TITLE: Hypodermic syringes with reuse prevention feature

Specification reference:	E013/RUP01.0
Product verification protocols:	E013/RUP01.0
Issue date:	6th October, 2025
Date of previous revision:	New specification

Contents

1. Scope

This combined specification and testing protocol defines the immunization device requirements for World Health Organization (WHO) prequalification of hypodermic syringes with reuse prevention feature. Description of the general prequalification process can be found in *Guidelines for WHO IMD-PQS Applicants & Prequalification Holders*[1]; however, syringe-specific guidance within this specification supersedes the general guidance. This document is intended to be used in conjunction with ISO 7886-4:2018 *Sterile hypodermic syringes for single use — Part 4: Syringes with re-use prevention feature*, which provides the primary technical specification for hypodermic syringes with reuse prevention features.

2. Normative references

Where normative references are referenced without a specific edition, it is implied that the latest edition of the standard is applicable.

Reference number	Standard
ISO 7886-4:2018	Sterile hypodermic syringes for single use — Part 4: Syringes with re-use prevention feature
ISO 13485	Medical devices — Quality management systems — Requirements for regulatory purposes
ISO/IEC 17025	General requirements for the competence of testing and calibration laboratories
ISO 7886-1:2017	Sterile hypodermic syringes for single use — Part 1: Syringes for manual use
ISO 23908:2024	Sharps injury protection — Sharps protection mechanisms for single-use needles, introducers for catheters and needles used for blood testing, monitoring, sampling and medical substance administration — Requirements and test methods
ISO 10993-1	Biological evaluation of medical devices — Part 1: Evaluation and testing within a risk management process
ISO 14971	Medical devices — Application of risk management to medical devices
ISO 7864:2016	Sterile hypodermic needles for single use — Requirements and test methods
IEC 62366	Medical devices — Part 1: Application of usability engineering to medical devices AND Amendment 1 Medical devices — Part 2: Guidance on the application of usability engineering to medical devices
ISO 8537:2016	Sterile single-use syringes, with or without needle, for insulin
ISO 9626	Stainless steel needle tubing for the manufacture of medical devices — Requirements and test methods

1 World Health Organization (WHO). *WHO Immunization Devices (IMD-PQS) Prequalification of Cold Chain-Related Products: Guidelines for WHO IMD-PQS Applicants & Prequalification Holders*. WHO/VAX/IMD/PQS/GUIDE 2.0. Geneva: WHO; July 2024. https://extranet.who.int/prequal/sites/default/files/document_files/WHO%3AIMD%3APQS%20Prequalification%20Guideline%202.0_3.pdf

Reference number	Standard
ISO 80369-7	Small-bore connectors for liquids and gases in healthcare applications — Part 7: Connectors for intravascular or hypodermic applications
ISO 15223-1:2021	Medical devices — Symbols to be used with medical device labels, labelling and information to be supplied — Part 1: General requirements
ISO 7000	Graphical symbols for use on equipment
ISO 780	Packaging — Distribution packaging — Graphical symbols for handling and storage of packages
ASTM D999-01	Standard Test Methods for Vibration Testing of Shipping Containers
ASTM D5276-98	Standard Test Method for Drop Test of Loaded Containers by Free Fall
ISO 2859	Sampling procedures for inspection by attributes
ISO 16269-6	Statistical interpretation of data — Part 6: Determination of statistical tolerance intervals

Abbreviations: ASTM, ASTM International; IEC, International Electrotechnical Commission; ISO, International Organization for Standardization.

3. Terms and definitions

The following definitions apply to this document.

