Method for the Separation of Tc-99m from Low Specific Activity Mo-99

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-Mo-99 production and solution stability testing

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- Ci level Process Testing

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- mCi level testing
- accelerator Mo-99 feasibility testing

Certus International (Robert Wolfangle, Vic Becker)
- FDA consultation, Solution Stability

American Medical Isotope Production Act

Promote Domestic US production of Mo-99

US uses half of the worlds Mo-99/Tc-99m, but since 1989 has no domestic supply

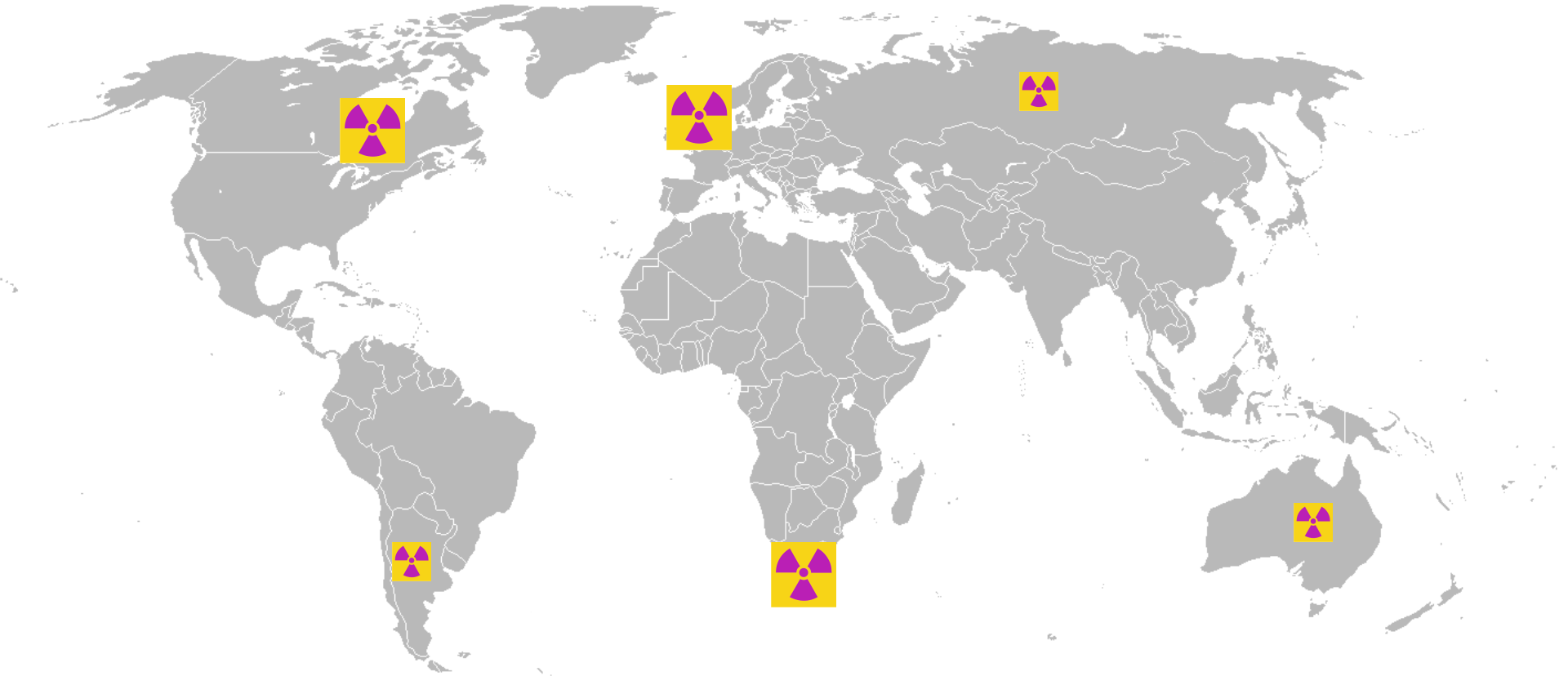
Phase out export of highly enriched uranium for the production of medical isotopes (GTRI).

- Top four suppliers of Mo-99/Tc-99m (98%)

HEU Cost(+10%) Reliable Supply
$11 - 30 mCi dose

American Medical Isotopes Production Act, 111th Congress, 2nd Session, Senate Report 111-120, January 28, 2010.

Nuclear Reactor Based Production



Medical Isotope Production without highly enriched uranium, NRC, National Academies Press, Washington, D.C. (2009).

American Medical Isotopes Production Act, 111th Congress, 2nd Session, Senate Report 111-120, January 28, 2010.

Highly Enriched U-235 Targets

- 40-50 kg of HEU used annually for medical isotope production

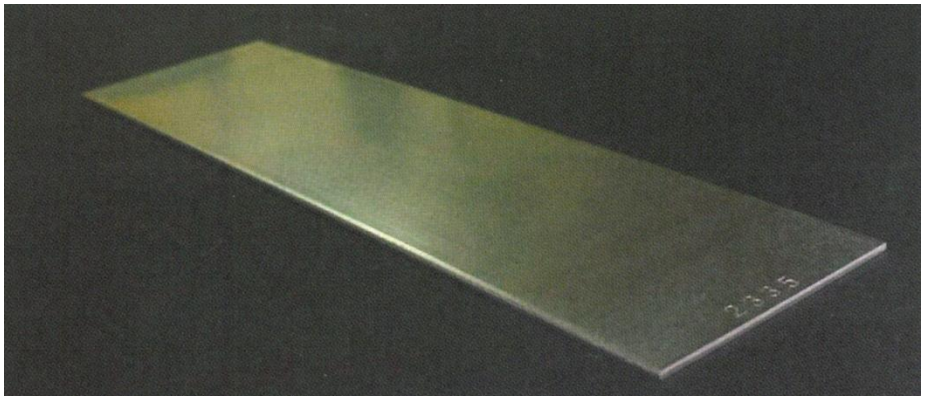
-U.S. is primary supplier (Euratom Supply Agency)

-93% U-235

-45% U-235 (South Africa)

