臺北榮民總醫院
Taipei Veterans General Hospital

核醫105學年度實習放射師專題課表

上課日期	時間	題目	主講者
2016/10/27	13:30 ~ 14:20	核醫臨床藥物	吳元鍾 藥師
	14:30 ~ 15:20	核醫正子藥物	張智偉 放化師

授課地點：中正樓2F放射線部大會議室

臺北榮民總醫院
Taipei Veterans General Hospital

Nuclear pharmacy practice

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Outline

- What is radiopharmaceutical ?
- Category of radiopharmaceuticals.
- Mo-99/Tc-99m generator systems.
- Quality Control of Radiopharmaceuticals.
- Radiochromatographic analysis for determining radiochemical purity.

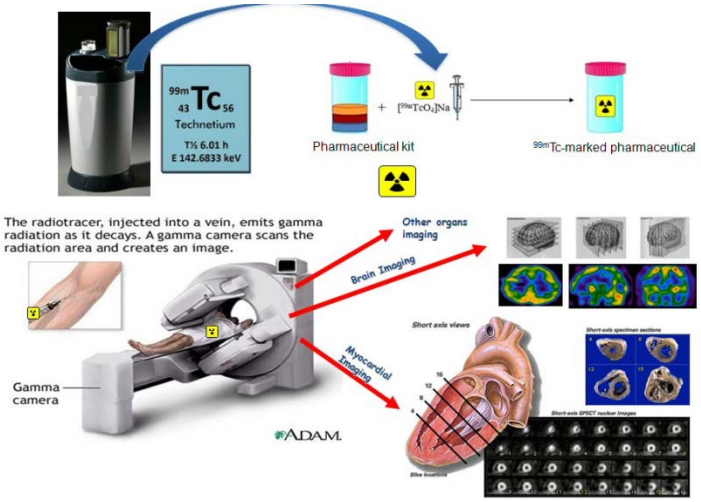
What is radiopharmaceutical ?

Radiopharmaceuticals

A radiopharmaceutical is a radioactive drug used for diagnosis or therapy in a tracer quantity ,masses so small that they do not produce pharmacologic effects , It is composed of two parts ;a radionuclide and a pharmaceutical.

ex : Tc-99m 5270mCi/ μg → Tc-99m 1.8×10^{-4} μg/mCi

MDP 7.5mg
Phytate 2.9mg
DMSA 1.4mg



Frequency of Adverse Reactions and Death Related Drugs		
Drug Category	Adverse Reactions	Death
Radiopharmaceuticals	~ 3 /100,000	< 1/10,000,000
Iodine contrast media,ionic	3.8 ~ 12.7%	~ 1/ 75,000
Iodine contrast media,nonionic	0.6 ~ 3.1%	~ 1/ 75,000
Pharmacologic drugs	0.6 ~ 6%	~ 1/ 7,500

Ideal Properties of Radionuclides for Diagnostic Imaging

- Decay mode:

  Electron capture or isomeric transition from metastable states ; no particulate radiation; gamma or x-ray only.

- Photon energy :

  100 ~ 200 keV is ideal

  Below 100 keV = tissue absorption and scatter (decreases resolution)

  Above 200 keV there is low detection efficiency. (decreases sensitivity)

- Half-life :

  Effective half-life equal to 1 to 1.5 times the imaging time.

- Chemical properties:

  Can be compounded into different chemical forms.

Characteristics of commonly used radionuclides

Nuclide	Physical half life	Mode of decay (%)	γ ray energy[a] (MeV)	Abundance (%)	Common production method
$^{3}_{1}H$	12.3 years	β (100)			$^{6}Li(n, \alpha)^{3}H$
$^{11}_{6}C$	20.4 min	β^+(100)	0.511 (annihilation)	200	$^{10}B(d, n)^{11}C$ $^{14}N(p, \alpha)^{11}C$
$^{13}_{7}N$	10 min	β^+(100)	0.511 (annihilation)	200	$^{12}C(d, n)^{13}N$ $^{16}O(p, \alpha)^{13}N$ $^{13}C(p, n)^{13}N$
$^{14}_{6}C$	5,730 years	β (100)			$^{14}N(n, p)^{14}C$
$^{15}_{8}O$	2 min	β^+(100)	0.511 (annihilation)	200	$^{14}N(d, n)^{15}O$ $^{15}N(p, n)^{15}O$
$^{18}_{9}F$	110 min	β^+(97) EC(3)	0.511 (annihilation)	194	$^{18}O(p, n)^{18}F$
$^{32}_{15}P$	14.3 days	β (100)			$^{32}S(n, p)^{32}P$
$^{51}_{24}Cr$	27.7 days	EC(100)	0.320	9	$^{50}Cr(n, \gamma)^{51}Cr$
$^{52}_{26}Fe$	8.3 h	β^+(56) EC(44)	0.165 0.511 (annihilation)	100 112	$^{55}Mn(n, 4n)^{52}Fe$ $^{50}Cr(\alpha, 2n)^{52}Fe$
$^{57}_{27}Co$	271 days	EC(100)	0.014 0.122 0.136	9 86 11	$^{56}Fe(d, n)^{57}Co$
$^{58}_{27}Co$	71 days	β^+(14.9) EC(85.1)	0.811	99.5	$^{55}Mn(\alpha, n)^{58}Co$
$^{59}_{26}Fe$	45 days	β (100)	1.099 1.292	56 43	$^{58}Fe(n, \gamma)^{59}Fe$
$^{60}_{27}Co$	5.2 years	β (100)	1.173 1.332	100 100	$^{59}Co(n, \gamma)^{60}Co$
$^{62}_{28}Zn$	9.3 h	β^+(8) EC(92)	0.420 0.511 0.548 0.597	25 31 15 26	$^{63}Cu(p, 2n)^{62}Zn$
$^{62}_{29}Cu$	9.7 min	β^+(97) EC(3)	0.511 (annihilation)	194	$^{62}Ni(p, n)^{62}Cu$ $^{62}Zn \xrightarrow[9.3h]{\beta^+, EC} {}^{62}Cu$
$^{67}_{29}Cu$	2.6 days	β (100)	0.185	49	$^{67}Zn(n, p)^{67}Cu$
$^{201}_{81}Tl$	73 h	EC(100)	0.167 x ray (0.069 0.083)	9.4 93	$^{203}Tl(p, 3n)^{201}Pb$ $^{201}Pb \xrightarrow[9.3\ hr]{EC} {}^{201}Tl$

Nuclide	Physical half life	Mode of decay (%)	γ ray energy[a] (MeV)	Abundance (%)	Common production method
$^{67}_{31}Ga$	78.2 h	EC(100)	0.093 0.184 0.300 0.393	40 20 17 5	$^{68}Zn(p, 2n)^{67}Ga$
$^{68}_{31}Ga$	68 min	β^+(89) EC(11)	0.511 (annihilation)	178	$^{68}Zn(p, n)^{68}Ga$
$^{68}_{32}Ge$	270.8 days	EC(100)			$^{66}Zn(\alpha, 2n)^{68}Ge$
$^{82}_{37}Rb$	75 s	β^+(95) EC(5)	0.511 (annihilation) 776	190 13	$^{82}Sr \xrightarrow[25.5\ days]{EC} {}^{82}Rb$
$^{82}_{38}Sr$	25.5 days	EC(100)			$^{85}Rb(p, 4n)^{82}Sr$ $Mo(p, spallation)^{82}Sr$
$^{89}_{38}Sr$	50.6 days	β (100)			$^{88}Sr(n, \gamma)^{89}Sr$
$^{90}_{38}Sr$	28.6 years	β (100)			$^{235}U(n, f)^{90}Sr$
$^{90}_{39}Y$	2.7 days	β (100)			$^{89}Y(n, \gamma)^{90}Y$ $^{90}Sr \xrightarrow[\beta]{28.6y} {}^{90}Y$
$^{99}_{42}Mo$	66 h	β (100)	0.181 0.740 0.780	6 12 4	$^{98}Mo(n, \gamma)^{99}Mo$ $^{235}U(n, f)^{99}Mo$
$^{99m}_{43}Tc$	6.0 h	IT(100)	0.140	90	$^{99}Mo \xrightarrow[66\ hr]{\beta} {}^{99m}Tc$
$^{111}_{49}In$	2.8 days	EC(100)	0.171 0.245	90 94	$^{111}Cd(p, n)^{111}In$
$^{113m}_{49}In$	100 min	IT(100)	0.392	64	$^{112}Sn(n, \gamma)^{113}Sn$ $^{113}Sn \xrightarrow[117\ days]{EC} {}^{113m}In$
$^{123}_{53}I$	13.2 h	EC(100)	0.159	83	$^{121}Sb(\alpha, 2n)^{123}I$
$^{124}_{53}I$	4.2 days	β^+(23) EC(77)	0.511 (annihilation)	46	$^{124}Te(p, n)^{124}I$
$^{125}_{53}I$	60 days	EC(100)	0.035 x ray (0.027 0.032)	7 140	$^{124}Xe(n, \gamma)^{125}Xe$ $^{125}Xe \xrightarrow[17\ hours]{EC} {}^{125}I$
$^{131}_{53}I$	8.0 days	β (100)	0.284 0.364 0.637	6 81 7	$^{130}Te(n, \gamma)^{131}Te$ $^{235}U(n, f)^{131}Te$ $^{131}Te \xrightarrow[25\ min]{\beta} {}^{131}I$ $^{235}U(n, f)^{131}I$
$^{133}_{54}Xe$	5.3 days	β (100)	0.081	37	$^{235}U(n, f)^{133}Xe$
$^{137}_{55}Cs$	30.0 years	β (100)	0.662	85	$^{235}U(n, f)^{137}Cs$
$^{153}_{62}Sm$	1.9 days	β (100)	70 103	5 28	$^{152}Sm(n, \gamma)^{153}Sm$
$^{186}_{75}Re$	3.8 days	β (92) EC(8)	137	9	$^{185}Re(n, \gamma)^{186}Re$

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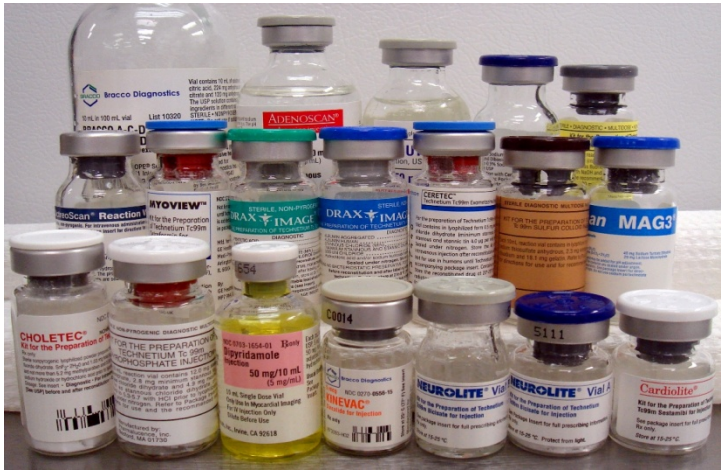
^{99m}Tc-labeled radiopharmaceuticals

- Pulmolite ® MAA kit
- Techne ® MDP kit
- Techne ® Pyrophosphate kit
- Techne ® DTPA kit
- Techne ® DMSA kit
- Techne ® Phytate kit
- Hepatolite ® DISIDA kit
- Ceretec ® HMPAO kit
- Neurolite ® ECD kit
- Cardiolite ® MIBI kit



Radiopharmaceutical kit

- Ligand :
  The properties of the ligand are primarily responsible for dictating how the product will behave in the body.

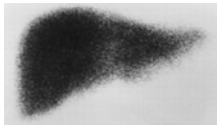
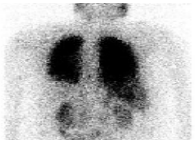
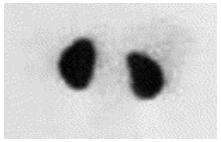
- Reducing agent :
  Stannous ion ..

- Other agent :
  Stabilizers , transfer ligands , buffer , solubilizing agent ..

Oxidation State of Technetium in Various Compounds	
Oxidation State	Chemical Form
Tc(VII)	Pertechnetate , Sulfur Colloid
Tc(V)	DMSA(high pH) , ECD , HMPAO ,MAG_3
Tc(IV)	DTPA , MDP , PYP
Tc(III)	DMSA(low pH) , HIDA analogues
Tc(I)	Sestamibi

Exchange reaction	
Radiopharmaceutical	Transfer ligand
^{111}In-Ibritumomab tiuxetan	Acetate
^{90}Y-Ibritumomab tiuxetan	
^{99m}Tc-Sestamibi	Citrate
^{111}In-Pentetreotide	
^{99m}Tc-ECD	EDTA
^{99m}Tc-MAG_3	Tartrate
^{99m}Tc-Trodat-1	Glucoheptonate

Radiopharmaceuticals

Radionuclide	(Non-radioactive Component)	Organ System		Study parameter
^{99m}Tc	+ Phytate	Liver		Reticuloendothelial system function
^{99m}Tc	+ Macroaggregated Albumin (MAA)	Lungs		Regional pulmonary perfusion
^{99m}Tc	+ DTPA	Kidneys		Renal Blood Flow

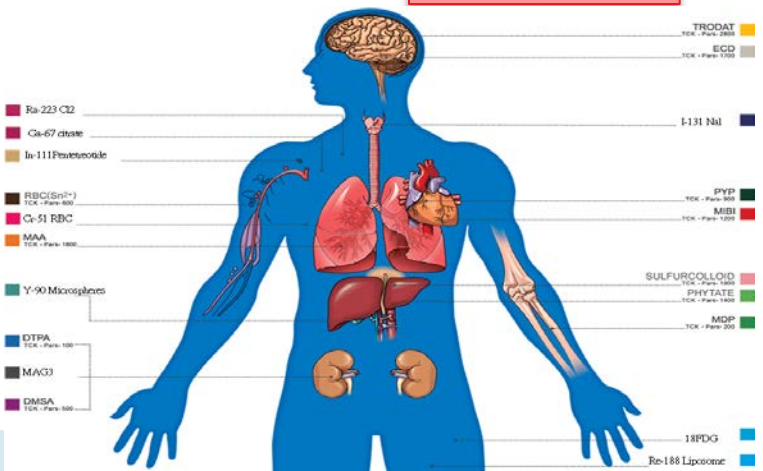
Mechanism(s) of Localization of Radiopharmaceuticals

Mechanism	Radiopharmaceutical
Isotope dilution	^{99m}Tc-red blood cells (RBC)
Capillary blockade	^{99m}Tc-macroaggregated albumin (MAA)
Phagocytosis	^{99m}Tc-SC
Cell migration	^{111}In-oxine-white blood cells (WBC), ^{99m}Tc-HMPAO-WBCs
Cell sequestration	^{99m}Tc-RBCs (heat damaged)
Simple diffusion	^{133}Xe gas, ^{99m}Tc-pertechnegas [^{15}O]water
Diffusion and mitochondrial binding	^{99m}Tc-sestamibi (Cardiolite®)
	^{99m}Tc-tetrofosmin (Myoview®)
Diffusion and intracellular binding	^{99m}Tc-exametazine (HMPAO) (Ceretec®)
	^{99m}Tc-bicisate (ECD) (Neurolite®)
	^{99m}Tc-(DMSA)
Diffusion and increased capillary permeability	^{67}Ga-citrate
Facilitated diffusion	[^{18}F]fluorodeoxyglucose (FDG)
Active transport	
Na^+/I^- sodium iodide symporter (NIS)	^{123}I and ^{131}I sodium iodide (I^-)
Na^+/K^+ ATPase pump	^{201}Tl-thallous chloride (Tl^+)
	^{82}Rb-chloride (RB^+)
	[^{13}N]ammonia as ammonium ion (NH_4^+)
Ion exchange with hydroxyapatite	
Exchange with OH^- ion	[^{18}F]fluoride (F^-)
Exchange with Ca^{2+} or calcium phosphate	^{99m}Tc-medronate (MDP)
	^{99m}Tc-oxidronate (HDP)
Glomerular filtration	^{99m}Tc-pentetate (DTPA)
Tubular secretion	^{99m}Tc-merteatide (MAG3)
Metabolic trapping	
Glucose metabolism	[^{18}F]fluorodeoxyglucose (FDG)
Tissue hypoxia and acidic pH	^{67}Ga-citrate
Specific receptor binding	
Hepatocyte anionic receptor	^{99m}Tc-disofenin, DISIDA (Hepatolite®)
	^{99m}Tc-mebrofenin (Choletec®)
Somatostatin (SSTR2) receptor	^{111}In-pentetreotide (octreotide) (OctreoScan®)
Dopamine transporter	^{123}I-ioflupane (DaTSCAN)
Norepinephrine and serotonin transporters and energy-dependent type I amine uptake mechanism	^{123}I and ^{131}I-meta-iodobenzylguanidine (mIBG)

Category of radiopharmaceuticals

Classification

- Radiopharmaceuticals
  - Diagnosis
    - SPECT
      - ^{99m}Tc kits
      - ^{67}Ga-citrate
      - ^{201}Tl-chloride
      - ^{133}Xe gas
      - ^{51}Cr-RBC
      - ^{131}I-NP59
      - ^{131}I-Nal
      - ^{111}In-Pentetreotide
    - PET
      - ^{18}FDG
      - ^{13}N-Ammonia
      - ^{11}C-sodium acetate
  - Therapy
    - ^{131}I-Nal
    - ^{90}Y-Microspheres (SIR-Spheres®)
    - ^{90}Y-Ibritumomab tiuxetan (Zevalin ®)
    - ^{223}Ra-Cl_2
    - ^{188}Re-liposome



	Examples
Ready-to-use prepared product	^{133}Xe gas , ^{131}I-Hippuran ^{67}Ga-citrate , ^{201}Tl-chloride , $^{99m}TcO_4^-$ $^{223}Ra\text{-}Cl_2$
Instant ^{99m}Tc kit	DTPA , MDP , DISIDA , MAA PYP , HMPAO , Phytate ….
^{99m}Tc kits requiring heating	Sestamibi , MAG_3 , Sulfur colloid
Products requiring significant manipulation	^{99m}Tc-Trodat-1 , ^{99m}Tc-ECD ^{131}I-NP59 , ^{111}In-pentetreotide , ^{51}Cr -RBC , ^{99m}Tc-RBC ^{90}Y-Microspheres (SIR-Spheres®) ^{90}Y-Ibritumomab tiuxetan (Zevalin ®) ^{18}FDG , $^{13}NH_3$, ^{11}C-sodium acetate…

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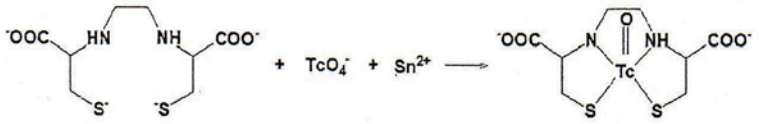
Labeling with ^{99m}Tc

Fig. 2.5. Direct labeling can be performed if ligand is present in metal binding form



