force is not an EDDC.

794 **Table 2: Injectors**
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| Device platform | Delivery of intended dose | Delivery to the target site | Product preparation | Initiation of dose delivery | Dose delivery progression | Dose delivery completion |
|---|---|---|---|---|---|---|
| **Auto-injector** | Dose accuracy | Extended needle length | • Cap removal force<br>• Activation force (e.g., to start reconstitution process)[86]<br>• Audible/visual/ tactile feedback, as applicable, of successful drug preparation/ reconstitution[87] | • Activation force (shield)<br>• Activation force (button) | N/A | • Injection time<br>• Audible/ visual/ tactile feedback, as applicable |
| **On-body injector** | • Dose accuracy/ dose effic-iency, as applicable<br>• Injection time[88]<br>• Interval of delivery[89] | Extended needle/cannula length | • Cap removal force<br>• Activation force (e.g., to start reconstitution process)[90]<br>• Audible/visual/ tactile feedback, as applicable, of successful drug preparation/ reconstitution[91] | Activation force | Adhesion force | • Injection time<br>• Audible/ visual/ tactile feedback, as applicable<br>• Adhesion force |

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[86] Depending on the design of the automated mixing/reconstitution feature, there may be alternate or additional EDDCs.
[87] If the injector design automates reconstitution of the drug prior to injection, features that ensure and/or indicate successful mixing of the drug are EDDCs because if the drug is not mixed then the efficacy is diminished. If the device does not allow for drug delivery when the drug is not well mixed, this may be considered adequate feedback depending on the drug/indication to address the EDDC(s) of audible/visual/tactile feedback.
[88] On-body injectors are often intended to deliver a large volume (e.g., 1-3mL) of drug. Therefore, injection time is an EDDC for delivery of intended dose because if the speed is too high then there is a higher risk of tolerability issues impacting the delivered dose. In addition, injection time is an EDDC for dose delivery completion similar to an autoinjector.
[89] On-body injectors may be used to replace two separate autoinjectors and may be designed to deliver injections at intervals. Therefore, that interval of delivery would be an EDDC.
[90] See footnote 86.
[91] See footnote 87.

**Continued – Table 2: Injectors**

| Device platform | Delivery of intended dose | Delivery to the target site | Product preparation | Initiation of dose delivery | Dose delivery progress-ion | Dose delivery completion |
|---|---|---|---|---|---|---|
| **Pen injector** | Dose accuracy | N/A | • Cap removal force<br>• Activation force (e.g., to start reconstitution process)[92]<br>• Audible/visual/tactile feedback, as applicable, of successful drug preparation/reconstitution[93] | Injection force[94] | N/A | • Injection time[95]<br>• Audible/ visual/ tactile feedback, as applicable |
| **Jet injector** | Dose accuracy | Penetra-tion depth | • Cap removal force<br>• Activation force (e.g., to start reconstitution process)[96]<br>• Audible/visual/tactile feedback, as applicable, of successful drug preparation/reconstitution[97] | • Activation force (shield)<br>• Activation force (button) | N/A | • Injection time<br>• Audible/ visual/ tactile feedback, as applicable |

[92] See footnote 86.
[93] See footnote 87.
[94] If the pen injector is automated (i.e., does not manually deliver the dose), the EDDC may be activation force rather than injection force.
[95] If the pen injector is automated, then injection time is an EDDC.
[96] See footnote 86.
[97] See footnote 87.

805 **Table 3: Nasal Sprays**[98]
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| Delivery of intended dose | Delivery to the target site | Product preparation | Initiation of dose delivery | Dose delivery progression | Dose delivery completion |
|---|---|---|---|---|---|
| • Pump delivery (spray weight)<br>• Spray content uniformity (SCU) | • Spray pattern<br>• Droplet size distribution<br>• Particle size distribution (suspensions) | N/A | Activation force | N/A | N/A |

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809 **Table 4: Inhalation Products**
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| Device Platform | Delivery of intended dose | Delivery to the target site | Product preparation | Initiation of dose delivery | Dose delivery progression | Dose delivery completion |
|---|---|---|---|---|---|---|
| **Metered dose inhaler (MDI) - non-breath actuated** | Delivered dose | Aerodynamic particle size distribution (APSD)[99] | Priming or repriming[100] | Device actuation force | N/A | • Counter accuracy [101]<br>• Counter actuation force |

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[98] For additional information on nasal spray products, see the guidance for industry *Nasal Spray and Inhalation Solution, Suspension, and Spray Drug Products – Chemistry, Manufacturing, and Controls Documentation* (July 2002).