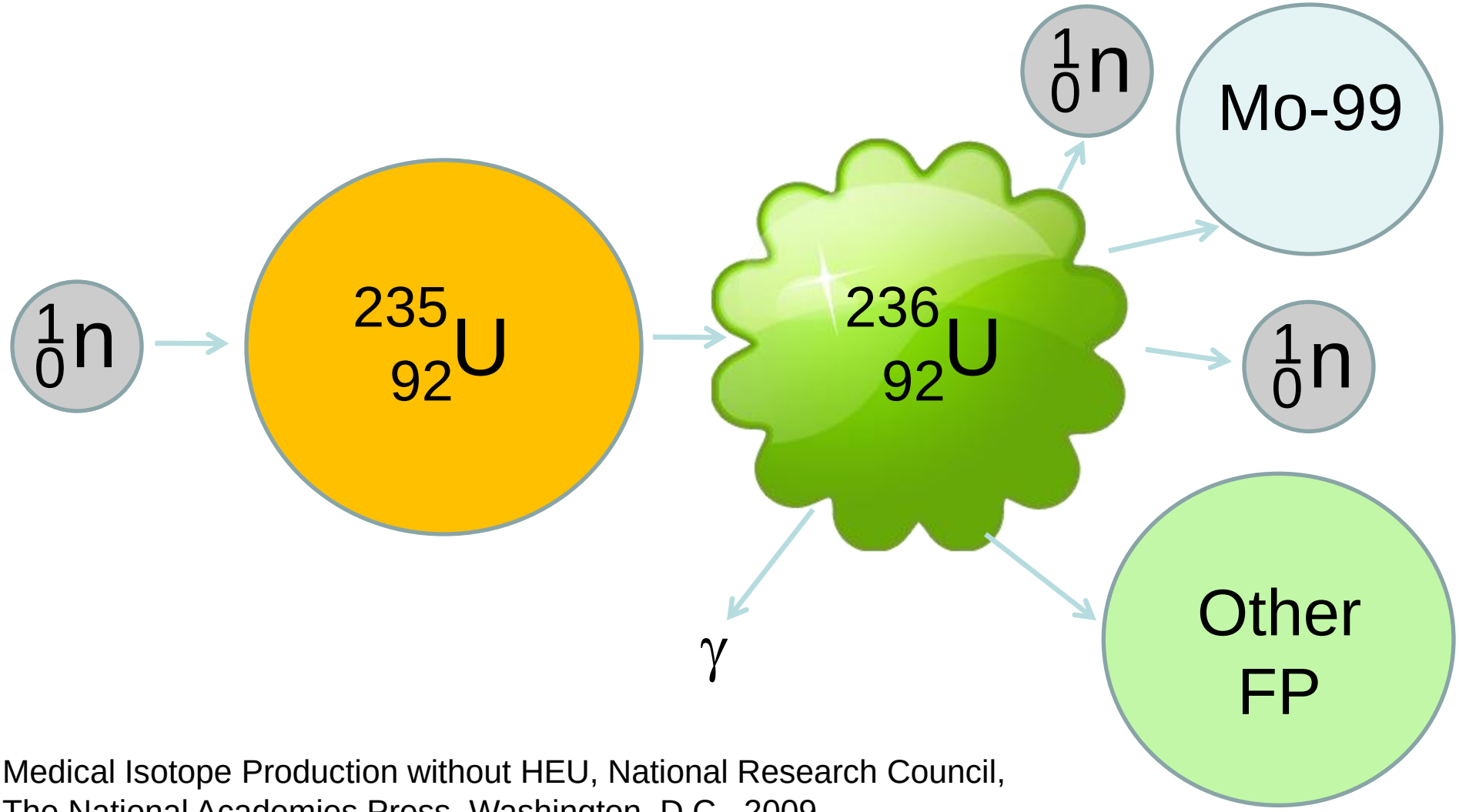
-IAEA “significant quantity” of HEU = 25 kg

“Quantity from which the possibility of constructing a nuclear explosive device cannot be excluded”



Medical Isotope Production without highly enriched uranium, NRC, National Academies Press, Washington, D.C. (2009).

Production of Mo-99/Tc-99m by HEU Fission



Medical Isotope Production without HEU, National Research Council, The National Academies Press, Washington, D.C., 2009.

Tc-99m Pharmaceuticals: Preparation and Quality Control in Nuclear Medicine, Ilse Zolle editor, Springer, New York, 2007.

Fission Yield for U-235

Activation Products

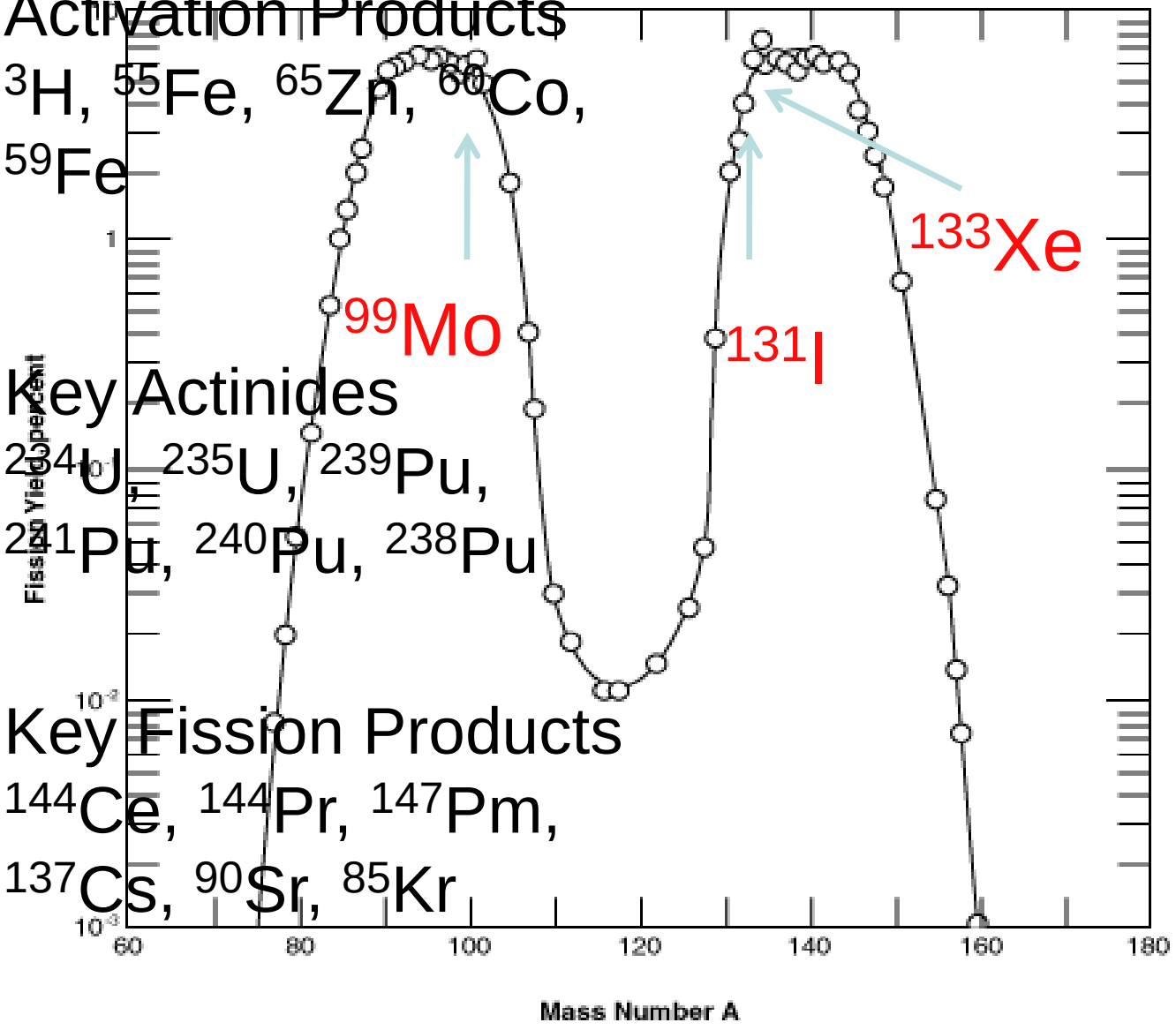
^{3}H, ^{55}Fe, ^{65}Zn, ^{60}Co, ^{59}Fe

