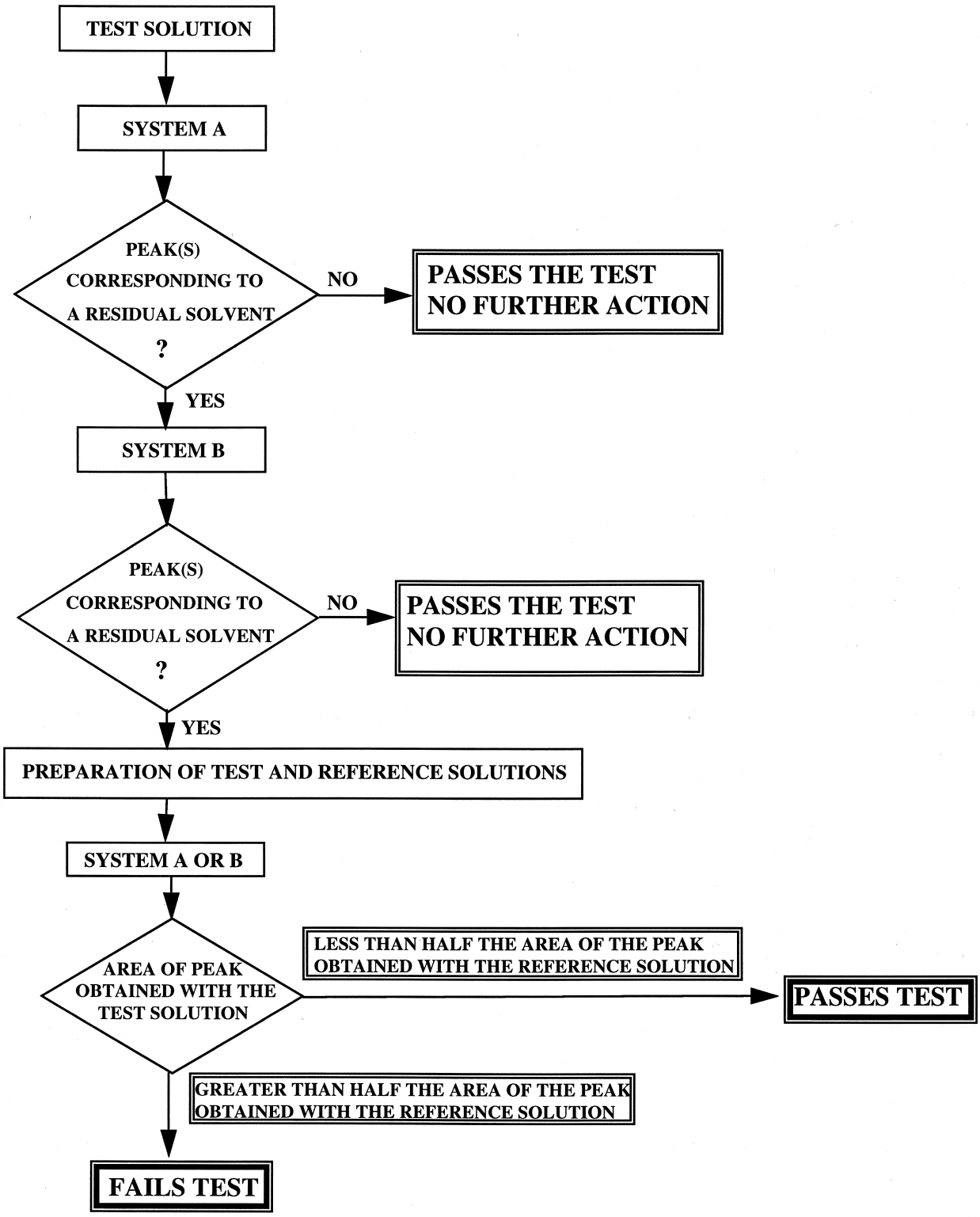

Figure 2.4.24.-5. – *Diagram relating to the identification of residual solvents and the application of limit tests*

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2.4.25. ETHYLENE OXIDE AND DIOXAN

The test is intended for the determination of residual ethylene oxide and dioxan in samples soluble in water or dimethylacetamide. For substances that are insoluble or insufficiently soluble in these solvents, the preparation of the sample solution and the head-space conditions to be employed are given in the individual monograph.

Examine by head-space gas chromatography (*2.2.28*).

A. For samples soluble in or miscible with water, the following procedure may be used.

Test solution. Weigh 1.00 g (M_T) of the substance to be examined in a 10 ml vial (other sizes may be used depending on the operating conditions) and add 1.0 ml of *water R*. Close and mix to obtain a homogeneous solution. Allow to stand at 70 °C for 45 min.

Reference solution (a). Weigh 1.00 g (M_R) of the substance to be examined into an identical 10 ml vial, add 0.50 ml of *ethylene oxide solution R3* and 0.50 ml of *dioxan solution R1*. Close and mix to obtain a homogeneous solution. Allow to stand at 70 °C for 45 min.