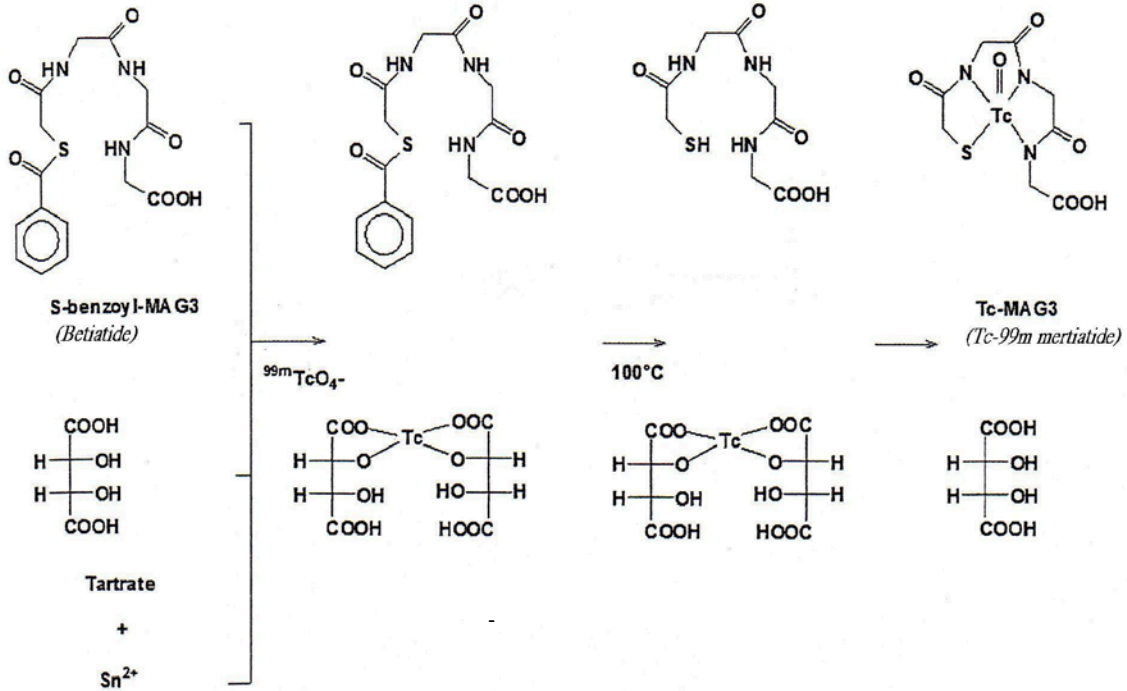


Fig. 2.6. Exchange labeling with ^{99m}Tc exemplified by ^{99m}Tc-MAG3

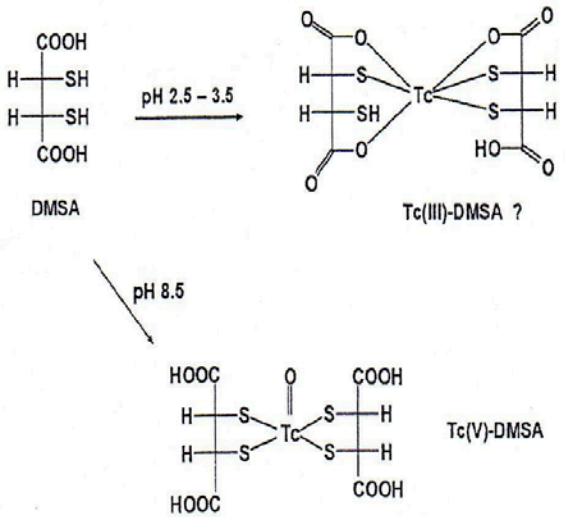


Fig. 2.4. pH determines valence of reduced Tc and nature of formed complex in the case of [^{99m}Tc]DMSA (the structure of Tc(III)-DMSA is a proposed structure)

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Preparation of a Technetium-99m labeled radiopharmaceutical

Tc-99m as sodium pertechnetate is added to the reaction vial

↓

Reduced ^{99m}Tc + chelating agent ⇌ ^{99m}Tc-chelate

Tc-99m radiopharmaceutical is ready for dispensing

↓

The patient dose is withdrawn from the vial

↓

Each dose is measured in the dose calibrator before it dispensed

- Common problems associated with ^{99m}Tc chelates:
    1. Excessive ^{99m}Tc
    2. Excessive ^{99}Tc
    3. Radiolytic oxidants
    4. Inadequate stannous ion

Mole Fractions of ^{99m}Tc and ^{99}Tc in Generator Eluates			
Time Since Prior Generator	Technetium Mole Fraction		Molar Ratio
	[^{99m}Tc / ^{99m}Tc + ^{99}Tc]	[^{99}Tc / ^{99}Tc + ^{99m}Tc]	^{99}Tc / ^{99m}Tc
3 hr	0.727	0.273	0.38
6 hr	0.619	0.381	0.62
12 hr	0.46	0.54	1.17
24 hr	0.277	0.723	2.61
48 hr	0.131	0.869	6.63
72 hr	0.077	0.923	11.99

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- Common problems associated with preparative manipulations :
    1. Improper mixing order
    2. Improper heating
    3. Incubation /time delays
    4. Component concentration
    5. Radiolytic effects

Particle Size Distribution of ^{99m}Tc-Sulfur Colloid	
Particle Size (nm)	% of Total
Standard Preparation method (5 minute heating)	
< 100	15 ~ 20
100 ~ 600	70 ~ 80
700 ~ 5000	2 ~ 4
> 5000	0.5 ~ 1.5
Modified Preparation method (3 minute heating)	
< 30	47
30 ~ 50	0
50 ~ 80	1
80 ~ 200	5
200 ~ 400	21
400 ~ 800	16
800 ~ 2000	5
2000 ~ 5000	1
5000 ~ 10000	0
> 10000	5

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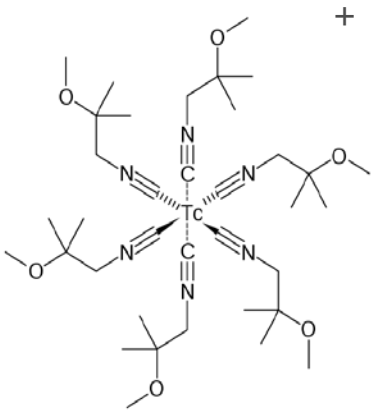
- Common problems associated with drug stability and delays before dispensing:

1. Aluminum ion
2. Radiolytic effects
3. Sedimentation particles
4. Interaction with container walls

Tc-99m sestamibi (Cardiolite ®)

Formulation

$Cu(MIBI)_4.BF_4$	1mg
L-Cysteine hydrochloride hydrate	1mg
Stannous chloride	0.075mg
Mannitol	20mg
Sodium citrate dihydrate	2.6mg



Prior to adding the Sodium Pertechnetate Tc99m Injection to the vial, inspect the vial carefully for the presence of damage, particularly cracks, and do not use the vial if found. Tear off a radiation symbol and attach it to the neck of the vial.

Remove the vial from the lead shield and place upright in an appropriately shielded and contained boiling water bath, such that the vial is suspended above the bottom of the bath, and boil for 10 minutes. Timing for 10 minutes is begun as soon as the water begins to boil again. Do not allow the boiling water to come in contact with the aluminum crimp.

Remove the vial from the water bath, place in the lead shield and allow to cool for fifteen minutes.

Biochemical Properties of SPECT and PET Myocardial Perfusion Imaging Agents

Property	^{201}Tl-Chloride	^{99m}Tc-Sestamibi	^{99m}Tc-Tetrofosmin	^{82}Rb-Chloride	^{13}N-ammonia
Molecular	+1 Cation	+1 Cation	+1 Cation	+1 Cation	Neutral
Charge	Hydrophilic	Lipophilic	Lipophilic	Hydrophilic	Lipophilic
Uptake mechanism	Active transport Na-K ATPase	Passive diffusion	Passive diffusion	Active transport Na-K ATPase	Passive diffusion $NH_4^+ \rightarrow NH_3 + H^+$ (19 μsec equilibrium)
First-pass extraction (at resting blood flow)	~85 % Diffusion limited > 2.5ml / min /gram	~66 % Diffusion limited > 2.0ml / min /gram	~54 % Diffusion limited > 1.7ml / min /gram	~59 % Diffusion limited > 1ml / min /gram	~82% Diffusion limited > 2ml / min /gram
Heart uptake (% injected dose at rest)	~ 4%	~ 1.2%	~ 1.0%		
Heart retention	Redistributes	Bound in mitochondria	Bound in mitochondria	Redistribution (not possible) (rapid physical Half-life = 76 sec)	$^{13}NH_3$+Glutaminic acid $\rightarrow$ ^{13}N-Glutamine Biologic half-life = 1~2hr) (rapid physical Half-life = 10min)

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Contraindications for use of pharmacologic agents in stress testing

Contraindications	Dipyridamole	Adenosine	Dobutamine
Unstable angina or resting ischemia	X	X	X
Poor LV function (EF<15%)	X	X	X
Hypertension (> 200mm Hg systolic)		X	X
Hypotension (< 90mm Hg systolic)	X	X	
Severe aortic stenosis			X
History of asthma	X	X	
Active bronchospastic disease	X	X	
History of tacharrhythmias			X
Second-degree AV block		X	
Oral dipyridamole		X	
Xanthine compounds	X	X	
Atrial fibrillation with rapid ventricular response			X

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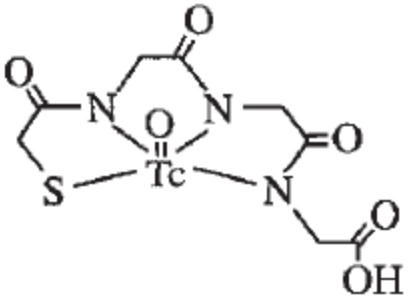
Tc-99m Mertiatide (MAG_3)

Formulation

	European	U.S
Betiatide	1mg	1mg
Disodium tartrate	16.9mg	40mg
Stannous chloride	40μg	200μg
Lactose	None	20mg



Immediately following the addition of sodium pertechnetate Tc 99m solution to the reaction vial, withdraw the syringe plunger to a volume of 2 mL, thus removing 2 mL of argon gas and adding 2 mL of filtered air to the vial. The air is required to oxidize excess stannous ion. Remove both needles from the vial.

↓

Invert the reaction vial several times to obtain complete mixing.

↓

Immediately transfer the reaction vial to the water bath. Place it inside the lead shield which has been equilibrated to the temperature of the boiling water bath. Allow the reaction vial to incubate for 10 minutes.

- Fractors that may cause radiochemical impurities :
  1、 >100mCi ^{99m}Tc
  2、 Volume < 4ml
  3、Waiting longer than 5min to place the vial into the boiling water bath .
  4、Not adding air to the vial during radiolabeling .

Biologic properties of renal imaging radiopharmaceuticals

Property	Tc-99m DTPA	Tc-99m GH	Tc-99m DMSA	Tc-99m MAG3	I-131 OIH
Glomerular filtration	Yes	Yes	Not significant	Not significant	Yes
Tubular transport	No	Yes (cortical binding)	Yes (cortical binding)	Yes (Secretion)	Yes (Secretion)
Tubular reabsorption	No	No	No	No	No
Collecting system	Yes	Yes	No	Yes	Yes
Cortical binding	No	Yes	Yes	No	No
Dosage	10mCi (blood flow) 3mCi (renogram)	10mCi (blood flow) 15mCi (static)	5mCi (static)	5mCi (blood flow) 1~3mCi (renogram)	75μCi (1kidney) 200μCi (2kidneys) (renogram)
Critical organ	Bladder wall	Bladder wall	kidney cortex	Bladder wall	Bladder wall
rad (cGy)/mCi (4.8hr void)	0.27	0.28	0.85	0.48	5.71

Radiopharmaceuticals in Nuclear Pharmacy and Nuclear Medicine ,p555

Tc-99m ECD (Neurolite ®)

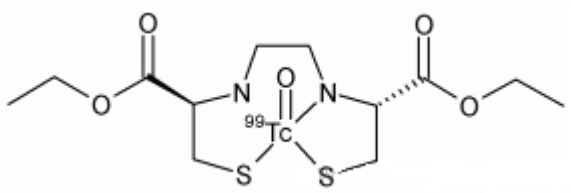
Vial A Bicisate ·2HCl (l,l-ECD·2HCl)
EDTA (Edetate disodium dihydrate)
$SnCl_2$ .. pH=2.7 ± 0.25
Vial B Phosphate buffer
pH=7.6 ± 0.4

With a sterile shielded syringe, aseptically add 3.70 GBq (100 mCi) sterile, non-pyrogenic, oxidant-free Sodium Pertechnetate Tc99m Injection, in approximately 2.0 ml, to vial B. Without withdrawing the needle, remove an equal volume of air to maintain pressure within the vial.

With a sterile syringe, rapidly inject 3.0 ml of Sodium Chloride Injection (0.9%) into vial A (the lyophilized vial) to dissolve the contents. Without withdrawing the needle, remove an equal volume of air to maintain pressure within the vial. Shake the contents of the vial for a few seconds.

With another sterile syringe, immediately (within 30 seconds) withdraw 1.0 ml of vial A and inject it into vial B.

Swirl the contents of the vial B for a few seconds and allow this mixture to stand for thirty (30) minutes at room temperature.



Cerebral retention

l.l > d.l > d.d

HMPAO vs ECD

Table 4.1. Pharmacokinetics of technetium radiopharmaceuticals for brain perfusion SPECT.

Parameter	^{99m}Tc-HMPAO	^{99m}Tc-ECD
In vitro Characteristics		
Stability	30 min (>4 h with stabilizer)	>6 h
Biologic Characteristics		
Plasma protein binding	Higher extraction	Hydrophilic
First extraction (%)	hydrophilic conversion	conversion by
Retention mechanism	by interaction with glutathion	de-esterification
Brain kinetics		
	2%–3%*	4%–7%
Brain uptake (% I.D)	2 min	2 min
peak brain activity	12%–15% over 15 min	12%–14% the first hour; then
Brain washout		6%/h
	50% liver–gut	15% liver–gut
Excretion (% at 48 h pi)	40% kidneys	75% kidneys
Dosimetry		
	555–1,100 MBq	555–1,100 MBq
injection dose (MBq)	Lachrymal glands	Urinary bladder
Target organs	Gallbladder wall	Gallbladder wall
Imaging		
Recommended imaging time	Upto 4 h p.i.	Up to 2 h p.i.
Ratio of Gray matter to white matter	2–3:1	4:1

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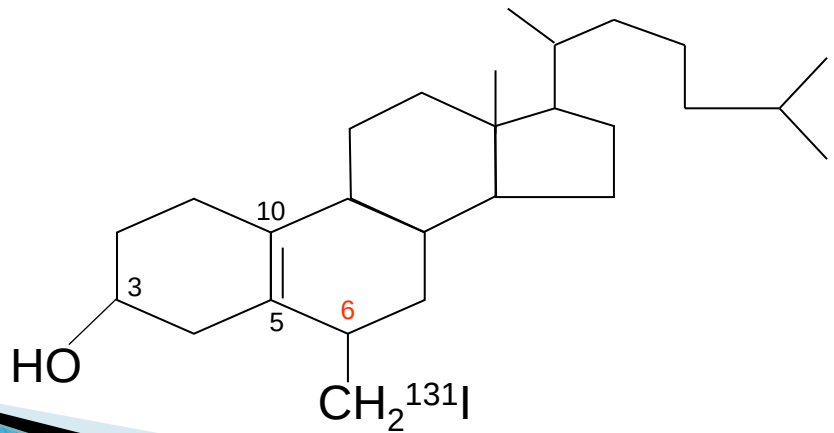
Adosterol ®

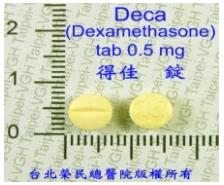
- ^{131}I-labeled NP-59 is use in Adrenocortical scan. (Cushing's syndrome, aldosteronism, adrenal adenoma, adrenal hyperplasia.)
- Radiocholesterols are dissolved in an alcoholic vehicle ontain Tween-80 and should be injected intravenously over 2~3min .

Vol.		0.5ml	1ml
6β-iodomethyl-19-nor-cholest-5(10)-en-3β-o1 (^{131}I) (inspection day)		18.5MBq	37.5MBq
Inactive ingredients	Ethanol	0.008ml	0.016ml
	Polysorbate 80	0.016ml	0.032ml
	physiological saline	appropriate amount	
Appearance		colorless transparent fluid	
PH		5.5 ~ 7.0	
Osmotic ration (vs. 9.9% saline)		Approx . 2	

Adosterol ®

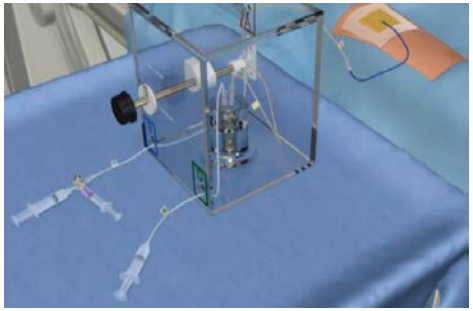
- Administer an appropriate iodine drug thyroid gland (such as Lugol` solution or SSKI).
- Dexamethasone suppression .
- At 4°C, NP-59 is stable for 2 weeks , an deiodination occurs at room or higher temperature





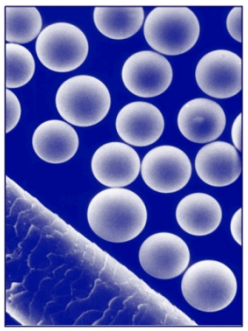
^{90}Y-Microspheres (SIR-Spheres®)

- Energy (Mean /Maximum) (MeV) : 0.94 /2.3
- Range (Mean /Maximum) (mm) : 2.5 /11
- SIR-Spheres® are intended for use on the day of calibration. (>24hr , Particle number ↑ 30%).
- SIR-Spheres® is intended for implantation into hepatic tumours via the hepatic artery.
- For treating unresectable liver metastasis from primary colorectal cancer.



Characteristics of Microspheres

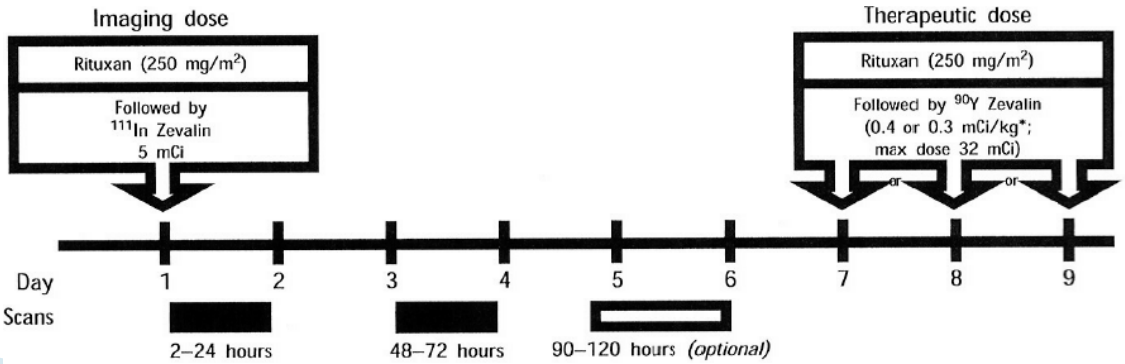
Parameter	Resin	Glass
Trade name	Sir-Spheres ®	TheraSphere ®
Manufacturer and location	Sirtex Medical (Singapore)	MDS Nordion (Canada)
Diameter (μm)	20 ~ 60	20 ~ 35
Particles /activity (million/3GBq)	40 ~ 80	1.2
Specific gravity	1.6g/dl	3.6g/dl
Specific activity per microsphere	50Bq	2500Bq



Microscopic view of yttrium-90 microspheres beside a strand of hair.

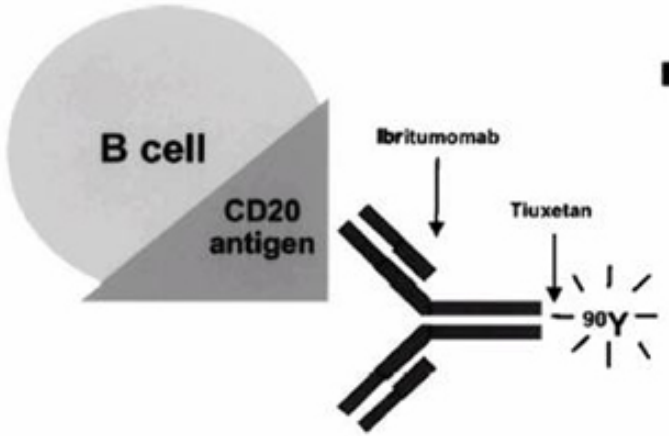
^{90}Y-Ibritumomab tiuxetan (Zevalin®)

- Zevalin® in the treatment of relapsed or refractory low-grade ,follicular,transformed B-cell Non-Hodgkin's Lymphoma.
- The Rituximab predose is given initially to block accessible CD 20 sites in the peripheral circulation and prevent indiscriminate uptake of the radiolabeled antibody in the reticuloendothelial system .



*0.4 mCi/kg in patients with a platelet count ≥150,000/μL or 0.3 mCi/kg with a platelet count 100,000–149,000/μL. Maximum dose is 32 mCi.

^{90}Y–Ibritumomab tiuxetan (Zevalin ®)



- ^{90}Y Ibritumomab tiuxetan
  - Ibritumomab (murine antibody parent of Rituximab)
  - Tiuxetan (MX-DTPA) conjugated to antibody forming strong urea-type bond
    - Stable retention of ^{90}Y
  - Yttrium-90
    - $T_{1/2}$ = 64 hours
    - Outpatient administration
    - Beta emission χ_{90} = 5 mm
- CD20 antigen
  - Hydrophobic, 35 kD phosphoprotein
  - Expressed only on B lineage cells
  - Important for cell cycle initiation and differentiation
  - Does not shed, internalize or modulate

Figure 1. Ibritumomab tiuxetan consists of a murine monoclonal anti-CD20 antibody (ibritumomab) covalently bound to a linker-chelator (tiuxetan), which securely chelates ^{111}In for imaging and ^{90}Y for therapy.

(Source: Wiseman GA et al. Cancer Biotherapy and Radiopharmaceuticals 18(2):165-178.)