Key Actinides

^{234}U, ^{235}U, ^{239}Pu, ^{241}Pu, ^{240}Pu, ^{238}Pu

Key Fission Products

^{144}Ce, ^{144}Pr, ^{147}Pm, ^{137}Cs, ^{90}Sr, ^{85}Kr



High Specific Activity Mo-99

Other useful medical radionuclides

Radio-active waste byproducts

Substantial processing to isolate Mo-99

Management of Radioactive Waste From Tc-99m Production, IAEA-TECDOC-1051, Nov. 1998.

Traditional Generator

High specific activity Mo-99

Simple Generator

Ease of Use

Decades of Experience

Alternative Methods for Mo-99/Tc-99m Production

Fission of LEU in current/modified reactor system

-Not immediate replacement for HEU

-Complete transfer possible in 7-10 years

U-238 Photo-Fission

Solution Reactor

Direct Tc-99m production: $^{100}Mo(p,2n)^{99m}Tc$

$^{98}Mo(n,\gamma)^{99}Mo$

$^{100}Mo(\gamma,n)^{99}Mo$

^{92}Mo	14.84%
^{94}Mo	9.28%
^{95}Mo	15.92%
^{96}Mo	16.68%
^{97}Mo	9.55%
^{98}Mo	24.13%
^{100}Mo	9.63%

Mo-99/Tc-99m Production from Natural/Enriched Mo

Low specific activity Mo-99

- 1-2 Ci/g (7.5cm) — Bennett, et al. Nuclear Tech. 126, 102 (1999)
- ≥10 Ci/g (0.5cm) — Lidsky US Patent 5,784,423

No Enriched Uranium Targets

Less long-lived radioactive byproducts (Nb-95, Tc-99)

Simpler upfront processing/more complex end process

Alternative Separation to Current Alumina Generator

Methods for Tc-99m from low specific activity Mo-99

Thermal Separation Bennett, et al. Nuclear Tech. 126, 102 (1999).

- 50-80% yield (geometry/size dependent)
- Heating sample at 800^{o}C for 30 min

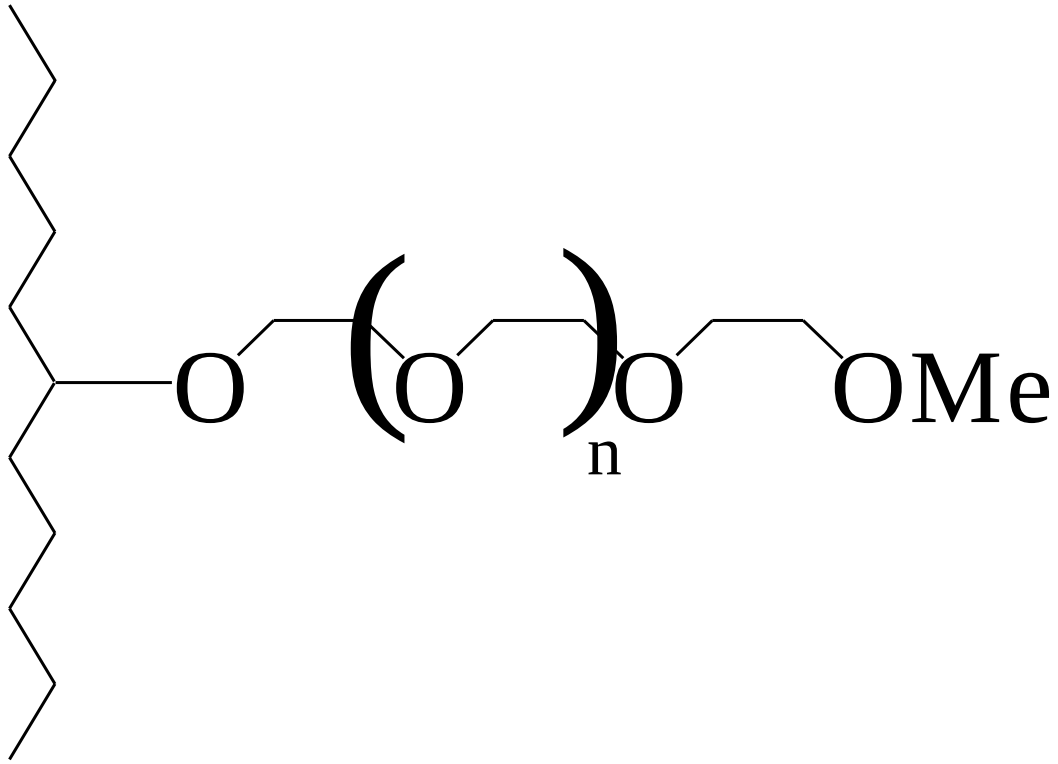
Anion Exchange Chattopadhyay, et al. Appl. Rad. Isotop. 66, 1814 (2008).

