Product Description: West Global Specification for Gold/Clear Lacquered Aluminum Caps **with Liner for Pen-injector, China**

Control ID: **MSPEC: WPSCH-0013** Rev.: 12

1 Scope

1.1 This Global Master Specification provides product acceptance criteria for the physical, microbiological and packaging properties of aluminum caps with liners for pen-injectors. The product consists either of halobutyl and synthetic polyisoprene dual rubber liner, or of a halobutyl rubber monolayer rubber liner and aluminum cap for Gold/Clear Lacquered Aluminum Caps with Liners for Pen-injectors supplied for the China Market.

1.2 The specification applies to non-sterile and sterile components. Products are listed in VAL: E.00047.

1.3 The process operates under applicable cGMPs.

1.4 All tests in this Master Specification are required for releasing product to China Market, as applicable.

2 Reference Documents: (Current Versions)

2.1 Policy on Customer Notification of Process/Material Changes

A copy may be obtained on West's website, www.westpharma.com; (Support/Quality Assurance Support/Global Change Policy)

2.2 ESOP-8105: Change Control

2.3 EPD-7001: Testing and Release Policy – China Market

2.4 EPD-7002: Product Grouping for Chinese Pharmacopeia and YBB methods

2.5 EPD -7003: Fragmentation Testing of Stoppers and Liners for Pen-Injectors (in accordance with YBB/ChP as applicable)

2.6 EPD-7005: Sample size for testing under MSPEC-0004, MSPEC-0013, MSPEC-0015, MSPEC-0016, MSPEC-0018, MSPEC-0021 and MSPEC-0024

2.7 EPD-7008 Justification for Compendial Test Methods

2.8 ESOP-3133: YBB Stability Studies for China

2.9 YBB00142004-2015: Aluminum Caps for Pen-injectors

2.10 YBB00152004-2015: Chlorobutyl Rubber Plungers and Liners for Pen-injectors

2.11 YBB00162004-2015: Bromobutyl Rubber Plungers and Liners for Pen-injectors

2.12 Chinese Pharmacopeia (2020 Edition): 4002 Test for Infrared Spectrum of Packaging Materials

2.13 YBB00262005-2015: Determination of Ash for Rubber

2.14 YBB00302004-2015: Determination of Volatile Sulfides

2.15 Chinese Pharmacopoeia (2020 Edition), Vol. IV General Rule 0401, 0631, 0821, 0901, 0902

2.16 YBB00022003-2015: Test for Pyrogen

2.17 Chinese Pharmacopeia (2020 Edition): 4013 Test for Hemolysis of Packaging Materials

2.18 Chinese Pharmacopeia (2020 Edition): 4011Test for Acute Systematic Toxicity of Packaging Materials

2.19 Inspection requirements: AQL GB/T 2828.1-2012

2.20 Chinese Pharmacopeia (2020 Edition): 1143 Method for Bacterial Endotoxin Test in accordance with harmonized BIO-22: Quantification of Endotoxins on Elastomeric Closures and Westar Lined Seal.

2.21 MSPEC: WPSCH_INS-0013: Justification Document – Specification for Gold/Clear Lacquered Aluminum Caps with Liner for Pen-injector.

2.22 WPSCH_ATT-0013: Attachment Document – Specification for Gold/Clear Lacquered Aluminum Caps with Liner for Pen-injector.

3 Specification Table

	Test	Acceptance Criteria
National Medical Products Administration (NMPA)	**Aluminium Caps**	
	Visual Inspection and Dimension	
	Appearance (YBB) [1]	Complies (see 4.1.1.1)
	Appearance [7]	Complies (see 4.1.1.2)
	Physical Properties	
	Compatibility	Whole assembly should be compatible
	Resistance to sterilization	No cracks or deformation
	Durability of Coating	No damages
	Liner retention force	Not less than 1.0 N
	Rubber Liners	
	Visual Inspection and Dimensions	
	Appearance (YBB) [2]	Complies (see 4.2.1.1)
	Appearance [7]	Complies (see 4.2.1.2)
	Dimensions (YBB) [2]	Complies (see 4.5)
	Dimensions [7]	Complies (see 4.5)
	Functional Tests	
	Fragmentation[4]	NMT 3 fragments
	Leakage [4]	No leakage is observed
	Biological Tests	
	Pyrogen [3]	No pyrogenic response is observed
	Hemolysis [3]	< 5%
	Acute systemic toxicity test [3]	No acute systemic toxic response is observed
	Chemical Tests	
	Identification [3]	(i)Positive for $AGNO_3$ Test[8] (ii)Comply to Reference Spectrum
	Clarity and Color	Clarity: Intensity ≤Number 2 turbidity standard solution Color: Intensity ≤Number 5 yellow green standard solution.
	Volatile Sulfides [3]	NMT 50 µg Na_2S/20 cm^2