Term	Definition
Acceptable regulatory authority	A regulatory authority defined as either a “Stringent Regulatory Authority” (SRA) or “WHO-Listed Authority” (WLA) by WHO.
Adverse event	An incident resulting in permanent impairment, hospitalization, congenital malformation, injury or death to patients or users of a single-use injection device.
Applicant	Legal manufacturer or licensed reseller of a product, in the process of submitting that product for prequalification assessment by WHO Immunization Devices Prequalification.
Application Review Template	A standardized form used by WHO Immunization Devices Prequalification to assess whether a product submission meets the required performance, quality, and safety (PQS) criteria. It is completed by the applicant and serves as a structured summary of the product’s compliance with relevant PQS specifications and guidelines.
Certified translation	A document translation that includes a signed statement by the translator or translation company attesting to the accuracy and completeness of the translated document.
Correspondence	Includes mail and email.

Term	Definition
Device	A cold chain-related product, unless specifically described as an 'injection device'.
Dossier	Refers to the comprehensive set of documents and data that an applicant must present for each product they submit for prequalification. Each dossier is product-specific and, if applicable, site-specific, meaning a separate dossier is required for each manufacturing site.
In writing	Communication by letter, fax or email.
Legal Manufacturer[2]	The natural or legal person with responsibility for the design, manufacture, packaging and labelling of a product or device before it is placed on the market under its own name, regardless of whether these operations are carried out by that group or on its behalf by a third party.
Manufacturer	The legal manufacturer.
Product	A cold chain-related product.
Production-run products	"Samples" of the product submitted for WHO Immunization Devices prequalification that are commercial-run / production-run products, NOT prototypes or models of products.
Quality system	A quality system that has been certified by the appropriate regulatory or notified body as specified in the relevant WHO Immunization Devices Performance Specification. This quality system must be in current and continuous compliance.
Reseller	A commercial entity, licensed to act on behalf of a legal manufacturer, and which carries product liability and warranty responsibilities no less onerous than those carried by the legal manufacturer.
Secondary carton	A carton, which contains a number of individual vaccine vials or vial pairs. Most countries have traditionally stored and distributed vaccines in these cartons.
Single-use injection device	Single-use injection device includes single-use syringes used in conjunction with single-use needles, auto-disable syringes designed specifically for immunization and syringes with a reuse prevention feature for general purposes.
Unit container[3] **Error! Bookmark not defined.**	The unit container is the sterile enclosure which encloses a single, self-contained syringe unit (otherwise known as the primary container.

4. Requirements

As part of the WHO Immunization Devices Performance, Quality and Safety (PQS) prequalification process, a technical review of a submitted dossier for each product will

2 Definition derived from Article 1 (2) (f) of the European Union Medical Device Regulation.
3 Definition derived from ISO 7886-3:2020 *Sterile hypodermic syringes for single use — Part 3: Auto-disabled syringes for fixed-dose immunization*

be conducted to ensure completeness and sufficiency of the technical documentation supplied. This technical review focuses on the following three main components:

- **Completeness:** Each dossier submission will be reviewed according to the relevant ISO specifications to ensure that every requirement is sufficiently addressed.
- **Compliance:** Each dossier will be reviewed to ensure it has sufficient raw data demonstrating compliance with every requirement.
- **Quality:** Each set of raw data demonstrating compliance with the relevant ISO standard will be evaluated for adherence to good documentation practices (as outlined in ISO 13485 *Medical devices — Quality management systems — Requirements for regulatory purposes*).

Relevant ISO specifications are determined by the features of the injection device being submitted for WHO prequalification.

4.1 Hypodermic syringe with reuse prevention feature

All performance requirements necessary for WHO prequalification of hypodermic syringes with reuse prevention feature and their associated packaging and labelling are defined in ISO 7886-4:2018 *Sterile hypodermic syringes for single use — Part 4: Syringes with re-use prevention feature.*

4.2 Sharps injury protection feature

If an injection device is being considered for prequalification contains a sharps injury protection (SIP) feature, the injection device shall be evaluated as a SIP syringe as defined by compliance with ISO 23908:2024 *Sharps injury protection* in addition to the evaluation outlined in 5.1.

4.3 Quality system compliance

This guidance outlines the marketing approvals and/or quality system certification required from applicants as evidence of quality system compliance and acceptable regulatory status.