- 500 mCi Mo-99 (200mCi/g) in 5M NaOH
- Tc-99m stripped with CH_2Cl_2/TBAB
- Alumina secondary column

ABEC Rogers, et al Solv. Extr. Ion Exch. 14(5), 919 (1996).

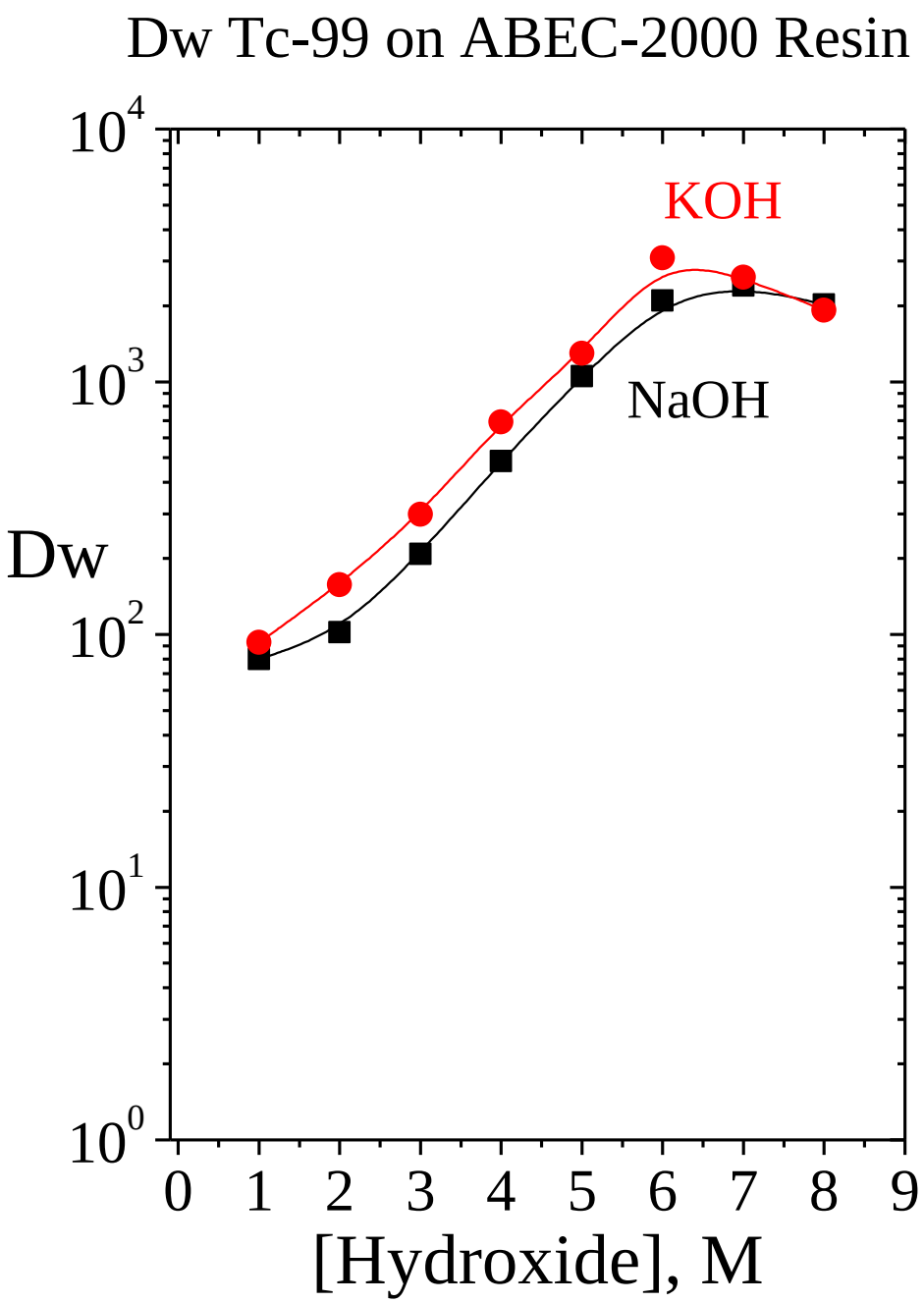
- Selective Extraction of Tc(VII) over Mo
- Alkaline, sulfate, phosphate, carbonate
- Can strip Tc(VII) with H_2O, saline
- High Mo enhances Tc(VII) extraction

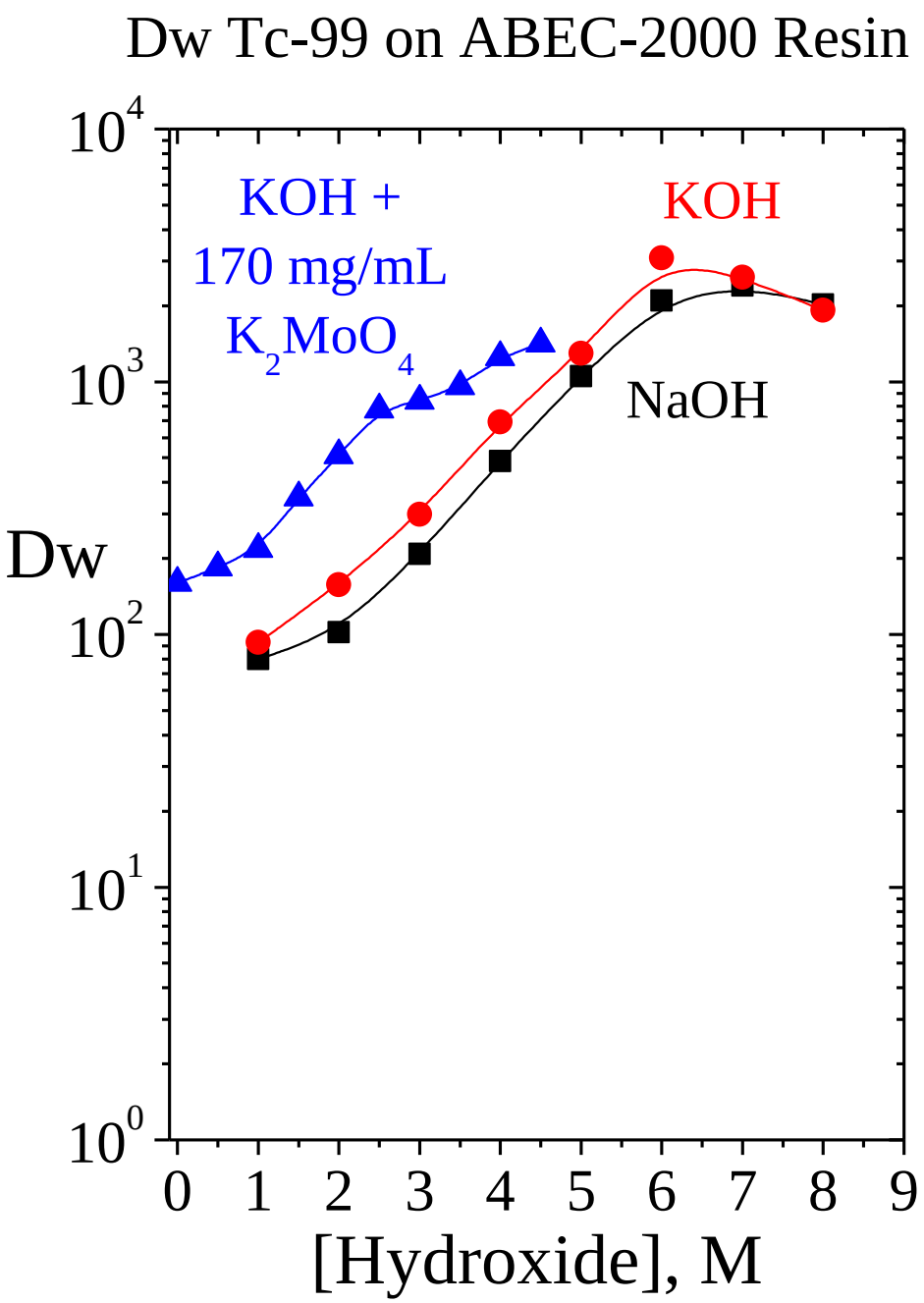
ABEC - Aqueous Biphasic Extraction Chromatography