^{90}Y-Ibritumomab tiuxetan (Zevalin ®)

TABLE 29-1 Radiolabeling of Ibritumomab Tiuxetan with ^{111}In and ^{90}Y

^{111}In Labeling Steps	^{90}Y Labeling Steps
1. Add required volume of 50 mM sodium acetate buffer to the reaction vial. (Buffer volume = 1.2 times the volume of 5.5 mCi $^{111}InCl_3$.) Coat entire surface of reaction vial with buffer.	1. Add required volume of 50 mM sodium acetate buffer to the reaction vial. (Buffer volume = 1.2 times the volume of 40 mCi $^{90}YCl_3$.) Coat entire surface of reaction vial with buffer.
2. Add 5.5 mCi $^{111}InCl_3$ to the reaction vial and mix the solutions.	2. Add 40 mCi $^{90}YCl_3$ to the reaction vial and mix the solutions.
3. Add 1.0 mL of the antibody to the reaction vial and roll/mix solutions gently. Do not cause foaming of the antibody.	3. Add 1.3 mL of the antibody to the reaction vial and roll/mix solutions gently. Do not cause foaming of the antibody.
4. Incubate at room temperature for 30 minutes.	4. Incubate at room temperature for 5 minutes.
5. Add the formulation buffer (FB) to quench the labeling. (FB volume = 10 mL minus the volumes of $^{111}InCl_3$ + acetate buffer + antibody.)	5. Immediately add the formulation buffer to quench the labeling. (FB volume = 10 mL minus the volumes of $^{90}YCl_3$ + acetate buffer + antibody.)

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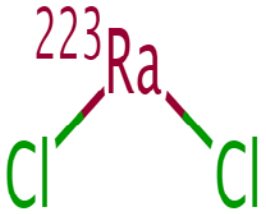
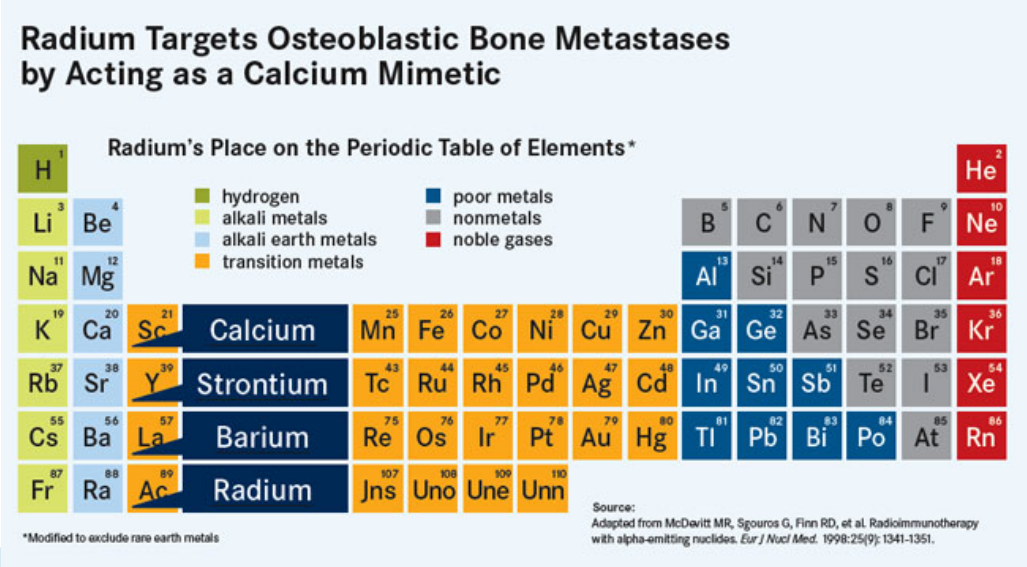
^{223}Ra–Dichloride (Xofigo®)

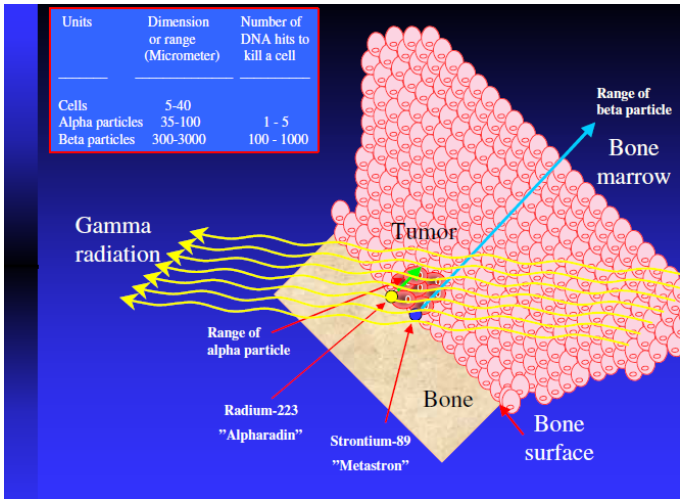


- Radium belongs to the same group of elements as Calcium.
- Radium-223 is a calcium mimetic that binds to newly formed bone stroma,



^{223}Ra-Dichloride (Xofigo®)

- Xofigo® is indicated for the treatment of patients with castration-resistant prostate cancer (CRPC), symptomatic bone metastases and no known visceral metastatic disease.
- $^{223}RaCl_2$ emits high-energy ionizing α- particle which cause lethal, double-strand DNA breaks in adjacent tumor cells in the bone.



^{223}Ra-Dichloride (Xofigo®)

- Recommended Dosage :
  50 kBq (1.35 μCi) / kg body weight, given at 4-week intervals for 6 injections
- Radium-223 emits mainly α-particles
- t1/2 = 11.43 days
- Of the total decay energy
  - 95.3 % emitted as α-particles
  - 3.6% emitted as β-particles
  - 1.1% emitted as γ- or X-rays

^{99m}Tc-Trodat-1

- A ^{99m}Tc labeled tropane derivative (cocaine), is a potential dopamine transporter (DAT) imaging agent for the central nervous system.
- N_2S_2 diaminedithiol type chelator with tropane at the 2β-position.

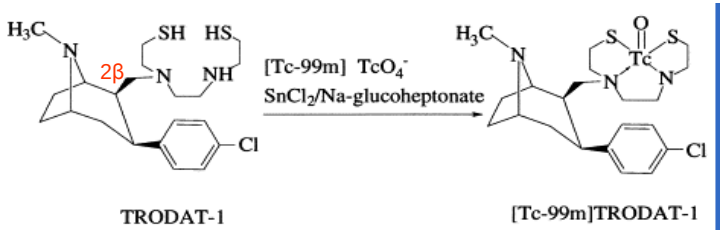
Forty mCi of elution of freshly $^{99m}TcO_4^-$ diluted in 5 ml of saline solution were injected in the kit

↓

submitted to 16 atm and temperature of 121ºC, during 30 minutes in an autoclave

↓

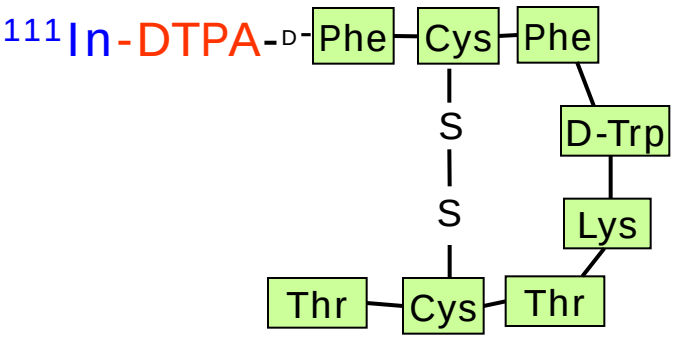
After cooling to room temperature in an water bath over 15 min.



^{111}In-Pentetreotide(OctreoScan®)

- 8-amino acid segment of somatostatin that maintains active binding properties ,It is resistant to enzymatic degradation in the body.
- The agent for the scintigraphic localization of Primary and metastatic neuroendocrine tumors bearing somatostatin receptors (SSTR2、5).

The components of Octreoscan® manufactured by INER		
Ingredient	**Amount**	**Purpose**
Reaction vial 10ml		
Pentetreotide ：	10 μg	Ligand
Gentisic acid ：	2 mg	Stabilizer
Trisodium citrate	4.9 mg	Buffer
Citric acid ：	0.37 mg	Stabilizer
Inositol ：	10mg	Stabilizer
Indium vial 10ml		
^{111}In-chloride ：	1.1ml (3mCi/ml)	Tracer



^{99m}Tc-Labeled Red blood Cells

- Mechanism :

$$\text{Cold-PYP+RBC} \longrightarrow {}^{99m}\text{Tc+RBC} \longrightarrow {}^{99m}\text{Tc-RBC}$$

10 ~20ug/kg

$^{99m}TcO_4^- + Sn^{2+} \rightleftharpoons$ reduces $^{99m}Tc + Sn^{4+}$

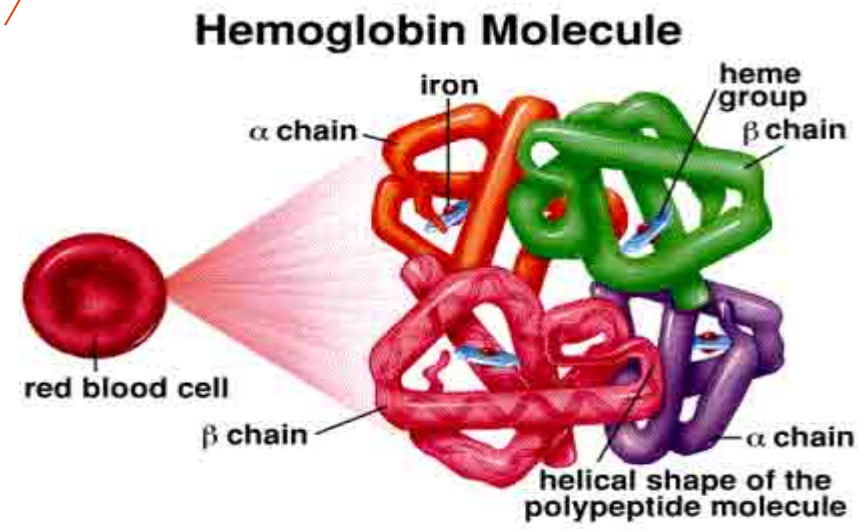
80% of reduced Tc binds to β chain of the globin part of hemoglobin And 20% to heme .

cell membrane

RBC

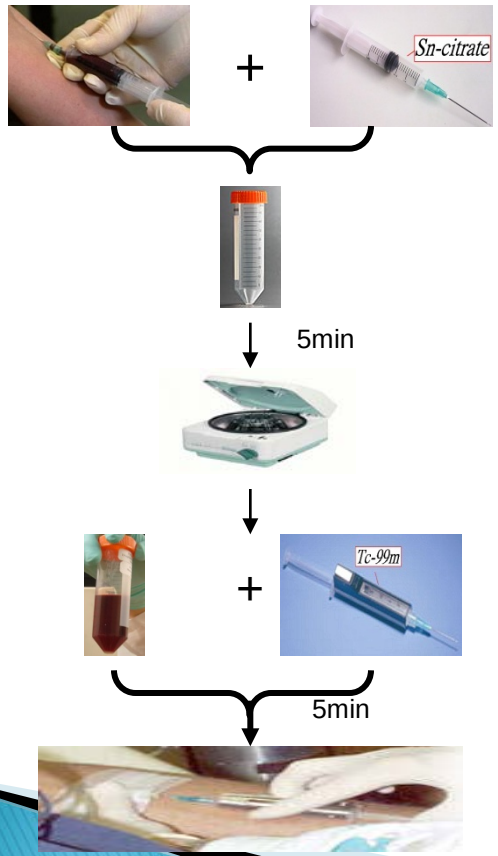
$TcO_4^- \rightleftharpoons TcO_4^- \rightarrow$ Reduced ^{99m}Tc

Bound



^{99m}Tc-Labeled Red blood Cells

In vitro

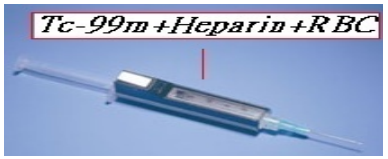


In vivo

20min

Modified in vivo

20min



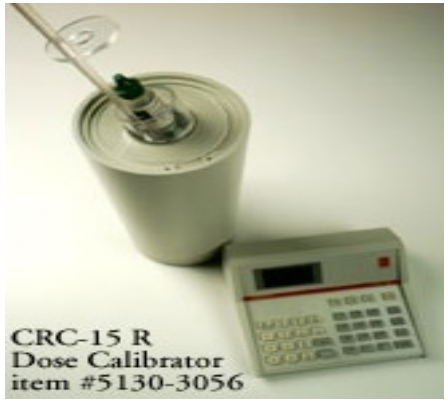
10min

Clinical applications of radiolabelled cells and radiolabelling approach

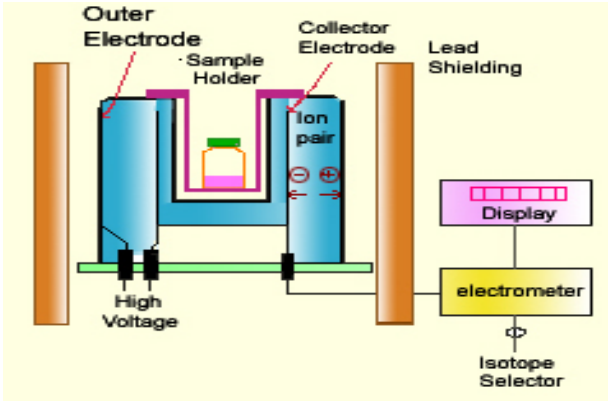
Clinical application	Blood cellular element	Radionuclide /radiolabel	Radiolabelling approach
Cardiac and vascular imaging	Red cells	^{99m}Tc-pertechnetate	In vivo In vivo/in vitro
Gastrointestinal bleeding	Red cells	^{99m}Tc-pertechnetate	In vivo In vivo/in vitro
Spleen imaging	Denaturated red cells	^{99m}Tc-pertechnetate	In vitro In vivo/in vitro
Blood volume and red cell volume	Red cells	^{99m}Tc-pertechnetate ^{51}Cr-chromate	In vitro
Red cell survival	Red cells	^{51}Cr-chromate	In vitro
Site of red blood cell destruction	Red cells	^{51}Cr-chromate	In vitro
Infection and inflammation	White blood cells	^{111}In-oxine ^{111}In-tropolone ^{99m}Tc-HMPAO	In vitro
Abnormal platelet deposition	Platelets	^{111}In-oxine ^{111}In-tropolone ^{99m}Tc-HMPAO	In vitro

Dose Calibrator

- Ionization chamber
  - Sealed chamber (Argon ,halogen..)
  - High pressure
  - Operating voltage(about 150 V)



- Isotope selector
  - Calibration factor
  - Feedback resistors

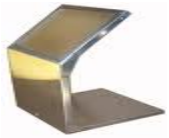


Basic storage and shielding equipment for radioactive material

Lead-lined storage cabinets

a. Radiopharmaceuticals
b. Radioactive sources
c. Radioactive waste

Lead L-block shields



Lead bricks

Lead vial shields and syringe shields

Lead foil or sheeting of various thickness

Radionuclide	Half value layer (cm)				
	lead	Iron	Al	Water	Concrete
Mo-99	0.49	1.11	3.16	7.6	3.54
Tc-99	0.05	0.25	0.73	1.73	0.82
Tc-99m	0.07	0.39	1.13	2.68	1.27
I-131	0.25	0.93	2.67	6.5	3.02
Xe-133	0.03	0.16	0.47	1.11	0.53
Co-60	1	1.66	4.65	10.99	5.2
Cr-51	0.17	0.82	2.38	5.69	2.68
Sr-89	0.74	1.4	4	9.35	4.42

Estimation of Attenuation Factors

Number of HVLs	Attenuation Factor
1	0.5
2	0.25
3	0.125
4	0.0625
5	0.03125
6	0.015625
7	0.0078125
8	0.00390625
3.3	0.10 (10%)
6.6	0.01 (1%)
9.9	0.001 (0.1%)

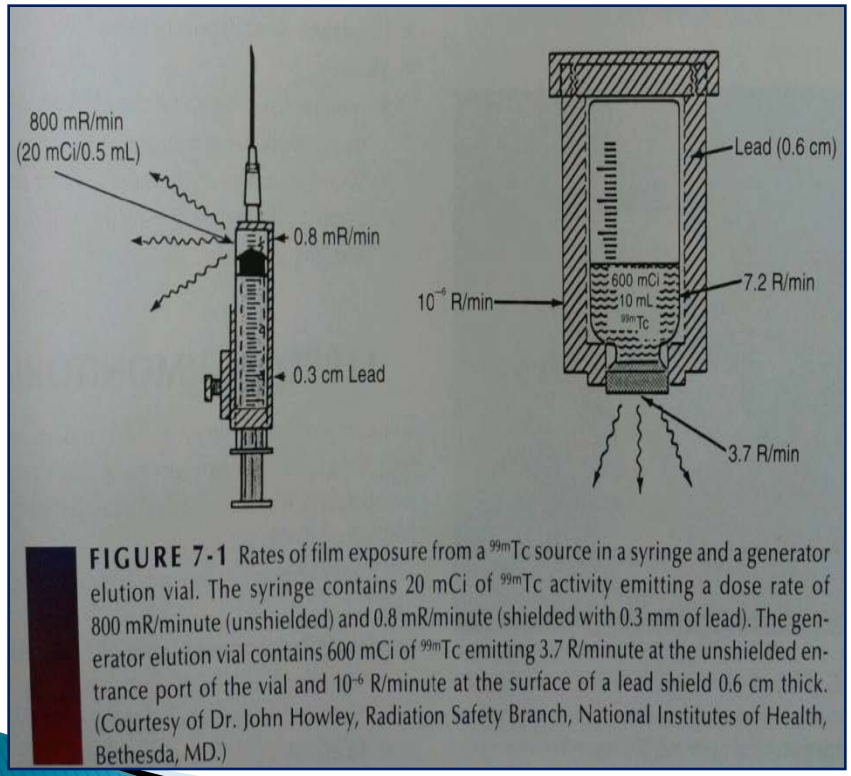


FIGURE 7-1 Rates of film exposure from a ^{99m}Tc source in a syringe and a generator elution vial. The syringe contains 20 mCi of ^{99m}Tc activity emitting a dose rate of 800 mR/minute (unshielded) and 0.8 mR/minute (shielded with 0.3 mm of lead). The generator elution vial contains 600 mCi of ^{99m}Tc emitting 3.7 R/minute at the unshielded entrance port of the vial and 10^{-6} R/minute at the surface of a lead shield 0.6 cm thick. (Courtesy of Dr. John Howley, Radiation Safety Branch, National Institutes of Health, Bethesda, MD.)

Volume (mL)	A	B	C
0.5	55	1.25	0.30
1.0	40	1.75	0.25
2.0	25	5.95	0.20

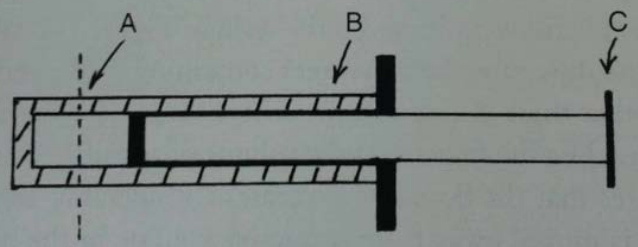


FIGURE 7-2 Exposure rate (in mrem per mCi per minute) of fingers at various positions on an unshielded 2 mL plastic syringe containing ^{99m}Tc. (Compiled from reference 9.)

