matography. If necessary use a guard column prepared by coating the inside wall of a fused silica tube, 0.53 mm in inside diameter and 5 m in length, to 5 μm thickness with 5% phenyl-methyl silicon polymer for gas chromatography.

Column temperature: Maintain at 35°C for 5 minutes, then increase to 175°C at 8°C per minute, further increase to 260°C at 35°C per minute if necessary, and keep at 260°C for 16 minutes.

Injection port temperature: A constant temperature of about 70°C

Detector temperature: A constant temperature of about 260°C

Carrier gas: Helium

Flow rate: 35 cm/second

Split ratio: Splitless

System suitability—

System performance: When the procedure is run with the standard solution under the above operating conditions, the resolution between the peaks is not less than 1.0. (Note: In the case that the number of substances to be tested is two or more.)

System repeatability: When the test is repeated 3 times with the standard solution under the above operating conditions, the relative standard deviation of the peak areas of the substance to be tested is not more than 15%.

Test conditions (3)

Operating conditions—

Detector: Hydrogen flame-ionization detector

Column: Coat the inside wall of a fused silica tube, 0.32 mm in inside diameter and 30 m in length, to 0.25 μm thickness with polyethylene glycol 20M for gas chromatography. Use a guard column if necessary.

Column temperature: Maintain at 50°C for 20 minutes, then increase to 165°C at 6°C per minute if necessary, and keep at 165°C for 20 minutes.

Injection port temperature: A constant temperature of about 140°C

Detector temperature: A constant temperature of about 250°C

Carrier gas: Helium

Flow rate: 35 cm/second

Split ratio: 1:5

System suitability—

System performance: When the procedure is run with the standard solution under the above operating conditions, the resolution between the peaks is not less than 1.0. (Note: In the case that the number of substances to be tested is two or more.)

System repeatability: When the test is repeated 3 times with the standard solution under the above operating conditions, the relative standard deviation of the peak areas of the substance to be tested is not more than 15%.

5. International Harmonization Implemented in the Japanese Pharmacopoeia Fourteenth Edition

Items for which harmonization has been agreed among the European Pharmacopoeia, the United States Pharmacopeia and the Japanese Pharmacopoeia are implemented in the Japanese Pharmacopoeia Fourteenth Edition (JP 14). They are shown in the table below. The column headed Harmonized items shows the harmonized items written in the Pharmacopoeial Harmonization Agreement Document, and the column headed JP 14 shows the items as they appear in JP 14. In the Remarks column, notes on any differences between JP 14 and the agreement are shown as occasion demands.

Harmonized items	JP 14	Remarks
Bacterial Endotoxin Test	Bacterial Endotoxin Test	
Apparatus	Apparatus	
Preparation of Standard Endotoxin Stock solution	Preparation of Standard Endotoxin Stock solution	
Preparation of Standard Endotoxin solution	Preparation of Standard Endotoxin solution	
Preparation of sample solutions	Preparation of sample solutions	
Determination of Maximum Valid Dilution	Determination of Maximum Valid Dilution	
Gel-clot technique	Gel-clot technique	
(1) Preparatory testing	(1) Preparatory testing	
(2) Limit test	(2) Limit test	
(3) Assay	(3) Assay	
Photometric techniques	Photometric techniques	
(1) Turbidimetric technique	(1) Turbidimetric technique	
(2) Chromogenic technique	(2) Chromogenic technique	
(3) Preparatory testing	(3) Preparatory testing	
(4) Assay	(4) Assay	
Reagents, Test Solutions	Reagents, Test Solutions	
Amebocyte lysate	Lysate reagent	
Lysate TS	Lysate TS	
Water for bacterial endotoxins test (BET)	Water for bacterial endotoxins test	

Note: The method for decision of the limit for bacterial endotoxins was agreed between the three pharmacopoeias, but in the Decision of Limit for Bacterial Endotoxins under the General Information in JP 14, the maximum adult dose is calculated based on an average body mass of an adult of 60 kg.

6. Media Fill Test

The media fill test (MFT) is one of the processing validations employed to evaluate the propriety of the aseptic processing of pharmaceutical products using sterile media, etc. instead of actual products. Therefore, media fill tests should be conducted with the manipulations normally performed in actual processing, e.g. filling and closing operation, operating environment, processing operation, number of personnel involved, etc., and conducted under processing conditions that include "worst case" conditions. Refer to GMP (1), WHO/GMP for pharmaceutical products (2), and ISO 13408 (3), etc. for necessary information to conduct this test.