Test Methods for Prefilled Syringes
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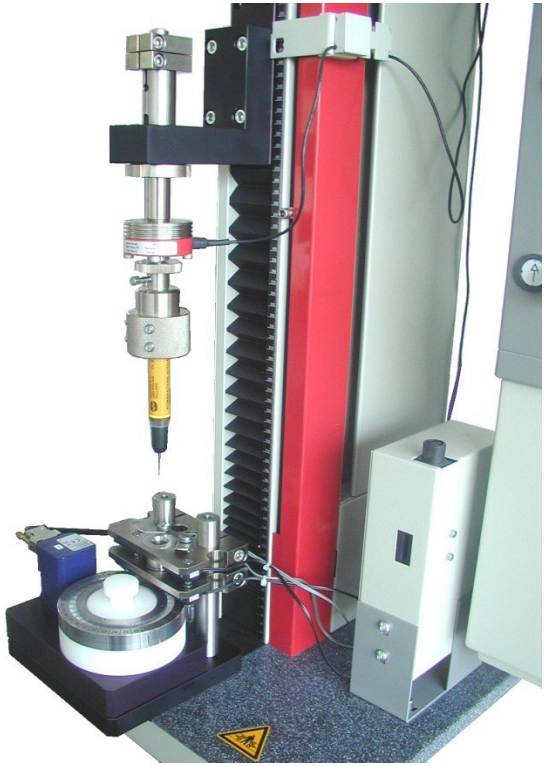
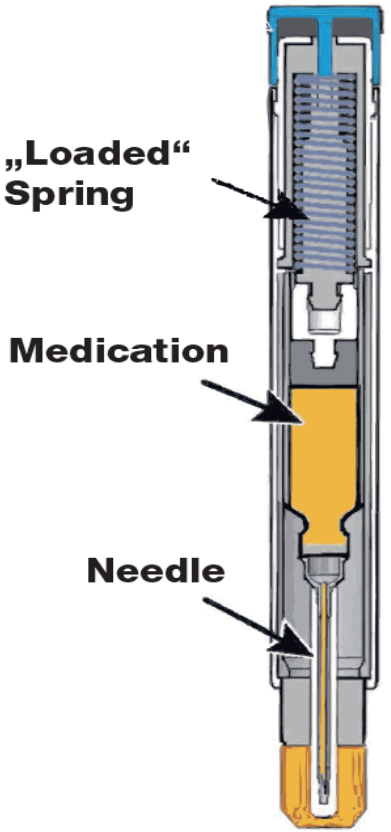
Test Methods for Prefilled Syringes