[99] Aerodynamic particle size distribution (APSD) characterizes the particle/droplet size distribution of delivered aerosolized drug. APSD is a critical parameter, and its control is crucial for maintaining the quality of inhalation drugs. This parameter is dependent on the formulation, container closure system, and device delivery mechanism. The optimum APSD for most oral inhalation products has generally been recognized in the range of 1 to 5 um. For more guidance conducting these tests, please refer to USP <601> for aerosols, sprays, and powders and USP <1601> for nebulizer products. For guidance on information to provide to FDA regarding test setups and data presentation in submissions, please refer to the draft guidance for industry, *Metered Dose Inhaler (MDI) and Dry Powder Inhaler (DPI) Drug Products—Quality Considerations* (April 2018). When final, this guidance will represent FDA's current thinking on this topic.

[100] This attribute is applicable to most MDIs where a priming and repriming function is present.

[101] If the counter is not accurately measuring the doses dispensed, the patient may dispense the drug and not receive a dose because the device is empty (under counting). For additional information to avoid undercounting, see design recommendations included in section III.B of the guidance for industry *Integration of Dose-Counting Mechanisms into MDI Drug Products* (March 2003).

**Continued – Table 4: Inhalation Products**

| Device platform | Delivery of intended dose | Delivery to the target site | Product preparation | Initiation of dose delivery | Dose delivery progression | Dose delivery completion |
|---|---|---|---|---|---|---|
| **Dry powder inhaler (DPI) - both pre-metered and device metered** | • Metered dose<br>• Delivered dose | APSD[102] | Dose loading[103] | Trigger mechanism[104] | Trigger mechanism | Counter accuracy[105] |
| **Nebulizers**[106] | • Total dose<br>• Rate of delivery | • Patient Interface[107]<br>• APSD[108] | N/A | Breath synchronization[109] | Breath synchronization[110] | Audible/visual /tactile feedback, as applicable |

[102] See footnote 99.
[103] Single-dose DPIs are designed to require loading of doses and multi-dose DPIs are designed with internal mechanisms to cycle to new dose blisters or load drug from an internal reservoir into a dosing chamber.
[104] Additionally, some device features dictate the appropriate airflow for activation (e.g., triggering flow rate) and may be considered an EDDC.
[105] See footnote 101.
[106] Applicable to inhalation solutions, inhalation suspensions, solutions for inhalation, and drugs for inhalation solutions dosage forms, as opposed to inhalation powder and aerosol.
[107] The amount of drug delivered to the lung will depend on the route of inhalation (e.g., full-face mask or mouthpiece) as well as seal and resistance to flow. Additionally, different materials which may have different electrostatic properties which can attract and capture smaller droplets, add sources of leak and dead space, and may decrease respirable dose.
[108] See footnote 99. For nebulizers, APSD is dependent on the patient interface, in addition to the formulation, container closure system, and device delivery mechanism. See also footnote 98.
[109] Some nebulizers are designed to attempt to nebulize only during patient inhalation. Design implementation of synchronization includes both simple one-way valve (selective flow during inhalation or exhalation) and more complex sensor-driven electromechanical actuation systems.
[110] See footnote 109.

822 **Table 5: Vaginal Systems (VS)[111]**
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| Delivery of intended dose | Delivery to the target site | Product preparation | Initiation of dose delivery | Dose delivery progression | Dose delivery completion |
|---|---|---|---|---|---|
| Drug release rate and consistency [112] | • VS physico-mechanical properties, such as:[113]<br>- Dimensions<br>- Durometer/ hardness<br>- Tensile strength<br>- % elongation/force at break<br>- Compression strength (including fatigue resistance)<br>- Twisting during compression<br>- Seal integrity (if applicable)<br><br>• Applicator/inserter physico-mechanical properties, such as:<br>- Dimensions<br>- Force needed for delivery<br>- Assessment of correct deployment | N/A | N/A | • VS physico-mechanical properties, such as:[114]<br>- Dimensions<br>- Durometer/ hardness<br>- Tensile strength<br>- % elongation/ force at break<br>- Compression strength (including fatigue resistance)<br>- Twisting during compression<br>- Seal integrity (if applicable) | N/A |