Product Description: West Global Specification for Gold/Clear Lacquered Aluminum Caps **with Liner for Pen-injector, China**

Control ID: **MSPEC: WPSCH-0013** Rev.: 12

	Ash	≤ 50%
	pH Change [4]	NMT 1.0
	Absorbance (wavelength 220 to 360nm)	NMT 0.1 AU
	Oxidizable Substance	NMT 3.0 mL of 0.01 M $Na_2S_2O_3$
	Non-volatile Matter	NMT 4.0 mg
	Heavy Metals	NMT 1 ppm
	Extractable Ammonium	NMT 0.0002%
	Extractable Zinc	NMT 0.0003%
	Conductivity [4]	NMT 40.0 µS/cm
	Tests for Ready to Use (RU) products	
	Bacterial Endotoxin [5]	≤ 1 EU/Piece (BIO-22)
	F_0 Lethality[6]	≥ 35.0 (minutes)

Notes:

[1] For product registration and stability testing, appearance and dimensions are performed according to YBB00142004-2015 for aluminum caps.

[2] For product registration and stability testing, appearance and dimensions are performed according to YBB00152004-2015 or YBB00162004-2015 for liners.

[3] Tests performed for product registration only. Not required for release testing except in events as described in EPD -7001

[4] Not required for standard washed product. Tests are for pharmaceutical-washed products only and not for soft/purified water-rinsed products that have not undergone pharmaceutical washing. For West Standard items, the final washing is done by the customer.

[5] Applies to Ready to Use (RU) components only. The result will be extracted from release batch testing by the method BIO-22: Quantification of Endotoxins on Elastomeric Closures and Westar Lined Seal.

[6] Applies to Ready to Use (RU) steam sterilized components only. Sterilization achievement will be determined using the parametric review of critical process parameters and achieved F_0 Lethality during the autoclave cycle.

[7] For release testing, appearance and dimension checks are done according to West's procedures and inspection plan as stated in MSPEC: WPSCH_INS-0013.

[8] This test is not required for Non-halogenated Butyl Rubber products.

4 NMPA Test Methods

4.1 Aluminum Caps

4.1.1 Appearance

4.1.1.1 Product Registration

Take sufficient samples and inspect visually under natural light. The samples should be clean with no residual lubricant, burr, damage. The Acceptable Quality Limits (AQL) according to paragraph 4.4 The Aluminum Cap should comply with the requirement.

4.1.1.2 Routine Release

Take sufficient samples and visually inspect these samples according to West's procedures and inspection as stated in MSPEC: WPSCH_INS-0013.

4.1.2 Compatibility

Collect sufficient samples, fix onto suitable pre-filled borosilicate pen-injectors and crimp. The assembly should be compatible.

4.1.3 Resistance to Sterilization

Collect sufficient samples, crimp and autoclave at 130±2°C for 30 minutes. The surface should be free of cracks and deformation.

4.1.4 Durability of Coating

This test is applicable to aluminium caps with a lacquered surface. Collect sufficient samples and autoclave at 130±2°C for 30 minutes. Remove the rubber liner, rub the surface for 30 seconds with a cotton swab soaked in 80% ethanol followed by a cotton swab soaked in 70% isopropanol for 30 seconds. The surface should be free of damages.

4.1.5 Liner Retention Force

Collect sufficient samples, place the samples facing up on the instrument. Using a metal rod with a diameter smaller than the target ring, exert force on the liner at a rate of 10±2 mm/min. Record the force when the liner starts to dislodge in the aluminum cap.

4.2 Rubber Liners

4.2.1 Appearance

4.2.1.1 Product Registration

Take sufficient samples and inspect visually under natural light. Surface color should be even, there shall be no stain, contamination (≥0.2 mm2), bubbles, cracks lines, rough, glue silk, rubber scraps, sponge-like and burrs as listed in the Acceptable Quality Limits (AQL) according to paragraph 4.4. The rubber liner should comply with the requirement

4.2.1.2 Routine Release

Collect several samples and visually inspect these samples according to West's procedures and inspection as stated in MSPEC: WPSCH_INS-0013.