- **Requirements of the use in devices**

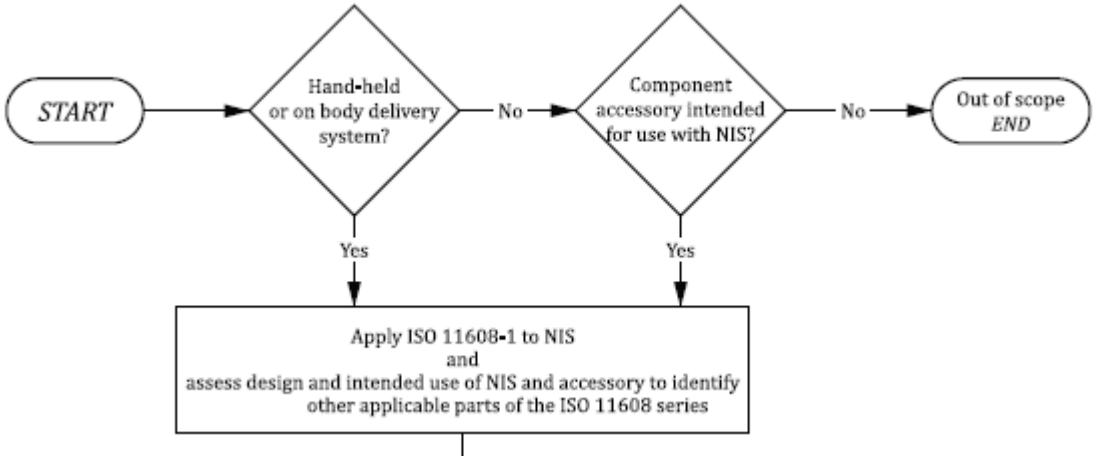


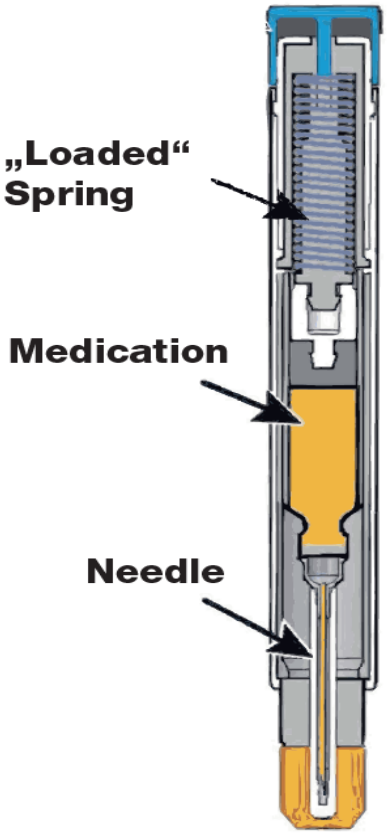
Test assembly



TM for the Use of PFS in Delivery Devices

ISO 11608-1
Needle-based injection systems for medical use - Requirements and Testmethods
Part 1: NIS (TC 84)





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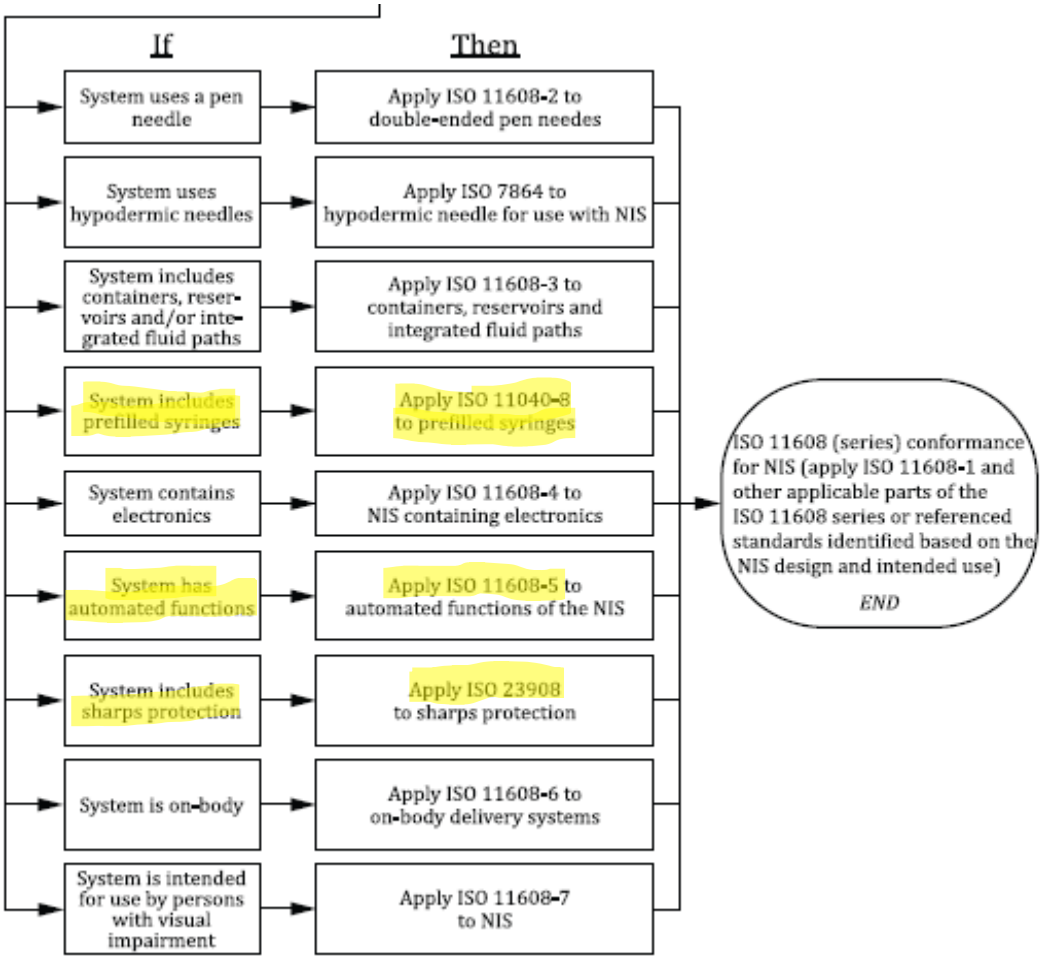
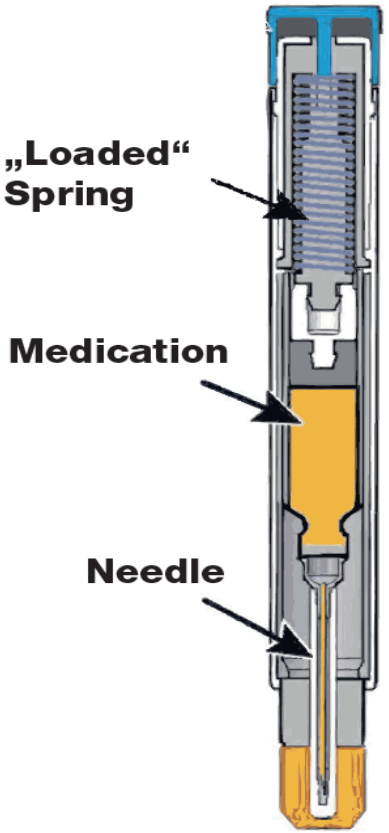


