Testing - additional guidance

End-user testing

End-user testing is an important step in the quality management of radiopharmaceutical preparations and for the safety of patients especially for those radiopharmaceutical preparations that are dispensed or compounded in the end-user facility (for example, nuclear medicine clinics). Application of the tests specified in the relevant monograph may not be possible at this stage either because of the short half-life of the radioisotope or due to other analytical limitations. The use of alternative, simple, tests that adequately identify the radiopharmaceutical preparation is therefore advisable.

Such tests fulfil a similar role to the Basic tests provided for pharmaceutical substances and dosage forms which are published by WHO[1] to provide simple and readily applicable methods for confirmation of identity especially useful when a fully equipped quality control laboratory and/or analytical expertise are not available and when indicative and rapid control is necessary.

[1] For current publications in the series consult the WHO Medicines web site http:/www.who.int/medicines.

f non-licensed or non-approved/registered radiopharmaceutical preparations under national rules are used, a detailed certificate of analysis or certificate of compliance is essential. In addition, the essential tests which give sufficient assurance of quality must be undertaken to allow safe use in patients.

Thin-layer chromatography of common radiopharmaceuticals

The following table gives an indication of thin layer chromatographic tests that may be suitable as end-user tests for identifying certain radiopharmaceuticals.

In chromatographic tests included within the monographs of the International Pharmacopoeia, the type of TLC plate or coating material to be used is stated but reference to commercial sources of these chromatographic supports is not given within the monograph. Where such information is given in the table below, it is intended to indicate a commercially available material that has been found to be suitable but does not imply that a different but equivalent commercial brand may not be used. Whatever chromatographic support is chosen, the person carrying out the analysis is responsible for ensuring that the chromatographic system is suitable.

Radiopharmaceutical	Stationary phase	Mobile phase	Rf Unbound radionuclide	Rf Bound radionuclide
^{14}C-urea	cellulose	butanol-water-acetic acid (12:5:3)	0	0.6
$^{123/131}$I-hippuran	silica gel	chloroform-acetic acid (9:1)	0.0	0.2-0.3
$^{123/131}$I-MIBG	silica gel	ethyl acetate-ethanol (1:1)	0.6	0.0
^{111}In-DTPA	ITLC-SG	10% ammonium acetate- methanol (1:1)	0.1	1.0
^{111}In-octreotide	ITLC-SG	0.1 M citrate buffer pH 5	1.0	0.0
^{18}F-FDG	silica gel	acetonitrile-water (95:5)	0.0	0.45
^{123}I- ioflupane	ITLC-SG spot must be dry	chloroform-methanol (9:1)	0.0	1.0
^{123}I-iomazenil	silica gel	ethyl acetate-ammonia (200:1)	0.0	0.7
^{123}I-iomazenil	silica gel	chloroform-acetic acid- water (65:35:5)	0.0	0.3
^{131}I-iodocholesterol	silica gel	chloroform-ethanol (1:1)	0.0	0.66

Radiochemical purity measurement systems of radiopharmaceuticals: thin-layer chromatography of technetium-99m radiopharmaceuticals

Stationary phases:

ITLC-SG Instant thin-layer chromatography, silica gel, e.g. Pall life Sciences

3MM	Whatman 3MM chromatography paper
No 1	Whatman No 1 chromatography paper
silica gel	Silica gel 60, e.g. Merck
alumina	aluminium oxide, e.g. Bakerflex
cellulose	cellulose, e.g. Merck

Mobile phases:
butanone = 2-butanone = methyl ethyl ketone = MEK
saline = 9g/l solution of sodium chloride
1 M sodium acetate = 82 mg/mL anhydrous sodium acetate
or 136 mg/mL sodium acetate trihydrate
0.1 M citrate = 21 mg/mL monosodium citrate dihydrate
1 M ammonium acetate = 77 mg/mL ammonium acetate
Mixtures of volatile solvents should be made freshly each day

Thin-layer chromatography of technetium-99m radiopharmaceuticals

The following table gives an indication of thin layer chromatographic tests that may be suitable for identifying certain technetium-99m radiopharmacauticals.