To be considered for WHO prequalification, an injection device must be produced in compliance with the requirements of an acceptable quality system standard for manufacturers of medical devices. Compliance of a manufacturer's quality system with this requirement may be demonstrated via submission of the necessary documentation, but site assessments may be conducted to further evaluate the acceptability of a manufacturer's quality system if deemed necessary by WHO. Acceptability of a manufacturer's quality system shall be demonstrated in one of two ways:

Option 1: Market authorization by an acceptable regulatory authority

If an injection device has been given market authorization or license (approval to supply) by an acceptable regulatory authority, compliance will be demonstrated by submission of the following:

- Proof of marketing authorization or license from an acceptable regulatory authority

AND

- ISO 13485 certification

WHO previously identified acceptable regulatory authorities as “Stringent Regulatory Authorities” (SRAs) but is transitioning to defining these regulatory bodies as “WHO-Listed Authorities” (WLAs).

Note: Although WHO has begun to define WLAs for medicines and vaccines, WLAs for medical devices have not yet been identified. Until this transition of SRAs to WLAs is complete, applicants may demonstrate evidence of quality system compliance by attaining marketing authorization/approval from either an SRA or WLA for medical devices (once established). No further quality system evidence (audit reports) will be required, as compliance is inferred.

Marketing authorization granted by an SRA must be demonstrated by one of the following:

Regulatory body	Evidence provided to WHO	Description of evidence
Notified Bodies (EU)	CE Certificate	A CE Certificate issued by Notified Bodies designated by the medical device regulators of European Union (EU) member states.
FDA (United States)	De Novo Summary or 510(k) summary	Indication of marketing approval from the United States Food and Drug Administration (FDA), either through the De Novo pathway (for novel devices) or the 510(k) pathway (for substantial equivalence).
Health Canada	Device license	Approval and device license issued by Health Canada to confirm the device has met Canada’s requirements for safety, effectiveness and quality.
TGA (Australia)	Conformity Assessment Certificate	Conformity Assessment Certificate issued by the Therapeutic Goods Administration (TGA) of Australia.
MHLW, PMDA, RCB (Japan)	Pre-market approval [document]	Pre-market approval from Japan, issued by the Ministry of Health, Labour and Welfare (MHLW), the Pharmaceutical and Medical Devices Agency (PMDA) or a Registered Certified Body (RCB).
HSA (Singapore)	Registration document	Registration indicates the device has been approved for marketing and sale in Singapore by the Health Sciences Authority (HSA).

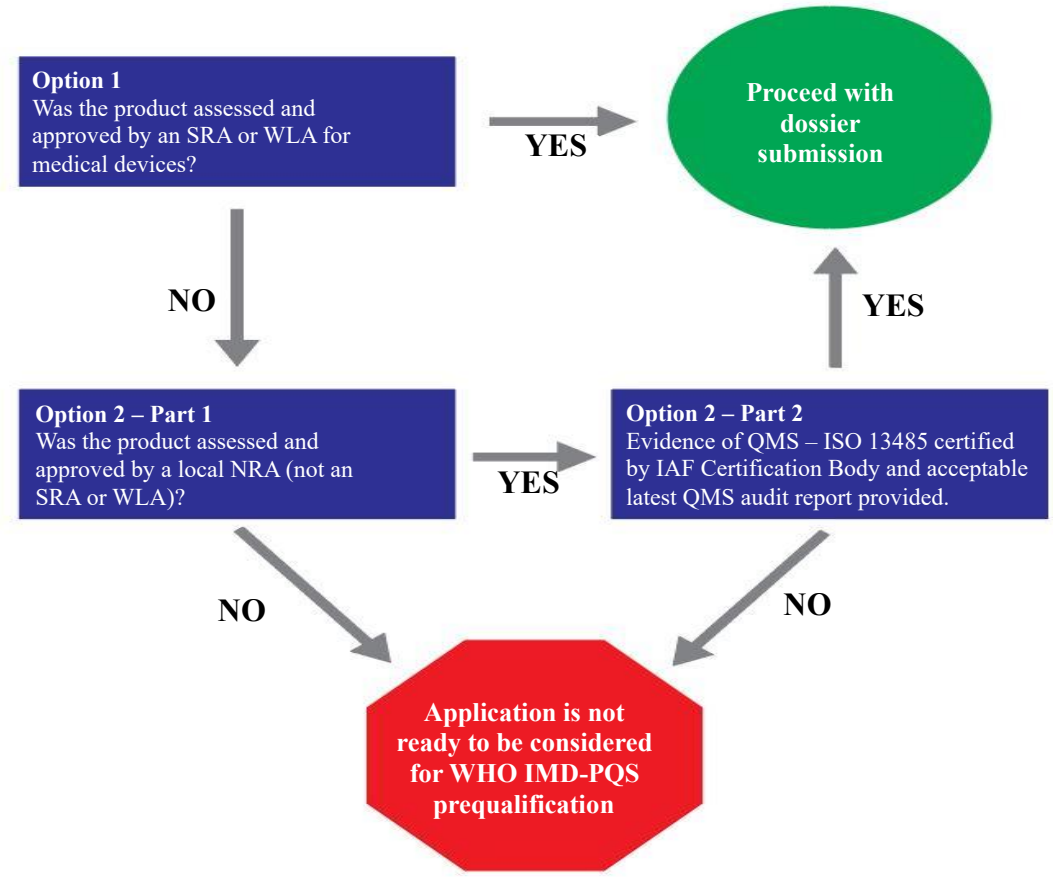
Option 2: Market authorization by a local National Regulatory Authority