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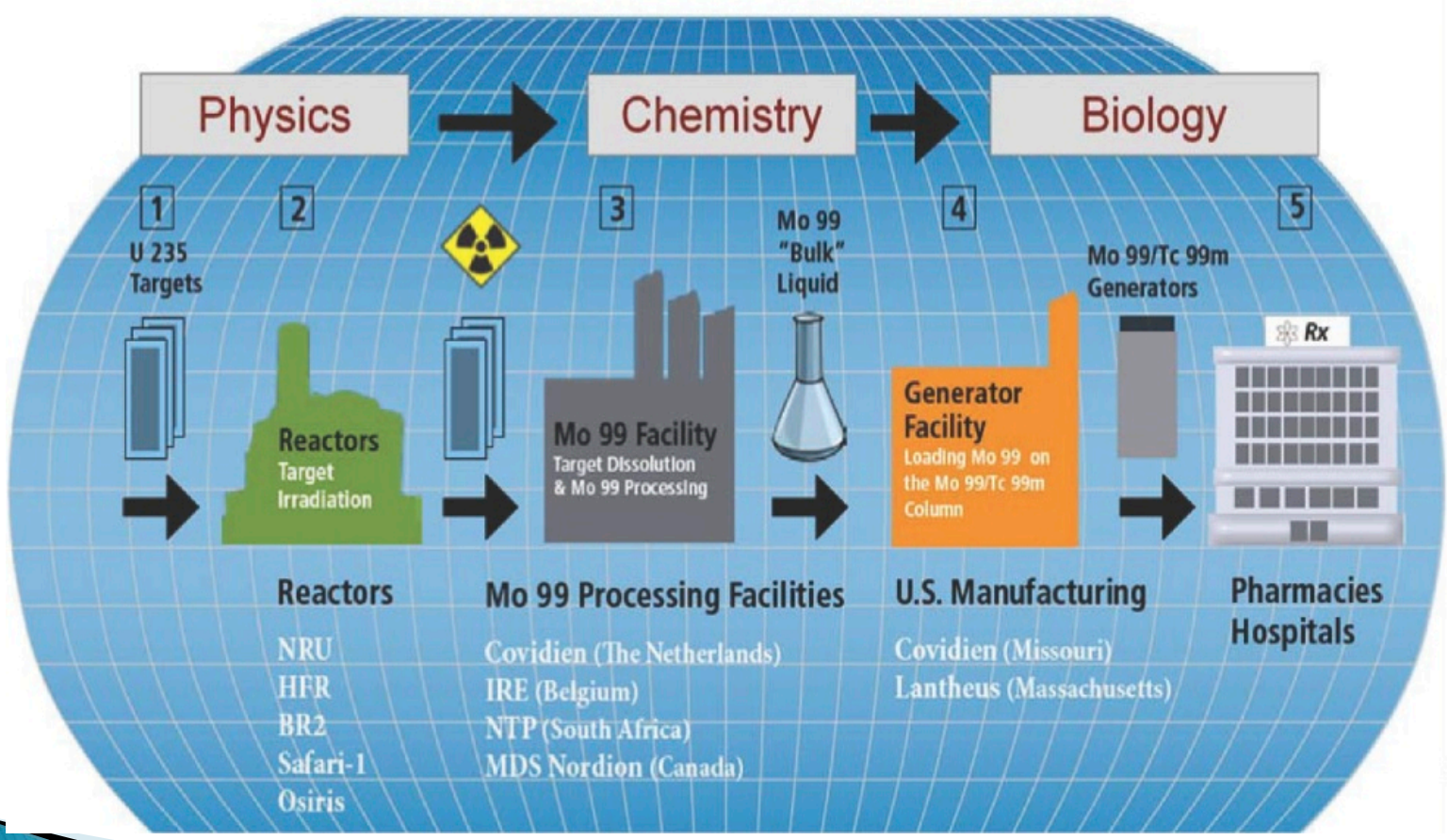
Mo-99/Tc-99m generator systems

The supply chain

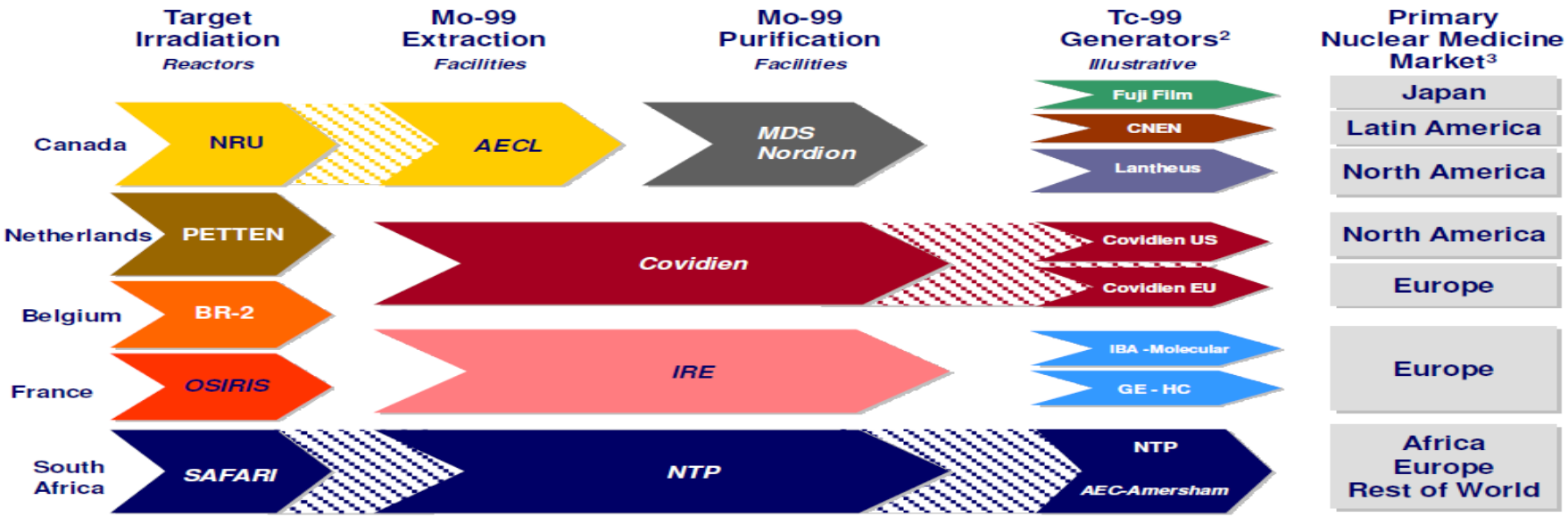


Tc-99 Global Distribution Channels

SNM 2009 Annual Meeting

Five nuclear reactors serve global demand through four distribution channels[1]

Wholesale Processor of Bulk Mo-99



1. Distribution channels illustrate markets where majority of sales occur
2. Most Bulk Mo-99 processors also cross-sell to some other generator companies
3. Indicates markets where majority of sales occur; distributors also serve other markets

Source: SECOR Analysis

SECOR CONSULTING

^{99}Mo-^{99m}Tc

Ultra-Techne Kow® (^{99}Mo-^{99m}Tc Generator)

Indications / Effects	- Diagnosis of cerebral tumor and cerebral vessel disorders - Diagnosis of thyroid diseases - Diagnosis of salivary gland diseases - Diagnosis of ectopic gastric mucosa diseases - Test of regional pulmonary ventilation function in combination with medical device,"Techne Gas Generator"	
Size	925 MBq, 1.85, 3.70, 5.55, 7.40, 11.1, 14.8 and 18.5 GBq (25, 50, 100, 150, 200, 300, 400 and 500 mCi) *37.0 GBq is exclusive size for export.	
Contents	Sodium pertechnetate (^{99m}Tc) injection generator	1 pc
	Saline solution	1 bottle (200 ml)
	Collecting vial (5 or 10 or 20)	8 vials
	Injection needle for elution	8 pieces
	Tube for elution (when needed)	2 pieces
	Elution shield (when needed)	1 piece
pH	4.5 - 7.0	
Storage	Room temperature	
Expiration	12 days after calibration	

The ELUMATIC® III GENERATOR has an activity expressed in ^{99m}Tc at the date indicated on the label.

Elution solution : aqueous sterile and pyrogen free 0.9 % sodium chloride and 0.005% sodium nitrate solution.

Availability and Calibration	on Monday calibrated Saturday 12 a.m. on Tuesday calibrated Saturday or Wednesday (following week) 12 a.m. on Wednesday calibrated Wednesday (following week) 12 a.m. on Thursday calibrated Wednesday 12 a.m. on Friday calibrated Wednesday or Saturday (following week) 12 a.m.
Ordering deadline	3 days before the shipment day, before 11 a.m.
Expiry	20 days after the manufacturing date
Elution volume	5, 10 or 15 mL
Radiochemical purity	⩾ 95 %
Radionuclidic purity	$^{99}Mo \leqslant 0.1$ %, $^{131}I \leqslant 5.10^{-3}$ %, $^{103}Ru \leqslant 5.10^{-3}$ %, $^{89}Sr \leqslant 6.10^{-5}$ %, $^{90}Sr \leqslant 6.10^{-6}$ %, $\alpha \leqslant 1.10^{-7}$ %, other $\gamma \leqslant 0.01$ % at the date indicated on the label
pH	4.0-8.0
Storage	- Generator : 20 days. Not above 25°C. - Sodium (^{99m}Tc) pertechnetate solution : store at 2-8°C and use within 10 hours after elution.
Precalibred quantities	2 - 4 - 6 - 8 - 10 - 12 - 16 - 20 GBq
Indications	1. Reagent for labelling various kits to be used with ^{99m}Tc 2. Administered intravenously the eluate might be used in : • Thyroid scintigraphy • Salivary gland scintigraphy • Localization of ectopic gastric mucosa • Cerebral scintigraphy 3. In conjunction with a reducing agent for labelling red blood cells for : • Cardiac and vascular scintigraphy • Diagnosis and localisation of occult gastrointestinal bleeding 4. Administered by instillation into the eye for : • Lacrymal duct scintigraphy

- $(NH_4)_2{}^{99}MoO_4$
  Ammonium molybdate
- $^{99}MoO_4^{-2}$ → $^{99m}TcO_4^{-1}$
- $Na^{99m}TcO_4$
  Sodium pertechnetate

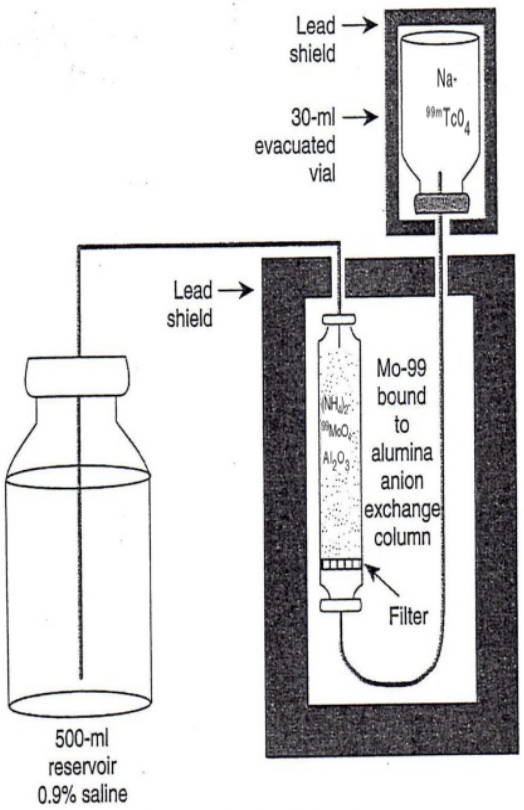


Figure 1-3 "Wet" radionuclide generator system.

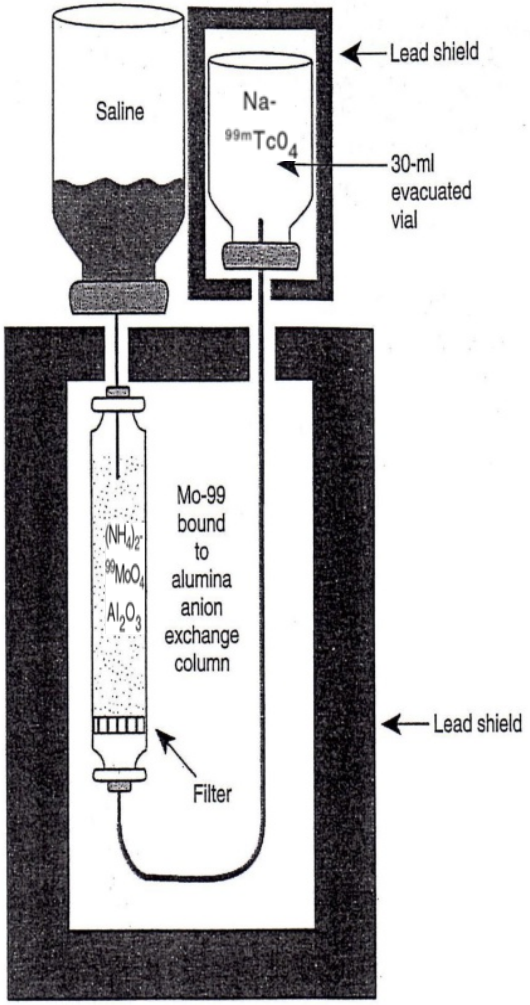


Figure 1-4 "Dry" radionuclide generator system.

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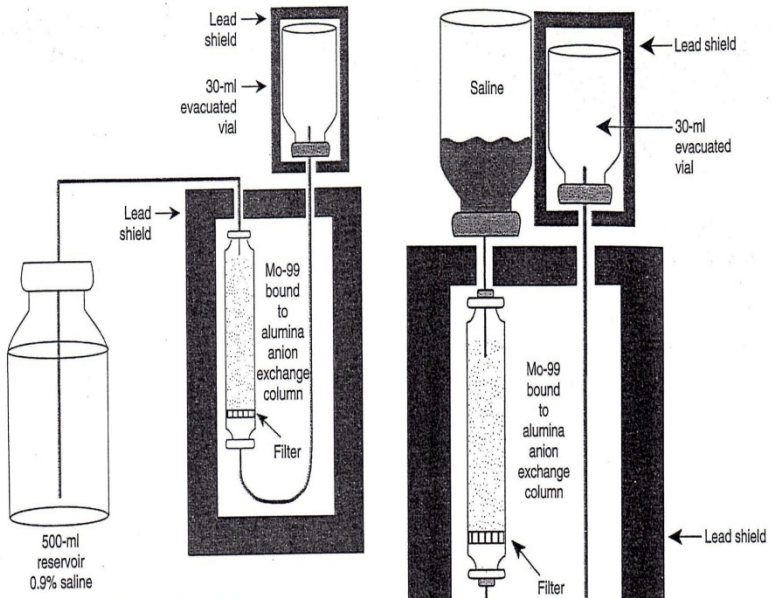

Figure 1-3 "Wet" radionuclide generator system.

Figure 1-4 "Dry" radionuclide generator system.

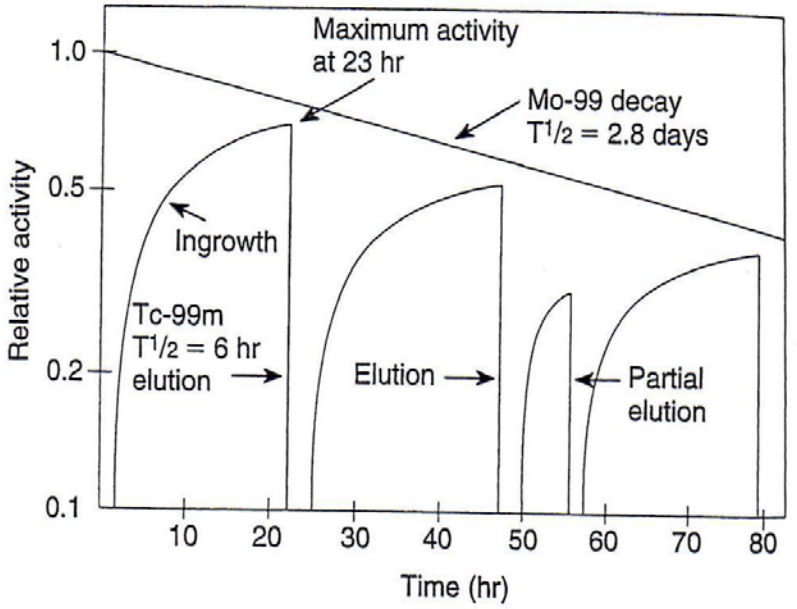

Figure 1-2 Decay curve for molybdenum-99 and ingrowth curves for Tc-99m. Successive elutions, including a partial elution are illustrated. Relative activity is plotted on a logarithmic scale, accounting for the straight line of Mo-99 decay.

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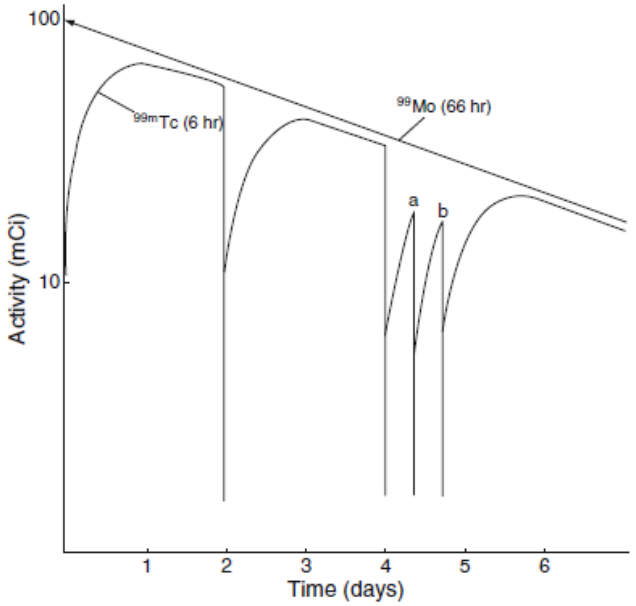

FIGURE 5.2. Typical decay growth relationship of ^{99}Mo and ^{99m}Tc activities in a Moly generator. On day 2, ^{99m}Tc activity is eluted with saline and then starts growing after elution. The yield of ^{99m}Tc is approximately 80 90%. It takes approximately 24 h to reach maximum activity of ^{99m}Tc after elution. Positions *a* and *b* indicate elutions of ^{99m}Tc activity at 8 and 17 h after elution on day 4.

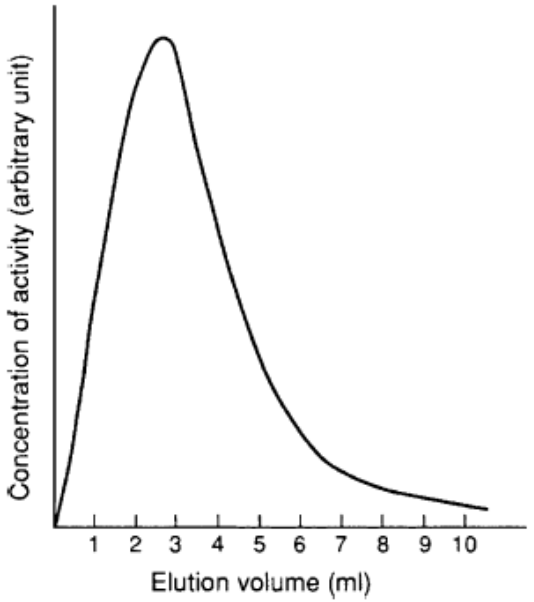

FIGURE 5.4. Elution profile of the ^{99m}Tc activity expressed as concentration of radio activity versus eluate volume. The profile may be broader or narrower depending on the type of generator. For generators using fission produced ^{99}Mo, the eluate volume is about 2 3 ml due to the smaller alumina column.

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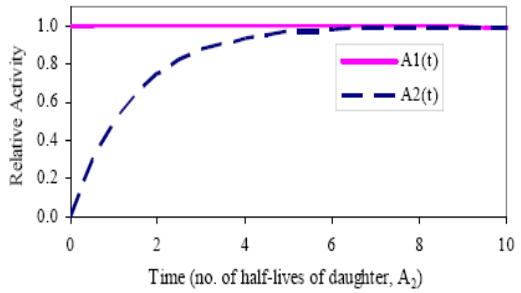
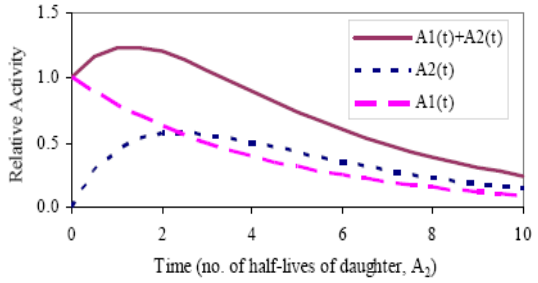
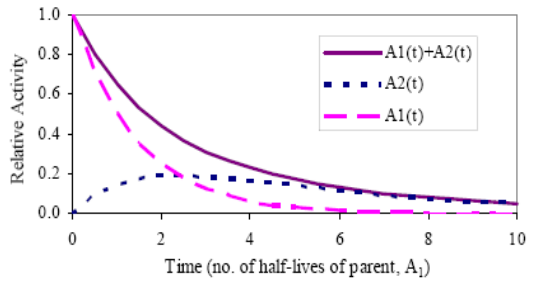
永久平衡 (Seqular equilibrium)	暫態平衡 (Transient equilibrium)	不平衡 (No equilibrium)
母核 $T_{1/2}$>>子核$T_{1/2}$ 100倍以上	母核 $T_{1/2}$>子核$T_{1/2}$ 10-100倍	母核 $T_{1/2}$<子核$T_{1/2}$
		
達平衡時放射活度： $A_2 \fallingdotseq A_1$	$A_2 = \frac{\lambda_2}{\lambda_2 - \lambda_1} A_1$	
$^{68}Ge \xrightarrow{\beta^-} {}^{68}Ga$ $T_{1/2}$=275d　$T_{1/2}$=68 min	$^{99}Mo \xrightarrow{\beta^-} {}^{99m}Tc$ $T_{1/2}$=67h　$T_{1/2}$=6h	$^{218}Po \xrightarrow{\alpha} {}^{214}Pb$ $T_{1/2}$=3 min　$T_{1/2}$=27 min

TABLE 5.1. Several generator systems useful in nuclear medicine.

