



**Savannah River  
National Laboratory™**

OPERATED BY SAVANNAH RIVER NUCLEAR SOLUTIONS

We put science to work.™

# Rapid Methods for Radionuclides in Bioassay Samples

**Sherrod L. Maxwell**  
Senior Fellow Scientist

9-16-14

# SRNL Bioassay Lab

---

- **Need rapid bioassay capabilities for emergency response**
  - IND, RDD, nuclear accident
- **Analyze over 2500 urine samples/year**
  - 10,000 actinide/strontium determinations per year
  - ~5000 Tritium determinations per year
- **Specialize in emergency response rapid analysis techniques**
  - Rapid bioassay technology
  - 3200 square meters lab space



# SRNL – Rapid Extraction Chromatography

- Vacuum box technology
  - 1980's with ion exchange
- SRNL Bioassay lab-switch to TEVA and TRU Resin -1998
  - higher chemical yields
  - better alpha peak resolution
  - *lowers costs significantly*



**New Technology For Faster Analysis!**  
*The Vacuum Box System*



Eichrom continues its tradition of being your "time saver" by introducing its Vacuum Box System and extraction cartridge line. By employing vacuum in our already advanced separation methods, analysis time can easily be cut in half over traditional gravity flow Eichrom columns. Customer comments and research in our Rail-lab indicate the same consistently high yields for actinides and strontium as with our conventional columns. Chromatography is improved with the new cartridges that use our smaller 'S' grade resin beads. Another advantage of the cartridge design is the ability to stack two together for tandem separations. Many of our actinide procedures use a common load solution that passes through two

resins, for example UTEVA and TRU Resin in our ACWOS method. Using the Luer connections, the cartridges can easily be stacked during sample loading and initial rinse steps and then be separated for final analyte stripping. For sample loading to our cartridges, a standard syringe barrel is recommended, although many reservoirs with a male Luer connection can be used. The cartridges are connected to the vacuum box by two disposable tips. The white inner tip provides an excellent seal with the cartridge and the yellow outer tip provides support. As with our columns, each cartridge is labeled with an identifying lot number. In addition to St, Ln, TEVA, TRU and UTEVA cartridges currently in stock, our other resins are available by special order in the cartridge format. Though inventory is limited on the Vacuum Box at this introductory stage, we are now accepting orders. Please inquire for an up to date delivery schedule when placing your order.

The Vacuum Box
Clear polycarbonate construction
24 sample capacity
Sample collection via inner 50 mL C tube rack
Inexpensive cartridge to box connection

The Extraction Cartridge
Standard 2 ml resin volume
50-100µ beads
Available in St, Ln, TEVA, TRU and UTEVA
Stackable for multiple analyte separation

**Eichrom and Westinghouse Savannah River Site Strive for Faster Bioassay Methods**



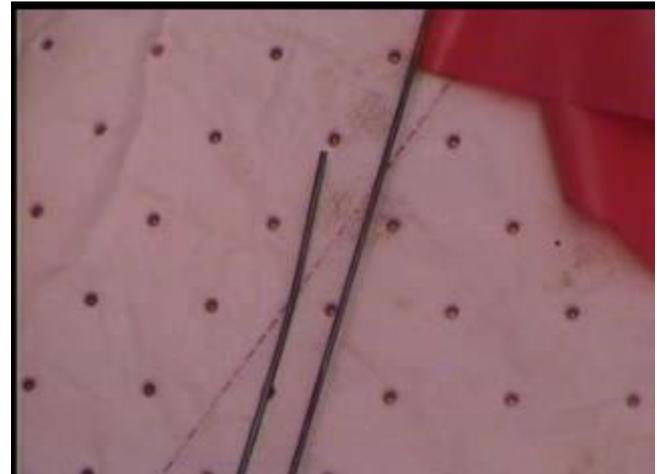
# SRS Emergency Response Bioassay Capabilities

- **Participate in NIST NRIP Emergency Response exercises**
  - Typically have fastest analysis times for actinides/Sr-90
  - Actinides and Sr-90 in urine in <4 hours (Sr-90 in 2.5 hrs)
- **Recently provided rapid analytical support for Japan (environmental)**
  - One of 4 labs nationally providing lab analyses for Japan
  - *Assisted CDC with Sr-90 and Ra-226 in urine methods*
- **Recently demonstrated value of rapid bioassay analyses**
  - June, 2010 incident at SRS
  - assess the magnitude of the uptake and in guiding efforts to mitigate dose (tissue excision and chelation therapy)



# June 14, 2010 TRU Puncture Wound Can/Flag Pictures Causing Puncture

---



# Post Core Punch Tissue Excision

---



**Initial core punch 13,976 dpm  $^{238}\text{Pu}$  (3.5 hrs post injury)**

# Tissue Excision

---



2nd surgical excision 3180 dpm  $^{238}\text{Pu}$   
(5.5 hrs post injury)



3rd surgical excision 3777 dpm  $^{238}\text{Pu}$   
(9 days post injury)

