Product Description: **Justification Document –Halogenated Butyl Rubber Plunger for Prefilled Syringes, China**

Control ID: MSPEC: WPSCH_INS-0015 Rev.: 7

This Justification document applies to halogenated butyl rubber plungers for prefilled syringes. for inhalation and injection Drug Product Type. In the development of this standard, reference was made to YBB00082004-2015 Bromobutyl Rubber Plungers for Prefilled Syringes or YBB00072004-2015 Chlorobutyl Rubber Plungers for Prefilled Syringes and YBB00112004-2015: Assemblages for Prefilled Syringes (with Stainless Steel Needles).

The tests and specifications for this standard are carried out per applicable Chinese Pharmacopoeia and YBB standards in accordance with EPD 7008:

1.1 Dimensions and Appearance

1.1.1 Product Registration

Appearance is performed according to YBB00162004-2015 or YBB00152004-2015.
VAL: E.00078 Justification Report: Registration and Stability testing T0 of Dimensional characteristics aligned with YBB Requirements, justifies that Dimensions do not have to be performed for Registration and Stability T0 testing.

1.1.2 Routine Release

The inspection is conducted according to West's procedures and inspection plans.

1.2.2.1 Dimensions

All dimensions defined in YBB are controlled by either mold qualification, tool monitoring or releasing testing.

For release testing and per ESOP-7111 ''Dimensional control in Final Inspection", West carries out measurement on dimensions that are process dependent and important for the article functionality for each batch prior to release. Dimensional Inspections are controlled by inspection of specific or critical dimensions as specified on the approved specification, e.g. height h1 and rib diameter d1, etc.

If tested samples are all within the limits of the article drawing, the product can be released. If not, a batch of the product should be declared as non-conforming and an investigation is performed.

For mold qualification, measurements are completed as defined in the ESOP 6179 Tooling Approval Guidelines. Upon mold approval, the mold is released for use in a plant. West also ensures the usability of the molds through a mold monitoring program. The Tool Life Cycle Management program is defined in ESOP 4171 Mold Life Cycle Monitoring (Frequency & Sampling Plan). At defined intervals, molds are cleaned and then a full panel of molded stoppers are 100% inspected for defects.

As part of the tool/mold life cycle procedure, a risk assessment is completed to determine the effect of the type and frequency of cleaning on all dimensions. Affected dimensions are measured by sampling parts from representative sections of the molds. Measurements are taken and trended. This is done throughout the life cycle of the tools. Dimensions are plotted and controlled within upper and lower limits; any point occurring outside of these limits will result in the relevant mold being quarantined for repair or for retirement.

West's existing controls and monitoring programs provide sufficient confidence that the plunger elastomer product will conform to the YBB dimensional requirements. VAL: E.00078 Justification Report: Registration of Dimensional characteristics aligned with YBB Requirements, justifies that Dimensions do not have to be performed for registration testing.

1.2.2.2 **Appearance**

In YBB00072004-2015 Chlorobutyl Rubber Plungers for Prefilled Syringes and YBB00082004-2015 Bromobutyl Rubber Plungers for Prefilled Syringes is stated:

Take sufficient samples and inspect visually under natural light. The surface color should be even; there shall be no stains, impurities, bubbles, crack lines, non-fill, roughness, trim trash, sponge or loose rubber threads. There should be no molding damages. If there is an opening, the edges of the opening should not protrude from the plunger surface.

For purposes of analysis, it is assumed the categories are cumulative.

Comparisons between West visual inspection plan and YBB requirements are shown on a product basis. Additionally, for the articles that are part of China DMF, West performs review of the appearance inspection data. Product analysis and capability is determined by summing appropriate West categories and comparing to the YBB specification.

1.2 **Identification**

1.2.1 **Silver Nitrate Method**

The method and specification were based on YBB00162004-2015 or YBB00152004-2015. West will add the silver nitrate solution dropwise until a precipitate is formed.

1.2.2 **Infrared Spectrum Method**

The method references the Chinese Pharmacopoeia 2020 Edition 4002 Test for Infrared Spectrum of Packaging Materials. West is using a Diamond ATR Crystal instead of Zinc Selenide.

1.3 **Coordination Performance of Plunger and Push Rod**

The method and specification reference YBB00112004-2015 – Assemblages for Prefilled Syringes (with Stainless Steel Needles). The test is for pharmaceutical washed products only and not for soft water rinsed products that have not undergone pharmaceutical washing.

1.4 **Lubricity of Plunger**

The method and specification reference YBB00112004-2015 – Assemblages for Prefilled Syringes (with Stainless Steel Needles). The test is for pharmaceutical washed products only and not for soft water rinsed products that have not undergone pharmaceutical washing.