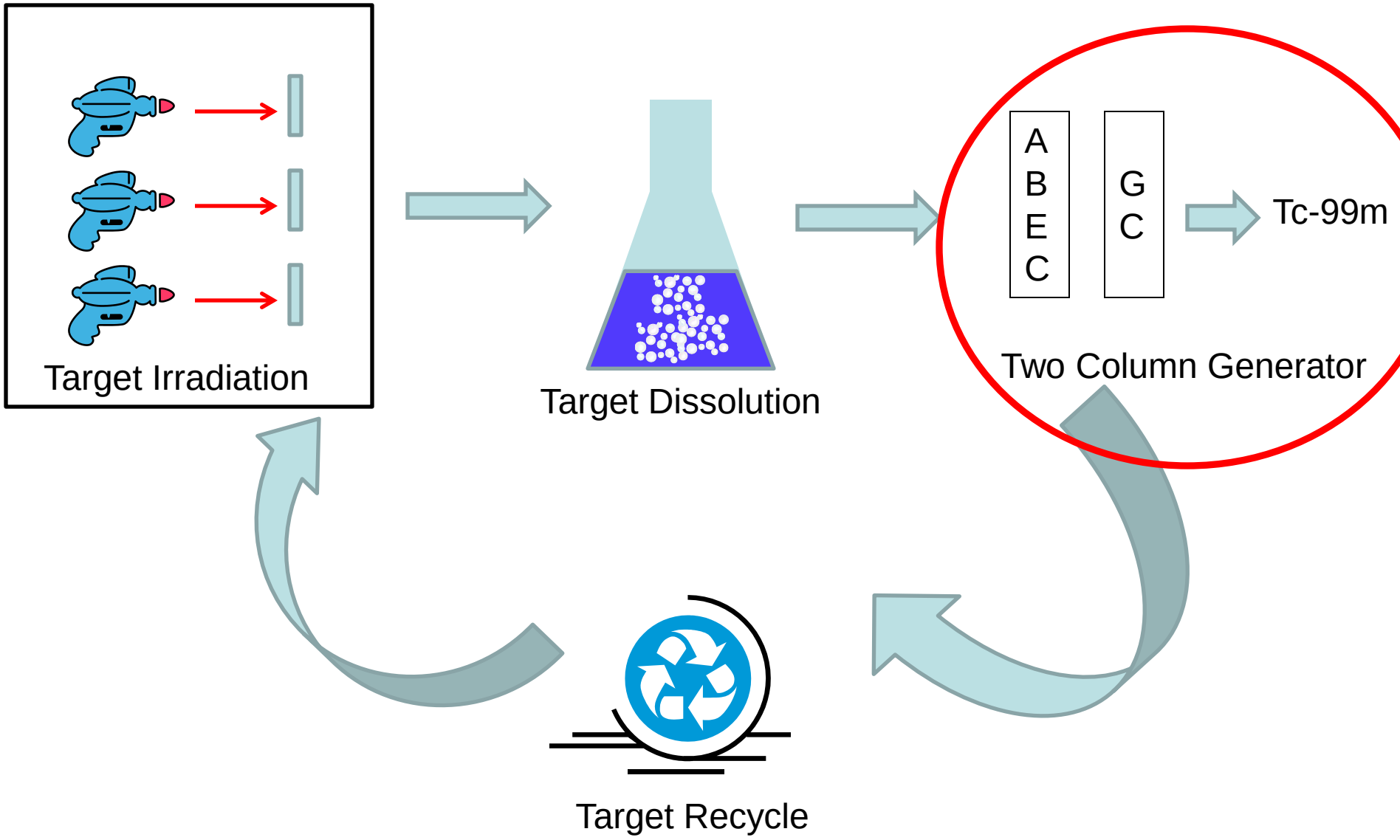
Support
Polystyrene
Divinylbenzene

n = 50

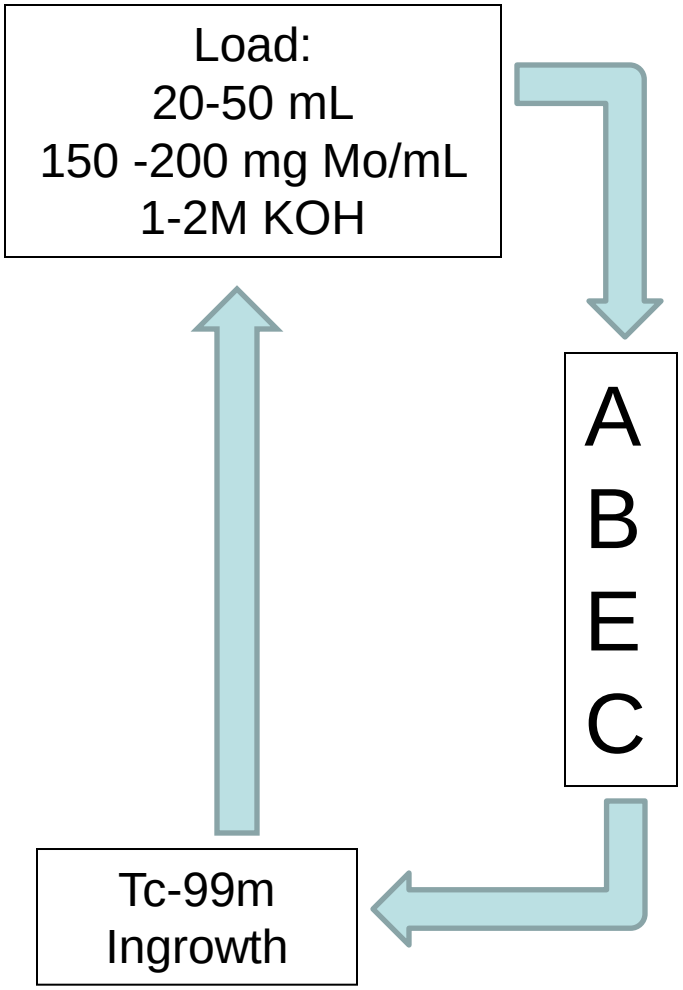

Dw Tc-99 on ABEC-2000 Resin
KOH
NaOH
Dw
10^4
10^3
10^2
10^1
10^0
0 1 2 3 4 5 6 7 8 9
[Hydroxide], M


Dw Tc-99 on ABEC-2000 Resin
KOH +
170 mg/mL
K2MoO4
KOH
NaOH
Dw