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[111] Examples of vaginal systems include drug-eluting intravaginal rings, inserts, discs.
[112] This includes the initial burst effect, if applicable. Release rate is a reflection of dose accuracy over time.
[113] For vaginal systems, the VS physico-mechanical properties ensure that the vaginal system can be inserted, remains in place for the duration of the use period, and can be removed. If these fail after the vaginal system is inserted, the vaginal system may fall out, leading to an incomplete dose, or may cause physical harm to the user.
[114] See footnote 113.

827 **Table 6: Infusion Products**
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| Device platform | Delivery of intended dose | Delivery to the target site | Product preparation | Initiation of dose delivery | Dose delivery progression | Dose delivery completion |
|---|---|---|---|---|---|---|
| **Infusion pumps** [115, 116] | • Flow rate accuracy/ consisten-cy[117]<br>• Dose accuracy [118] (if applicable) | • Needle/ cannula depth (if applicable)<br>• Secure connection to IV or to separate administration set for SQ, etc.<br>• Needle/ cannula insertion force | Drug cartridge insertion force (if applicable) | • Button activation force (mechani-cal)<br>• Dose status[119] | • Adhesion force (if applicable)<br>• Dose status | Dose status |
| **Subdermal implants (and applicators if applicable)** [120] | Dose accuracy or Drug release rate and consisten-cy | Implantation depth indicators | Implant connection/fit with applicator (e.g., dimensional connection) | Applicator ejection force | N/A | Dose status (if applicable) |

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[115] When bolus feature is present the EDDCs for on-body injectors also apply.
[116] The form factor of infusion pumps can vary significantly. However, this table is meant to apply to a wide array of form factors such as body-worn, body-attached, and conventional infusion pumps. Additional EDDCs may exist depending on the functionality and intended use of the infusion pump.
[117] Accuracy and/or consistency depending on the drug characteristics, indication, and/or safety profile.
[118] For pumps that include a bolus dose function, in addition to continuous infusions.
[119] Dose status is applicable throughout the initiation, progress, and completion of the infusion; however, whether dose status communication is achieved through audio, visual, tactile or other means is dependent on the pump design. Furthermore, this guidance does not address the causes that might result in interruption of a dose such as occlusion, motor failure, etc., since each pump design is different. Therefore, depending on the design and technology of the pump, characteristics other than dose status may be EDDCs for dose initiation, progression, and completion.
[120] The examples of potential EDDCs identified for subdermal implants and applicators are based on the two most common forms: passive delivery moderated by polymer degradation and active delivery using an osmotic engine.

## APPENDIX D – EXAMPLE OF A CONTROL STRATEGY FOR THE EDDC OF EXTENDED NEEDLE LENGTH FOR AN AUTOINJECTOR

The following is an example control strategy for the extended needle length for an autoinjector assembled with the prefilled syringe (PFS) at the final finished combination product[121] manufacturing facility. The applicant is ultimately responsible for the control of the essential drug delivery device performance characteristic (EDDC). This example shows how the applicant can leverage information regarding the design and manufacturing from suppliers and purchasing agreements (e.g., certificate of analysis), which are part of the purchasing information (ISO 13485, subclause 7.4.2),[122] to adequately control the EDDC upstream.

In this example, supplier A is the syringe and needle manufacturer, supplier B is the autoinjector subassembly manufacturer, and the applicant is the manufacturer of the final finished combination product. The applicant performs the following manufacturing steps, which include:

(1) Manufacturing the primary container (PFS) – filling and stoppering the syringes from supplier A with drug,
(2) Manufacturing the autoinjector – Inserting and securing the PFSs into autoinjector subassemblies from supplier B, and
(3) Final packaging and labeling of autoinjector.

As shown in the table below:

- The length of the syringe and needle are not subject to change after filling or assembly into the autoinjector, or over the autoinjector shelf life. Therefore, control of the length of the syringe and needle is effective at supplier A (the syringe and needle manufacturer).

