5511 General Chapter of Subassembled Prefilled Syringes

1 Scope

This general chapter specifies the application requirements and product quality requirements for subassembled prefilled syringes.

This general chapter applies to sterile subassembled prefilled syringes for pharmaceutical packaging that are packaged in nest tubes. Non-sterile prefilled syringes for pharmaceutical packaging can refer to this general chapter.

2 Terms and definitions

2.1 Syringe barrel

Cylindrical glass or plastic body with front end (Luer conical fitting or staked needle) and finger flange as back end.

2.2 Syringe barrel with staked needle

Barrel with a staked needle front end. The needle can be fixed by inserting molding, gluing, or other bonding methods.

2.3 Syringe barrel with Luer conical fitting

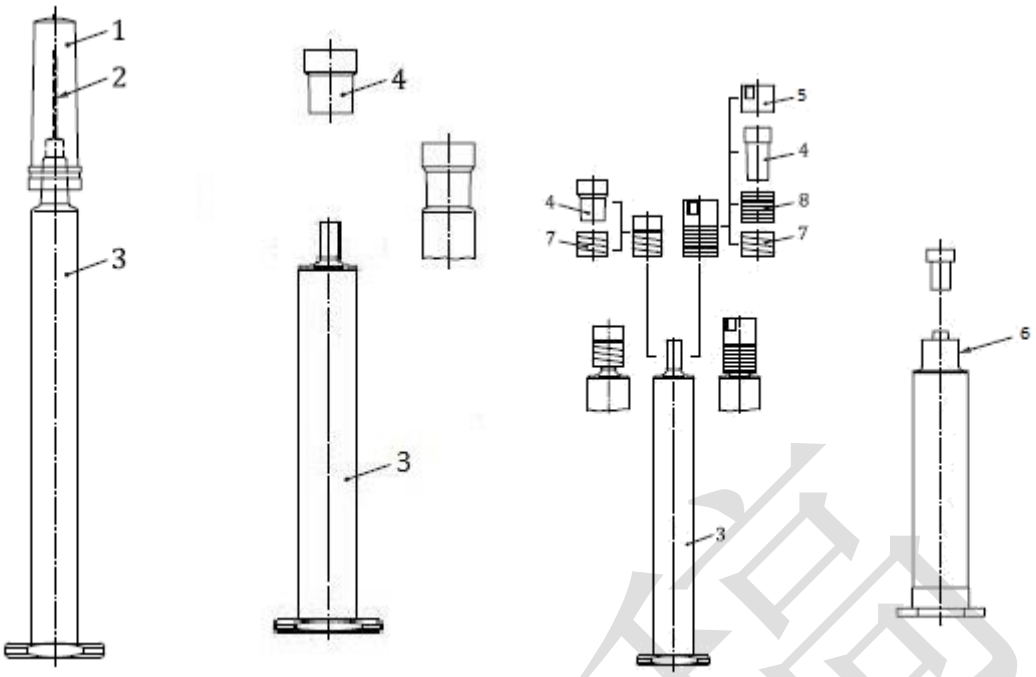
Barrel with a Luer conical fitting front end.

2.4 Tip cap/needle shield

Component or multi-component systems designed to close the syringe system at the front end that is designed to allow the sterilization of cone or staked needle and maintain sterility of the contents of the syringe up to the time of injection, such as tip cap, needle shield. According to the connection type with the barrel, it can be divided into locked tip cap/needle shield and unlocked tip cap/needle shield.

2.5 Subassembled prefilled syringes

Packaging components that have been sterilized, consisting of a barrel and a tip cap/needle shield. Examples of subassembled prefilled syringes are illustrated in Figure 1.



a) Syringe with staked needle **b) Syringe with Luer cone** **c) Syringe with Luer lock cone and Luer lock adaptor** **d) Syringe with integrated Luer lock**

Key

1	needle shield	5	protective tamper-evident cap
2	needle	6	integrated Luer lock
3	syringe barrel	7[1]	Luer lock adaptor
4	tip cap	8[1]	semi-rigid sleeve

Notes 1: 7 and 8 are usually integrated, that is, Luer lock adaptor collar.

Fig.1 Examples of subassembled prefilled syringes

3 Classification

Subassembled prefilled syringes are mainly classified according to the material of the barrel and the form of the front end.