Parent	Parent $t_{1/2}$	Nuclear reaction	Daughter	Daughter $t_{1/2}$	Mode of daughter decay	Principal photon energy (keV) (% abundance)	Column	Eluant
^{99}Mo	66 hr	Fission ^{98}Mo(n, γ)	^{99m}Tc	6 hr	IT[a]	140 (90)	Al_2O_3	0.9% NaCl
^{113}Sn	115 days	^{112}Sn(n, γ)	^{113m}In	99.5 min	IT	392 (64)	ZrO_2	0.05 *N* HCl
^{87}Y	80 hr	^{88}Sr(p, 2n)	^{87m}Sr	2.8 hr	IT	388 (82)	Dowex 1 × 8	0.15 *M* $NaHCO_3$
^{68}Ge	271 days	^{69}Ga(p, 2n)	^{68}Ga	68 min	β^+	511 (178)	Al_2O_3 SnO_2	0.005 *M* EDTA 1 *N* HCl
^{62}Zn	9.3 hr	^{63}Cu(p, 2n)	^{62}Cu	9.7 min	β^+	511 (194)	Dowex 1 × 8	2 *N* HCl
^{137}Cs	30 yr	Fission	^{137m}Ba	2.6 min	IT	662 (85)	Ammonium molybdophosphate	0.1 *N* HCl + 0.1 *N* NH_4Cl
^{81}Rb	4.6 hr	^{79}Br(α, 2n)	^{81m}Kr	13 sec	IT	190 (67)	BioRad AG 50	Water or air
^{82}Sr	25.5 days	^{85}Rb(p, 4n)	^{82}Rb	75 sec	β^+	511 (190)	SnO_2	0.9% NaCl
^{191}Os	15.4 days	^{190}Os(n, γ)	^{191m}Ir	4.9 sec	IT	129 (26)	BioRad AG1	4% NaCl
^{195}Hg	41.5 hr	^{197}Au(p, 3n)	^{195m}Au	30.6 sec	IT	262 (68)	Silica gel coated with ZnS	Sodium thiosulfate solution

Data from Browne E, Firestone RB. *Table of Radioactive Isotopes*. 1st ed. New York: Wiley; 1986.
[a]IT, isomeric transition.

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Molybdenum-99/Technetium-99m generator systems

Radionuclides	Parent(Mo-99)	Daughter(Tc-99m)
Half-life	66hr	6hr
Mode of decay	β^-	Isomeric transition
Daughter products	Tc-99m ,Tc-99	Tc-99
Principal photon energies	740keV ,780keV	140keV(89%)
Generator function		
Composition of ion exchange column		Al_2O_3
Eluant		Normal saline
Time from elution to maximum daughter yield		23hr

Purity Checks: Mo-99 / Tc-99m Generator System

	Problem	Standard
Radionuclidic purity	Excessive Mo-99 in eluant	< 0.15μCi Mo-99/mCi Tc-99m at time of administration
Chemical purity	Al_2O_3 from generator ion exchange column in elution	< 10μg/ml (fission generator)
Radiochemical purity	Reduced oxidation states of Tc-99m (i.e ,+4,+5, or +6 instead of +7)	95% of Tc-99m activity should be in +7 oxidation state

Purity Checks: Mo-99 / Tc-99m Generator System

Aluminum ion breakthrough:

Al^{3+} ion is measured colorimetrically. A drop of the eluate is placed on one end of a special test paper; a drop of a standard solution of Al^{3+}, concentration 10 ppm, is placed on the other end of the test strip (Figure 6). If the colour at the centre of the drop of eluate is less red than that of the standard solution, the eluate has passed the Aluminum Ion Breakthrough Test. Units may be expressed as ug/ml.

Figure 6: Aluminium breakthrough test (courtesy of VirRAD)

Detection of impurities

Method	Type of Impurity
Dose calibrator/multichannel analyzer	Radionuclidic
Thin layer chromatography	Radiochemical
Colorimetric	Chemical

Classification of impurities

Type of Impurity	Example	Effect
Radionuclidic	^{99}Mo	Increased radiation dose; poor image quality
Radiochemical	Free ^{99m}Tc-pertechnetate	Poor image quality; increased radiation
Chemical	Al^{3+}	Poor image quality due to labelling problems

Calculating generator yields

- How much Mo-99 activity is present on the generator column?

$$A = A_0 e^{-\lambda p t}$$

A_0 = Mo-99 activity on generator column at time of calibration

t = time elapsed since calibration

$\lambda p = 0.693 / Mo\ t_{1/2}$

- How much Tc-99m activity has formed by Mo-99m decay at any given time?

Transient equilibrium $A_{Tc} = 0.957 (A_{Mo})_t$ $\quad (A_{Mo})_t = (A_{Mo})_0 e^{-\lambda p t}$

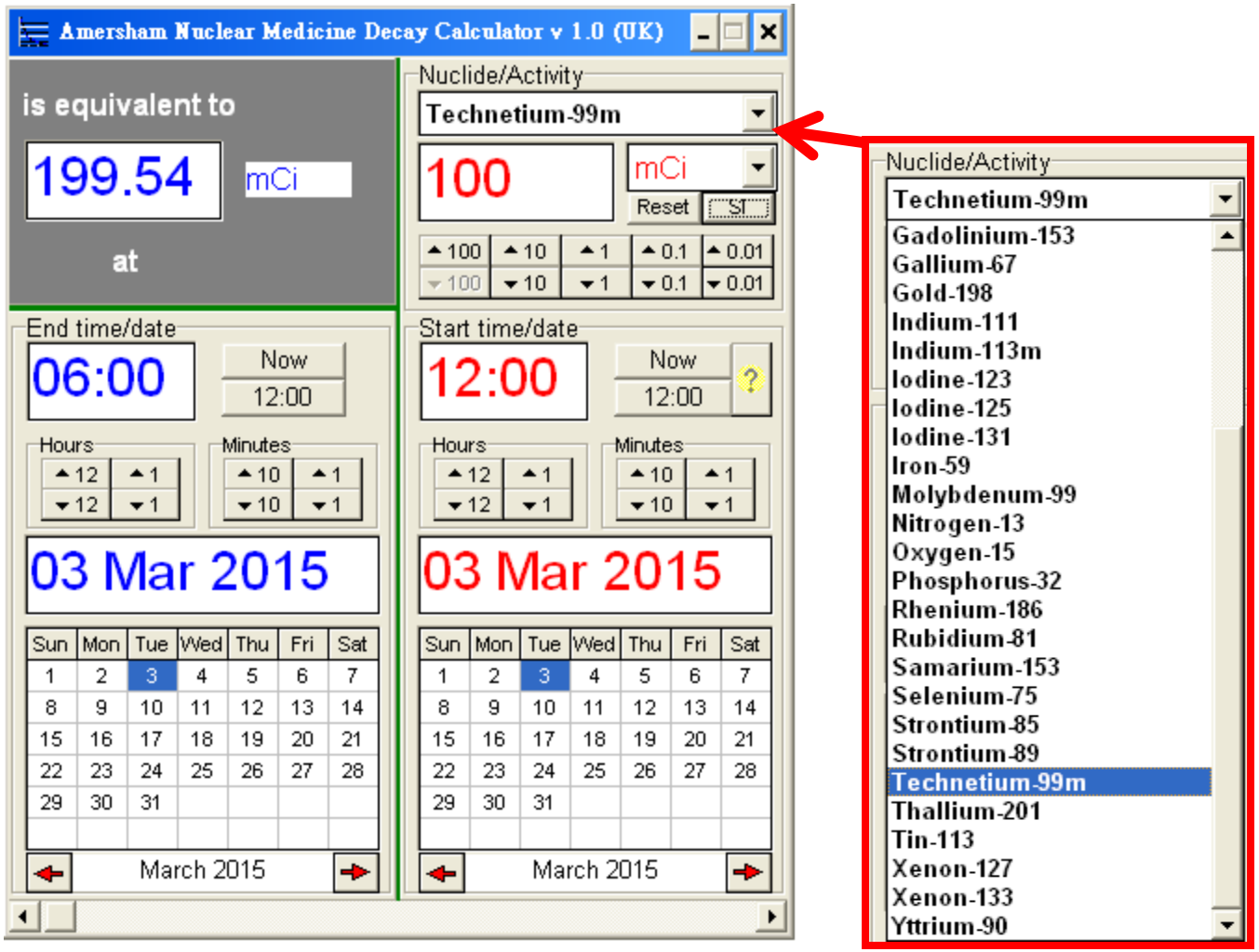
t = time elapsed since calibration

Previous elution $A_{Tc} = 0.957\ (A_{Mo})_0 (e^{-\lambda p t} - e^{-\lambda d t}) + (A_{Tc})_0 e^{-\lambda d t}$

t = time in hours elapsed after previous elution

- What fraction of available Tc-99m is removed (the efficiency of elution)?

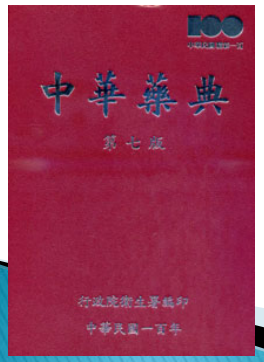
80% ~ 95%

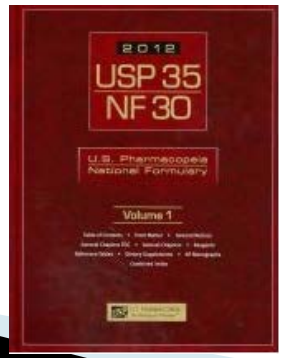

Amersham Nuclear Medicine Decay Calculator v 1.0 (UK)
is equivalent to
199.54
mCi
at
Nuclide/Activity
Technetium-99m
100
mCi
Reset
ST
End time/date
06:00
Now
12:00
Start time/date
12:00
Now
12:00
Hours
Minutes
03 Mar 2015
Sun Mon Tue Wed Thu Fri Sat
March 2015
Nuclide/Activity
Technetium-99m
Gadolinium-153
Gallium-67
Gold-198
Indium-111
Indium-113m
Iodine-123
Iodine-125
Iodine-131
Iron-59
Molybdenum-99
Nitrogen-13
Oxygen-15
Phosphorus-32
Rhenium-186
Rubidium-81
Samarium-153
Selenium-75
Strontium-85
Strontium-89
Technetium-99m
Thallium-201
Tin-113
Xenon-127
Xenon-133
Yttrium-90

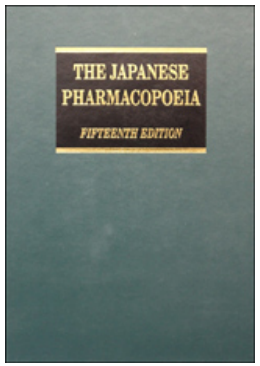
Quality Control of Radiopharmaceuticals

Pharmacopoeia

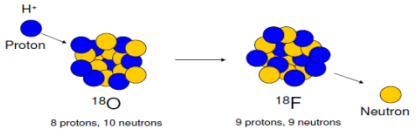
- 中華藥典
- U.S. Pharmacopoeia
- European Pharmacopoeia
- British Pharmacopoeia
- Japanese Pharmacopoeia



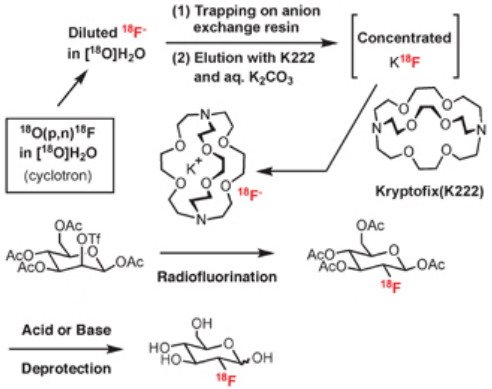


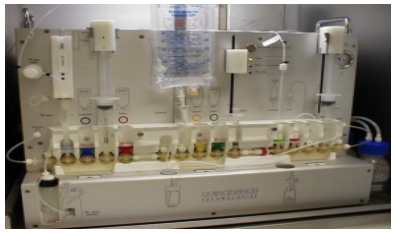


2-[^{18}F]-fluoro-2-deoxy-D glucose (^{18}FDG)synthesis overview



- Production of radioactive ^{18}F
- Labeling dried ^{18}F to a precursor (mannose triflate)
- Preliminary purification
- Hydrolysis step changes the sugar to ^{18}FDG
- Purification steps and final filtration during synthesis remove product impurities





Coincidence TracerLab MXFDG

Cassette for GE TRACERlab MX Synthesis Module

Reagents Kit for production of 2-[^{18}F]-fluoro-2-deoxy-D-glucose with GE TRACERlab Module

行政院衛生署　令

發文日期：中華民國100年9月28日
發文字號：署授食字第1001405359號

訂定「中華藥典第七版」，並自中華民國一百年十月十日生效。

附「中華藥典第七版」

署長 邱文達

明。

(2)乾燥減重——本品於 105° 乾燥三小時，其減失重量不得超過 0.5%（通則 3001）。

(3)熾灼殘渣——本品 0.5g 經熾灼遺留殘渣不得超過 0.1%（通則 3002）。

(4)鐵——取本品 0.5g，精確稱定，置一試管中，加乙醇 5mL 溶解後，加水 5mL 混合之，按鐵檢查法（通則 3045）檢查之，其所含鐵之限量為 20ppm。

(5)類緣化合物——

層析條件檢測液——以標準品溶液供用。

標準品溶液——取下列各對照標準品，氟康那唑、氟康那唑類緣化合物 A、B 及 C 各適量，精確稱定，置一適當容量瓶中，加乙腈溶解後，用移動相溶媒必要時作定量稀釋，作成已知濃度含各標準品均為每 mL 各 10μg 之溶液。

檢品溶液——取本品 30mg，精確稱定，置 10-mL 容量瓶中，加移動相溶媒溶解並加至容量，混合之。

層析裝置——液相層析裝置，具波長 260-nm 檢測器，4.6-mm×15-cm 層析管，充填直徑 3～5μm 十八矽烷鍵結多孔性矽石或陶瓷微粒，移動相溶媒流速每分鐘約 0.5mL，層析管維持於 40°，取標準品溶液按下述測定法層析之，記錄各波峯值：其具代表性滯留時間氟康那唑類緣化合物 A 約 4.9，B 為 8.0，C 為 8.5，氟康那唑為 9.9 分鐘，B 與 C 化合物之時距，不得小於 1.5，重複注入相對標準差不得大於 0.5%。

測定法——取標準品溶液及檢品溶液等量（約 20μL）分別注入層析裝置層析之，記錄其層析圖譜，測計各波峯值，按下列公式計算氟康那唑類緣化合物 A、B、C 或其他不純物含量之百分數：

$$100\,(C / W)\,(r_U / r_S)$$

C：標準品溶液含氟康那唑類緣化合物 A、B 或 C 濃度每 mL 之 mg 數。

W：製作檢品溶液所取氟康那唑重量之 mg 數。

r_U：檢品溶液測得之波峯值。

r_S：標準品溶液重複注入測得氟康那唑或其類緣化合物 A、B 或 C 測得波峯值之平均值。

每一不純物之檢出量不得超過 0.1%，不純物檢出總量不得超過 0.3%。

貯　藏　法：本品應置於緊密容器中於 30° 以下貯之。

用途分類：抗真菌劑。

〔氟-18〕氟去氧葡萄糖注射液

Fludeoxyglucose F18 Injection

本品為 2-去氧-2-[氟-18] 氟-D-葡萄糖分子中標誌放射性氟-18 之無菌溶液，適於靜脈注射。本品所含氟-18 放射活性應為標誌量之 90.0～110.0%，本品可含適當之安定劑或保藏劑。

性　　狀：本品為無色或淡黃色之澄清液。

比 活 性：無載體。

鑑　　別：

(1)放射核種鑑別——使用適當的偵檢系統測定其半衰期，應介於一百零五至一百一十五分鐘之間。

(2)放射化學鑑別——按放射化學純度測定法操作層析之，檢品溶液與標準品溶液所呈現 [氟-18] 氟去氧葡萄糖主斑點之 R_f 值相若。

一般檢查及其他規定：

(1) pH 值——取本品依 pH 值測定法（通則 1009）以適當之玻璃電極裝置或其他適當方法測定，其 pH 值應為 4.5～7.5。

(2)無菌試驗——本品應符合無菌試驗法（通則 7001）之規定，惟依其放射特性，本品可在無菌試驗完成前放行使用。

(3)細菌內毒素——本品每 mL 所含細菌內毒素不得超過 175EU/V（V 為於效期終止時之最大體積總劑量，以 mL 表示之；通則 7008）。

(4)放射化學純度——

標準品溶液——取氟去氧葡萄糖對照標準品 10mg，溶於 100mL 乙腈：水（95：5）混液中。本試驗所指氟去氧葡萄糖對照標準品為非放射性 2-氯-2-去氧-D-葡萄糖（分子量 182.15）。

檢品溶液——取本品注射液。

測定法——取稀釋後之檢品溶液適量，點注於活化後之矽膠薄層層析板上，其放射量適用於放射性檢測系統。標準品溶液取約 10μg 點注同一層析板上，以乙腈：水（95：5）之混液為展開溶媒層析之。俟溶媒上昇達層析板高度約四分之三處，取出層析板，風乾後以適當之準直放射檢測器掃描層析板以測定放射性分佈。噴以 2N 硫酸，於 110° 加熱十分鐘，以確定氟去氧葡萄糖的位置。放射檢測器掃描之 [氟-18] 氟去氧葡萄糖與標準溶液所呈現主斑點之 R_f 值（約 0.4）相若。[氟-18] 氟去氧葡萄糖的放射活性不得低於總放射活性之 90%。

(5)放射核種純度——取適量注射液，使用一適當的加馬射線光譜儀，計測一段時間使足以收集一個加馬射線能譜，其測定結果應可分析及鑑別非氟-18 放

射圖譜之特性，其檢測結果不小於 99.5% 的加馬射線須在 0.511MeV、1.022MeV 上，或氟-18 康普敦散射峯上。

(6) 化學純度——〔註：本節說明以酸水解法合成注射劑可能產生的不純物，特別是胺基聚醚（Kryptofix®）與 2-氨-2-去氧-D-葡萄糖之檢驗方法與限值。如果使用之合成方法會產生不同的不純物，則未標誌之成份、試劑及與製程相關的副產物必須受到管制，其可能產生的生理或藥理作用應予考慮。任何具有潛在毒性之成份亦必須規範在適當限值內，並使用一種或一種以上已被確效之限量試驗來確認這些限值。〕

胺基聚醚之限值——〔註：使用此化學品以任何方式合成 [氟-18] 氟去氧葡萄糖時，必須執行這項試驗。〕

吸附劑——0.25mm 厚層析矽膠。

檢品溶液——取本品注射液。

標準品溶液——精確稱取胺基聚醚對照標準品，溶在生理食鹽水中，配製成已知濃度為每 mL 含 50μg 之溶液。

取用體積——約 1μL。

層析溶媒——甲醇與 30% 氫氧化銨（9：1）之混合液。

測定法——將點有檢品溶液及標準品溶液之層析板，用層析溶媒展開，把已展開之層析板放入含有碘粒之展開槽內，直到在層析板上之標準溶液部份出現可見斑點。檢品溶液所呈現斑點的大小及明暗度，不能超過標準品溶液。

2-氨-2-去氧-D-葡萄糖之限值——〔註：使用親核合成方式包括酸水解或陰離子交換樹之方式合成 [氟-18] 氟去氧葡萄糖時，必須執行這項試驗。〕

移動相溶媒——取 50% 氫氧化鈉溶液約 16g 溶於 1000mL 水中，過濾並用氮氣去空氣。

層析條件檢測液——精確稱取氟去氧葡萄糖對照標準品及 2-氨-2-去氧-D-葡萄糖對照標準品溶於移動相中，配製成已知濃度為每 mL 分別含 1mg 及 0.1mg 之溶液。

標準品溶液——精確稱取 2-氨-2-去氧-D-葡萄糖對照標準品溶於水中，配製已知濃度為每 mL 含 0.1mg 之溶液。

檢品溶液——取本品注射液。

層析裝置——液相層析裝置，具脈衝電流檢測器，4.0-mm×25-cm 層析管，重填直徑 10μm 聚苯乙烯—苯二乙烯與四級胺聚合乳化微粒，移動項溶媒流速每分鐘 0.5mL。取標準品溶液及層析條件檢測液按下述測定法層析之，記錄其波峯值：氟去氧葡萄糖與 2-氨-2-去氧-D-葡萄糖和氟去氧葡萄糖主波峯間之分離率 R 不得小於 1.5，重複注入之相對標準差不得大於 5%。