# Puncture Wound Incident Lab Support

---

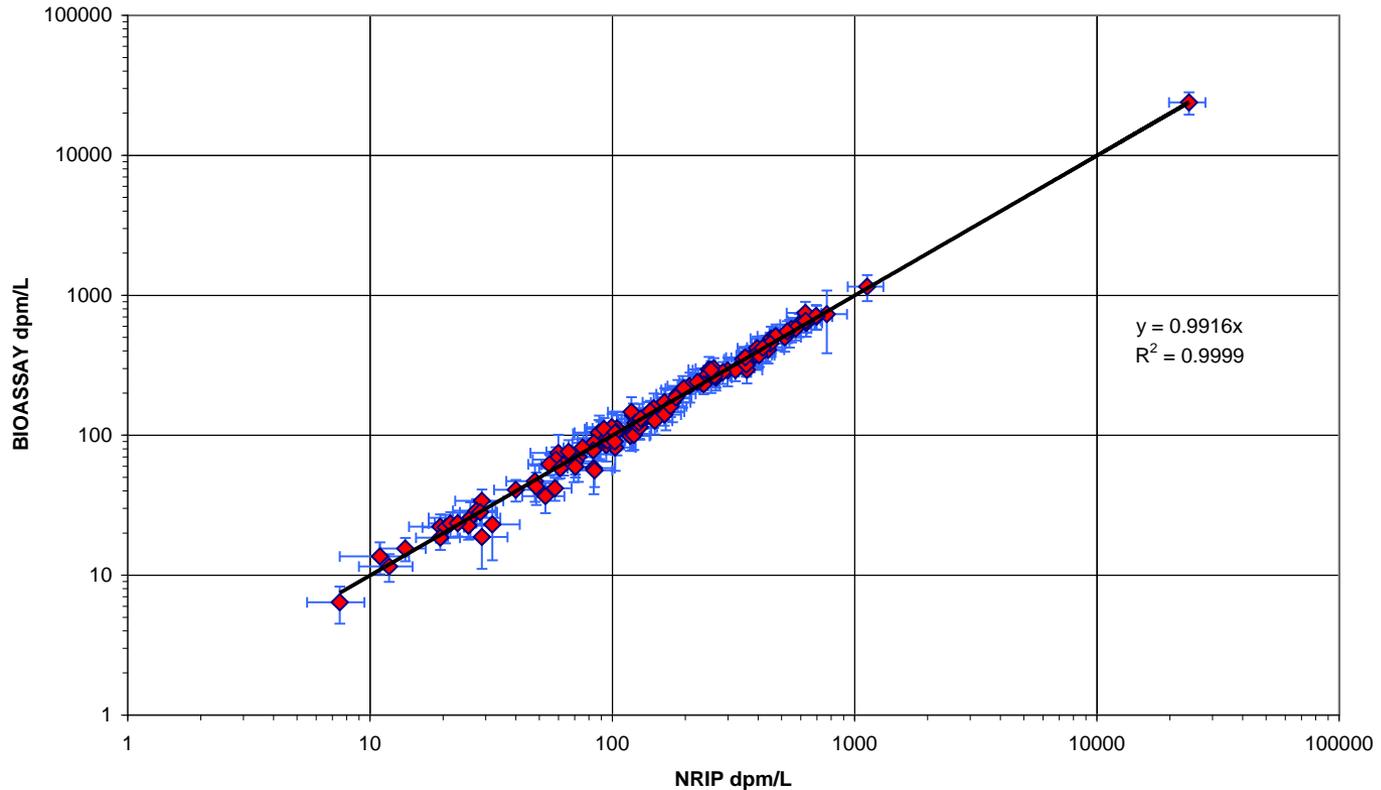
- **Sample receipt puncture wound** **6/16/10**
- **NRIP emergency method <sup>1</sup> results (EM lab)** **6 hrs.**
- **Rapid Bio Lab results (initial)** **4 days**
- **Rapid Bio Lab <sup>2</sup> results (final)** **7 days**

<sup>1</sup> NRIP method provided HPT 8 data points in first 10 days into event to support dose mitigation  
(tissue excision and chelation therapy)

<sup>2</sup> DOELAP accredited method official results 7 days earlier than 14 day TAT requirement for Incident samples  
Method: Wet-ashing with HNO<sub>3</sub> and H<sub>2</sub>O<sub>2</sub> to destroy chelation agent + TEVA Resin (vacuum box)

# NRIP Emergency Method vs. Rapid Bioassay (routine)

BIOASSAY vs. NRIP Results  
Log-Log Plot for all Data



Emergency method-cerium fluoride source preparation

Routine rapid method-electrodeposition



## Rapid bioassay incident support

---

***The response to this incident by all involved (both BIO and EM folks) has been exceptional. We are seeing data (both official DOELAP and rapid screening) come through in remarkable time-frames.***

***The rapid analysis screening has been THE most powerful tool (in addition to some retention counting work we have performed) I essentially have a new data point daily because of the efforts of your team in aiding me in getting a handle on the magnitude of this uptake and guiding Medical in efforts to mitigate dose (tissue excision and chelation therapy).***

***As I mentioned to you when we last spoke directly, if this event had occurred two years ago the quantity of good quality excreta data simply would not have been available. ...***

***Mitch Findley -HPT***



# Rapid bioassay incident support

---

- *“It should be noted that the **prompt medical intervention of wound excision and DTPA therapy** has drastically reduced the dosimetric consequences of this **incident**, and the health physics and medical personnel at SRS should be commended for their prompt action.*
- *In addition, **the development of a rapid analysis technique for Pu-238 in urine** has provided important data in a very timely manner, and contributed greatly to the effective management of this incident”*

*Dr. Richard Toohey*

*REAC/TS Trip Report*

*ORISE*

*7/23/2010*



# Sample Preparation Challenges for Bioassay

- **Actinides (Pu, Np, U, Th, Am, Cm)**
  - Requires low levels of detection
  - Alpha Spectrometry and ICP-MS options
- **Remove spectral interferences**
  - Rapidly and effectively
- **Flexibility**
  - Direct urine aliquot (Ex. 10 mL)
  - Preconcentration (Ex. 100 mL +)
- **Rapid, effective sample preparation is essential**
  - Rapid column extraction technology
  - *Reduces costs for routine analyses*



# Rapid Flow Rates

---



# Actinides and Sr-90 in Urine

Calcium phosphate precipitation

- 1) Redissolve in 8 mL 6M HNO<sub>3</sub> and 8 mL 2M Al(NO<sub>3</sub>)<sub>3</sub>
- 2) Add 0.5 mL 1.5M Sulfamic Acid + 1.25 mL 1.5M Ascorbic Acid
- 3) Add 1 mL 3.5 M Sodium Nitrite