4.2.2 Identification

4.2.2.1 Silver Nitrate Method

This method is applicable to both monolayer and bilayer products. For bilayer products, separate the two layers and test the product contact side only. Cut sufficient samples into small pieces. Weigh 2.0 g and place in a crucible, add 2.0 g of sodium bicarbonate and cover with a lid. Heat gently in an electric burner until the sample is thoroughly charred. Allow to cool, place in a high temperature furnace and heat at 300°C until completely reduced to ash. Allow to cool, add approximately 10 mL of water, dissolve and filter. In a test tube, place 1.5 mL of filtrate, acidify with nitric acid and a silver nitrate solution dropwise until a precipitate is formed. A pale yellow (bromobutyl) or white (chlorobutyl) precipitate should appear.

4.2.2.2 Infrared Spectrum Method

This method is applicable to both monolayer and bilayer products. For bilayer products, separate the two layers and test each layer individually as per Chinese Pharmacopoeia 2020 Edition 4002 Test for Infrared Spectrum of
Packaging Materials, ATR Method. The spectrum should comply with the reference spectrum provided in Appendix 1.
West is using a Diamond ATR Crystal instead of Zinc Selenide.

4.2.3 Fragmentation

The test is carried out in accordance with EPD-7003. Take 50 samples, add water corresponding to two times the surface area of the 50 samples and boil for 5 minutes. Rinse 5 times, each time using the same amount of water. Transfer the washed samples to a conical flask, add the same amount of water, cover with a piece of aluminum or borosilicate glass beaker and autoclave by raising the temperature to 121±2°C over 30 minutes. Maintain the temperature for another 30 minutes. Then cool to room temperature. Transfer the autoclaved samples into a suitable glass bottle, seal and dry at 60°C for 60 minutes.

Half-fill 50 pen-injectors fitted with plungers with water, assemble the rubber liners (with the non-drug surface facing up) and aluminum caps onto the pen-injectors. Rest the pen-injector on a stable flat surface during the test, fill a syringe with water, then fit with a sterile hypodermic needle of external diameter 0.4 mm and bevel angle (refer to Diagram 1 and Table 1). Ensure the tip of the needle is free of water. Pierce the rubber liner in an upright position and inject 1 mL of water, clean the needle with acetone or MIBK after every pierce. Change a new needle after every 20 pierces. Remove the aluminum caps after the test is completed and filter the content of the 50 pen-injectors using one filter paper, ensure no fragments are left behind in the pen-injectors. Inspect the filter paper at a distance of 25 cm and record the number of fragments. The total number of fragments for 50 samples should not be more than 3.

Diagram 1: Bevel Angle (unit: mm)

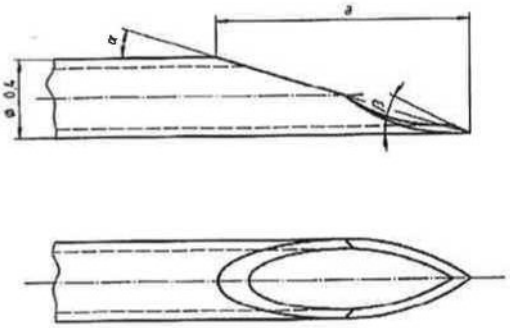


Table 1: Bevel Angle (with reference to Diagram 1)

	a, mm		α	β
Bevel type M (Medium)	Min.	Max.	Normal	
	1.35	1.55	15°30'	26°±1°

4.2.4 **Leakage Test**

The samples shall be autoclaved prior to assembly into the cartridge by raising the temperature to 121±2°C over 30 minutes. Maintain the temperature for another 30 minutes. Then, cool to room temperature in 20-30 minutes. Fill 10 cartridges (with silicone oil-treated inner surfaces) with water. Fit the cartridges with plungers and seal with the rubber liners and aluminum caps. Mount the first cartridge in the cartridge clamp (with flat surface in direct contact with the plunger) and apply a force F, where F = 0.64 N/mm^2 x d_2^2 (d_2 is the inner diameter, expressed in millimeter (mm) of the glass cylinder & 0.64 is a correction factor), to the plunger for 1 minute. After this time interval, check for leakage at the plunger and rubber liner. Repeat above procedure for remaining cartridges. There should be no leakages on either end.

