Criteria for medical adhesive

(August 10, 1970)
(MHW Ministerial Announcement No. 299)

In accordance with provisions in Article 42, Paragraph 2 of the Pharmaceutical Affairs Act (Act No. 145 of 1960), the criteria for medical adhesive shall be established as follows and applied from August 10, 1970.

Criteria for medical adhesive

I Definition

Medical adhesive is a product that is used to bond human tissues, contains "poly α-cyanoacrylate ester" as the main ingredient, and may remain in the body.

II Quality and test methods of medical adhesive

(1) Physical tests

A Appearance

Medical adhesive is an almost clear and colorless liquid.

B Infrared spectrophotometry

Spread the medical adhesive thin on a rock salt plate, and determine the infrared absorption spectrum of the solidified adhesive: It exhibits maxima at the wave numbers of about 2220 cm^{-1}, 1740 cm^{-1} and 1250 cm^{-1}.

(2) Adhesion test

Cut a gut sheet (0.06-0.08 mm in thickness) into pieces 6 cm in length and 1 cm in width, and use these as test pieces. Place 1 drop of the medical adhesive on the 1 cm wide edge of 1 test piece, spread thin, and overlay the 1 cm wide edge of another test piece on the part with the adhesive spread. Place a polyethylene plate on the test piece assembly, and apply the load at 1.96 N for 3 minutes to proceed with adhesion. Then, take the adhered gut sheet pieces out, fix one of the pieces, and apply the load at 9.8 N to the other piece: The adhered pieces do not separate. When this procedure is repeated 5 times, the adhered pieces shall not separate in any replicate.

(3) Chemical tests

A Residue on ignition

Perform the test with 5 g of the medical adhesive as directed in Residue on Ignition Test under the General Tests, Processes and Apparatus of the Japanese Pharmacopoeia (hereinafter referred to as "JP") (MHW Ministerial Announcement No. 44 of April 1976): The residue is not more than 0.1%.

B Extractable substances

Insert the medical adhesive between 2 polyethylene sheets, spread, and allow to stand for solidification. Place 1.0 g of the above assembly in an appropriate container, add 100 mL of water, attach a reflux condenser, and boil for 30 minutes. After cooling, filter the extract, and add water to the filtrate to make 100 mL. Use this solution as the test solution, and perform the following tests: The test solution meets the requirement for the tests.

(A) pH

Perform the test with 20 mL each of the test solution and water as directed in pH Determination in the JP: The difference in pH between these solutions is not more than 1.0.

(B) Heavy metals

Perform the test with 10 mL of the test solution as directed in Method 1 of the Heavy Metals Limit Test in the JP. Prepare the control solution with 1.0 mL of Standard Lead Solution.

(C) Potassium permanganate-reducing substances

To 5 mL of the test solution in a glass-stoppered Erlenmeyer flask, add 20 mL of 0.002 mol/L potassium permanganate solution and 1.0 mL of dilute sulfuric acid, and boil for 3 minutes. After cooling, add 0.1 g of potassium iodide, and titrate with 0.01 mol/L sodium thiosulfate solution (indicator: 5 drops of starch TS). Perform the blank test in the same manner, using 5 mL of water instead of the test solution. The difference in mL of potassium permanganate solution required between the tests is not more than 2.0 mL.

(4) Biological tests

Spread about 20 g of the medical adhesive to make thin pieces about 0.1 mm in thickness, cut the pieces into small pieces of about 1 cm^2, wash with a neutral detergent, water, and distilled water for injection in this order, and place these in a 500 mL glass container meeting the requirements for Soluble alkali test under the Test for Glass Containers for Injections in the JP. To the container, add 125 mL of saline solution, close tightly by melting glass of the opening or with a suitable stopper, proceed with extraction at 121°C for 1 hour, allow to stand until the temperature falls to room temperature, and use this solution as the test solution. Separately, prepare the blank solution in the same manner.

A Pyrogen test

Perform the test as directed under Pyrogen Test in the JP: The test solution meets the requirement for the test.

B Acute toxicity test

Use male mice of inbred strain or from a closed colony, weighing 17 to 23 g, and inject intravenously each of the test solution and the blank solution into 10 mice at 50 mL/kg. Observe the animals for 5 days after injection: No death occurs.

C Skin reaction test

To the shaved skin of 3 healthy rabbits, apply 1 drop of the test solution each on 2 sites of a certain area, and press the application site slightly using a polyethylene sheet. No skin reactions (erythema, edema, necrosis, etc.) occur within 1 week after the application.

Revised text (Excerpt) (MHW Ministerial Announcement No. 42 of March 6, 1978)

To products manufactured or imported until March 5, 1978, the provisions then in force shall remain applicable.

Revised text (Excerpt) (MHW Ministerial Announcement No. 211 of September 30, 1997)

It shall be applied from October 1, 1997.