10^4
10^3
10^2
10^1
10^0
0
1
2
3
4
5
6
7
8
9
[Hydroxide], M

Production Scheme



Tc-99m Generator



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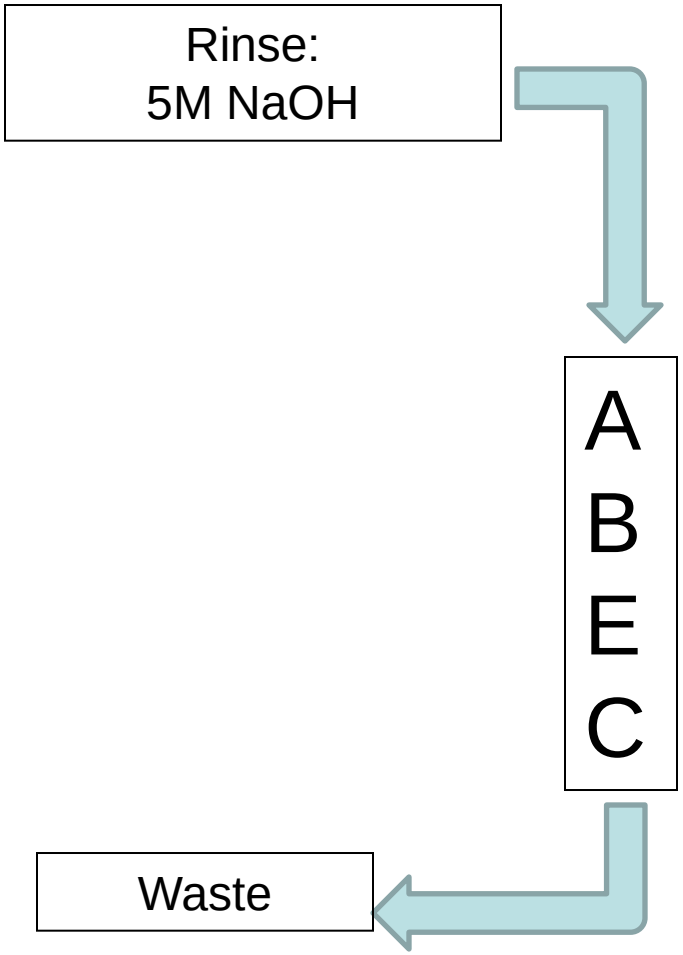

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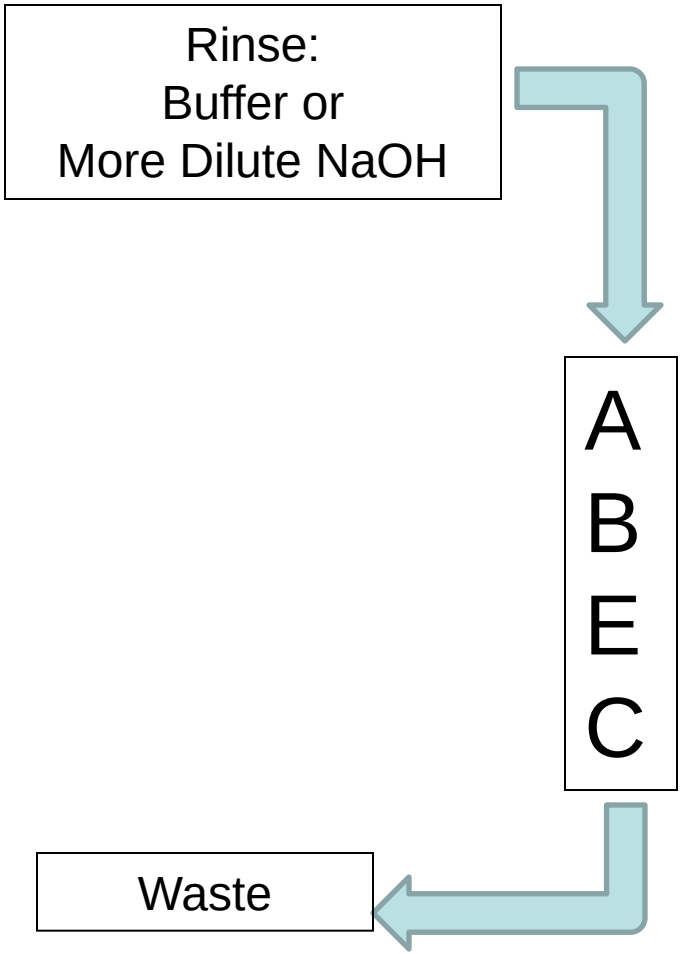