4.2.5 **Ash Content**

Separate the two layers，weigh 1.0 g of each layer and test as per YBB00262005-2015 "Determination of Ash for Rubber", the mass of the residue for each layer should meet the applicable product ash limit in the Specification Table.

4.2.6 **Volatile Sulfides**

Use samples corresponding to 20±2 cm^2, cut the sample if necessary. Test as per YBB00302004-2015 "Determination of Volatile Sulfides". The test results obtained should comply with the outlined requirements.

4.2.7 **Chemical Characteristics**

Test solution: Place uncut samples corresponding to a surface area of about 200 cm^2 into a beaker. Add water corresponding to a ratio of 1:2 (Surface Area: Water) and boil for 5 minutes.

Rinse 5 times, each time using the same amount of water. Transfer the washed samples to a conical flask, add the same amount of water and autoclave by raising the temperature to 121±2°C over 30 minutes. Maintain the temperature for another 30 minutes. Then, cool to room temperature in 20-30 minutes. Separate the closures to obtain the extract.

Blank: Prepare a blank in same manner. Carry out the following tests:

4.2.7.1 **Clarity and Color**

Obtain 10 mL of test solution, test as per (Chinese Pharmacopoeia 2020, Vol. IV General Rule 0902, 0901), the test solution should be clear and colorless. If it appears turbid, compare with No.2 turbidity reference solution, the solution should not be more turbid than the reference. If it appears colored, compare with Yellow-Green No. 5 standard solution, the color of the test solution should not be more intense than the reference.

4.2.7.2 **pH Change**

Obtain 20 mL of test solution and blank solution. Add 1 mL of potassium chloride solution (1→1000) to each and test as per (Chinese Pharmacopoeia 2020, Vol. IV General Rule 0631). The pH difference between the two should not exceed 1.0.

4.2.7.3 **UV Absorbance**

Obtain sufficient test solution, using the blank solution as reference, test as per (Chinese Pharmacopoeia 2020, Vol. IV General Rule 0401). Measure the absorbance at wavelength of 220-360 nm, the greatest absorbance should not exceed 0.1.

4.2.7.4 **Oxidizable Substances**

Add 20.0 mL of 0.002 mol/L potassium permanganate and 2 mL dilute sulfuric acid to 20.0 mL test solution. Boil for 3 minutes and cool rapidly. Add 0.1 g potassium iodide and leave in the dark for 5 minutes. Titrate with 0.01 mol/L sodium thiosulfate solution until light brown. Add 5 drops of starch indicator solution and titrate until colorless. Carry out a titration using the blank. The titration volume difference between the two should not exceed 3.0 mL.

4.2.7.5 **Non-volatile Matter**

Measure 100 mL of test solution and place in an evaporating dish weighed to constant mass. Evaporate to dryness by placing the samples in an oven at 105 °C for 16 hours. Repeat for 100 mL of blank solution. The weight difference between the two should not exceed 4.0 mg.

4.2.7.6 **Heavy Metals**

Add 2 mL of acetate buffer solution (pH 3.5) to 10 mL of test solution and test as per (Chinese Pharmacopoeia 2020, Vol. IV General Rule 0821, Method One). The heavy metal level should not exceed 1 ppm.

4.2.7.7 **Extractable Ammonium**

Add 2 mL of Nessler's reagent to 10 mL of test solution and allow to stand for 15 minutes. The sample solution should remain colorless. If color appears, prepare a reference solution by adding 2.0 mL of ammonium chloride solution (dissolve 31.5 mg of ammonium chloride with ammonium-free water and dilute to 1000.0 mL) to

8 mL of blank and 2 mL of Nessler's reagent. The test solution shall not be darker than the reference (0.0002%).

4.2.7.8 Extractable Zinc

Filter the test solution through a 0.45 µm filter. Collect 10 mL of filtrate and add 1 mL of 2 mol/L hydrochloric acid and 3 drops of freshly prepared potassium hexacyanoferrate solution (dissolve 4.2 g of potassium hexacyanoferrate trihydrate in water and dilute to 100 mL). The solution should be freshly prepared. The sample solution should remain colorless. If color appears, prepare a reference by adding 3.0 mL of zinc standard solution (dissolve 44.0 mg of zinc sulfate heptahydrate in cooled freshly boiled water and dilute to 1000.0 mL, the solution should be freshly prepared), 7 mL of blank solution, 1 mL of 2 mol/L hydrochloric acid, and 3 drops of potassium hexacyanoferrate. The test solution should not be darker than the reference (0.0003%).