Figure 1 — ISO 11608 series road map



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Requirements and Testmethods
Part 1: NIS

Stand-alone prefilled syringes defined by ISO 11040-8 are not covered by this document (see exclusions below). However, when the prefilled syringes are provided to the user with an integrated addition, certain portions of the ISO 11608 series apply as follows:

— prefilled syringes that are provided to the user with an integrated electronic addition (e.g. electronic dose counter) are covered by relevant requirements of ISO 11608-4, but only to assess the function, feature or performance of the "addition" not the prefilled syringe;

— prefilled syringes that are provided to the user with an integrated addition that provides an automated function (e.g. an automated inserter that inserts to a predetermined insertion depth or needle safety device) are covered by relevant requirements of ISO 11608-5, but only to assess the function, feature or performance of the "addition" (as integrated into the NIS) not the prefilled syringe.

It is important to note that other functions and characteristics of the prefilled syringe, such as dose accuracy, are subject to the requirements (delivered volume) in ISO 11040-8 and not this document, unless the addition impacts the delivery function (e.g. a mechanism that intends to restrict or stop the plunger movement, which would limit the dose delivered). In that case, the system is completely covered by this document and applicable requirements of the ISO 11608 series.

Excluded from the scope are:

— stand-alone prefilled syringes defined by ISO 11040-8 (with noted exceptions above);

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ISO 11608-1
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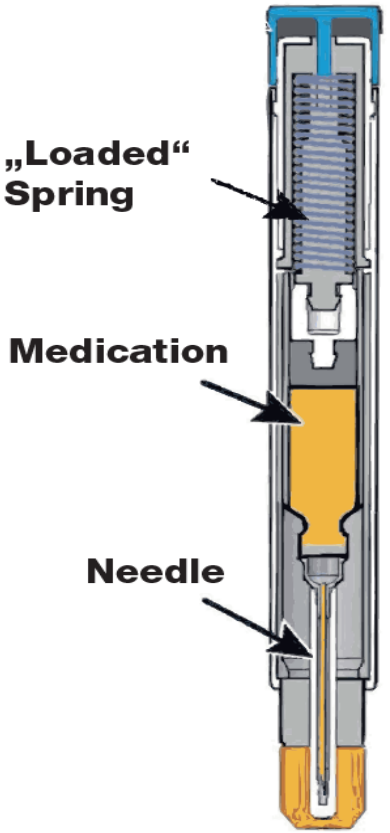
Part 1: NIS