If an injection device has been given market authorization or license (approval to supply) by a local National Regulatory Authority (NRA) that is not yet accepted as an SRA or WLA for medical devices by WHO, compliance will be demonstrated by

submission of all of the following:

- Proof of marketing authorization by the NRA.
- ISO 13485 certificates issued by a body that is accredited by a signatory to the Multilateral Recognition Arrangement of the International Accreditation Forum (IAF).
- A copy of the most recent audit report, issued by the manufacturer's ISO 13485 certification body. If the most recent audit report is a surveillance report, a copy of the most recent full audit report (certification or recertification audit report) should also be provided.

A process diagram of the above options can be found below.



Abbreviations: IAF, International Accreditation Forum; ISO, International Organization for Standardization; NRA, National Regulatory Authority; PQS, WHO Performance, Quality and Safety program; QMS, quality system; SRA, Stringent Regulatory Authority; WLA, WHO-Listed Authority.

5. Testing body

Testing of injection devices may be conducted by either the prequalification holder (product manufacturer or product reseller) or a third-party testing laboratory. Third-party testing laboratories are not required to have WHO accreditation, but they must provide proof of [International Electrotechnical Commission] 17025 *General requirements for the competence of testing and calibration laboratories certification.*

6. Product dossier

For a **generic list** of supporting documents required for a prequalification application refer to: *Guidelines for WHO IMD-PQS Applicants & Prequalification Holders*.

The applicant shall provide WHO with a dossier containing at a minimum the following:

- Fully completed Application Review Template[4]
- Injection device certifications/regulatory approvals (according to one of the two options outlined in Section 4.3)

For each requirement of the product defined within the ISO 7886-4:2018 and any other referenced standards there within, complete documentation to prove compliance shall be submitted. Depending on the requirement this shall include:

- Internal (manufacturer) or third-party laboratory testing reports with complete, raw data,
- Internal (manufacturer) or third-party laboratory testing protocols used to generate the testing data Risk analysis documentation (compliant with ISO 14971 *Medical devices — Application of risk management to medical devices*),
- User testing documentation,
- Equipment calibration certificates corresponding to submitted testing datasets, and/or
- Supporting rationale or justification accompanying testing data or protocols (if present).