4.2.7.9 Conductivity

Perform the test within 5 hours of test solution preparation: The conductivity of the blank solution should not exceed 3.0 µS/cm at 20±1°C . The conductivity of the sample should not exceed 40.0 µS/cm at 20±1℃, adjustments should be made if the measurement is not done under conditions of 20±1°C .

4.2.8 Biological Tests

4.2.8.1 Pyrogen

Take sufficient samples, add sodium chloride injection in the ratio of 0.2 g/mL and place it in autoclave oven at 115±2°C for 30 minutes, test the extraction solution as per YBB00022003-2015 "Test of Pyrogen." The result should comply with the stated requirements.

4.2.8.2 Hemolysis

Take sufficient samples and test as per Chinese Pharmacopoeia 2020 Edition 4013 Test for Hemolysis of Packaging Materials. The results should comply with the stated requirements.

4.2.8.3 Acute Systemic Toxicity

Take sufficient samples, add sodium chloride injection in the ratio of 0.2 g/mL and place it in an autoclave oven at 115±2°C for 30 minutes. Test the extraction solution as per Chinese Pharmacopoeia 2020 Edition 4011 Test for Acute Systematic Toxicity of Packaging Materials. The result should comply with the stated requirements.

4.3 Microbiological Tests

4.3.1 Bacterial Endotoxin*

Transfer 10 aluminum caps with rubber liner to a depyrogenated flask. Add LAL reagent water with Tween 80 and shake at approximately 350 RPM for 1 hour at room temperature. A fixed volume of resulting solution is tested in duplicate. Test sample preparation as per US

Pharmacopoeia: <85>Bacterial Endotoxins, European Pharmacopoeia 2.6.14 Bacterial Endotoxins and Chinese Pharmacopoeia (2020 Edition) : 1143 Method for Bacterial Endotoxin Test.

The specification as per globally aligned BIO-22 Test Method is ≤ 1 EU/Piece.

4.3.2 **Biological Indicators**[+]

Use standard biological indicators (BI). This method is applicable for qualification production sterilization cycles. Following sterilization, the biological indicators are removed from the sterilizer load and forwarded to the lab for testing. Under appropriate environmental conditions, each BI is transferred to a Tryptic Soy Broth (TSB) jar. A positive and negative control is tested per autoclave cycle. Samples are incubated and monitored: BI's not less than 7 days at 55-60°C.

Results are reported as follows:
N = No Growth
P = Growth

For results to be valid, the positive control must show growth.
All biological indicators subjected to the sterilization cycle should not have any growth. The specification is 0 positive.
The sterilization achievement for release testing will be determined using the parametric review of critical process parameters and achieved F_0 Lethality during the autoclave cycle.
The specification is F_0 Lethality calculation minutes**.** ≥ 35.0

* Applies to Ready to Use product only.

[+] Applies to Ready to Use steam sterilized product only.

4.4 Sampling requirements

Conduct the sampling procedure Part I: AQL limits based on the sampling plan (GB/T2828.1 -2012). The liner and cartridge caps should comply in accordance to the tabulated table below. Inspection of resistance to sterilization, durability of coating, compatibility and liner retention force are carried out in accordance with EPD-7005.

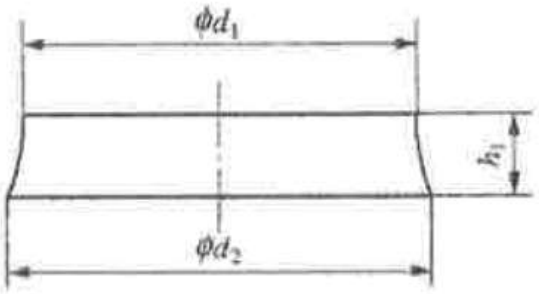
Section	Inspection Item	General Inspection Level (IL)	Acceptable Quality Limits (AQL)
Rubber Liner	Appearance	I	0.65
Aluminum Cap	Appearance	I	4.0
	Compatibility	S-2	4.0
	Resistance to Sterilization	S-2	4.0
	Coating Integrity	S-2	4.0
	Liner Adhesive Force	S-2	4.0

Table 2: Inspection Level and Acceptable Quality Limits (AQL)

4.5 Dimension for Liner

Dimensions for liner should comply to Diagram 2 & Table 3.

