



► Leaders in Life Science and Technology

TEST RESULT CERTIFICATE

Sponsor	Saint-Gobain PPL	Technical Initiation	9/30/2009
Address	3910 Terry Diane Drive Beaverton, Michigan 48612	Technical Completion	10/2/2009
Contact	Nancy Tremaine	Report Date	10/23/2009
P.O. Number	P586084	Project Number	09-4101-N5

Test Article	SPT-50
Lot/Batch #	363399
Study	Tests for Elastomeric Closures for Injection – USP
Comments	None

REFERENCES: The study was conducted based upon the following references: USP 32, NF 27, 2009. <381> Elastomeric Closures for Injections.

ISO/IEC 17025, 2005, General Requirements for the Competence of Testing and Calibration Laboratories.

PROCEDURE:

Preparation of Solutions: Prior to extraction, the test article with a surface area of $100 \pm 10 \text{ cm}^2$ was placed in a suitable extraction container. The test article was covered with 200 mL of purified water and boiled for 5 minutes. After boiling, it was rinsed 5 times with cold purified water. The washed test article was placed into a suitable wide-neck glass flask. Purified water (200 mL) was added to the container and then it was weighed. The mouth of the flask was covered with a glass beaker. The test articles were extracted by autoclaving to $121 \pm 2 \text{ }^\circ\text{C}$ for 30 ± 2 minutes. The extracted test article was cooled to room temperature over a 30 minute period. Purified water was added to bring it to the original mass. The flask was agitated and then Solution S was immediately decanted into a suitable clean container.

Appearance of Solution: The degree of opalescence was determined by turbidity measurement against a Reference Suspension. The turbidity of the test solution S was 0.65 NTU and 0.2 NTU for the method blank. It was less than the turbidity of Reference Suspension 1 (3 NTU).

Color: The color of 50 mL of Solution S was compared with the color of 50 mL of color Standard in a color comparison tube against a white background. The color of Solution S was lighter than color Standard.

Acidity or Alkalinity: To 20 mL of solution S, 0.1 mL of Bromothymol blue solution was added. The solution was yellow, so it was titrated with 0.01N sodium hydroxide (NaOH) until blue endpoint was reached.

Absorbance: This test was performed within 5 hours of Solution S preparation. Solution S was filtered through a $0.45 \text{ }\mu\text{m}$ filter. The first few milliliters were rejected. The absorbance of the filtrate at 220 nm to 360 nm wavelengths was recorded; the blank was used as compensation liquid.

Reducing Substances: To 20 mL of Solution S, 1.0 mL of dilute sulfuric acid and 20 mL of 0.002M potassium permanganate were added. The solution was boiled for 3 ± 1 minutes, and immediately cooled. To cooled solution, 1.0 g of potassium iodide and 0.25 mL of starch solution were added. It was immediately titrated with 0.01M sodium thiosulfate. The volume of sodium thiosulfate was recorded. A blank titration was carried out, exactly in the same manner with the extracted control solution. The difference between the titration volumes was calculated.

TOXIKON

Tests for Elastomeric Closures for Injection – USP

Toxikon Final NON–GLP Report: 09–4101–N5

Test Article: SPT-50

PROCEDURE (Cont.):

Heavy Metals: The Test Preparation was prepared by placing 10 mL of Solution S into 50 mL color comparison tube. Lead Standard solution was prepared by placing 2 mL of standard lead solution into the second 50 mL color-comparison tube which was then diluted with 10 mL of water. The monitor preparation was prepared by placing 10 mL of Solution S and 2.0 mL of standard lead solution into a third color comparison tube. To each of the tubes, 1.2 mL of thioacetamide – glycerin base TS and 2 mL of pH 3.5 Acetate Buffer were added, and mixed. Any brown color produced within 2 minutes in the tube containing the test solution did not exceed that in the tube containing the lead standard solution and the monitor solution, all tubes being viewed downward over a white surface.

Extractable Zinc: The solution S (10 mL) was digested with 0.6 mL of nitric acid and 1.0 mL of 1:1 hydrochloric acid water. After the digestion was complete, the mixture was cooled and the volume was brought to 10 mL with purified water. The blank was prepared in the similar manner. The solutions were analyzed by Inductively Coupled Plasma/Emission Spectroscopy (ICP/ES).

Ammonium: Solution S (5 mL) was diluted with purified water so that the total volume was 14 mL. The solution was made alkaline with dilute NaOH and then diluted to 15 mL with purified water. To the mixture, 0.3 mL of alkaline potassium tetraiodomercurate was added. A standard was prepared by mixing 10 mL of ammonium standard solution with 5 mL of water and 0.3 mL of alkaline potassium tetraiodomercurate. The test tubes were covered and examine after 5 minutes. The yellow color in the test solution was not darker than the yellow color produced in the Standard Solution.

Volatile Sulfides: The test Article with the surface area of 20 ± 2 cm² was placed in a 100 mL conical flask, and 50 mL of 20 g/L citric acid solution was added. The mouth of the flask was covered with lead acetate paper. The flask was heated in an autoclave at 121 ± 2 °C for 30 minutes. The color of the paper was compared with the standard prepared at the same time in the same manner by adding 0.154 mg of sodium sulfide to 50 mL of 20 g/L citric acid solution.

RESULTS: The results presented in table below were obtained by employing the methods described in USP Elastomeric Closure guidelines.

Parameter	Results	Acceptance Limits	Meet Criteria
Turbidity	0.65 NTU	< 3 NTU is Clear	Yes
Color	Less intense than the Color Standard	Less intense than the color standard	Yes
Acidity or Alkalinity	0.05 mL 0.01N sodium hydroxide	≤ 0.3 mL of 0.01N sodium hydroxide or ≤ 0.8 mL of 0.01N hydrochloric acid	Yes
Absorbance	< 0.20	≤ 0.2 for Type I	Yes
Reducing Substances	0.6 mL	≤ 3.0 mL difference between titration for Type I	Yes
Heavy Metals	< 2.0 ppm	≤ 2.0 ppm	Yes
Extractable Zinc	ND	≤ 5.0 ppm	Yes
Ammonium	< 2.0 ppm	≤ 2.0 ppm	Yes
Volatile Sulfides	< 0.154 mg	≤ 0.154 mg of sodium sulfide	Yes

ND = Not Detected

TOXIKON

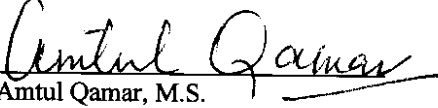
Tests for Elastomeric Closures for Injection – USP


Toxikon Final NON-GLP Report: 09-4101-N5

Test Article: SPT-50

CONCLUSION: The test article meets the criteria described in the USP Elastomeric Closures Test based on the results presented in the table above.

AUTHORIZED PERSONNEL:


Amtul Qamar, M.S.
Study Director


Paula Mazzio, B.S., M.P.H.
Quality Assurance