Beaker rinse: 3mL 3MHN03  
10 mL 3M HN03 to stacked cartridges

Separate cartridges:  
TEVA Resin alone: 10 mL 3M HN03

Sr Resin alone:  
15 mL 8MHN03  
10 mL 0.05M strip Sr

Evaporate/ beta counting

Th Elution  
20mL 9M HCl

Pu (and/or Np) Elution  
20mL  
0.10M HCl - 0.05M HF - 0.01M TiCl<sub>3</sub>

2 mL TEVA Resin  
(50-100 um)

Add 0.5 mL 30 wt% H<sub>2</sub>O<sub>2</sub>

Cerium fluoride

2 mL TRU-Resin  
(50-100 um)

Alpha spectrometry

Cerium fluoride

2 mL Sr-Resin  
(50-100 um)

Enhanced Po-210 removal

TRU Resin alone:  
Elute Am/Cm with 15 ml 4M HCL/add  
15 ml H<sub>2</sub>O + 50 ug Ce+ 3 ml HF  
12 ml 4M HCl-0.2M HF -0.002M TiCl<sub>3</sub>  
Elute U with 15 ml 0.1M NH<sub>4</sub>HC<sub>2</sub>O<sub>4</sub>

Vacuum box procedure

# Improvements in NRIP -2008 Urine Samples

**Radiological Preparedness Exercise (NRIP) administered by NIST**  
-emergency analysis samples with 1 day notice

	<b>NRIP 2006</b>	<b>NRIP 2007</b>	<b>NRIP 2008</b>
<b>Radionuclides</b>			
<b>Am-241</b>	<b>7.4 hrs</b>	<b>4.6 hrs</b>	<b>3.1 hrs</b>
<b>Pu-238, 239</b>	<b>7.4 hrs</b>	<b>4.8 hrs</b>	<b>3.3 hrs</b>
<b>U-234, 235, 238</b>	<b>7.4 hrs</b>	<b>5.2 hrs</b>	<b>4.2 hrs</b>
<b>Strontium-90</b>	<b>5.8 hrs</b>	<b>3.9 hrs</b>	<b>2.9 hrs</b>

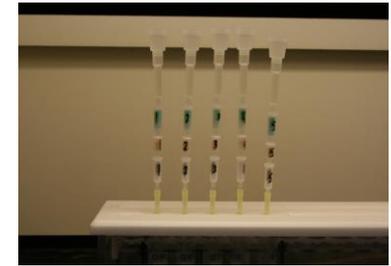


# Alpha Spectrometry vs. ICP-MS

- **ICP-MS**
  - shorter measurement time; sequential
  - can differentiate nuclides with overlapping alpha energies ( $^{239}\text{Pu} + ^{240}\text{Pu}$ )
  - can be hampered by isobaric, polyatomic interferences ( $^{238}\text{UH}^+$  on  $^{239}\text{Pu}$ )
  - may be limited for shorter-lived isotopes with very low mass, ex.  $^{238}\text{Pu}$
- **Alpha Spectrometry**
  - Simultaneous counting with large numbers of detectors
  - works for long or short-lived actinide isotopes
  - typically requires chemical separation
  - cannot differentiate well between alpha isotopes with overlapping alpha energies
- **Both may require separation of interferences**
- **Both may have MDA challenges for some actinides depending on variables such as inhalation, ingestion, days post exposure**
- **Instead of either/or...maybe both**
  - *can be complementary for short-lived and long-lived actinides*