Diagram 2



A Type – Lined Seal

Table 3

Lined Seals group as determined in VAL:HOS.00176	**Φ d_1 (mm)**	**Φ d_2 (mm)**	**h_1 (mm)**
Group 1.1	6.9±0.6	7.8±0.4	2.0±0.3
Group 1.2	6.9±0.6	7.8±0.4	1.5±0.3

5 Testing Program

5.1 **The testing as outlined in this Master Specification:**

The batch release criteria in accordance with EPD-7001

The stability testing plan in accordance with ESOP-3133

The registration testing plan in accordance with EPD-7002

The sample size in accordance with EPD-7005

Testing will be carried out per applicable Chinese Pharmacopoeia and YBB standards in accordance with EPD 7008.

5.2 Changes impacting the product will be evaluated in accordance with West's change control procedure. Full inspection may be carried out if needed.

6 Revision History

Revision 12

- The release criteria on Ready-to-Use (RU) steam sterilized components will change according to CC # 200040017. The parametric release replaces biological indicator (BI) specification and results with the F0, Lethality specification and results. There is no product impact from removing the BIs from the production sterilization cycles. The autoclave cycles have been validated to achieve a sterility assurance level of 10^{-6}. This leads to the following updates:
- Section 1 removal of ChP reference Biological Indicator Section 3

- Section 3 Specification Table updated Biological Indicator to F_0 Lethality[6]≥ 35 (minutes) and the related footnote accordingly,
- Section 4.3.2 Biological Indicators[+] updated the wording to reflect the F_0 Lethality calculation. Removal of the self-contained indicators (SCBI) in the method as West does not use SCBIs.

Revision 11

- Remove Violet from title and sections in accordance with the latest update dated 04Jan2024 in the Change Control #200051183.

Revision 10

- Section 2.15 update from ChP 2015 to ChP 2020.
- Rename title and sections from Aluminum Caps to Gold/Clear/Violet Lacquered Aluminum Caps in accordance with Change Control #200051183.

Revision 9

- Correction of Product Registration section 4.1.1.1 Aluminum caps as the wording for rubber was included erroneously and detailed the information for Section 4.2.1.1.as per YBB and product standard. The error occurred in revision 7.

Revision 8:

- Section 2 Reference Documents exchanged the pervious YBB references to Chinese Pharmacopoeia 2020 Edition 4002, 4011 and 4013 as the Chinese Pharmacopoeia superseded the YBB standards for the aforementioned methods. The related Change Control # is 435342. Updated title of EPD 7008. Updated title of EPD 7008. Revision 2 of EDP 7003 leads to the update of the title to Fragmentation Testing of Stoppers and Liners for Pen-Injectors (in accordance with YBB/ChP as applicable).
- Section 3 Specification Table added to footnote 8 "[8]This test is not required for Non-halogenated Butyl Rubber products." For non-halogenated butyl rubber, the silver nitrate testing is not possible, no precipitate can be formed. Deleted YBB Ash limits to be followed for all formulation with the exceptions as listed below, as this was a copy paste error. Endotoxin: Deleted the BIO-018 reference, as BIO 22 is implemented now and supersedes Bio-018.
- Updated the Chinese Pharmacopeia 2015 references where applicable to Chinese Pharmacopeia 2020, the related Change Control # is 435342.
- Resistance to Sterilization 4.1.3 and Durability of Coating 4.1.4 according to Change Control # 200023111 removed the previous reference autoclaving by 121+/-2°C for 30 minutes inclusive of 130 +/-2°C for 5 minutes to 130 +/-2°C for 30 minutes. Exchanged Coating Integrity title to Durability of Coating as in harmonization with YBB and the other related MSPECs 0004 and 0016.
- Rephrased Silver Nitrate Method 4.2.2.1 and as per global method: This procedure is applicable to both monolayer and bilayer products. For bilayer products, separate the two layers and test each layer individually following the Deviation 200022209 and Change Control # 200022796.
- Incorporated to Infrared Spectrum Method 4.2.2.2 the Chinese Pharmacopeia 2020 Edition 4002 and deleted the previous YBB references, as the Chinese Pharmacopoeia superseded the YBB standards for the aforementioned method. The related Change Control # is 435342.
- Added to Acute Systemic Toxicity Test 4.2.8.3 and Hemolysis 4.2.8.3 the applicable Chinese Pharmacopoeia 2020 Edition 4011 and 4013 and deleted the previous YBB references as the

Chinese Pharmacopoeia superseded the YBB standards for the aforementioned methods. The related Change Control # is 435342.