1.5 **Plunger Gliding property**

The method and specification reference YBB00112004-2015 – Assemblages for Prefilled Syringes (with Stainless Steel Needles). The test is for pharmaceutical washed products only and not for soft water rinsed products that have not undergone pharmaceutical washing.
As per the agreement outlined in the memo enclosed in the Infocard in MasterControl (Memo Title: Schott Plunger Gliding exclusion July2023), the specific design SCHO 2225 4432/50/GREY, SKU: 7001-6121, in combination with the plastic syringe purchased by Schott Pharma AG & Co KGaA, is exempt from this test.

1.6 Syringe Seal integrity

The method and specification reference 052/QA/KKL/2019 (Justification for Modification to Body Sealing Property Test Method for MSPEC: WPSCH-0015). The test is for pharmaceutical washed products only and not for soft water rinsed products that have not undergone pharmaceutical washing.

1.7 Ash

The method refers to Determination of Ash for Rubber (YBB00262005-2015), the specification reference YBB00082004-2015 or YBB00072004-2015. The parameters and deviation for ash content are specified in accordance to the European Pharmacopoeia.

1.8 Volatile Sulfide

The method refers to Determination of Volatile Sulfides (YBB00302004-2015), the specification reference YBB00082004-2015 or YBB00072004-2015.

1.9 Insoluble Particles

The method refers to Test for Insoluble Particulate Matter of Packaging Materials (YBB00272004-2015) Method I, the specification reference YBB00082004-2015 or YBB00072004-2015. Insoluble Particles test is for pharmaceutical washed products only and not for soft water rinsed products that have not undergone pharmaceutical washing.

1.10 Chemical Characteristics

The method reference YBB00082004-2015 or YBB00072004-2015.

1.10.2 Clarity and Color

The method reference Chinese Pharmacopoeia 2020 Edition, Vol. IV General Rule 0902 and 0901, the specification refers to YBB00082004-2015 or YBB00072004-2015.

1.10.3 pH Change

The method reference Chinese Pharmacopoeia 2020 Edition, Vol. IV, General Rule 0631, the specification refers to YBB00082004-2015 or YBB00072004-2015. This method applies for pharmaceutical washed products only and not for soft water rinsed products that have not undergone pharmaceutical washing.

1.10.4 UV Absorbance

The method basically refers to Chinese Pharmacopoeia 2020 Edition, General Rule 0400, the specification refers to YBB00082004-2015 or YBB00072004-2015.

1.10.5 Non-volatile Matter

The method and specification reference YBB00082004-2015 or YBB00072004-2015. West will perform drying by placing the samples in an oven at 105 °C for 16 hours as referenced in EPD 7008.

1.10.6 **Oxidizable Substances**

The method and specification reference YBB00082004-2015 or YBB00072004-2015.

1.10.7 **Heavy Metal**

The method basically refers to Chinese Pharmacopoeia 2020 Edition, Vol IV General Rule 0821, First Act, the specification reference YBB00082004-2015 or YBB00072004-2015.

1.10.8 **Extractable Ammonium**

The method and specification reference YBB00082004-2015 or YBB00072004-2015.

1.10.9 **Extractable Zinc**

The method and specification reference YBB00082004-2015 or YBB00072004-2015.

1.10.10 **Conductivity**

The method and specification reference YBB00082004-2015 or YBB00072004-2015. This method applies for pharmaceutical washed products only and not for soft water rinsed products that have not undergone pharmaceutical washing.

1.11 **Biological Test**

1.11.2 **Pyrogen**

The method and specification reference YBB00082004-2015 or YBB00072004-2015.

1.11.3 **Acute Systemic Toxicity Test**

The method and specification reference as per Chinese Pharmacopoeia 2020 Edition 4011 Test for Acute Systematic Toxicity of Packaging Materials.

1.11.4 **Hemolysis**

The method and specification reference as per Chinese Pharmacopoeia 2020 Edition 4013 Test for Hemolysis of Packaging Materials.

1.12 **Microbiological Test**

1.12.2 **Bacterial Endotoxin**

The method references Chinese Pharmacopoeia 2020 Edition (1143 Method for Bacterial Endotoxin Test).

1.12.3 **Biological Indicator**

The method is conducted in accordance with ISO 17665, West's procedures, and inspection plans.

1.12.4 **Dosimeter**

The method references ISO 11137: Sterilization of health care products – Radiation.

2 Revision History

Revision 7

- Section 1.12.3 removal of ChP reference Biological Indicator Section 3 to "The method is conducted in accordance with ISO 17665, West's procedures, and inspection plans," to reflect the current process in accordance to CC # 200040017.