- The needle cover retraction distance is also a dimensional function that is not impacted by aging and subsequent assembly steps at the final manufacturing stage. Therefore, control of the needle cover retraction distance is effective at supplier B.

- The compatibility of the length of the syringe and needle with the needle cover retraction distance is demonstrated by the applicant's engineering analysis. This analysis validates the extended needle length specification.

The applicant determines that the final extended needle length for the autoinjector is dependent on the process steps to assemble the syringe into the subassemblies. Therefore, the applicant provides a process risk assessment to support which steps impact this EDDC, the applicant's in-process work instructions relating to this process step, and process validation data to show this process step is controlled and yields autoinjectors with adequate extended needle lengths. See sections VII.B and VII.C for control strategy information to include in applications.

[121] For purposes of this guidance, the final finished combination product is the product intended for marketing and submitted in the marketing application.

[122] 21 CFR 820.10(a) and 4.4(b)(1)(iii); see 21 CFR 820.7(b) and 4.4(f)(2) for incorporation by reference.

870 **Table 1 – Example of a control strategy for extended needle length, an EDDC for an**
871 **autoinjector**

| Feature or manufacturing process step | Control at supplier A[123] | Control at supplier B[124] | Control at final manufacturer | Documentation used to verify the control at final manufacturer/applicant and submitted |
|---|---|---|---|---|
| Length of syringe and needle | 100% dimensional check of overall syringe/ needle | N/A | Incoming acceptance per certificate of analysis (COA) | Engineering drawing (#XXXX) |
| Length of syringe and needle | In-process control (IPC) check of syringe dimensions | N/A | Incoming acceptance per COA | Engineering drawing (#XXXX) |
| Length of syringe and needle | COA for each syringe batch released | N/A | Incoming acceptance per COA | COA |
| Needle cover retraction distance | N/A | IPC dimensional check for autoinjector components/ subassem-blies | Tolerance analysis ensuring needle extension is compatible with design to 'X' CpK level | • Engineering report explaining tolerance analysis and justification of CpK values<br>• Engineering drawing (Doc# XXXX) of component A<br>• Engineering drawing (Doc# XXXX) of component B |

[123] In a marketing application, a proposed control strategy does not need to include the referenced documentation (e.g., from sources other than the applicant) to verify the control. However, the Agency may request the referenced documentation. Additionally, the Agency may request protocols, test methods, or work instructions for controls at suppliers during review of the application depending on the criticality of the EDDC and the method of control upstream (e.g., if the applicant is relying on the supplier's control information). When requested, the supplier can provide this information directly to the applicant or through reference to a master file with an appropriate Letter of Authorization.

[124] Ibid.

| **Feature or manufacturing process step** | **Control at supplier A**[123] | **Control at supplier B**[124] | **Control at final manufacturer** | **Documentation used to verify the control at final manufacturer/applicant and submitted** |
|---|---|---|---|---|
| Step #x - subassembly assembly | N/A | 100% check to ensure key components were assembled correctly and interact to ensure needle extension | Adequate change control and purchasing control agreements are in place to ensure notification of any changes to components | Purchasing control agreement between final manufacturer and supplier B |
| Step #y - assembling subassemblies and syringe | N/A | N/A | Process risk assessment to determine assembly steps impacting needle extension | Process risk assessment |
| Step #y - assembling subassemblies and syringe | N/A | N/A | Push/snap force of fixture | • Work instruction<br>• Validation of snap force |
| Step #y - assembling subassemblies and syringe | N/A | N/A | Fixture height | • Tolerance analysis of fixture height and impact on overall needle extension length<br>• Work instruction for fixture set up and calibration |
| Step #y - assembling subassemblies and syringe | N/A | N/A | Performed process validation and verified that device manufacturing from PQ engineering runs[125] met needle extension specifications | Process validation report (includes autoinjector extended needle length testing) |

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[125] An engineering run is representative of the intended manufacturing process for the to-be-marketed product.

| **Guidance History*** | **Date** | **Description** |
|---|---|---|
| Level 1 Revised Draft Guidance | October 2026 | See Introduction section of this document |
| Level 1 Draft Guidance | June 2024 | See Notice of Availability for more information** |

*This table was implemented beginning October 2026 and previous guidance history may not be captured in totality.

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