

Lawrence Livermore National Laboratory

# Determination of $^{235}\text{U}/^{238}\text{U}$ Ratio in Urine by ICP-MS

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Lori Collins, Alfonso Gobaleza, Robert Langston, Radoslav Radev, Chit Than, Carolyn Wong,  
Annmarie Wood-Zika

Radiation Protection Functional Area, Environment, Safety & Health

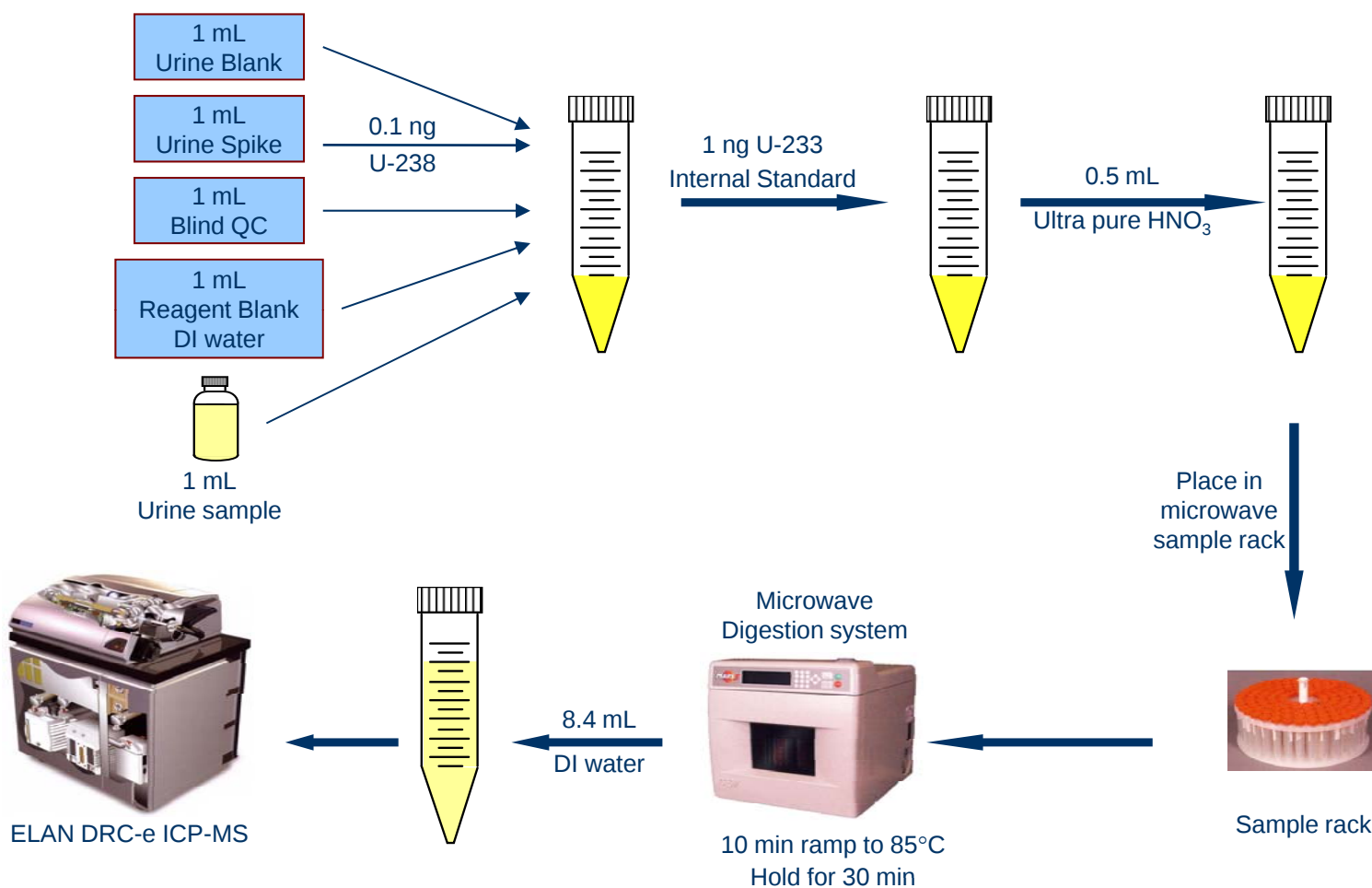
Lawrence Livermore National Laboratory, P. O. Box 808, Livermore, CA 94551

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# LLNL Bioassay Laboratory DOELAP Accredited Uranium Standard Operating Procedure