- 4.3.1. Bacterial Endotoxin, reworded the method description, deleted BIO-018 reference and included USP and EP reference as BIO -022 is applicable to all Pharmacopoeias. Added Tween 80 detergence in alignment with the BIO-022 method.
- Section 5 Testing Program: introduced EPD 7008 to this section to enable to delete the previous redundant references to EDP 7008 within the NMPA Test methods of Section 4. Reworded "Full testing may be carried out per applicable YBB standards" to "Testing will be carried out per applicable Chinese Pharmacopoeia and YBB standards in accordance with EPD 7008."

Revision 7:

- Rephrased 2.19 in Reference Documents Chinese Pharmacopeia (2015 Edition): 1143 Method for Bacterial Endotoxin Test in accordance with harmonized BIO-018 : Determination of Endotoxins on Lined Seals or BIO-22: Quantification of Endotoxins on Elastomeric Closures and Westar Lined Seal added EPD 7008, MSPEC 0018 to EPD 7005 to Section 2 Reference Documents.
- Incorporated BIO-22 method to the Section 3 Specification Table Bacterial Endotoxin test, added acceptance criteria ≤1 EU/Piece (BIO-22) and rephrased footnote 5 for the transition period. In 4.3.1 Bacterial Endotoxin* deleted the words "100 mL of", as the amount of LAL reagent water vary, and added "The specification is during transition period either ≤ 0.10 EU/mL/10 Lined Seals (BIO-018) or ≤ 1EU/Piece (BIO-22)".
- Rephrased 4.1.1. Product Registration to include contamination (≥ 0.2mm2). Exchanged collect several samples to take sufficient samples in section 4.1.1 and 4.1.2
- Corrected Section 4.2.2.1. the silver nitrate solution is now added dropwise until a precipitate is formed, reference EPD 7008, instead of one drop.
- Build into Section 4.2.2.2Infrared Spectrum Method the sentence "Reference EPD 7008, West is using a Diamond ATR Crystal instead of Zinc Selenide".
- In Section 4.2.7.5 Non-volatile Matter deleted "waterbath" and detailed that the samples are placed in an oven at 105 °C for 16 hours (Reference EPD 7008). Deleted the sentence "Continue heating at 105°C until constant mass" consequently.
- Revised in 4.5 Dimension for Liner table 3, based on the VAL: HOS.00176 added the detailed H1 dimension for group 1.2 1.5±0.3, the applicable designs are listed in the reference document VAL: HOS.00176.

Revision 6:

- Re-phrased the scope to "The product consists either of halobutyl and synthetic polyisoprene dual rubber liner, or of a halobutyl rubber monolayer rubber liner and aluminum cap for Aluminum Caps with Liners for Pen-injectors supplied for the China Market" to differentiate between the monolayer and dual rubber liner to include further registered monolayer items.
- The overarching MSPEC change: ESW 2019-138: YBB Master Spec Change, required an update of all existing MSPECs including several changes as listed below:
- Corrected error in 2.15 MSPEC: WPSCH_INS-0013: Justification Document – Specification for Aluminum Caps with Liner for Pen-injector and 2.17 Chinese Pharmacopeia (2015 Edition): 1143 Method for Bacterial Endotoxin Test in accordance with harmonized BIO-018: Determination of Endotoxins on Lined Seals, Bio 005 was referenced before corrected Footnote within Section 3 Specification Table to "Applies to Ready to Use (RU) components only. Result will be extracted from release batch testing per harmonized BIO-018: Determination of Endotoxins on Lined Seals."