3.1 Classification according to syringe barrel material

In terms of syringe barrel material, it is classified as glass subassembled prefilled syringes and plastic subassembled prefilled syringes. The glass barrel is mainly made of borosilicate glass, and the common plastic barrel materials are cyclic olefin (e.g. cyclopentene, norbornene) polymer (COP), cyclic olefin (e.g. cyclopentene, norbornene) and olefins (e.g. ethylene or propylene) copolymer (COC) and polypropylene (PP).

3.2 Classification according to the form of the front end of the syringe

In terms of the form of the front end of the syringe, it is classified as subassembled prefilled syringes with staked needle and subassembled prefilled syringes without staked needles. In addition, subassembled prefilled syringes without staked needle can

be classified as subassembled prefilled syringes with Luer cone and subassembled prefilled syringes with Luer lock cone according to Luer cone type at the front end.

4 Requirements

4.1 Production requirements

The production of subassembled prefilled syringes shall comply with relevant good manufacturing practices to ensure that the products meet the requirements for pharmaceutical use.

4.1.1 If it is necessary to spray silicone oil on the inner surfaces of the syringe barrel to improve gliding properties, the silicone oil shall comply with the requirements for pharmaceutical use.

4.1.2 For subassembled prefilled syringes with staked needle, if it is necessary to treat the needle surface with a lubricant (e.g., silicone oil), the silicone oil shall meet the requirements for pharmaceutical use. At the same time, the needle penetration force shall be comprehensively evaluated through risk assessment and clinical use.

4.1.3 For plastic subassembled prefilled syringes, special focus shall be given to the impact of the sterilization process on the colour and transparency of the syringe barrel.

4.1.4 If the syringe barrel is sprayed with graduation markings or indicator lines, the accuracy verification shall be carried out.

4.1.5 Sterilization shall be carried out using a suitable validated method to a Sterility Assurance Level of 10^{-6}.

4.1.6 The packaging system for subassembled prefilled syringes shall ensure product sterility over its shelf-life. It is necessary to consider the compatibility between the size of the nest tub and the filling equipment of the drug manufacturer.

4.1.7 The protective bag can protect the product from external contamination like dust or dirt. If it is claimed that the protective bag can maintain the sterility of the product over its shelf-life, its sterility retention capacity shall be evaluated.

4.2 Biological evaluation

The biological safety of subassembled prefilled syringes shall be evaluated according to the Guideline on Biological Evaluation and Test Selection of Pharmaceutical Packaging Materials and Containers (Guideline 9651).

4.3 Component and material requirements

4.3.1 Tip cap/needle shield

The tip cap/needle shield shall comply with Section 5 of General Chapter of Rubber Closures for Pharmaceutical Packages (General Chapter 5200).

4.3.2 Stainless steel needle

The stainless steel needle shall comply with General Chapter on Metal Containers and Components for Pharmaceutical Packaging (General Chapter 5400). The stiffness, resistance to breakage, and resistance to corrosion of the stainless-steel needle shall be evaluated.

4.3.3 Syringe barrel

The glass barrel shall comply with General Chapter on Glass Barrel for Prefilled Syringes (General Chapter 5104).

The plastic barrel shall comply with Section 5 of General Chapter of Plastic Containers and Components for Pharmaceutical Packaging (General Chapter 5300).

5 Product quality control

With the purpose of ensuring the controllable quality of drugs, meeting clinical needs and safety in use, manufacturers and users of the subassembled prefilled syringes shall choose appropriate quality control items according to the real situation of production and use, and develop the enterprise specification or quality agreements. In addition to meeting the requirements for components and materials in 4.3, the subassembled prefilled syringes shall also meet the following requirements.

5.1 Appearance

It is used to evaluate the appearance quality of the product. In bright natural light, visually inspect the appearance of the product in front of the eye, the result shall comply with the enterprise specification or quality agreements.

5.2 Luer conical fitting

It is used to evaluate the adaptability and clinical safety of the Luer conical fitting for subassembled prefilled syringes without staked needle.

5.2.1 General Requirements

Test according to the Examination Method of Luer Conical Fitting of Prefilled Syringes (General Chapter 4040), and the result shall comply with the requirements.

5.2.2 Luer lock adaptor collar pull-off force

It is used to evaluate the connection strength of the non-integrity Luer lock adaptor collar. Test according to the Determination of Performance for Luer Lock Adaptor Collar of Prefilled Syringes (General Chapter 4043 method 2), the adaptor collar shall withstand a pull-off force of at least 22N to avoid detachment from the syringe barrel.