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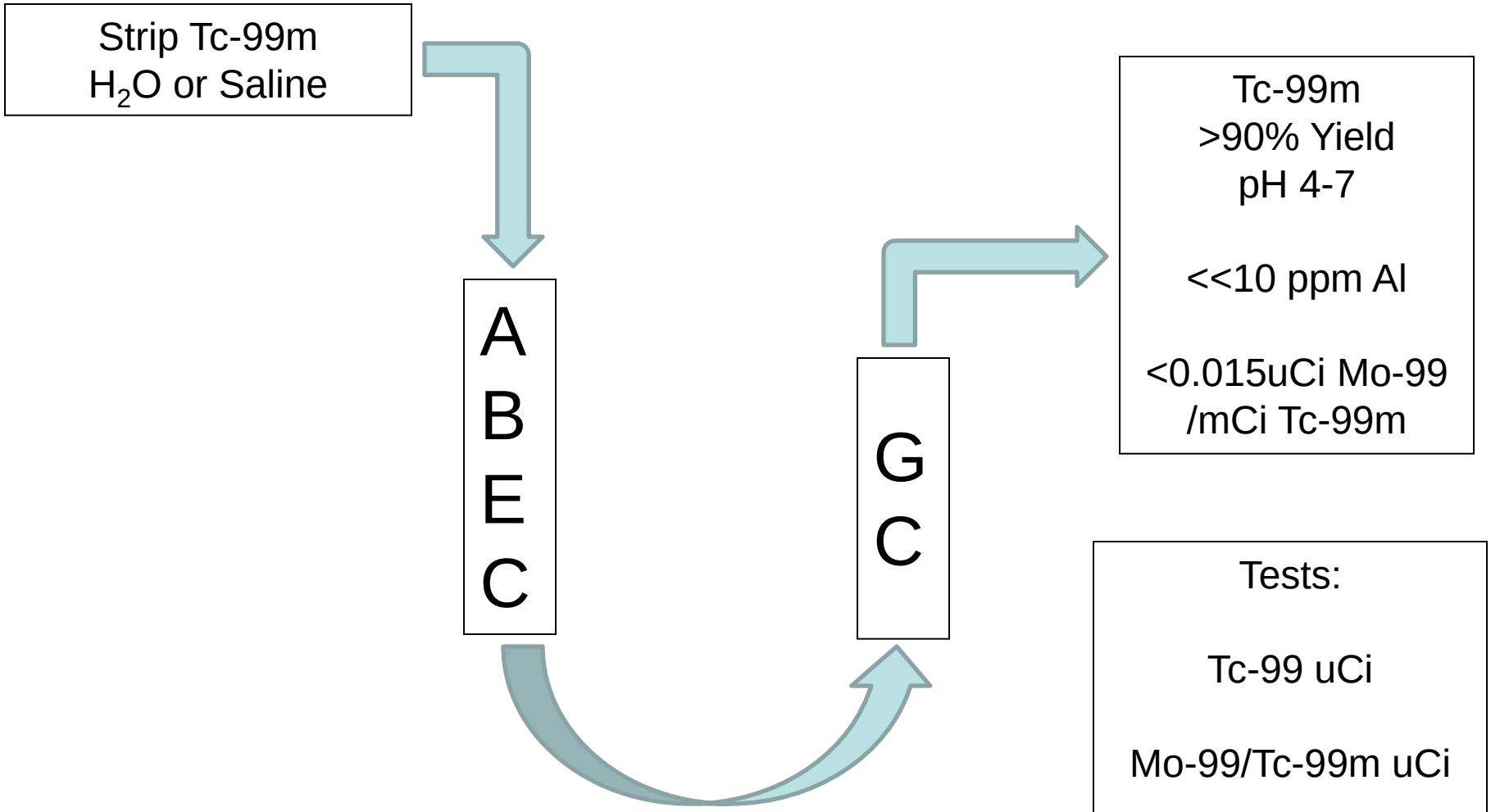
Tc-99m Generator



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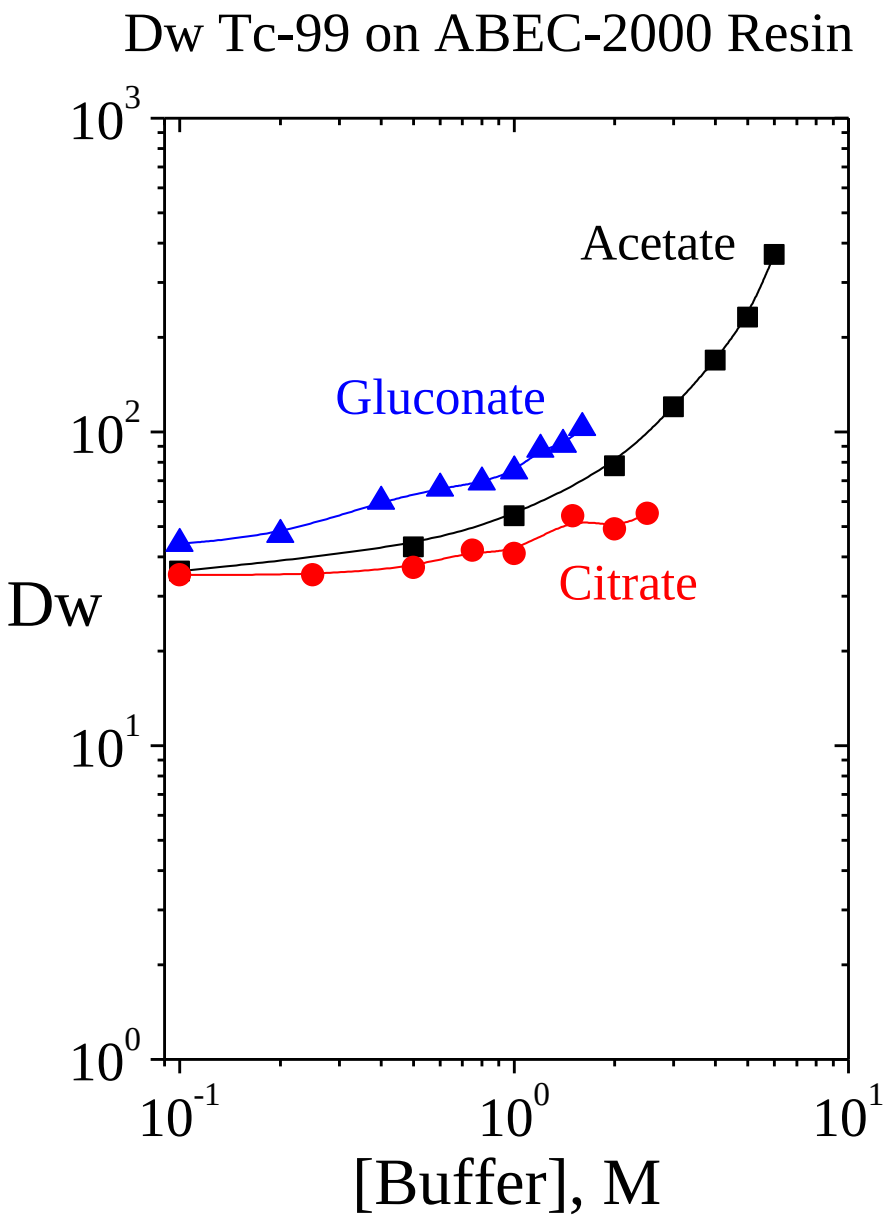
pH Control/GC column Chemistry