- Added MSPEC: WPSCH_INS-0013 to Reference Documents of Section 2.13
- Deleted the sentence “Products will be listed in Appendix 2” in 1.3 as Appendix 2 will be removed from the Attachment according to VAL: E.00047. Therefore added “Products are listed in VAL: E00047
- Added EPD-7001: Testing and Release Policy – China Market, EPD-7002: Product Grouping for Chinese Pharmacopeia and YBB methods, EPD -7003: Fragmentation Testing of Stoppers and Liners for Pen-Injectors for YBB, EPD-7005: Sample size for testing under MSPEC-0004, MSPEC-0013, MSPEC-0015 and MSPEC-0016 ESOP-3133: YBB Stability Studies and WPSCH_ATT-0013: Attachment Document – Specification for Aluminum Caps with Liner for Pen-injector for China to the Reference Documents.
- Deleted columns R and RT in the table.
- Divided the test within the Specification table into Chemical, Functional, Biological tests, Visual Inspection and Dimension and Tests for Ready to Use (RU) products in alignment with the YBB Standard.
- Deleted ≤ for Section 3 Specification table to Biological Indicator[6] 0 Positive as the ≤ was not applicable.
- Exchanged CFDA to NMPA
- Deleted biological in footnote 3 and added following tests Identification[3] and Volatile Sulfides[3]
- Deleted footnote: For individual ash limits, refer to respective formulation characteristic. The deletion then requires a renumeration of the footnotes.
- Added footnote 4 into the Specification Table of Section 3 “[4] Not required for standard washed product. Tests are for pharmaceutical washed products only and not for soft/purified water rinsed products that have not undergone pharmaceutical washing. For West Standard items, the final washing is done by the customer”.
- Added footnote 4 to the following tests: pH Change[4], Fragmentation[4] Conductivity[4] and Leakage [4].
- Corrected Bio -005 reference to BIO-018: in Footnote 6.
- Regrouped the footnotes accordingly.
- 4.1.2 Routine Release exchanged several to sufficient in alignment with the verbiage of the other MSPECs.
- Corrected Section 4.2.1 Identification text. The word “Into” should be read “of”, based on a translation error from Chinese to English. The sentence “Let the mixture stand for five minutes” was deleted, as it is not referenced in YBB.
- Rephrased Section 4.2.3 Fragmentation according to Change Control 200018248 added the reference EPD to the test description ”The test is carried out in accordance with EPD-7003”
- Added additional space between number and Si units except for % and °C.
- Renamed min into minutes, hr into hours, min to minimum and max to maximum.
- Corrected small and capital letters.
- Exchanged the term rubber stopper to aluminum cap with rubber liner in 4.3.1.
- Added “The solution should be freshly prepared” to 4.2.7.8. Extractable Zinc
- Rephrased Section 5: deleted the testing listed in this Master Specification may be subject to a reduced testing program in accordance with West procedures, as applicable. And added EPD-7001, 7002, 7005 and ESOP-3133, added Full testing may be carried out as per applicable YBB standards.
- Added ‘Inspection of resistance to sterilization, durability of coating, compatibility and liner retention force are carried out in accordance with EPD-7005’ to section 4.4.

Revision 5:

- Added Appearance (YBB) and Dimension (YBB) to Specification Table of Section 3
- Added footnote [1 and 2] to Appearance (YBB) and Dimension (YBB) to Specification Table of Section 3
- Re-phrased footnote[1] to explain the appearance and dimension inspection requirement for product registration and stability testing
- Added footnote [8] for release testing requirement for appearance and dimension tests
- Re-phrased sections 4.1 and 4.2 to state the requirements for appearance and dimension checks for product registration and routine release.
- Added section 4.3
- Simplified section 4.5

Revision 4:

- Updated the list of documents under Section 2 Reference Documents.
- 4.2.1 Rubber Liners Appearance – Replaced "impurities" with "contamination (≥ 0.2mm^2)" to align with West AQL standard.

Revision 3:

- 3. Specification Table – Added "X" to fragmentation and leakage tests in release and reduced testing columns.
- 3. Specification Table – Added a footnote [4] to indicate functional tests are for pharmaceutical washed products only and not for soft water rinsed products that have not undergone pharmaceutical washing.

Revision 2:

4.2.7.7 – Changed chloride-free water to ammonium-free water to align the description in the YBB standards.

Revision 1: History on file

Signature Manifest

Document Number: MSPEC: WPSCH-0013 **Revision:** 12

Title: West Global Specification for Gold/Clear Lacquered Aluminum Caps with Liner for Pen-injector, China

Effective Date: 21 Mar 2024

All dates and times are in UTC-Coordinated Universal Time.

Approve MSPEC-0013

Author Approval

Name/Signature	Title	Date	Meaning/Reason
Jeanette Hampe (HAMPEJ)	Sr. Specialist, QA	19 Mar 2024, 07:01:53 AM	Approved

Approval

Name/Signature	Title	Date	Meaning/Reason
Jenny Wong (WONGJ02)	Dir, Global Reg Affairs	19 Mar 2024, 03:40:09 PM	Approved
Laura Simpson (SIMPSONL)	Sr. Specialist, Quality System	20 Mar 2024, 01:49:41 PM	Approved
MeiYeng Kok (KOKMY)	Sr Dir, Quality, Seals	21 Mar 2024, 06:30:36 AM	Approved