測定法——取標準品溶液及檢品溶液等量（約 100μL），分別注入層析裝置層析之，記錄其層析圖譜，測計各主波峯值。按照下列公式計算所取檢品每 mL 含 2-氨-2-去氧-D-葡萄糖之 mg 數：

$$C\,(r_U / r_S)$$

C：標準品溶液每 mL 含 2-氨-2-去氧-D-葡萄糖對照標準品之 mg 數。

r_U 及 r_S：分別為檢品溶液及標準品溶液 2-氨-2-去氧-D-葡萄糖波峯值。

於每批注射劑生產總量中 2-氨-2-去氧-D-葡萄糖不得超過 1mg。

(7) 殘留溶劑——〔註：如果準備及合成過程不會導致注射劑含有下列任何一項殘留溶劑，則該溶劑的檢驗可以不必執行。假使注射劑含有任何不屬於下列的三種殘留溶劑，則該溶劑可能產生的生理或藥理作用應予考慮，任何具有潛在毒性之成份亦必須規範在適當限值內，並使用一種或一種以上已被確效之限量試驗來確認這些限值。〕

標準品溶液——分別配製 0.1% 乙醚、0.01% 乙腈及 0.1% 無水酒精。

檢品溶液——取本品注射液。

層析裝置——氣相層析裝置，具火焰離子檢測器、無分岔注射系統及 0.53-mm×30-m 以 0.25μm 化學交聯之聚乙二醇類固定相包覆的融合矽管柱。以氦氣為載體，流速每分鐘 10mL。（氦氣可用作補充氣體）。層析儀程式設定如下：開始前二分鐘維持溫度在 40°，然後溫度以每分鐘 20° 的速率增加至 130°，並維持五點五分鐘。在注射端及偵檢器溫度分別維持在 250° 及 300°。取標準品溶液按下述測定法層析之，記錄其波峯值：其鑑定波峯在任二成份間之分離率 R 不得小於 1.0，重複注入之相對標準差不得大於 5%。

測定法——取標準品溶液及檢品溶液等量（約 100μL），分別注入層析裝置層析之，記錄其層析圖譜，測計各主波峯值。按照下列公式計算檢品中所含乙醚、乙腈及酒精之百分比：

$$C\,(r_i / r_S)$$

C：標準品溶液中相關分析物之百分比。

r_i：檢品溶液測得相關分析物之波峯值。

r_S：標準品溶液測得相關分析物之波峯值。

乙醚不得超過 0.5%，乙腈不得超過 0.04%，酒精不得超過 0.5%。

放射活性分析：使用適當之計數裝置測定本品之放射活性，以 MBq/mL（mCi/mL）表示。

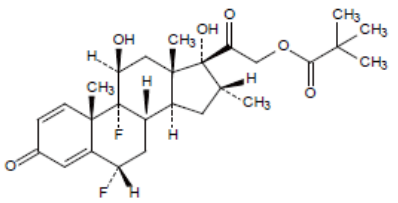
貯藏法及有效期限：本品應置於無菌中性玻璃容器內密封，其有效期限則依產品之放射活性及安定性試驗結果計算。

標　　誌：本品之包裝標籤上除依藥事法之規定外，應載明安定劑或保藏劑的名稱及劑量、放射活性校正的日期及時間、校正時每 mL[氟-18] 氟去氧葡萄糖放射活性、放射性物質標誌及警語。應附以載明因放射性衰減所作劑量校正之計算方式，並標示「若溶液混濁或含顆粒物質，請勿使用」。

用途分類：核子醫學診斷用。

三甲乙酸氟皮質醇

Flumethasone Pivalate



$C_{27}H_{36}F_2O_6$　　分子量：494.57

本品所含 $C_{27}H_{36}F_2O_6$ 按乾品計算應為 97.0～103.0%。

性　　狀：

(1) 一般性狀——本品為白色至類白色結晶性粉。

(2) 溶解度——本品微溶於甲醇；極微溶於氯仿及二氯甲烷；幾不溶於水。

(3) 比旋光度——本品二氧六環溶液（1→100）按旋光度測定法（通則 1007）測定之，其比旋光度為 +71°～+82°。

鑑　　別：

(1) 本品按紅外光吸光吸光度測定法（通則 1008）糊漿法測定之，其吸收光譜與本品對照標準品（注意一使用前於 105° 乾燥四小時）以同法測得者，僅於相同波長處呈最大吸收。

(2) 本品之甲醇溶液（1→50000）按紫外光吸光度測定法（通則 1008）測定之，其吸收光譜與本品對照標準品同法配置之溶液，於相同波長處呈最大及最小吸收；且二者於波長 237nm 附近呈最大吸收處測得之吸收係數差，以乾品計算亦不超過 3.0%。

雜質檢查及其他規定：

(1) 乾燥減重——本品於 105° 乾燥四小時，減失重量不得超過 1.0%（通則 3001）。

(2) 層析法純度檢查——取本品適量，加二氧六環溶成每 mL 含 20mg 之檢品溶液。另取本品對照標準品三份各適量，分別溶於二氧六環使成每 mL 含 200(1%)、400(2%) 及 600(3%)μg 之三種標準品溶液。取檢品溶液及三種標準品溶液各 5μL，按薄層層析法（通則 1010.3）分別點注於矽膠薄層上，乾後，以甲苯：乙酸乙酯（7：3）混液為展開溶媒層析之。展開並取出層析板風乾後，以稀硫酸（1→2）輕輕噴霧，於 100° 加熱三十分鐘，置長波紫外光下檢視之：與標準品溶液所呈現之斑點相比對，檢品溶液所呈現不純物斑點之總和不得超過 3.0%。

含量測定：

標準品溶液——取本品對照標準品適量，精確稱定，加乙醇使溶後，續作次第定量稀釋成每 mL 含約 20μg 之溶液。精確量取此溶液 10.0mL，移置 20-mL 玻塞錐形瓶中。

檢品溶液——取本品約 20mg，精確稱定，置 100-mL 容量瓶中，加乙醇使溶後，續加至容量，混勻。取此溶液 10.0mL，移置另一 100-mL 容量瓶中，加乙醇稀釋至容量，混勻。取所成溶液 10.0mL，移置 20-mL 玻塞錐形瓶中。

測定法——取上述貯有標準品溶液及檢品溶液之二錐形瓶，並另取一內貯作空白對照用乙醇 10.0mL 之第三 20-mL 錐形瓶。三瓶分別作下述完全相同之處理：加氫氧化四甲銨試液 1.0mL，混勻後，精確計時靜置二十分鐘。加四吡唑啉藍試液 1.0mL，混勻，靜置四十分鐘。再各加冰醋酸 1.0mL 分別混勻後，按分光吸光度測定法（通則 1008）用 1-cm 貯液管，以第三錐形瓶所得溶液為空白對照，於波長 520nm 附近呈最大吸收處測定其吸光度。按下列公式計算所取檢品中含 $C_{27}H_{36}F_2O_6$ 之 mg 數：

$$C\,(A_U / A_S)$$

C：標準品溶液每 mL 含本品對照標準品之 μg 數。

A_U 及 A_S：分別為檢品溶液及標準品溶液之吸光度。

貯 藏 法：本品應置於緊密、阻光容器內貯之。

用途分類：抗炎性皮質醇（外用）。

1.Physicochemical Tests

- Physical characteristics
- pH
- Radionuclidic purity
- Radiochemical purity

2.Biological Tests

- Sterility test
- Apyrogenicity test

Physical characteristics

- Recognize the color and state of Radiopharmaceutical
- Colloidal or aggregated preparations :
  size identify visualization of the reticuloendothelial system :
  10nm ~ 1 μm
  ^{99m}Tc-sulfur colloid : 80 ~500nm
- ^{99m}Tc-MAA，Tc-label albumin microsphere : 10 ~90μm
  (checked with hemocytometer under a light microscope)
  larger than 150 μm → pulmonary arterial blockade → embolism
  smaller than 10 μm → localize in the reticuloendothelial system

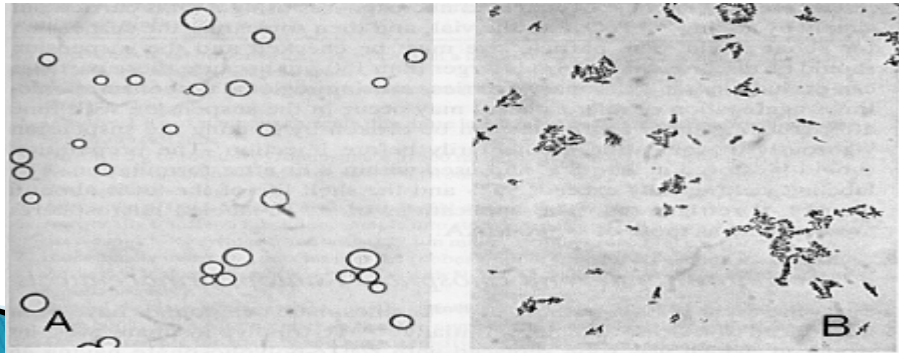
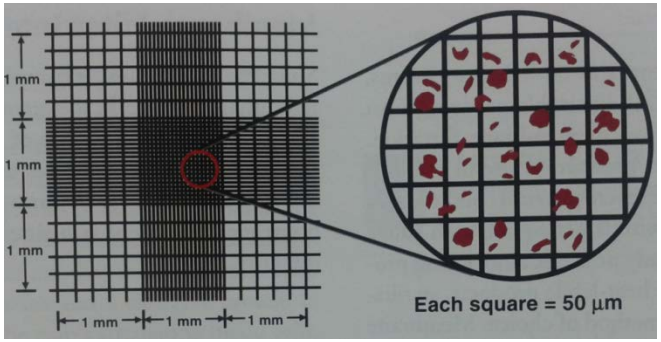
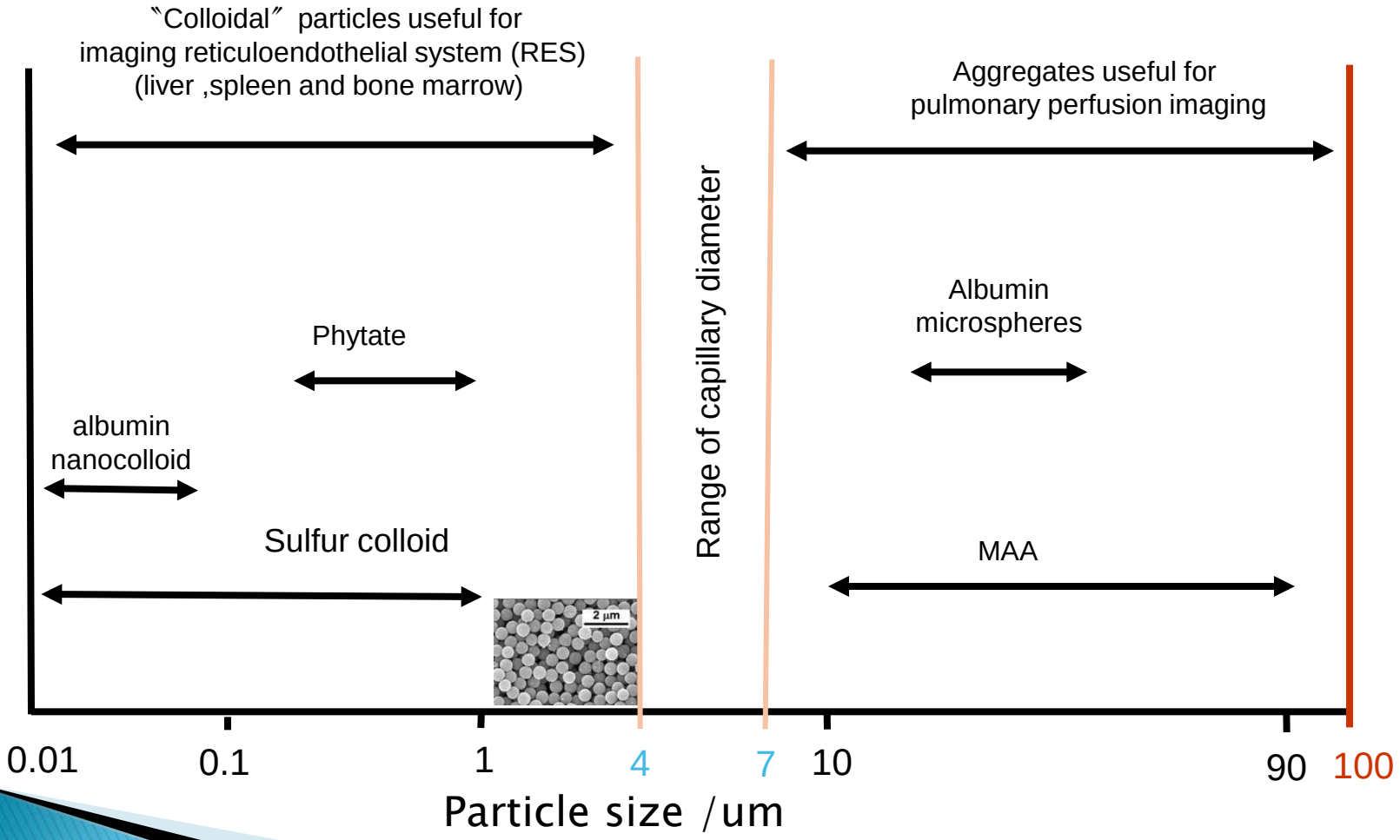


FIGURE 7.1. Comparison of albumin microspheres (A) and macroaggregates of albumin (B) as seen under a light microscope. Note the irregular shape of the MAA particles as compared to the spherical shape of the microsphere particles.

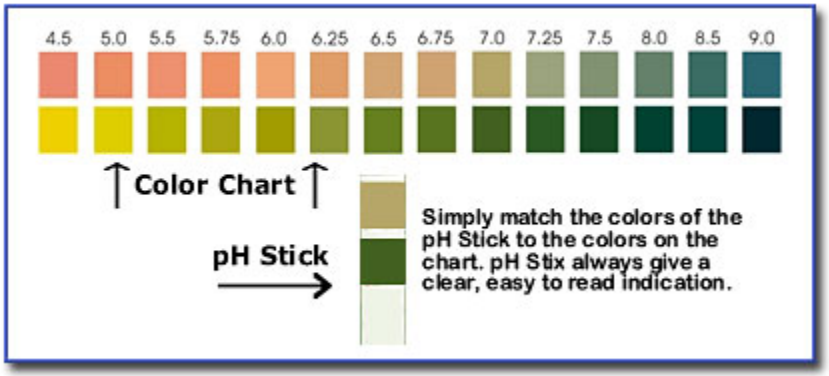




Nuclear pharmacy .H M Chilton et al;41

PH

- Ideal pH radiopharmaceutical should be7.4 (pH of the blood)
- However， radiopharmaceutical can vary between 2 ~ 9 because of high buffer capacity (緩衝能力) of blood.



	PH
$Na^{99m}TcO_4$	4.0 ~ 8.0
MDP	5.0 ~ 6.0
DTPA	4.0 ~ 4.5
DMSA(III)	2.5 ~ 3.5
DMSA(V)	7.5 ~ 8.0
MAA	5.0 ~ 8.0
Phytate	6.0 ~ 7.0
PYP	4.5 ~ 5.5
DISIDA	4.0 ~ 5.0
Trodat-1	6.5 ~ 8.5
ECD	7.2 ~ 8.0
MIBI	5.3 ~ 5.9
In-111 Pentetreotide	3.8 ~ 4.3

Radionuclidic purity

- Impurity sources from :
  ^{99}Mo-^{99m}Tc generator : ^{99}Mo breakthrough from the alumina column
  ^{131}I : contain many other iodine isotopes

- Radionuclidic purity is determined by measuring the half-live and characteristic radiation emitted by individual radionuclides.
  γ-ray emission radionuclides : checked with multi-channel analyzer
  pure β emission radionuclides : checked with β-spectrometer or a liquid scintillation counter

Radiochemical purity

- Radiochemical impurities arise from decomposition due to
  1. action of solvent
  2. change in temperature or pH
  3. light
  4. presence of oxidizing or reducing agents
  5. radiolysis(輻射分解)
- Analytical methods
  - Paper chromatography (PC)
  - Thin-layer chromatography (TLC)
  - Instant thin-layer chromatography (ITLC)
  - High performance liquid chromatography (HPLC)

Sterility test

- 1. To prove that radiopharmaceuticals are in essence free of viable microorganisms.
- Incubate the radiopharmaceutical sample in

(1) fluid thioglycollate medium at 30 ~ 35℃ for 14 days

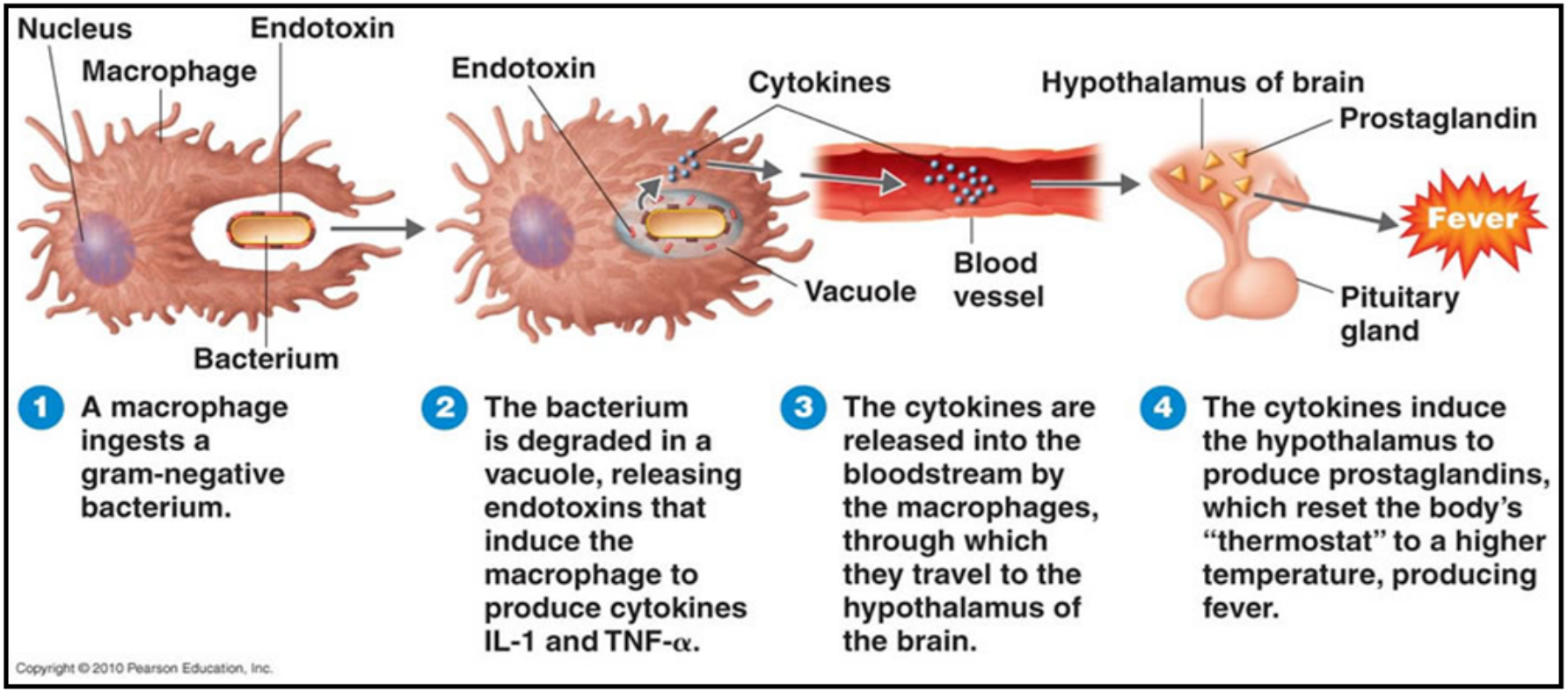
(2) sobean-casein digest medium for incubation at 20 ~ 25℃ for 14 days

培養基	試驗微生物	培養14天	
	菌種	培養溫度	培養狀態
硫醇乙酸鹽培養基 Fluid Thioglycollate Medium (FTM)	金黃色葡萄球菌 (Staphylococcus aunreus)	30 ~ 35℃	有氧
	綠膿桿菌 (Pseudomonas aeruginosa)		
	產芽孢梭菌 (Clostridium sporogenes)		無氧
大豆分解蛋白質-乾酪素 Soybean-Casein Digest (SCD)	枯草桿菌 (Bacillus subtilis)	20 ~25℃	有氧
	白色念珠菌 (Candida albicans) (fungi)		
	黑麴菌 (Aspergillous niger) (fungi)		