# Uranium Standard Operation Procedure $MDL_{99}$ , $MDA_{95}$ , $L_{C95}$ and CSU

Detection limit for  $^{238}\text{U}$  required by LLNL  
Internal Dosimetry Team =  $0.01 \mu\text{g/L}$

$$MDL_{99} = 0.0033 \mu\text{g/L}$$

$$MDA_{95} = 0.0042 \mu\text{g/L}$$

$$L_C = 0.0021 \mu\text{g/L}$$

Combined standard uncertainty (CSU,  $1\sigma$ )

$$^{238}\text{U} < 0.1 \mu\text{g/L} \quad \text{CSU} = 0.0015 \mu\text{g/L}$$

$$^{238}\text{U} \geq 0.1 \mu\text{g/L} \quad \text{CSU} = 0.0100 (\mu\text{g/L } ^{238}\text{U}) + 0.0005 \mu\text{g/L}$$



# Determination of $^{235}\text{U}/^{238}\text{U}$ Ratio

## ❖ Uranium Standard Operation Procedure

- ❖ Fast
- ❖ Microwave digested dilute & shoot method
- ❖  $\text{MDA}_{95} = 0.0042 \mu\text{g/L}$

$^{238}\text{U}$  Notification Level =  $0.05 \mu\text{g/L}$   
(Based on evaluation of non-uranium exposed  
worker population)

## ❖ Procedure to determine $^{235}\text{U}/^{238}\text{U}$ Ratio

We need to know the  $^{235}\text{U}$  content along with  $^{238}\text{U}$ , in order to determine whether the uranium uptake of the employee was due to:

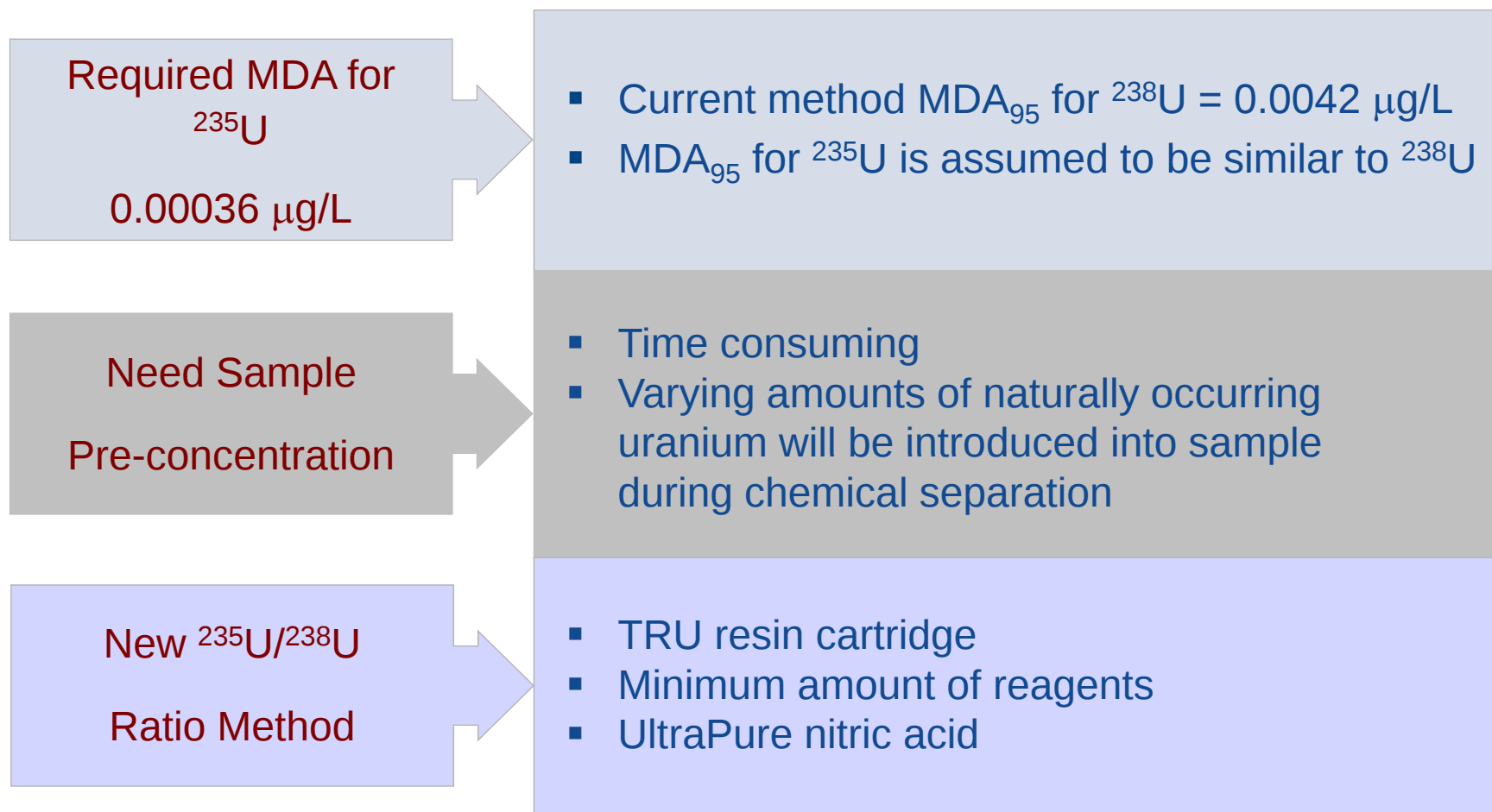
- Natural
- Enriched OR
- Depleted

At  $0.05 \mu\text{g/L}$  Notification level for  $^{238}\text{U}$

$$\begin{aligned} ^{235}\text{U} &= 0.05 \times 0.0072 \\ &= 0.00036 \mu\text{g/L} \end{aligned}$$