Revision 6

- Section 1.5 Pluger Gliding Property added the exception for this test as per customer agreement, as detailed by inclusion of the wording " As per the agreement outlined in the memo enclosed in the Infocard in MasterControl (Memo Title: Schott Plunger Gliding exclusion July2023), the specific design SCHO 2225 4432/50/GREY, SKU: 7001-6121, in combination with the plastic syringe purchased by Schott Pharma AG & Co KGaA, is exempt from this test."

Revision 5:

- Added Sections 1.1.1 and 1.1.2 Routine Release to this document as it was missing up to now to be in line with the structure of all the other INS documents.
  Product Registration amended stability T0 to the text and updated VAL: E.00078 title, reference CC # 200002279.
- Section 3: Attachment list, updated the text and included the following . The Val: E 00091 Justification Report: Registration of Visual characteristics aligned with YBB Requirements This document justifies the removal of individual PINS generation and covers this product application. Reference CC# 200002240 " One general PINS development

Revision 4:

- Reworded the scope from "The tests and specifications for this standard are as follows:" to "The tests and specifications for this standard are carried out per applicable Chinese Pharmacopoeia and YBB standards in accordance with EPD 7008:" to outline that the EPD 7008 has to be followed in association with the respective document. The redundant references to EPD 7008 were deleted consequently. Added "for inhalation and injection Drug Product Type" to include further registered application types.
- Incorporated to Product Registration 1.1. the following: VAL: E.00078 Justification Report: Registration of Dimensional characteristics aligned with YBB Requirements, justifies that Dimensions do not have to be performed for registration testing.
- Updated the Chinese Pharmacopeia 2015 references where applicable to Chinese Pharmacopeia 2020, the related Change Control # is 435342
- Added to Infrared Spectrum Method 1.2.2 the Chinese Pharmacopoeia 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 1.11.3 and Hemolysis 1.11.4 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.

Revision 3:

- Include 1.2.1 Silver Nitrate Method "As per EPD 7008 West will add the silver nitrate solution dropwise until a precipitate is formed". One drop cannot not form a precipitate reliably, therefore West is using up to 4 drops as referenced in EPD 7008.
- Add 1.2.2 Infrared Spectrum "As referenced in EPD 7008 West is using a Diamond ATR Crystal instead of Zinc Selenide". Using the Diamond is the more appropriate method for West.
- Renamed the following Test methods titles in Test methods 1.5 and 1.6: Sliding Performance of Plunger to Plunger Gliding property and Body Sealing Property to Syringe Seal integrity. The naming is now in accordance to the titles as referenced in the applicable YBB.
- Add 1.10.5 Non-volatile Matter the sentence "West will perform drying by placing the samples in an oven at 105 °C for 16 hours as referenced in EPD 7008". West is using the oven instead of a waterbath.

Revision 2:

- The overarching MSPEC change: ESW 2019-138: YBB Master Spec Change, required an update of all existing MSPECs including the Justification documents as listed below:
- Deleted Attachment list and inserted. "The West Pharmaceutical Services, plants practices for Appearance & Dimensions as a justification to meet the NMPA requirements (PINS) may be obtained via issuing PINS report overview by MasterControl".
- Added the phrase "This method applies for pharmaceutical washed products only and not for soft water rinsed products that have not undergone pharmaceutical washing." To Conductivity 1.9, pH change 1.10.3 and Conductivity 1.10.10
- Added: YBB00112004-2015: Assemblages for Prefilled Syringes (with Stainless Steel Needles).
- Reformatted document

Revision 1:

- Re-phrased paragraph 1.1. Added justification for applying West procedures and inspection plans.
- Changed reference from YBB00112004-2015 to 052/QA/KKL/2019 in paragraph 1.6
- Added paragraph 1.12.2 and 1.12.3

Revision 0:

- New

3 Attachment list

The West Pharmaceutical Services, plants practices for Appearance & Dimensions as a justification to meet the NMPA requirements (PINS) may be obtained via issuing PINS report overview by MasterControl.
Therefore, there is no attachment list listed within this document anymore.
The Val: E 00091 Justification Report: Registration of Visual characteristics aligned with YBB Requirements justifies the removal of individual PINs generation and covers this product application.

Signature Manifest

Document Number: MSPEC: WPSCH_INS-0015 **Revision:** 7

Title: Justification Document - Specification for Halogenated Butyl Rubber Plungers for Prefilled Syringes, China

Effective Date: 20 Mar 2024

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

Approve MSPEC-0015

Author Approval

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