Reference solution (b). To 0.50 ml of *ethylene oxide solution R3* in a 10 ml vial add 0.1 ml of a freshly prepared 10 mg/l solution of *acetaldehyde R* and 0.1 ml of *dioxan solution R1*. Close and mix to obtain a homogeneous solution. Allow to stand at 70 °C for 45 min.

B. For samples soluble in or miscible with dimethylacetamide, the following procedure may be used.

Test solution. Weigh 1.00 g (M_T) of the substance to be examined in a 10 ml vial (other sizes may be used depending on the operating conditions) and add 1.0 ml of *dimethylacetamide R* and 0.20 ml of *water R*. Close and mix to obtain a homogeneous solution. Allow to stand at 90 °C for 45 min.

Reference solution (a). Weigh 1.00 g (M_R) of the substance to be examined into a 10 ml vial, add 1.0 ml of *dimethylacetamide R*, 0.10 ml of *dioxan solution R* and 0.10 ml of *ethylene oxide solution R2*. Close and mix to obtain a homogeneous solution. Allow to stand at 90 °C for 45 min.

Reference solution (b). To 0.10 ml of *ethylene oxide solution R2* in a 10 ml vial, add 0.1 ml of a freshly prepared 10 mg/l solution of *acetaldehyde R* and 0.10 ml of *dioxan solution R*. Close and mix to obtain a homogeneous solution. Allow to stand at 70 °C for 45 min.

The following static head-space injection conditions may be used:

- equilibration temperature: 70 °C (90 °C for solutions in dimethylacetamide),
- equilibration time: 45 min,
- transfer-line temperature: 75 °C (150 °C for solutions in dimethylacetamide),
- carrier gas: *helium for chromatography R*,
- pressurisation time: 1 min,
- injection time: 12 s.

The chromatographic procedure may be carried out using:

- a capillary glass or quartz column 30 m long and 0.32 mm in internal diameter the inner surface of which is coated with a 1.0 µm thick layer of *poly(dimethyl)siloxane R*,
- *helium for chromatography R* or *nitrogen for chromatography R* as the carrier gas with a linear velocity of about 20 cm/s and a split ratio of 1:20,
- a flame-ionisation detector,

maintaining the temperature of the column at 50 °C for 5 min, then raising the temperature at a rate of 5 °C per minute to 180 °C and then raising the temperature at a rate of 30 °C per minute to 230 °C and maintaining at 230 °C for 5 min; maintaining the temperature of the injection port at 150 °C and that of the detector at 250 °C.

Inject a suitable volume, for example 1.0 ml, of the gaseous phase of reference solution (b). Adjust the sensitivity of the system so that the heights of the peaks due to ethylene oxide and acetaldehyde in the chromatogram obtained are at least 15 per cent of the full scale of the recorder. The test is not valid unless the resolution between the peaks corresponding to acetaldehyde and ethylene oxide is at least 2.0 and the peak of dioxan is detected with a signal-to-noise ratio of at least 5.

Inject separately suitable volumes, for example 1.0 ml (or the same volume used for reference solution (b)), of the gaseous phases of the test solution and reference solution (a). Repeat the procedure twice more.

Verification of precision

For each pair of injections, calculate for ethylene oxide and for dioxan the difference in area between the peaks obtained with the test solution and reference solution (a). The test is not valid unless the relative standard deviation of the 3 values obtained for ethylene oxide is not greater than 15 per cent and the relative standard deviation of the 3 values obtained for dioxan is not greater than 10 per cent. If the weighings used for the test solution and reference solution differ from 1.00 g by more than 0.5 per cent, the appropriate corrections must be made.

The content of ethylene oxide or dioxan in parts per million is calculated from the expressions:

$$\frac{A_T \times C}{(A_R \times M_T) - (A_T \times M_R)}$$

A_T = area of the peak corresponding to ethylene oxide in the chromatogram obtained with the test solution,

A_R = area of the peak corresponding to ethylene oxide in the chromatogram obtained with reference solution (a),

M_T = mass of the substance to be examined in the test solution, in grams,

M_R = mass of the substance to be examined in the reference solution, in grams,

C = the amount of ethylene oxide added to reference solution (a), in micrograms.

$$\frac{D_T \times C}{(D_R \times M_T) - (D_T \times M_R)}$$

D_T = area of the peak corresponding to dioxan in the chromatogram obtained with the test solution,

D_R = area of the peak corresponding to dioxan in the chromatogram obtained with reference solution (a),

C = the amount of dioxan added to reference solution (a) in micrograms.

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2.4.26. *N,N*-DIMETHYLANILINE

METHOD A

Examine by gas chromatography (*2.2.28*), using *N,N-diethylaniline R* as the internal standard.

Internal standard solution. Dissolve 50 mg of *N,N-diethylaniline R* in 4 ml of *0.1 M hydrochloric acid* and dilute to 50 ml with *water R*. Dilute 1 ml of this solution to 100 ml with *water R*.

Test solution. Dissolve in a ground-glass-stoppered tube 0.50 g of the substance to be examined in 30.0 ml of *water R*. Add 1.0 ml of the internal standard solution. Adjust the solution to a temperature of 26 °C to 28 °C. Add 1.0 ml of *strong sodium hydroxide solution R* and mix until