In chromatographic tests included within the monographs of the International Pharmacopoeia, the type of TLC plate or coating material to be used is stated but reference to commercial sources of these chromatographic supports is not given within the monograph. Where such information is given in the table below, it is intended to indicate a commercially available material that has been found to be suitable but does not imply that a different but equivalent commercial brand may not be used. Whatever chromatographic support is chosen, the person carrying out the analysis is responsible for ensuring that the chromatographic system is suitable.

Radiopharmaceutical	Stationary phase	Mobile phase	Rf RH-Tc (Tc-colloidal)	Rf TcO_4	Rf Tc-bound
^{99m}Tc-pertechnetate	ITLC-SG	MEK, acetone or saline	0.0	1.0	-
^{99m}Tc-MDP	ITLC-SG or 3MM	MEK or acetone	0.0	1.0	0.0
^{99m}Tc-MDP	ITLC-SG	1 M sodium acetate or saline	0.0	1.0	1.0
^{99m}Tc-DTPA	ITLC-SG or 3MM	MEK or Acetone	0.0	1.0	0.0
^{99m}Tc-DTPA	ITLC-SG or 3MM	saline	0.0	1.0	1.0
^{99m}Tc-colloid	ITLC-SG or 3MM	acetone or saline	0.0	1.0	0.0
^{99m}Tc-DMSA	3MM	MEK or acetone	0.0	1.0	0.0
^{99m}Tc-MAA	ITLC-SG or 3MM	MEK, acetone or saline	0.0	1.0	0.0
^{99m}Tc-pyrophosphate	ITLC-SG or 3MM	MEK or acetone	0.0	1.0	0.0
^{99m}Tc-pyrophosphate	ITLC-SG	Water	0.0	1.0	1.0
^{99m}Tc-HSA	ITLC-SG or 3MM	MEK or acetone	0.0	1.0	0.0
^{99m}Tc-HSA	ITLC-SG strip should be pre-saturated with human serum albumin and dried	ethanol-ammonia-water (2:1:5)	0.0	1.0	1.0

^{99m}Tc-HIG or IgG	ITLC-SG or 3MM	acetone, saline, or 0.1 M citrate	0.0	1.0	0.0
^{99m}Tc(V)-DMSA	ITLC-SG	butanone	0.0	1.0	0.0
^{99m}Tc(V)-DMSA	ITLC-SG	saline	0.0	1.0	1.0
^{99m}Tc(V)-DMSA	silica gel	butanol-acetic acid- water (3:2:3)	0.0	0.8	0.5
^{99m}Tc-IDAs	3MM spot must be dry	butanone	0.0	0.9	0.0
^{99m}Tc-IDAs	ITLC-SG	water or 50% acetonitrile	0.0	1.0	1.0
^{99m}Tc-sestamibi	Alumina Pre-spot with ethanol; do not allow spot to dry	ethanol	0.0	0.0	1.0
^{99m}Tc-tetrofosmin	ITLC-SG spot must be dry	acetone-dichloromethane (35:65)	0.0	1.0	0.5
^{99m}Tc-MAG3	ITLC-SG	ethyl acetate-butanone (3:2)	0.0	1.0	0.0
^{99m}Tc-MAG3	ITLC-SG	50% acetonitrile	0.0	1.0	1.0
^{99m}Tc-exametazime	ITLC-SG	butanone	0.0	1.0	1.0
^{99m}Tc-exametazime	ITLC-SG	saline	0.0	1.0	0.0
^{99m}Tc-exametazime	No 1	50% acetonitrile (freshly prepared)	0.0	1.0	1.0
^{99m}Tc-sulesmurab	ITLC-SG or 3MM	acetone, saline, or 0.1 M citrate solution	0.0	1.0	0.0
^{99m}Tc-depreotide	ITLC-SG	saturated solution of sodium chloride	0.0	1.0	0.0
^{99m}Tc-depreotide	ITLC-SG	1 M ammonium acetate-methanol (1:1)	0.0	1.0	1.0

Substitutions:

-in most cases, 2-butanone (methyl ethyl ketone, MEK) can be substituted for acetone

-in most cases, water can be substituted for saline

-in most cases, Whatman No 1 can be substituted for Whatman 3MM paper

-acid citrate dextrose solution (ACD) can be substituted for 0.1 M citrate