The applicant shall also send 20 production-run products randomly selected from the validated production line packaged in unit carton and associated secondary cartons.[5]

IMPORTANT:

- A **separate dossier is required for each nominal volume of syringe**; for example, if an applicant is applying for prequalification of 0.25 mL and 0.5 mL versions of a syringe with a reuse prevention feature, two dossiers will be required.
- Additionally, if a syringe is manufactured at more than one manufacturing site, a **separate dossier will be required for each named site**.

7. Application submission

As outlined in *Guidelines for WHO IMD-PQS Applicants & Prequalification Holders*, all dossier documentation must be submitted via the WHO electronic prequalification system (ePQS). Detailed learning materials for applicants via the ePQS system are available on WHO's Prequalification of Immunization Devices website: https://extranet.who.int/prequal/key-resources/documents/epqs-learning-materials-imd-pqs-pq-holders-applicants.

4 The Application Review Template contains the comprehensive list of required documents for inclusion in a device prequalification dossier submission.
5 Products-run products do not need to be packaged in the secondary container. They can be folded up and included in the general package contents.

7.1 ePQS folder structure

Submission of an electronic dossier (not including the initial pre-submission form) shall contain the following folder/file structure unless otherwise directed:

I. Dossier submission information
   a. Pre-submission application
   b. Injection device technical specification
   c. Laboratory/Manufacturer quality certification(s)
   d. Injection device marketing approval(s) (as relevant)
II. Completed Application Review Template
III. Submission data
   a. Test reports
   b. Inspection reports
   c. User-testing reports
   d. Risk analysis
IV. Equipment calibration certificate
V. Test protocols

7.2 File naming taxonomy

All dossier documentation must adhere to specific file name conventions. Please refer to Annexes 2 through 4 in *Guidelines for WHO IMD-PQS Applicants & Prequalification Holders* for the list of required file name conventions. Applications containing documents with incorrectly named files will be returned for correction.

If possible, please use a sequential numbering system included as a preface to each file name for ease of reference.

7.3 Product samples

Packages of product samples should be clearly marked "IMMUNIZATION DEVICES PREQUALIFICATION APPLICATION" and addressed to:

Vaccines & Immunization Devices Assessment Team (VAX)
Prequalification Unit (PQT)
Regulation and Prequalification Department (RPQ)
Access to Medicines and Health Products Division (MHP)
Avenue Appia 20
World Health Organization
1211 Genève
Switzerland

8. Injection Device testing

To demonstrate compliance with ISO 7886-4:2018, technical evaluation of the injection device must be conducted according to the guidance below.

8.1 Number of samples

Demonstration of compliance with each relevant requirement shall be achieved by evaluation of no fewer than 10 samples (units) per test unless otherwise specified in one of the following:

- Elsewhere in this performance specification or the Application Review Template
- ISO test procedure
- Manufacturer sampling strategy (if present and in compliance with the ISO 2859 *Sampling procedures for inspection by attributes* specification family)

Note: Sample strategies are prioritized accordingly: 1.) This performance specification or the Application Review Template, 2.) ISO test procedure, 3.) Manufacturer sampling strategy.

8.2 Testing procedures

Testing procedures to demonstrate compliance with the requirements outlined in ISO 7886-4:2018 shall follow the relevant methods specified in the respective standards. For all relevant testing, the manufacturer shall develop and implement test methods according to their quality system and include these methods in the dossier submission for reference.

8.2.1 Usability testing

Usability testing for demonstration of compliance with relevant ISO standards may take one of two forms:

- **External usability testing:** Evaluation of injection device characteristics by representative users in a simulated use scenario to assess acceptability or functionality. (See Annex A guidance in ISO 23908:2024 for reference.)
  Note: For external usability testing, the number of users should not be less than 15 to ensure sufficiency of data[6].
- **Internal usability testing:** Evaluation of injection device characteristics by laboratory technicians (or similar) to verify specific qualities or features.

8.2.2 Visual inspection

For any visual requirements (scale markings, labelling, etc.), compliance shall be demonstrated via a first article inspection report from the production line that references all relevant requirements. While clear images of the product should still be included as supplemental references for verification, WHO will not accept images alone as sufficient proof of compliance with visual requirements.