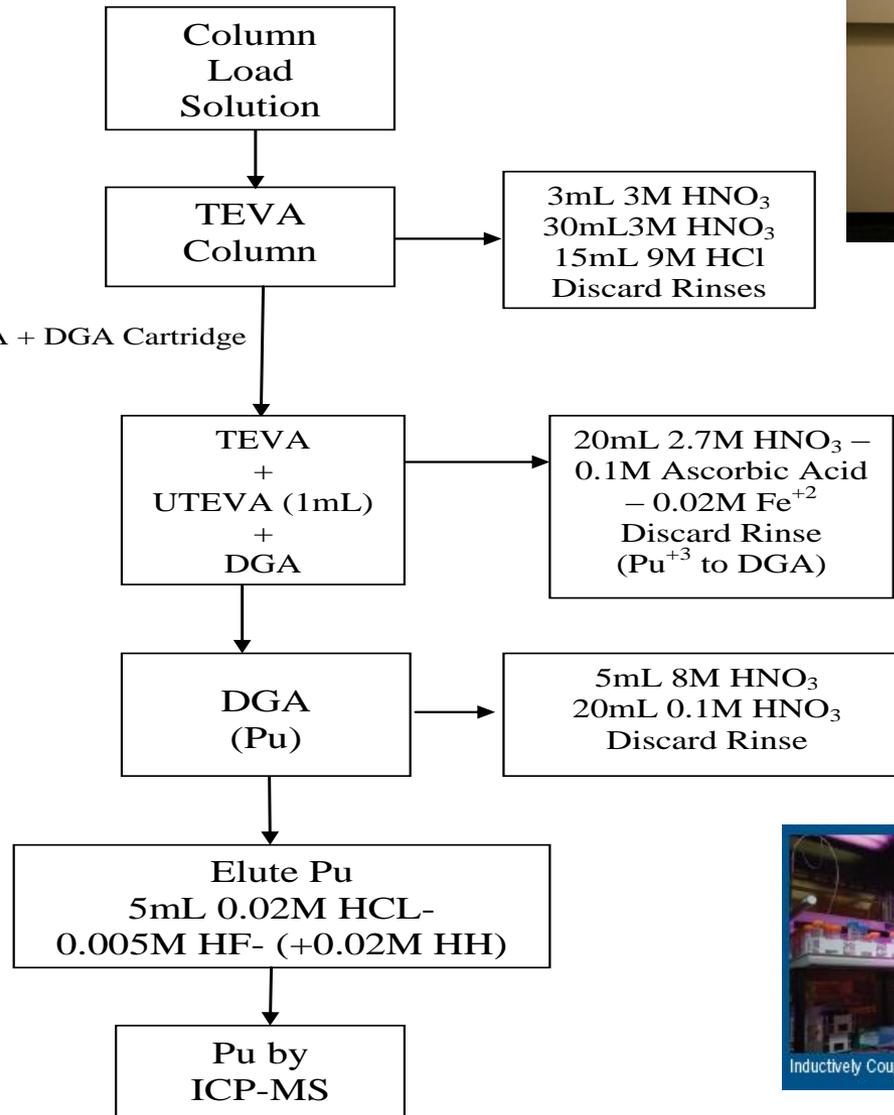
# Rapid Purification of Pu for ICP-MS



>10<sup>6</sup> removal  
of U-238 from Pu-239

Split Cartridges  
Discard UTEVA

Health Physics Journal, August 2011  
– Vol 101 - Issue 2 - pp 180-186



# Rapid Fecal Sample Furnace Heating



Place fecal sample in 1L beaker lined with vellum paper

Add Tracers (2x since sample is split later)  
[<sup>242</sup>Pu/<sup>236</sup>Pu, <sup>243</sup>Am, <sup>232</sup>U]

Place in furnace and heat @ 250°C for 30 min

Ramp 1 to 350°C and heat for 20min \*  
Ramp 2 to 450°C and heat for 20min  
Ramp 3 to 550°C and heat for 45min



\* Routine analysis heating option to 550°C in 1 liter overnight without ceramic crucible

Wet ash residue in 1L beaker

Transfer ash to 250mL ceramic crucible



Wet ash residue with 15.8M HNO<sub>3</sub> and 30wt% H<sub>2</sub>O<sub>2</sub> on hot plate

Place ceramic crucible in furnace @ 850°C for 1-1.5hr until ash is white

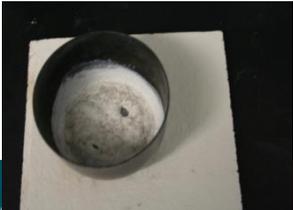
Transfer wet ashed residue (after evaporation to small volume) into 250mL Zr crucible with 15.8M HNO<sub>3</sub>

Transfer ash from ceramic crucible to 250mL Zr crucible with 15.8M HNO<sub>3</sub>