Apyrogenicity test

- Pyrogens include any substance capable of eliciting a febrile (or fever) response upon injection or infection 。
- The severity of response is dependent upon the amount of pyrogen administered。(Myalgia 、headache 、nausea 、sepsis …)
- The USP set a limit for radiopharmaceutical at 175EU/ V 。 (EU=Endotoxin Units) (V = maximum dose in ml)
- Sterile ≠ Pyrogen free
- Pyrogen (熱原) ≠ Endotoxin (內毒素)

Endotoxins and the Pyrogenic Response



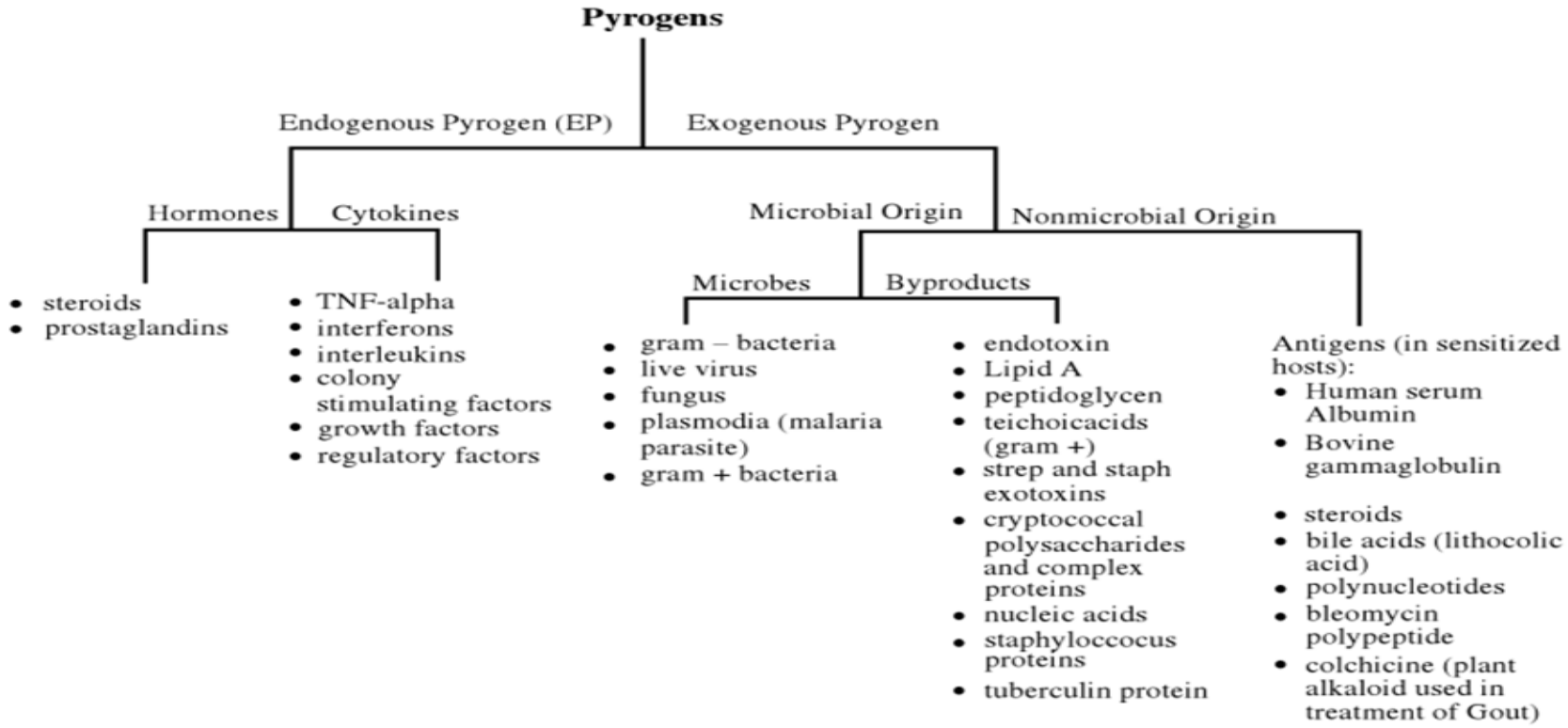


FIGURE 1 Microbial and nonmicrobial pyrogens and associated host active microbial products.

Endotoxins Pyrogens, LALtesting and Depyrogenation 3th ,p28

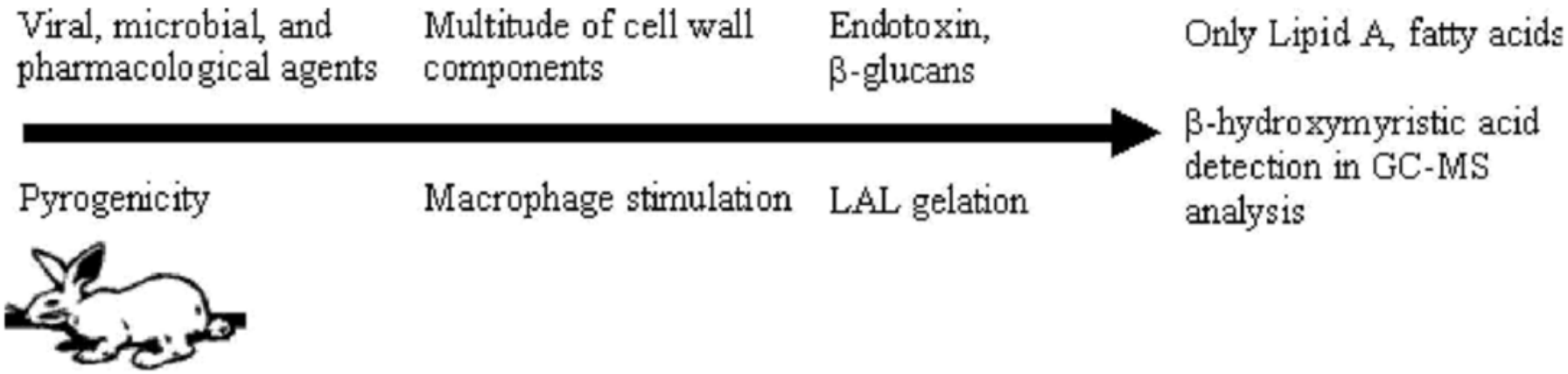


FIGURE 2 Increasing specificity of host response recognition by various methods. *Abbreviations*: LAL, *Limulus* amebocyte lysate; GC-MS, gas chromatography-mass spectroscopy.

Apyrogenicity test

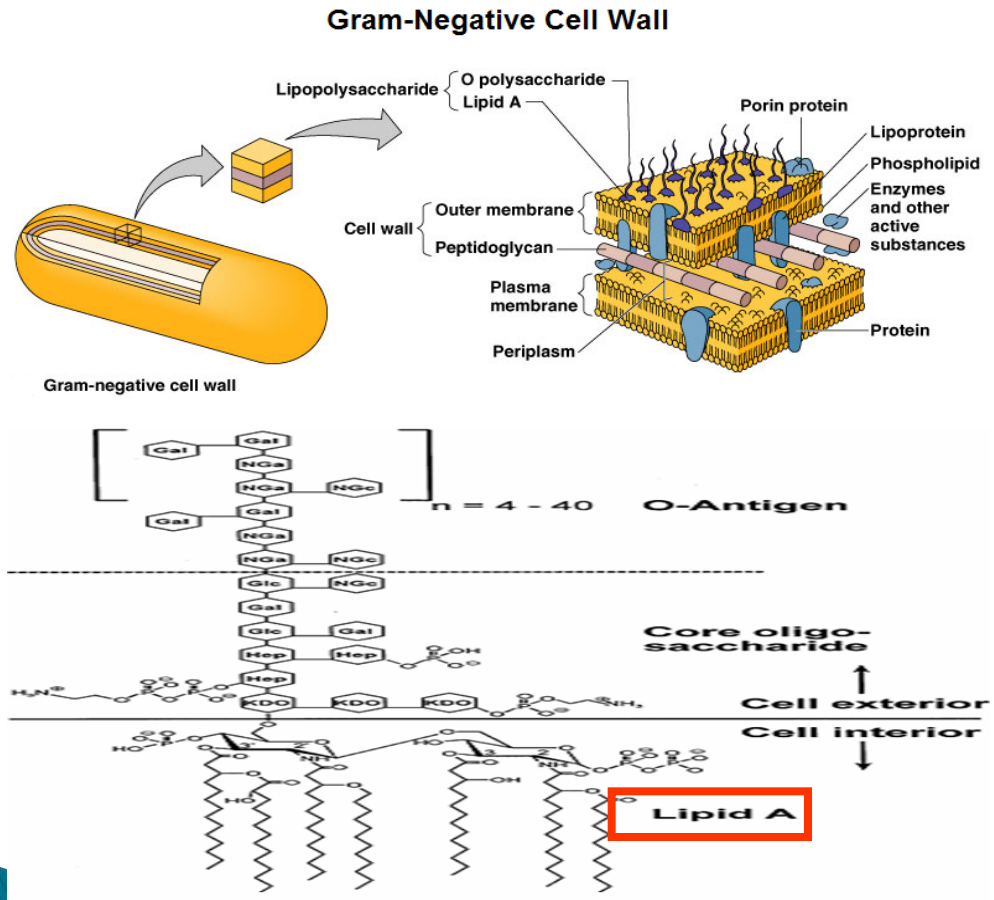


Figure 2: Chemical structure of endotoxin from *E. coli* O111:B4 according to Ohno and Morrison 1989 (25). (Hep) L-glycerol-D-manno-heptose; (Gal) galactose; (Glc) glucose; (KDO) 2-keto-3-deoxyoctonic acid; (NGa) N-acetyl-galactosamine; (NGc) N-acetyl-glucosamine.

Table 1. Characteristics of bacterial endotoxins and classic exotoxin

PROPERTY	ENDOTOXIN	EXOTOXIN
CHEMICAL NATURE	Lipopolysaccharide (mw = 10kDa)	Protein (mw = 50-1000kDa)
RELATIONSHIP TO CELL	Part of outer membrane	Extracellular, diffusible
DENATURED BY BOILING	No	Usually
ANTIGENIC	Yes	Yes
FORM TOXOID	No	Yes
POTENCY	Relatively low (>100ug)	Relatively high (1 ug)
SPECIFICITY	Low degree	High degree
ENZYMATIC ACTIVITY	No	Often
PYROGENICITY	Yes	Occasionally

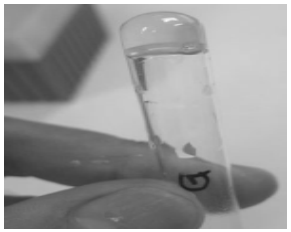
Apyrogenicity test

- Pyrogen Test (In vivo test)
  Rabbit fever test

- Bacterial Endotoxin Test (In vitro test)
  Limulus Amebocyte Lysate(LAL) test

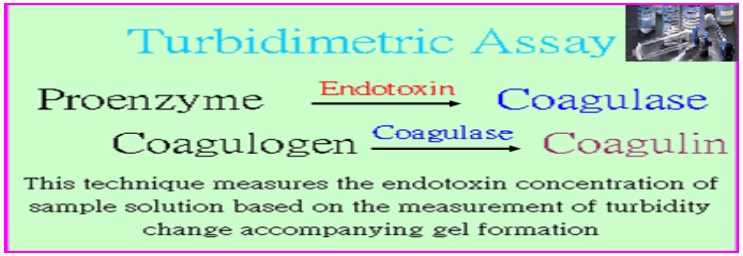
In vitro limulus amebocyte lysate(LAL) test

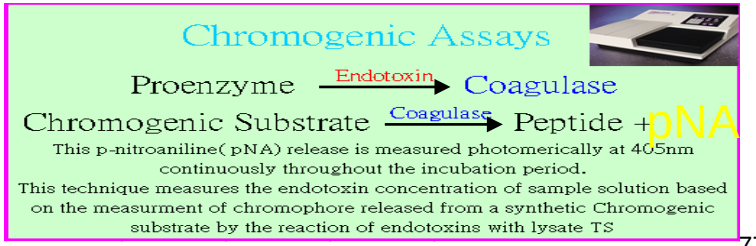
- Semi-quantitative method ：
  Gel-clot techniques (濁度法)



- Quantitative method ：
  Photometric techniques (呈色法)

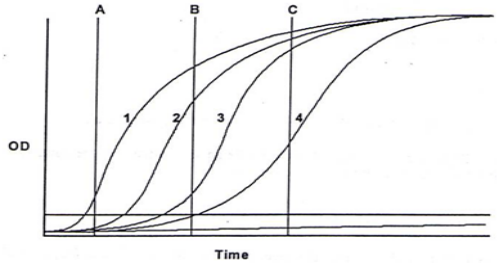
- Turbidimetric techniques
  - End-point
  - Kinetic
- Chromogenic techniques
  - End-point
  - Kinetic





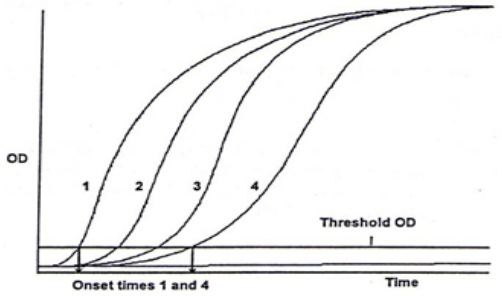
- 終點法 End-point ：

  根據反應混合物中的內毒素濃度和其在培養終止(相同反應時間)時的濁度 (釋放的呈色團的量)吸光度之間存在的量化關係。



- 動力學法 Kinetic ：

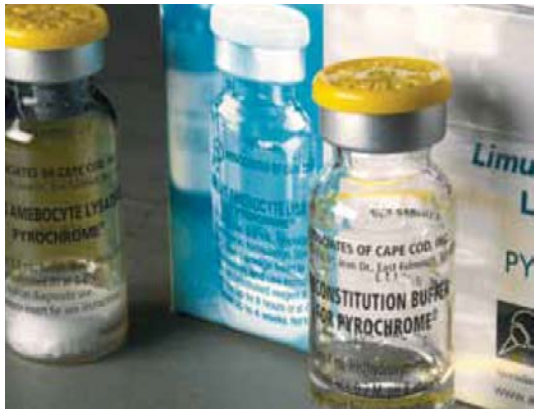
  測定反應混合物的濁度(釋放的呈色團)到達某一預先設定的吸光值所需要的反應時間(onset time)，或是檢測濁度(色度)增加速率的方法。



OD = optical density

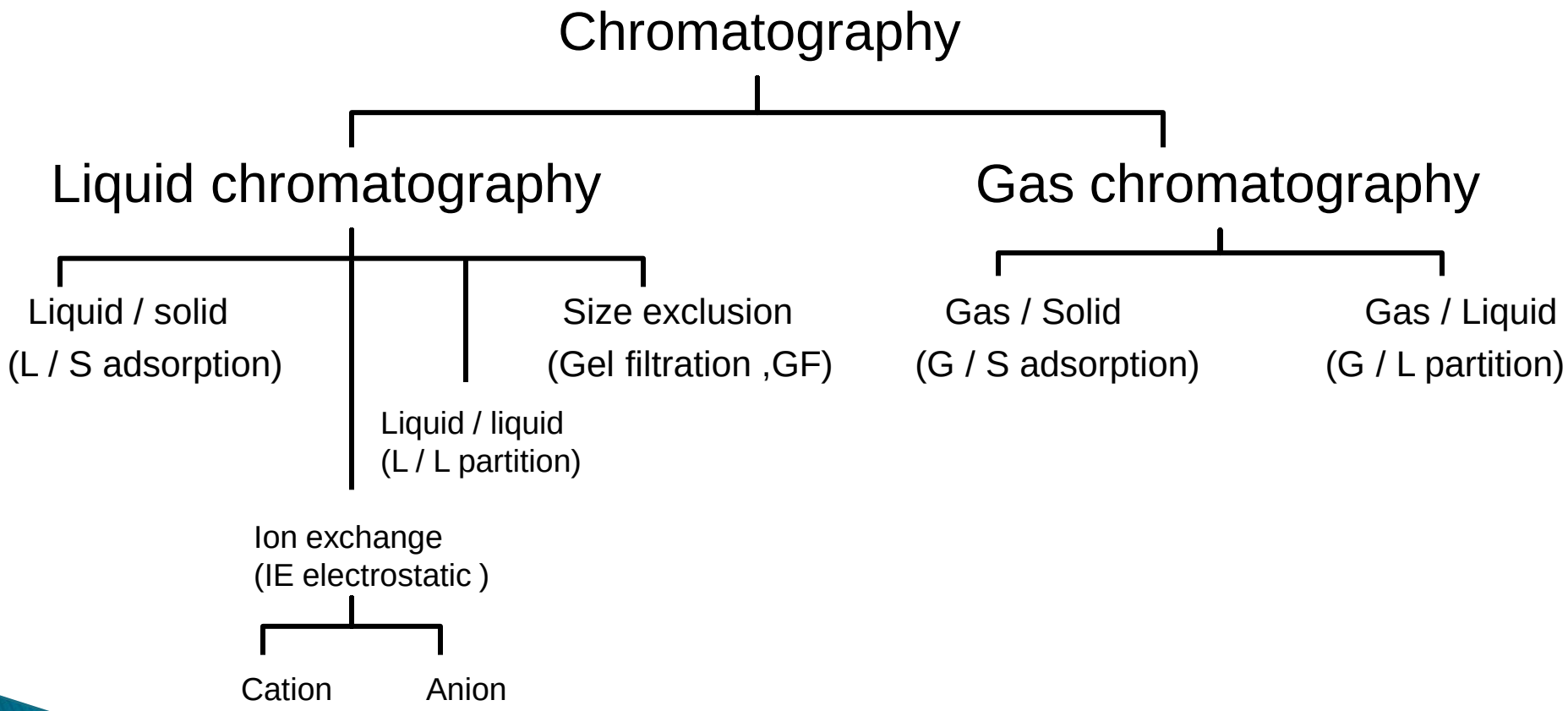
Chromogenic Endotoxin Test

- Incubating Microplate Readers (ELx808™)
- 無熱源水 (LAL Reagent Water)
- 標準品(Control Standard Endotoxin (CSE) E. Coli)
- 內毒素呈色劑 **(Pyrochrome®)**



Radiochromatographic analysis for determining radiochemical purity

Branches of chromatography according to mechanism of separation stationary phase



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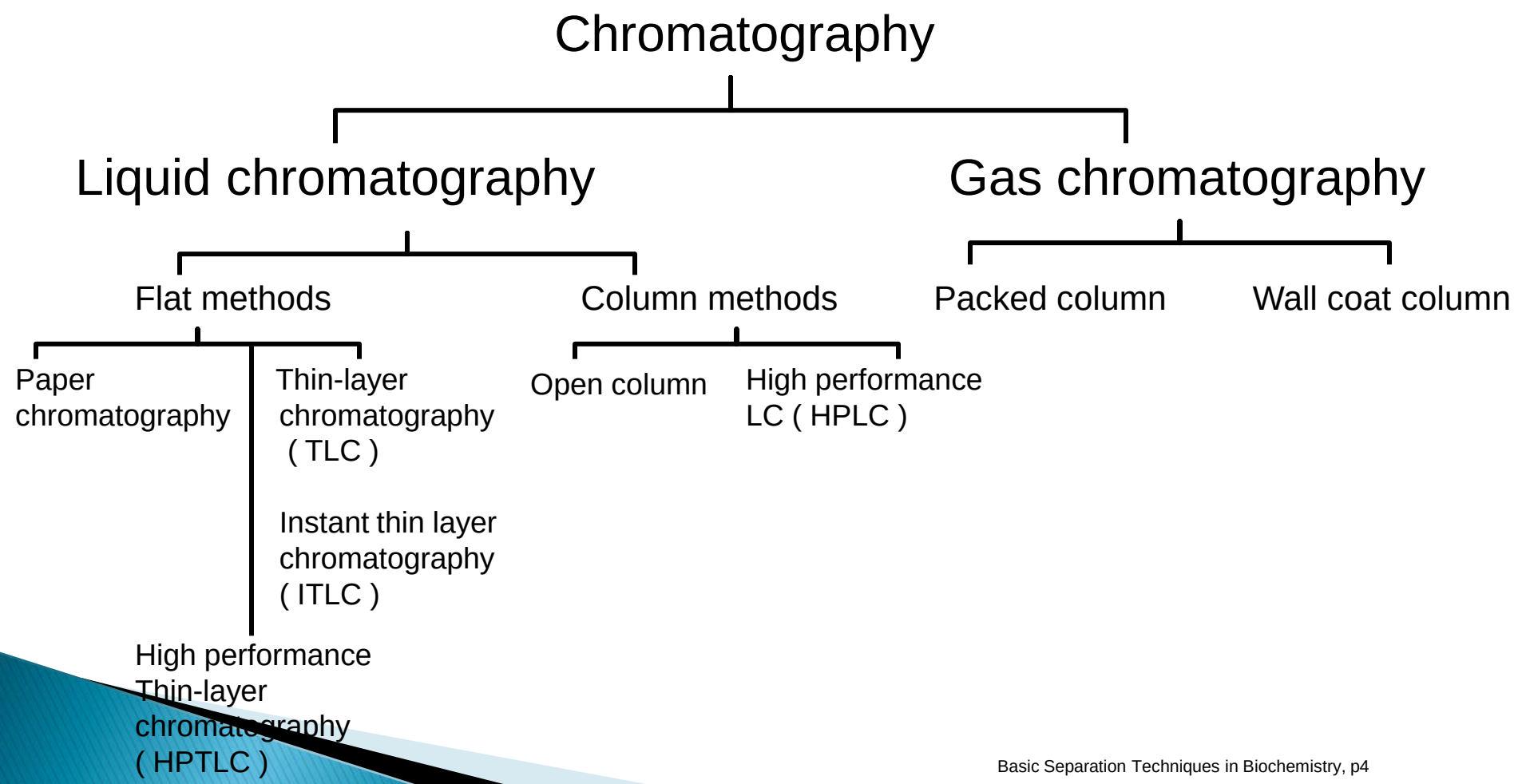
Branches of chromatography according to mobile phase and physical apparatus



Basic Separation Techniques in Biochemistry, p4

Paper and Thin-Layer Chromatography

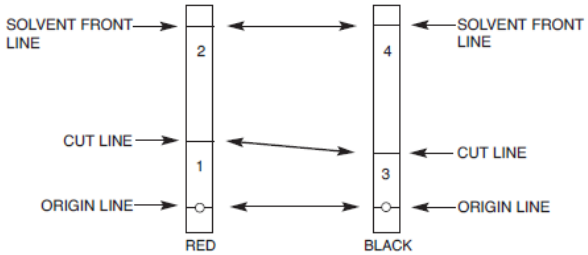
- The electrostatic forces (adsorption and capillary action) of the stationary phase and the polarity of the mobile phase are the two determining factors in the separation of different radiochemical components in a sample 。

- Rf = Retardation factor

$$Rf = \frac{\text{The distance traveled by the analyte}}{\text{The total distance traveled by the mobile phase}}$$

INTRODUCTION

Tec-Control is a miniaturized chromatography system for the radiochemical purity evaluation of specific radiopharmaceuticals.