Note: Inspection of digital graphic design files is not acceptable for demonstration of compliance.

9. Test data

9.1 Raw test data

The complete set of raw data (unaggregated or summarized) is required for demonstration of compliance with the relevant ISO requirements and must be included in each test report.

6 United States Food and Drug Administration (FDA). *Applying Human Factors and Usability Engineering to Medical Devices: Guidance for Industry and Food and Drug Administration Staff*. Silver Spring, Maryland, USA: FDA; February 3, 2016. https://www.fda.gov/media/80481/download

9.2 Qualitative requirements

For qualitative or binary requirements that cannot be addressed by quantitative testing results, compliance shall be demonstrated by reference to descriptive test results stating the resulting performance of each sample tested. Summary statements are not acceptable.

9.3 Predicate test data

All test data should be collected from the exact product being considered for prequalification. Test data from products that differ in design, nominal volume, or manufacturing location should not be included as part of the dossier unless preapproved by WHO in writing prior to dossier submission. Failure to secure pre-approval of predicate test data prior to dossier submission will result in an automatic rejection of the dossier.

10. Test report documentation

10.1 Good documentation practices

All documentation included as part of a dossier submission shall be recorded in a manner compliant with the good documentation practices outlined in ISO 13485 or comparable internal quality system policy.

10.2 Individual reporting

Test reports shall be individually saved as separate documents for ease of reference/review. Do not consolidate multiple test reports into a single document.

10.3 Report content

Unless otherwise specified by ISO test method, test result reports shall contain the following, as relevant:

- Document title, identification number and version
- ISO test reference if relevant; otherwise, document number/title of internal or external test method used
- Test sample description and preconditioning
- Test sample lot number
- Equipment identification, for reference to calibration certificate date and due date
- Raw test data
- Analysis calculations
- Comments
- Test data summary
- Requirement criteria
- Pass/fail designation
- Tester signature and date
- Reviewer signature and date

Test reports from external testing laboratories shall include evidence of ISO/IEC 17025 certification.

10.4 Calibrated equipment reference and certificates

Calibration certificates must be supplied for all calibrated test fixtures and equipment used in injection device testing. Certificates must be traceable to national or international standards, such as the National Institute of Standards and Technology or Physikalisch-Technische Bundesanstalt, and follow ISO/IEC 17025 or equivalent guidelines.

Calibration certificates should include essential details such as:

- Equipment identification (model and serial number)
- Calibration and next due dates
- Results and adjustments
- Referenced calibration standard compliant with ISO 13485 or ISO/IEC 17025
- Calibrator's name and signature
- Environmental conditions (if applicable)
- Measurement uncertainty

The frequency of calibration should be based on the equipment manufacturer's recommendations, syringe manufacturer usage and the criticality of the equipment.

10.5 Certified translation

Dossier submission shall be made in English. For any components in other languages, a certified translation shall be provided.

10.6 Images

Any photos included shall be of sufficient resolution and magnification to ensure that all text is legible and any injection device features referenced in the photo are clearly visible.

10.7 Raw data templates

All raw data results from manufacturer testing shall be recorded on controlled report templates according to the manufacturer's quality system policy.

11. Post prequalification reporting

11.1 Change notification

The applicant must advise WHO immediately in writing of any design or production changes which could potentially affect the performance, quality, or safety of the product after WHO prequalification has taken place. Any change that WHO determines may negatively impact the injection device's performance against the E013 category requirements may result in a request for the product to be retested.

IMPORTANT: A change to the manufacturing site or location automatically removes the product's prequalified status. The product must be resubmitted for evaluation and, if successfully prequalified, will receive a new IMD-PQS product code ("E013-XXX").

11.2 Defect/adverse event reporting

The applicant must advise WHO and any relevant United Nations purchasing agencies in writing in the event of any reported manufacturing defect, safety-related product recalls and reported adverse events or other similar events. If requested to do so, the manufacturer must implement a corrective and preventive action process according to ISO 13485 and submit a summary report regarding relevant findings. Reports of performance issues or failures will NOT automatically lead to the suspension of a product's prequalified status.