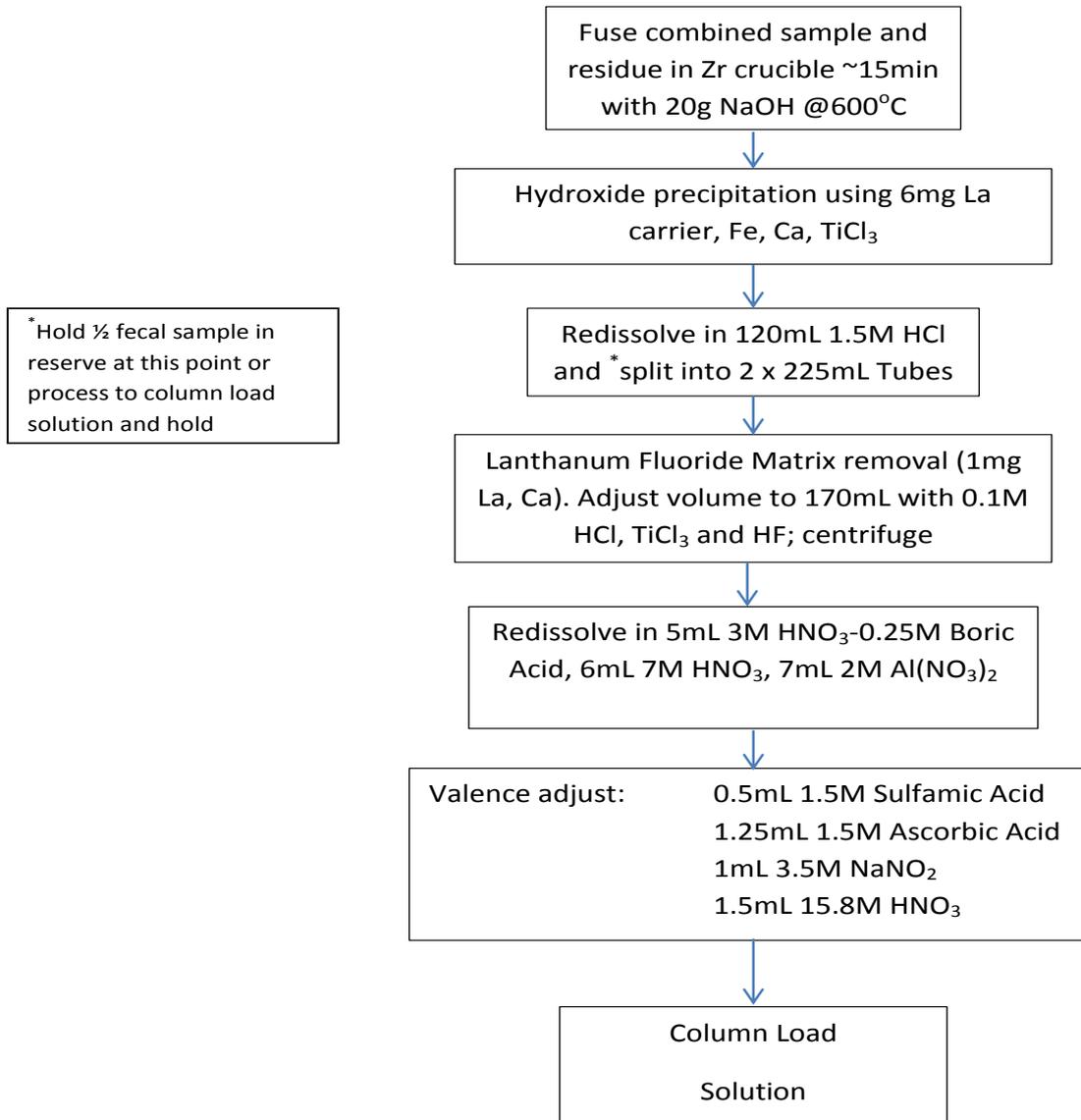


250mL Zr crucible  
Evaporate to dryness

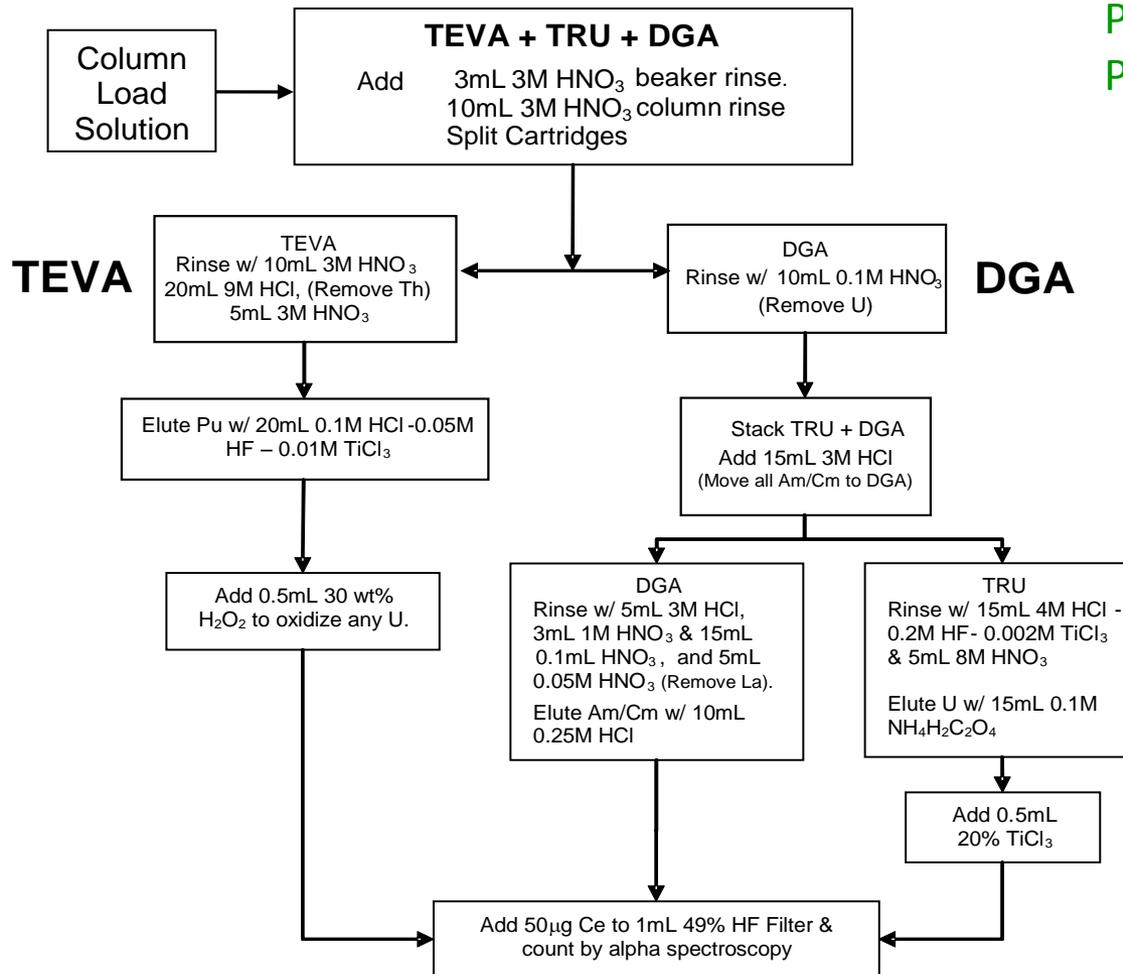
Place Zr crucible in furnace at ~450°C and increase heat (if necessary) until solids are white/light colored



# Rapid Fecal Sample Fusion



# Rapid Fecal Column Separation



Pu only: TEVA  
Pu and U: TEVA+TRU

# NRIP Fecal Results Pu-239/240

Sample ID	<sup>242</sup> Pu Yield (%)	<sup>239,240</sup> Pu Reference Value (Bq Smp <sup>-1</sup> )	Measured Value (Bq Smp <sup>-1</sup> )	Difference (%)
916	107.2	0.133	0.126	-5.3
918	87.5	0.101	0.104	3.0
931	89.0	0.204	0.198	-2.9
934	87.9	0.200	0.193	-3.5
956	101.6	0.085	0.081	-4.7
Avg	94.6			-2.7
SD	9.2			
% RSD	9.7			
<b>6 hour count</b>				

Maxwell, S. Culligan, B., Hutchison, J. and Spencer, R. Rapid fusion method for determination of actinides in fecal samples Radioanal Nucl Chem (2013) 298:1533–1542



# NRIP Fecal Results Am-241

Sample ID	<sup>243</sup> Am Yield (%)	<sup>241</sup> Am Reference Value (Bq Smp <sup>-1</sup> )	Measured Value (Bq Smp <sup>-1</sup> )	Difference (%)
916	89.2	0.310	0.315	1.6
918	88.5	0.237	0.210	-11.4
931	80.2	0.476	0.434	-8.8
934	81.9	0.469	0.464	-1.1
956	80.3	0.199	0.201	1.0
Avg	82.7			-3.7
SD	3.9			
% RSD	4.8			



# Rapid Ra-226 in Urine Method

---

- **What about Ra-226?**
  - *Could we develop a more rapid method?*
- **Ra-226**
  - *alpha emitter, 4.78 MeV (94.5%), 4.61 MeV (5.55%)*
  - *1600 year half-life (alpha spectrometry and ICP-MS)*
  - *radiotoxic, follows calcium in food chain into bones*
- **Urine**
  - Rapid assay needed
  - Simple, fast and reliable