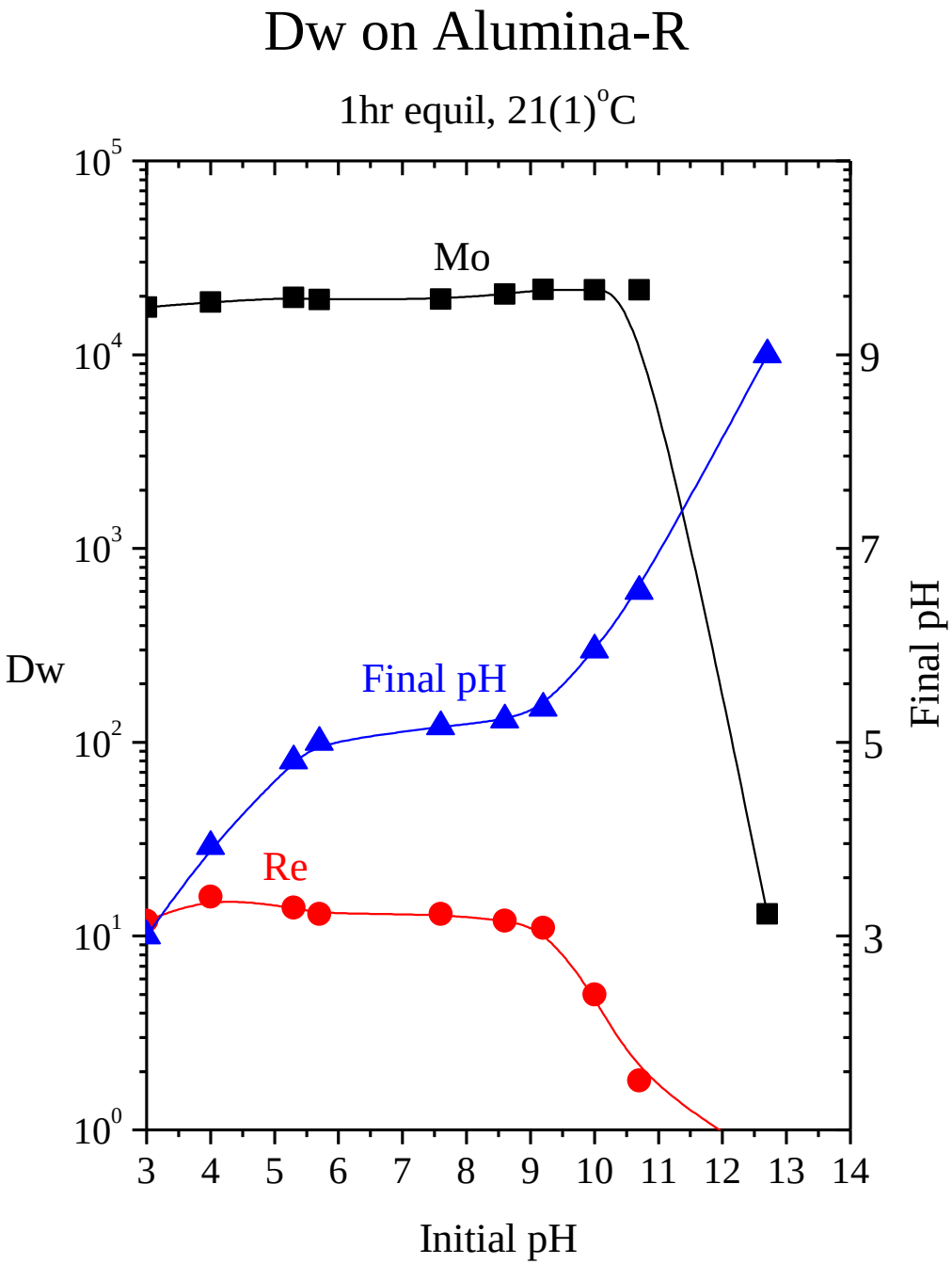


Alumina GC
Rinse: Buffer

Cation Exchange GC
Rinse: 0.1 - 1M NaOH

Cation/Alumina GC
Rinse: 0.1 - 1M NaOH

Alumina Performance



Concerns on Scale-up to 20 Ci

Tc can exist in several oxidation states: 7, 6, 4

Only Tc(VII) is retained by ABEC

Radiolysis at High Mo-99 activities (>1Ci/mL) can be sufficient to reduce Tc to 6 or even 4???

- Alumina increases reduction or stabilizes Tc(VI)

- High Mo concentrations increase reduction

Resin Stability

- 50 kGy Co-60 (Currently Testing to 250 kGy)

The chemistry of technetium in medicine, Joseph Steigman, William C. Eckelman, National Research Council (U.S.). Committee on Nuclear and Radiochemistry,National Academy Press, Washington, D.C.,1992.

Summary/Future Work

ABEC can be used to Separate Tc-99m from low specific activity Mo

Tc-99m meets USP specifications for pH, chemical and radiochemical purity

System and components stable up to 1-2 Ci Mo-99
- -Resin Tested to 1Ci Mo-99 and 50 kGy (Co-60)
- -Future Tests to 20Ci and 250 kGy (Co-60)

Mo-99/Tc-99m(VII) solution stable up to 1-2Ci Mo-99
- -6 separations over 8 days
- -Future tests to 20Ci Mo-99