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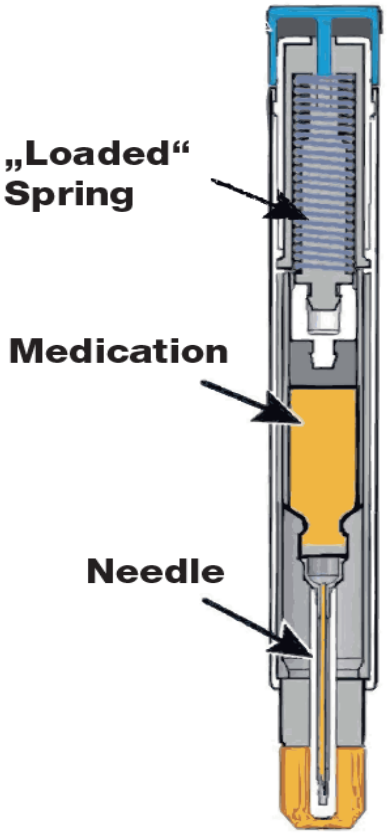
Needle-based injection systems for medical use - Requirements and Testmethods
Part 1: NIS

Table 1 — System designations

	Multi-dose container	Single-dose container
NIS with replaceable container	A Each container holds multiple doses, the size of which may be fixed or variable (set by the user)	B1 Each container holds a single dose, and the entire deliverable volume is expelled
		B2 Each container holds a single dose, and a portion of the deliverable volume is expelled
NIS with non-replaceable container which is integrated, or user assembled	C The container holds multiple doses, the size of which may be fixed or variable (set by the user)	D1 The container holds a single dose, and the entire deliverable volume is expelled
		D2 The container holds a single dose, and a portion of the deliverable volume is expelled



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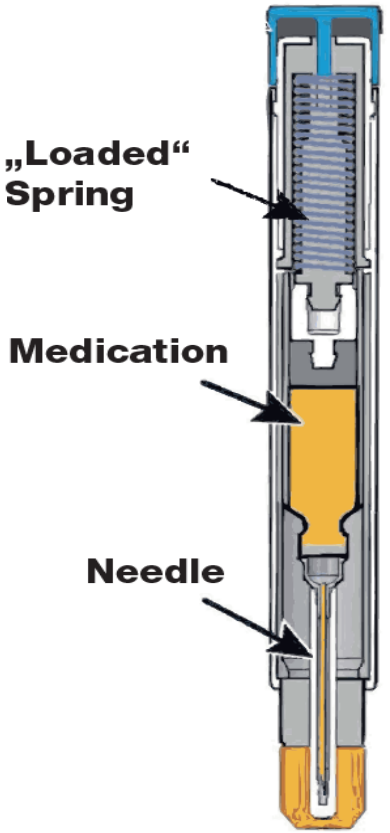
Needle-based injection systems for medical use - Requirements and Testmethods
Part 1: NIS

Table 2 — Dose accuracy assessment matrix

Dose accuracy matrix	System designation					
	A	B1	B2	C	D1	D2
Determine doses needed	7.2.3.1	7.2.3.2.1	7.2.3.2.2	7.2.3.1	7.2.3.2.1	7.2.3.2.2
Determine accuracy limits	7.4.2.1	7.4.2.2	7.4.2.1	7.4.2.1	7.4.2.2	7.4.2.1
Determine last-dose accuracy limits (variable dose only)	7.4.3	N/A	N/A	7.4.3	N/A	N/A
Calculate last-dose error (variable dose only)	7.4.3	N/A	N/A	7.4.3	N/A	N/A
Calculate dose delivery efficiency (user-filled only)	N/A	7.4.4	N/A	N/A	7.4.4	N/A
Calculate tolerance intervals	7.4.5	7.4.5	7.4.5	7.4.5	7.4.5	7.4.5

See Annex F for a detailed discussion of sampling plans for both variable and attribute data.