# Primary Laboratory Target CDG Levels (For Child or Pregnant Female)

Nuclide	Class*	Day 1		Day 2		Day 3		Day 5		Day 7		Day 10		Day 15		Day 20	
		Bq/L	µg/L														
Ra-226	M	2.44E+01	6.68E-04	4.74E+00	1.30E-04	3.21E+00	8.77E-05	1.68E+00	4.60E-05	8.71E-01	2.38E-05	4.13E-01	1.13E-05	2.14E-01	5.85E-06	1.68E-01	4.60E-06

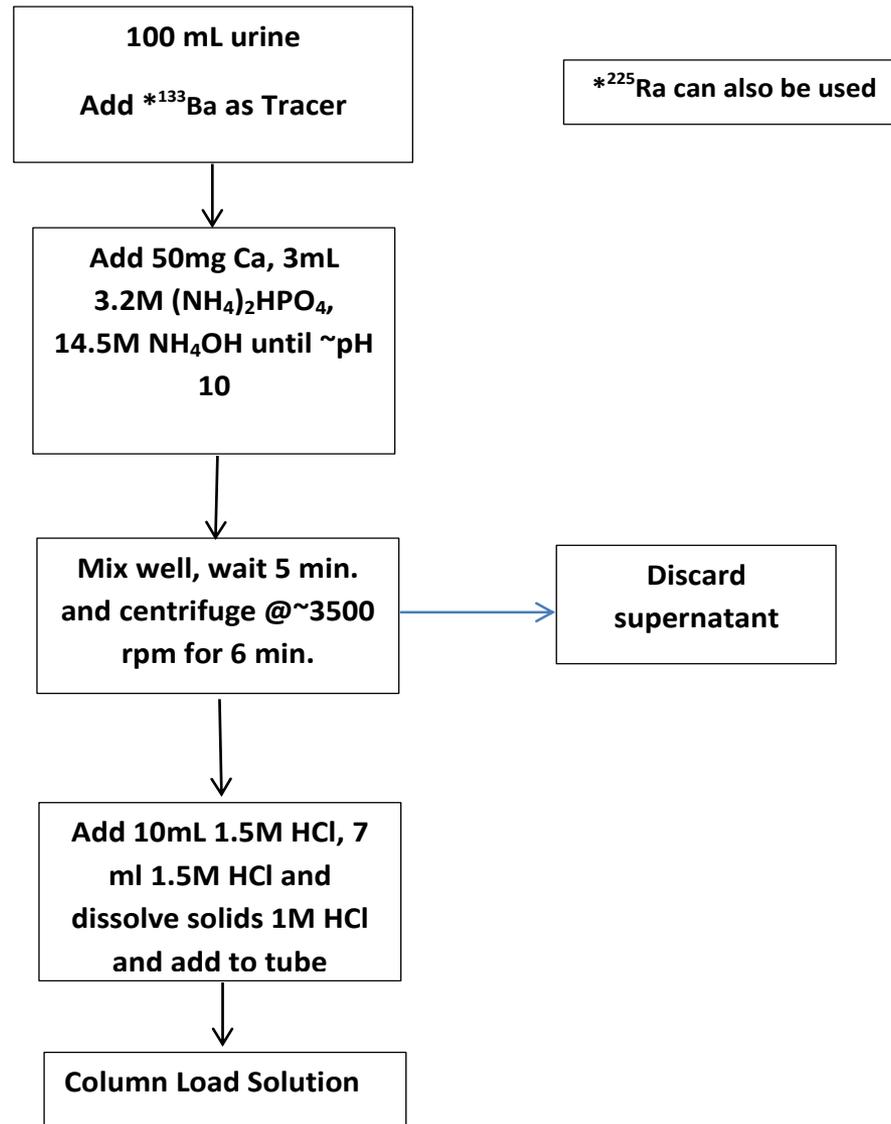
4.54pCi/L

The CDG levels for pregnant female and children are 1/5 the target levels for other adults.

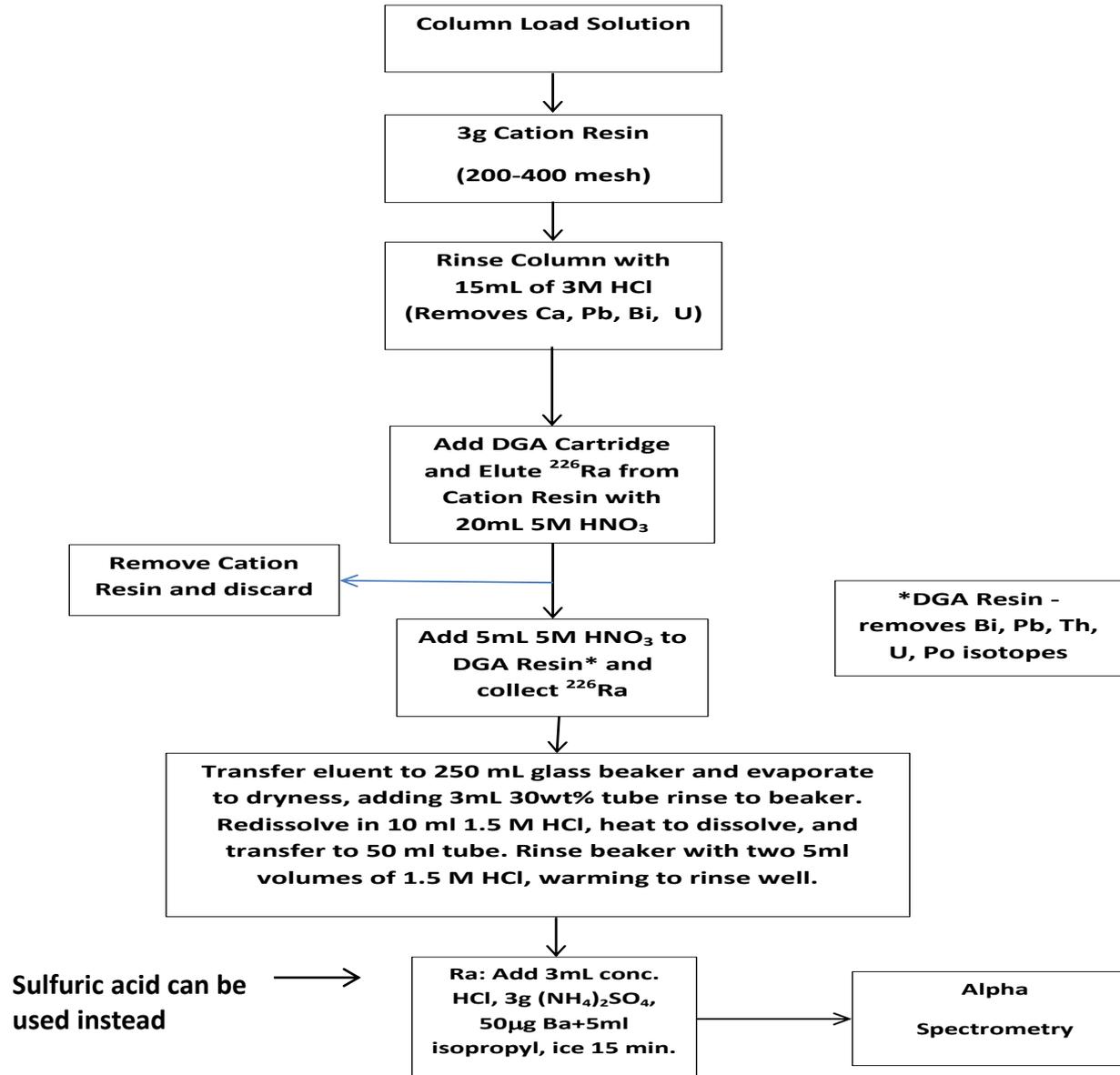
Calculations by Dr. David Saunders, CDC based on NCRP 161