If the identified issue is deemed severe, a product's prequalification status may be suspended until it is resolved. Further details of this process can be found in *Guidelines for WHO IMD-PQS Applicants & Prequalification Holders*.

Annex 1 – USL/LSL determination for ISO 23908:2024 requirements

Normative reference: International Organization for Standardization (ISO) 16269-6 *Statistical Interpretation of data — Part 6: Determination of statistical tolerance intervals*

Introduction

ISO 23908:2024 *Sharps injury protection* specifies the requirements and test methods for evaluation of sharps injury protection (SIP) features. As part of the requirements, manufacturers must measure the force/torque values associated with the SIP feature performance, such as activation and unlocking, to calculate their statistical tolerance interval as per ISO 16269-6. The manufacturer must then determine the upper and lower specification limits (USL and LSL, respectively) for the performance values using a risk-based approach that includes human factors considerations and statistical methodology outlined in ISO 23908:2024: *Part 6: Test methods — 6.2 Test procedure and results analysis methodology*. The measured tolerance interval is then compared with the USL and LSL values to demonstrate that the forces/torques are appropriate for the anticipated users of the injection device.

Example for determining and applying USL and LSL values

Note: All data and calculations given in the following example are theoretical only and are not based on real data. The values given in this example cannot be used to determine the statistical tolerance, USL or LSL for any SIP syringe.

Consider a SIP syringe that is activated by the user pinching two halves of a needle cover together using the thumb and forefinger until the two halves lock in place.

Steps

1. *Determine statistical tolerance of syringe performance*
   Measurement of the activation force required on a representative number of samples gives a statistical tolerance for the activation pinch force of 3.5 ± 0.5 kgf.

2. *Determine USL and LSL values*
   Surveys of health care workers in representative health care facilities indicate that the likely users of the SIP syringe are men and women between the ages of 22 and 60 years. Consulting published data on pinch strength finds that the maximum pinch strength decreases with increasing age, with values of 8 kgf and 6 kgf for 60-year-old men and women respectively. The manufacturer determines that it is unreasonable to expect users to exert the maximum pinch strength when activating the SIP feature and that a value of 80% of the maximum is appropriate.

   Further risk analysis and testing conducted by the manufacturer indicates that users may accidentally exert a maximum force on the SIP feature of 2.5 kgf. Thus, the USL to ensure that users can activate the SIP feature is 4.8 kgf (80% of 6 kgf) and the LSL to prevent accidental activation of the SIP feature is 2.5 kgf.

3. *Analysis of compliance*
   Since the tolerance of the measured activation force falls between the LSL and USL, the activation force meets the risk-based specification limits informed by human factors.

Additional considerations

- There may be cases (depending on the mechanism of action of the SIP feature) in which either the LSL or the USL for the activation or unlocking forces/torques is not applicable, and therefore irrelevant. For example, suppose the SIP feature is designed in such a way that accidental activation during use is not possible as determined by the risk analysis. In this case, determination of an LSL for the activation force/torque is not required as there is no risk of accidentally exerting the activation force/torque during use of the syringe. If determination of either an LSL or a USL is deemed to be unnecessary, the manufacturer must provide supporting evidence and rationale as for why this is the case. When calculating the tolerance interval, the manufacturer should use the two-sided tolerance interval given by the appropriate tables in ISO 16269-6 even when only one specification limit is applicable.

- If published human factors data relevant to the activation and unlocking forces/torques is not available, the manufacturer must collect the human factors data using a representative sample of likely users. The users should include a range of characteristics that are relevant to the activation and unlocking forces/torques (e.g., age, gender, hand size). USL and LSL values must not be determined from the syringe test data used to establish the tolerance interval.

Revision history

Revision history (since 6th October, 2025 revision)			
Date	Change summary	Reason for change	Approved
Monday 6th October, 2025	Version 1	NA	PM