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ISO 11608-1
Needle-based injection systems for medical use -
Requirements and Testmethods
Part 1: NIS

Test Liquid:
The test liquid shall be either medicinal product intended to be injected by the NIS, or a liquid with physical properties that mimic the original medicinal product for the respective test

Test Surface for the free-fall testing:
Shall be a smoth, hard, rigid steel of 3mm thickness, backed by wood whose thickness is greater than 10mm

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ISO 11608-1
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Part 1: NIS

Test Case	System Designation			
	A	B	C	D
Cool, standard and warm	x	x	x	x
Last-dose accuracy	x	N/A	x	N/A
Life-cycle	x	x	N/A	N/A
Free-fall (a and b)	x	x	N/A	N/A
Free-fall (c and b)	N/A	N/A	x	x
Dry-heat	x	x	x	x
Cold-storage	x	x	x	x
Damp-heat	x	x	N/A	N/A
Cyclical	x	x	N/A	N/A
Vibration	x	x	N/A	N/A
Transport	x	x	x	x
Functional stability	x	x	x	x
Fluid leakage	x	x	N/A	N/A

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ISO 11608-1
Needle-based injection systems for medical use - Requirements and Testmethods
Part 1: NIS

Condition		**Temperature** [°C]	**Humidity** [%RH]
Atmosphere	Cool	(5 ± 3)	No humidity requirement
	Standard	(23 ± 5)	(50 ± 25)
	Warm	(40 ± 2)	(50 ± 10)
Dry-heat	Dry-heat	(70 ± 2)	(50 ± 10)
Cold-storage	Cold-storage	(-40 ± 3)	No humidity requirement
Damp-heat	Damp-heat	(40 ± 2)	(93 ± 5)

Vibration			
Conditions	Frequency Range	Displacement / Acceleration (peak value)	Number of sweeps per direction
	3 Hz to 8 Hz	7.5mm	4
	3 Hz to 300 Hz	2g	4

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ISO 11608-3
Needle-based injection systems for medical use - Requirements and Testmethods
Part 3: Containers and integrated fluid path

Not applicable for PFS
Refere to ISO 11040-8

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ISO 11608-3
Needle-based injection systems for medical use - Requirements and Testmethods
Part 3: Containers and integrated fluid path

Not applicable for PFS
Refere to ISO 11040-8

5.4 Visible particulates

Prepare a test sample by filling or flushing the reservoir and/or integrated fluid path of 10 NISs with particle-free water as defined by pharmacopeia (using the filling device and/or mechanism specified in the instructions for use) into a container rinsed with particle-free water. Prepare a control sample (using the same filling device and/or mechanism specified in the instructions for use) to expel particle-free water into an appropriately cleaned container. The test sample shall be visually inspected for the presence of visible particulates (> 150 µm in diameter) in the test sample as compared to the control.

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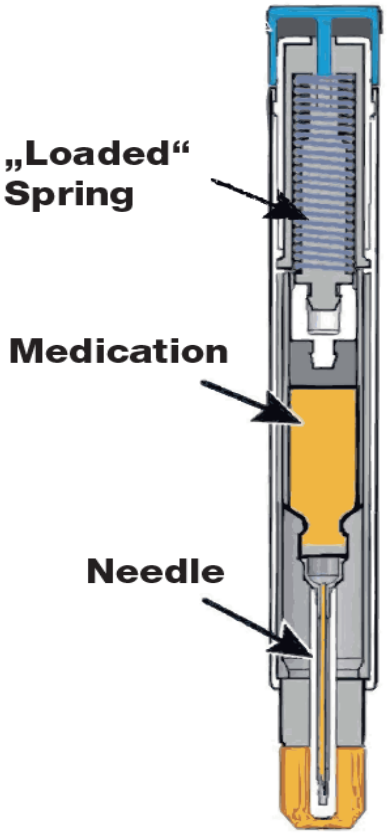
ISO 11608-5
Needle-based injection systems for medical use - Requirements and Testmethods
Part 5: Automated Functions