# Rapid Sample Preparation for Ra-226 in urine

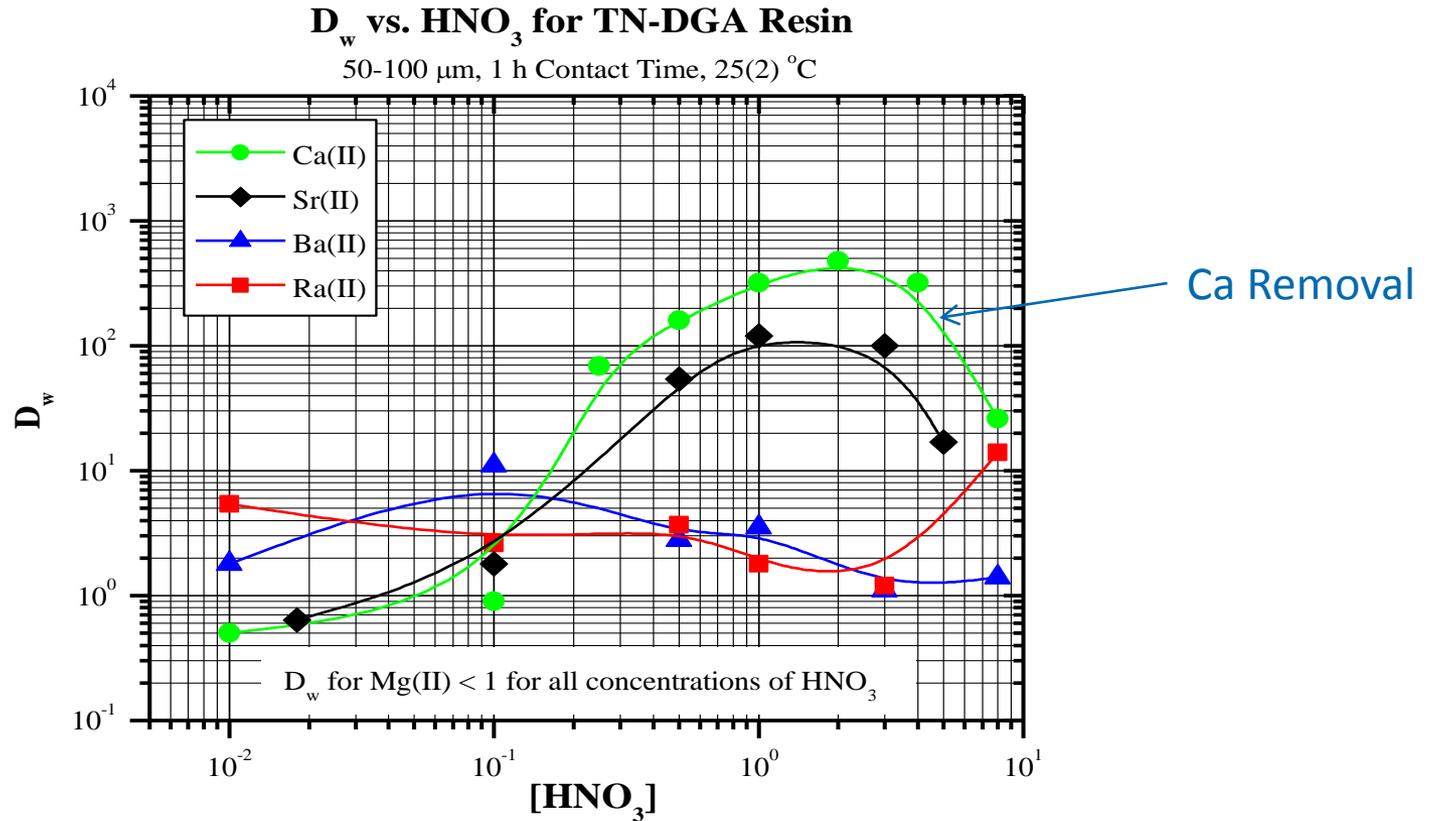
*Less Ca, PO<sub>4</sub> instead  
of carbonate to lower blanks*