Each red (150-001) and each black (150-005) chromatography strip have three distinct lines: an origin line, a cut line, and a solvent front line. For user convenience the back of each strip is marked with a soluble dye, located close to the line, that will migrate with the solvent front. The technologist can easily see the solvent front via the movement of the dye. Use a 10ml Wheaton Serum Vial as a developing vial. This test requires the technologist to "spot" approximately 10 microliters of the radiopharmaceutical sample onto the chromatography strip. This is easily accomplished using a 26G needle and syringe. One drop equals a volume of 0.01 cc (10µl or ten microliters).

NOTE: The Acetone HPLC grade solvent (Sigma-Aldrich part # 27972-5) and distilled H20 required to complete this procedure must be purchased separately.

Tec-Control Solvent Vendor:
Sigma-Aldrich Chemical Company
800-558-9160 www.sigmaaldrich.com

Customers outside the USA should visit the Sigma-Aldrich web site to locate a regional office.

NOTE: For each of the following procedures the strip should be placed on top or away from the well detector depending on count rate. If the strip is placed in the well, the dead time of the detector will give erroneous results.

NOTE: Black strip development time will take less than 1 minute.

NOTE: Red strip development time will take less than 1 minute.

DETERMINATION OF FREE PERTECHNETATE IN Tc-99m LABELED MAA, SULFUR COLLOID, STANNOUS CHLORIDE, ALBUMIN COLLOID AND GLUCOHEPTONATE

1. Add 1cc of acetone solvent to a developing vial.
2. Using a red chromatography strip, spot approximately 10 microliters of the test sample onto the bottom line (origin) of the test strip.
3. Immediately place the test strip into the developing vial containing acetone, and develop until the solvent front migrates to top line (solvent front).
4. Remove strip from the vial and allow to dry.
5. Cut strip at central line (cut line), producing sections 1 and 2.
6. Using a gamma counter, count background and calculate the net counts by subtracting the background counts from the number of counts registered for each strip section.

CALCULATION

% free pertechnetate

$$= \left[\frac{\text{(net cts sect. 2)}}{\text{(net cts sect. 1) + (net cts sect. 2)}} \right] \times 100$$

Artifacts in planar chromatography

- Reaction with the support，especially by drying the spots.
- Splashing when spotting.
- Grease from fingers.
- Strips touching wet walls of the developing chamber.
- Incorrect mobile phase.
- Insufficient mobile phase to allow full development to the required solvent front.

TABLE 14-2 Effect of Wet versus Dry Spot on Minichromatography Results (% Activity) for ^{99m}Tc-Labeled Compounds in ITLC-SG/Acetone System

Radiopharmaceutical	Wet Spot[a]		Dry Spot[a]	
	Origin	Solvent Front	Origin	Solvent Front
^{99m}Tc-gluceptate (^{99m}Tc-GH)[b]	74.01	25.99	99.81	0.19
^{99m}Tc-pentetate (^{99m}Tc-DTPA)[b]	60.04	39.96	99.70	0.30
^{99m}Tc-pyrophosphate (^{99m}Tc-PYP or ^{99m}Tc-PPi)[b]	85.37	14.63	99.39	0.61
^{99m}Tc-medronate (^{99m}Tc-MDP)[b]	82.60	17.40	99.82	0.18

[a]Results are means of five determinations on 5 cm ITLC-SG strips.
[b]Common chemical abbreviation.
Source: Reference 34.

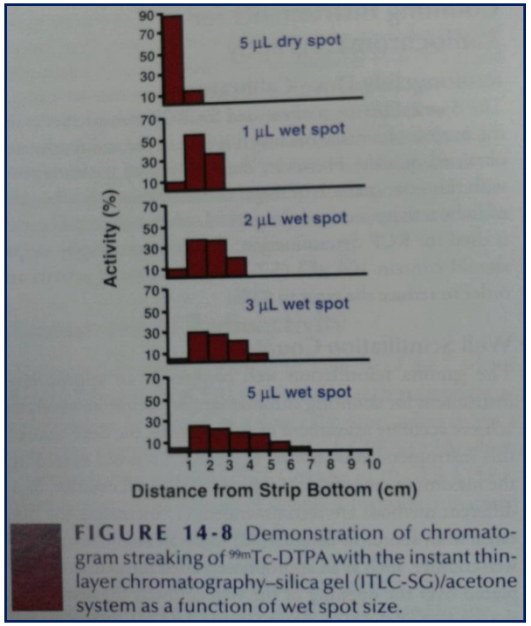


FIGURE 14-8 Demonstration of chromatogram streaking of ^{99m}Tc-DTPA with the instant thin-layer chromatography–silica gel (ITLC-SG)/acetone system as a function of wet spot size.

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Procedure for the determination of radiochemical purity by ITLC

Using fresh solvent into the developing tank to a depth of 3 ~ 4mm

↓

Prepare the strip: Mark the solvent front with a color pen and the start with a pencil

↓

Apply one small drop of the sample (<0.1ml) With a thin needle onto the strip;(the drop must not dry)

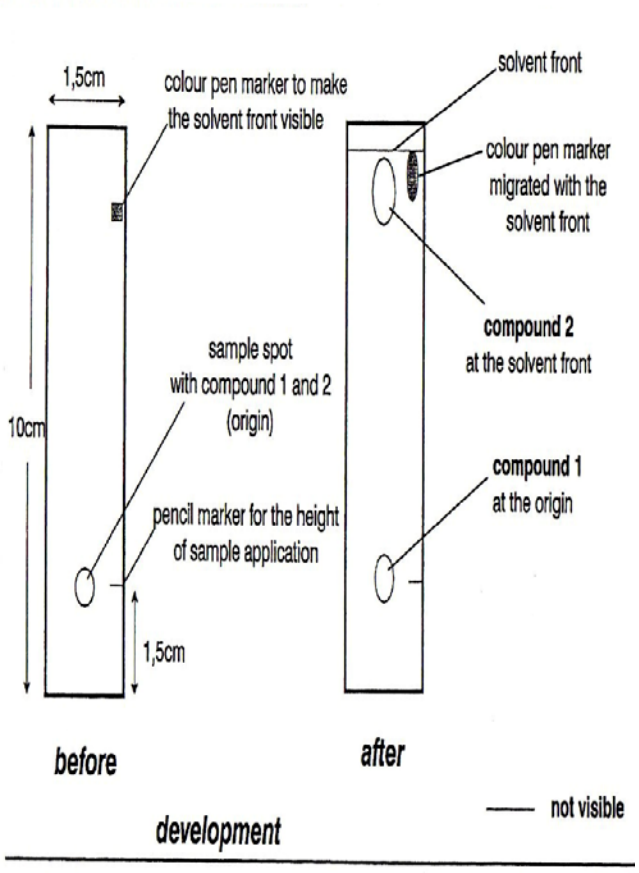
↓

Immediately put the strip into the developing tank ,the spot must remain above the solvent level .

↓

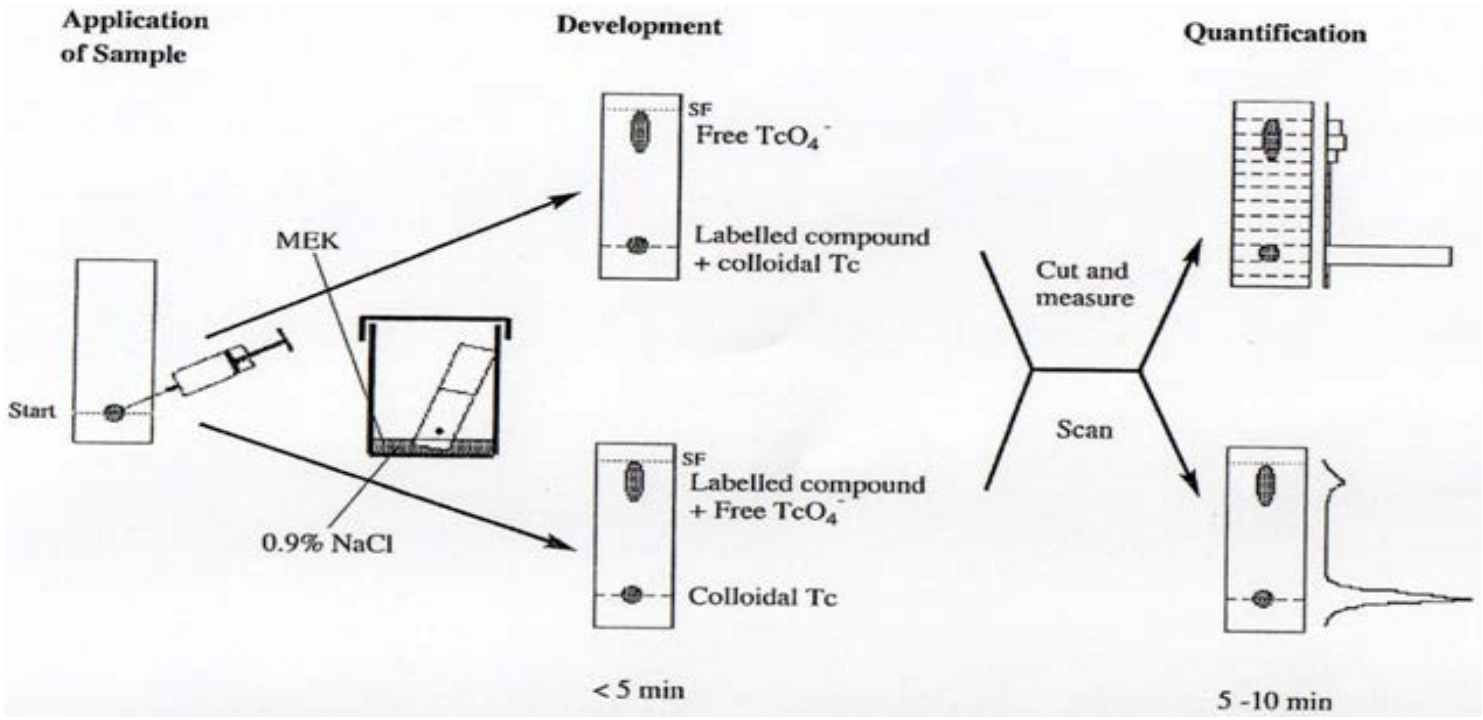
When the solvent has reached the front,Take the strip out and let it dry.

↓



Technetium-99m pharmaceuticals p130

Determination of the radiochemical purity of a radiopharmaceutical by ITLC using two different solvent



Technetium-99m pharmaceuticals p126

Materials for thin-layer chromatography (*TLC*)

Layer type	Format (cm)	Ordering no.	Quantity
TLC glass plates (layer thickness 0.2 and 0.25 mm)			
Silica gel 60 F_{254}	20×20	Merck 1.05715.000	25 plates
Silica gel 60 F_{254}	5×10	Merck 1.05789.000	25 plates
Silica gel 60 F_{254}	2.5×7.5	Merck 1.15327.000	100 plates
RP-18 F_{254}	20×20	Merck 1.15389.000	25 plates
RP-18 F_{254}	5×20	Merck 1.15683.000	50 plates
RP-18 F_{254}	5×10	Merck 1.15685.000	25 plates
HPTLC Si 60 F_{254}	5×5	Merck 1.05635.000	100 plates
HPTLC LiChrospher Si 60 F_{254}	20×10	Merck 1.15445.000	25 plates
TLC aluminum sheets (layer thickness 0.2 mm)			
Silica gel 60	20×20	Merck 1.05553.0001	25 sheets
Silica gel 60 F_{254}	5×10	Merck 1.16834.0001	50 sheets
Silica gel 60 F_{254}	5×7.5	Merck 1.05549.0001	20 sheets
Aluminum oxide 60 F_{254} neutral	20×20	Merck 1.05550.0001	25 sheets
Aluminum oxide 150 F_{254} neutral	20×20	Merck 1.05551.0001	25 sheets
HPTLC LiChrospher Si 60 F_{254}	20×20	Merck 1.05586.0001	25 sheets
TLC plastic sheets (layer thickness 0.2 mm)			
Silica gel 60 F_{254}	20×20	Merck 1.05735.0001	25 sheets
Aluminum oxide 60 F_{254}	20×20	Merck 1.05581.0001	25 sheets
Baker-flex silica gel 1B-F	20×20	J.T. Baker 4463-04	25 sheets
Baker-flex silica gel 1B-F	2.5×7.5	J.T. Baker 4463-02	200 sheets
Baker-flex aluminum oxide 1B-F	20×20	J.T. Baker 4467-04	25 sheets
Baker-flex aluminum oxide 1B-F	2.5×7.5	J.T. Baker 4467-02	200 sheets
ITLC fiberglass sheets (layer thickness 0.2 mm)			
Silica gel (ITLC-SG)	20×20	Pall Gelman 61886	25 sheets
Silica gel (ITLC-SG)	5×20	Pall Gelman 61885	50 sheets
Silicic acid gel (ITLC-SA)	20×20	Pall Gelman 51432	25 sheets

Materials for paper chromatography

Specification	Format (mm)	Ordering no.	Quantity
Whatman 1	100×300	3001845	100 sheets
Whatman 1	200×200	3001861	100 sheets
Whatman 3MM	50×250	30306122	50 sheets
Whatman 3MM	100×130	30306123	50 sheets
Whatman 3MM	150×150	3030286	100 sheets
Whatman 3MM	200×200	3030861	100 sheets
Whatman 31 ET	460×570	3031915	25 sheets

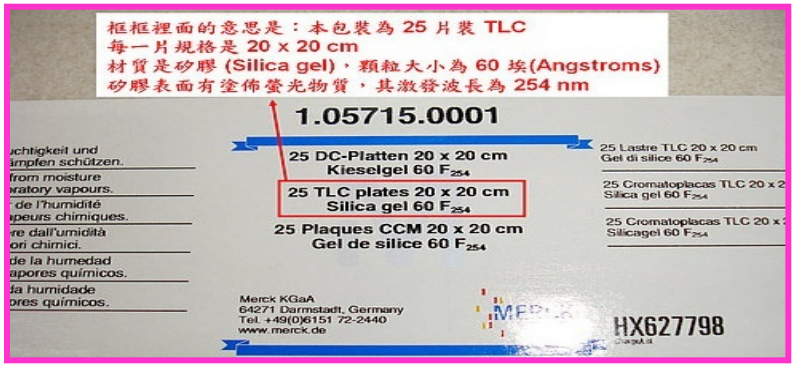


TABLE 8.1. Chromatographic data of ^{99m}Tc labeled radiopharmaceuticals

^{99m}Tc labeled radiopharmaceuticals	Stationary phase	Solvent	R_f $^{99m}TcO_4$	R_f ^{99m}Tc Complex	R_f Hydrolyzed ^{99m}Tc
^{99m}Tc PYP	ITLC SG	Acetone	1.0	0.0	0.0
	ITLC SG	Saline	1.0	1.0	0.0
^{99m}Tc HDP	ITLC SG	Acetone	1.0	0.0	0.0
	ITLC SG	Saline	1.0	1.0	0.0
^{99m}Tc MDP	ITLC SG	Acetone	1.0	0.0	0.0
	ITLC SG	Saline	1.0	1.0	0.0
^{99m}Tc DTPA	ITLC SG	Acetone	1.0	0.0	0.0
	ITLC SG	Saline	1.0	1.0	0.0
^{99m}Tc SC	ITLC SG	Acetone	1.0	0.0	0.0
^{99m}Tc MAA	ITLC SG	Acetone	1.0	0.0	0.0
^{99m}Tc Gluceptate	ITLC SG	Acetone	1.0	0.0	0.0
	ITLC SG	Saline	1.0	1.0	0.0
^{99m}Tc DISIDA	ITLC SA	20% NaCl	1.0	0.0	0.0
^{99m}Tc Mebrofenin	ITLC SG	Water	1.0	1.0	0.0
^{99m}Tc DMSA	ITLC SA	Acetone	1.0	0.0	0.0
^{99m}Tc sestamibi	Al_2O_3 coated Plastic plate	Ethanol	0.0	1.0	0.0
^{99m}Tc HMPAO	ITLC SG	Butanone (MEK)	1.0	1.0 (Primary)	0.0
	ITLC SG	Saline	1.0	0.0	0.0
	Whatman 1	50% Acetonitrile	1.0	1.0	0.0
^{99m}Tc tetrofosmin	ITLC SG	Acetone: dichloromethane (35:65 v/v)	1.0	0.5	0.0
^{99m}Tc MAG3	Whatman 3 MM	Acetone	1.0	0.0	0.0
	Whatman 3 MM	Water	1.0	1.0	0.0
^{99m}Tc bicisate	Whatman 3 MM	Ethylacetate	0.0	1.0	0.0
^{99m}Tc nanocolloid	Whatman ET 31	Saline	0.8	0.0	0.0

TABLE 8.2. Chromatographic data of radiopharmaceuticals other than ^{99m}Tc complexes[a]

Radiopharmaceuticals	Stationary phase	Solvent	R_f Values: Labeled product	R_f Values: Impurities
^{125}I RISA	ITLC SG	85% Methanol	0.0	1.0 (I^-)
^{131}I MIBG	Silica gel plated plastic	Ethylacetate:ethanol (1:1)	0.0	0.6 (I^-)
^{131}I NaI	ITLC SG	85% Methanol	1.0	0.2 (IO_3^-)
^{51}Cr sodium chromate	ITLC SG	*n* Butanol saturated with 1 N HCl	0.9	0.2 (Cr^{3+})
^{67}Ga citrate	ITLC SG	$CHCl_3$:acetic acid (9:1)	0.1	1.0
^{111}In DTPA	ITLC SG	10% Ammonium acetate: methanol (1:1)	1.0	0.1 (In^{3+})
^{111}In capromab[b] pendetide	ITLC SG	Saline	0.0	1.0 (In^{3+})
^{18}F FDG[b]	Silica gel	CH_3CN/H_2O (95:5)	0.37	0.0
^{90}Y , ^{111}In ibritumomab tiuxetan[b]	ITLC SG	0.9% NaCl sol	0.0	1.0

[a]Data are adapted from Procedure manual Radiochemical purity of radiopharaceuticals using Gelman Seprachrom™ (ITLC™) chromatography. Gelman Science, Inc., Ann Arbor, Michigan, 1977

[b]Data are from package insert

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Thank you for your attention ！