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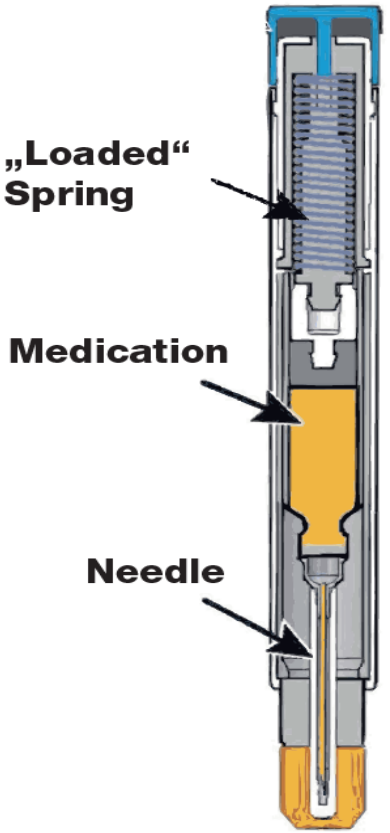
ISO 11608-5
Needle-based injection systems for medical use - Requirements and Testmethods
Part 5: Automated Functions

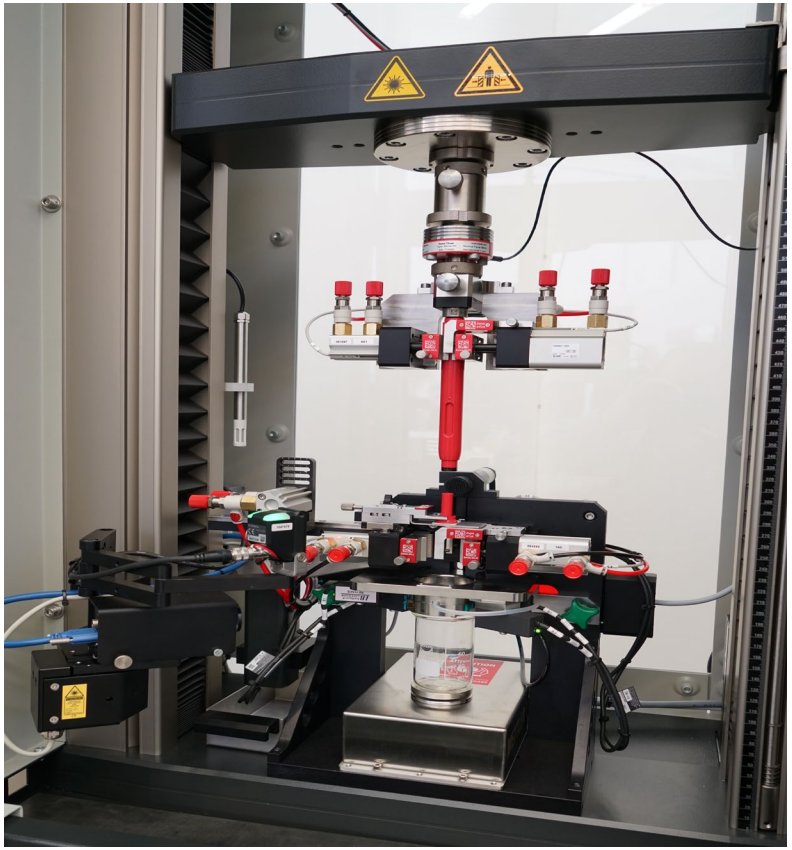


Workshop: Test Methods for Pre-filled Systems

ISO 11608-5
Needle Based Injection Systems (NIS) for medical use
Part 5: Automated functions

Customizable Testing Modules:

- Special low pressure grips
- Integrated high-precision scale
- Activation forces
- Sensor Needle length with removal last drop
- Sensor Ejection Time
- Sound detection via microphone
- Camera for needle tip/fluid stream recording



Workshop: Test Methods for Pre-filled