# Rapid Column Separation for Ra-226 in urine

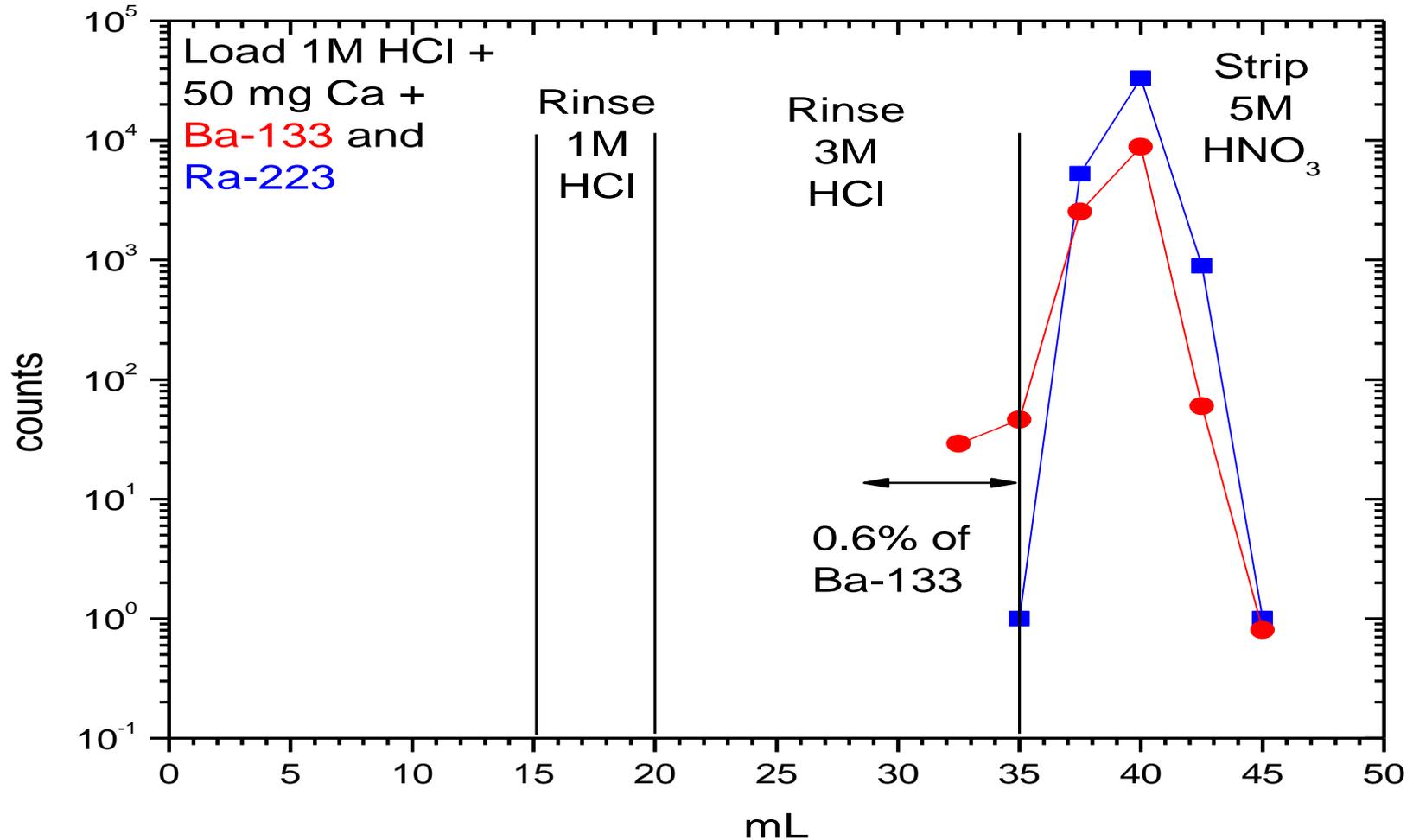


# Residual Ca Removal using DGA Resin



# Ba and Ra Behavior on Cation Resin

Elution on 3.0 g of 50Wx8, 200-400 mesh



Courtesy Dan McAlister, P&G Research

## Rapid Column Separation using Cation + DGA Resin : stacked elution

Sample ID	<sup>133</sup> Ba Yield (%)	<sup>226</sup> Ra Reference Value (mBq smp <sup>-1</sup> )	<sup>226</sup> Ra Measured Value* (mBq smp <sup>-1</sup> )	Difference (%)
1	100.4	18.42	18.4	-0.2
2	96.0	18.42	18.8	2.2
3	95.1	18.42	17.7	-3.9
4	101.2	18.42	17.9	-3.0
5	99.3	18.42	18.3	-0.8
6	96.1	18.42	16.5	-10.5
Avg	98.0		17.9	-2.7
SD	2.6		0.8	
% RSD	2.6		4.5	
For 100 ml aliquot 18.42 mBq/smp = 184.2 mBq/L				
16 hour count				



# Fast and Reliable

---

- **Ra-226 urine method validated and used by US Air Force Radioanalytical Laboratory**
  - **Same method works well with water samples**
- **High chemical yields**
  - <4-5 hours with simultaneous sample preparation
- **Ba-133: No waiting for Ra-225 in-growth**
  - but Ra-225 can be used with some adjustments if preferred
  - allows Ra-224 measurement
- **Can be adapted to smaller or larger urine aliquots as needed**
  - *Smaller aliquot if less urine available (spot urine sample)*
  - *Large aliquot if lower MDA needed*

Maxwell S, Culligan B, Hutchison J, Utsey R and McAlister, D (2014) Rapid determination of  $^{226}\text{Ra}$  in emergency urine samples. *Journal of Radioanalytical and Nuclear Chemistry*, online first, Feb. 2014

# Summary

---

- **Rapid methods are essential**
  - Emergency response-nuclear accident, RDD or occupational exposure
  - *Rapid, reliable screening is critical*
  - Improvements in emergency response can improve routine methods
  - *Reduced costs significantly with new rapid methods*
- **SRNL Bioassay Program**
  - Blind PT performance excellent
  - *Enhanced medical treatment and dose mitigation*
    - *Demonstrated by puncture wound treatment*
  - Effective routine occupational exposure monitoring
    - *Quality of results builds trust*