5.2.3 Luer lock adapter collar torque resistance

It is used to evaluate the torque resistance of the non-integrity Luer lock adaptor collar. Test according to the Determination of Performance for Luer Lock Adaptor Collar of Prefilled Syringes (General Chapter 4043 method 1), the result shall comply with the enterprise specification or quality agreements.

5.3 Needle

It is used to evaluate the clinical safety and related performances of the needle for subassembled prefilled syringes with staked needle.

5.3.1 Bonding strength

Fix the syringe barrel, conduct a non-impact pull test on the needle in the direction of needle extraction under a load of 22N, the needle and the syringe barrel shall not be loose or detached.

5.3.2 Needle lumen patency

Evaluate according to one of the following methods, and the needle lumen shall be patency.

a) A stainless steel stylet of the appropriate diameter selected from the diameters given in Table 1 shall pass through the needle;

b) The flow rate of water through the needle shall not be less than 80% of the standard needle of equivalent out diameter and length having a minimum inner diameter

given in Table 2, when tested under the same water pressure of no more than 100kPa.

Table 1 Diameter of stylet

Unit: mm

Designated metric size of needle	Outer diameter of stylet $^{0}_{0.01}$	
	for needle of regular walled tubing	for needle of thin-walled tubing
0.30	0.11	0.13
0.33	0.11	0.15
0.36	0.11	0.15
0.40	0.15	0.19
0.45	0.18	0.23
0.50	0.18	0.23

Table 2 Size of standard needle

Unit: mm

Designated metric size (Gauge)	Outer diameter		Minimum Inner Diameter	
	minimum	maximum	regular wall	thin wall
0.30（30G）	0.298	0.320	0.133	0.165
0.33（29G）	0.324	0.351	0.133	0.190
0.36（28G）	0.349	0.370	0.133	0.190
0.40（27G）	0.400	0.420	0.184	0.241
0.45（26G）	0.440	0.470	0.232	0.292
0.50（25G）	0.500	0.530	0.232	0.292

5.4 Tip cap/needle shield

5.4.1 Sealability between tip cap/needle shield and barrel

Test according to the Examination Method of Sealability for Components of Prefilled Syringes (General Chapter 4041 method 1), the caps are not falling off and no droplets are visible around the external surfaces of the tip cap/needle shield.

5.4.2 Pull-off force

It is used to evaluate the compatibility between the unlocked protective cap and barrel. Test according to the Determination of Opening Performance for Tip Cap/Needle Shield of Prefilled Syringes (General Chapter 4042 method 1), and the result shall comply with the enterprise specification or quality agreements.

5.4.3 Luer lock semi-rigid tip cap unscrewing torque

It is used to evaluate the compatibility between the Luer lock tip cap and barrel. Test according to the Determination of Opening Performance for Tip Cap/Needle Shield of Prefilled Syringes (General Chapter 4042 method 2), and the result shall comply with the enterprise specification or quality agreements.

5.5 Silicone oil content

It is used to evaluate the amount of silicone oil sprayed on the inner surface of the

syringe barrel. Test according to the Determination of Silicone Oil Content for Prefilled Syringes (General Chapter 4227), and the result shall comply with the enterprise specification or quality agreements.

5.6 Particulate matter

Test according to the Determination of Particulate Matter for Pharmaceutical Packaging Materials and Containers (General Chapter 4206), and the result shall comply with the enterprise specification or quality agreements.

5.7 Residual ethylene oxide

It is used to evaluate the amount of residual sterilant in products sterilized with ethylene oxide. If ethylene oxide is used for sterilization, it is necessary to consider the risks that ethylene oxide poses to patients and its impact on drugs. Test according to the Determination of Ethylene Oxide for Pharmaceutical Packaging Materials and Containers (General Chapter 4209), and the residual amount of ethylene oxide in each sample shall be less than 5μg.

5.8 Bacterial endotoxin

Prepare the test solution based on the container type specified in the Guideline for Bacterial Endotoxin Test (Guideline 9251) using plunger stoppers that are free of bacterial endotoxin or specified in the enterprise specification or quality agreements. Then test according to the Test for Bacterial Endotoxin (General Chapter 1143), and the result shall comply with the enterprise specification or quality agreements.

5.9 Sterility

Test according to the Guideline for Microbial Testing of Pharmaceutical Packaging Materials and Containers (Guidelines 9653), and shall be sterile.

5.10 Residual tungsten (if applicable).

It is used to evaluate the extractable tungsten for glass prefilled syringes. Test according to the Determination of Extractable Tungsten for Prefilled Syringes (General Chapter 4226), and the result shall comply with the enterprise specification or quality agreements.

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