# Developing New U Ratio Method Using ELAN DRC-e ICP-MS



## Separation Using 2 mL UTEVA<sup>®</sup> Resin Cartridges

| Sample Type   | Load Solution                                             | Cartridge          | Eluting Solution                                        | <sup>233</sup> U Recovery (%) |
|---------------|-----------------------------------------------------------|--------------------|---------------------------------------------------------|-------------------------------|
| Reagent Blank | 3M HNO <sub>3</sub>                                       | UTEVA <sup>®</sup> | 0.1M HNO <sub>3</sub>                                   | 99                            |
| Urine Spike   | 3M HNO <sub>3</sub>                                       | UTEVA <sup>®</sup> | 0.1M HNO <sub>3</sub>                                   | < 5                           |
| Reagent Blank | 3M HNO <sub>3</sub>                                       | UTEVA <sup>®</sup> | 0.075M (NH <sub>4</sub> )HC <sub>2</sub> O <sub>4</sub> | 94                            |
| Urine Blank   | 3M HNO <sub>3</sub>                                       | UTEVA <sup>®</sup> | 0.075M (NH <sub>4</sub> )HC <sub>2</sub> O <sub>4</sub> | 55                            |
| Urine Spike   | 3M HNO <sub>3</sub>                                       | UTEVA <sup>®</sup> | 0.075M (NH <sub>4</sub> )HC <sub>2</sub> O <sub>4</sub> | 44                            |
| Reagent Blank | 3M HNO <sub>3</sub> /1M Al(NO <sub>3</sub> ) <sub>3</sub> | UTEVA <sup>®</sup> | 0.075M (NH <sub>4</sub> )HC <sub>2</sub> O <sub>4</sub> | 98                            |
| Urine Blank   | 3M HNO <sub>3</sub> /1M Al(NO <sub>3</sub> ) <sub>3</sub> | UTEVA <sup>®</sup> | 0.075M (NH <sub>4</sub> )HC <sub>2</sub> O <sub>4</sub> | 79                            |
| Urine Spike   | 3M HNO <sub>3</sub> /1M Al(NO <sub>3</sub> ) <sub>3</sub> | UTEVA <sup>®</sup> | 0.075M (NH <sub>4</sub> )HC <sub>2</sub> O <sub>4</sub> | 80                            |



## Separation Using 2 mL TRU Resin Cartridges

| Sample Type   | Load Solution       | Cartridge | Eluting Solution                                        | <sup>233</sup> U Recovery (%) |
|---------------|---------------------|-----------|---------------------------------------------------------|-------------------------------|
| Reagent Blank | 3M HNO <sub>3</sub> | TRU       | 0.075M (NH <sub>4</sub> )HC <sub>2</sub> O <sub>4</sub> | 95                            |
| Urine Blank   | 3M HNO <sub>3</sub> | TRU       | 0.075M (NH <sub>4</sub> )HC <sub>2</sub> O <sub>4</sub> | 82                            |
| Urine Spike   | 3M HNO <sub>3</sub> | TRU       | 0.075M (NH <sub>4</sub> )HC <sub>2</sub> O <sub>4</sub> | 76                            |
| Reagent Blank | 3M HNO <sub>3</sub> | TRU       | 0.1M (NH <sub>4</sub> )HC <sub>2</sub> O <sub>4</sub>   | 93                            |
| Urine Blank   | 3M HNO <sub>3</sub> | TRU       | 0.1M (NH <sub>4</sub> )HC <sub>2</sub> O <sub>4</sub>   | 80                            |
| Urine Spike   | 3M HNO <sub>3</sub> | TRU       | 0.1M (NH <sub>4</sub> )HC <sub>2</sub> O <sub>4</sub>   | 75                            |
| Reagent Blank | 2M HNO <sub>3</sub> | TRU       | 0.075M (NH <sub>4</sub> )HC <sub>2</sub> O <sub>4</sub> | 92                            |
| Urine Blank   | 2M HNO <sub>3</sub> | TRU       | 0.075M (NH <sub>4</sub> )HC <sub>2</sub> O <sub>4</sub> | 55                            |
| Urine Spike   | 2M HNO <sub>3</sub> | TRU       | 0.075M (NH <sub>4</sub> )HC <sub>2</sub> O <sub>4</sub> | 68                            |



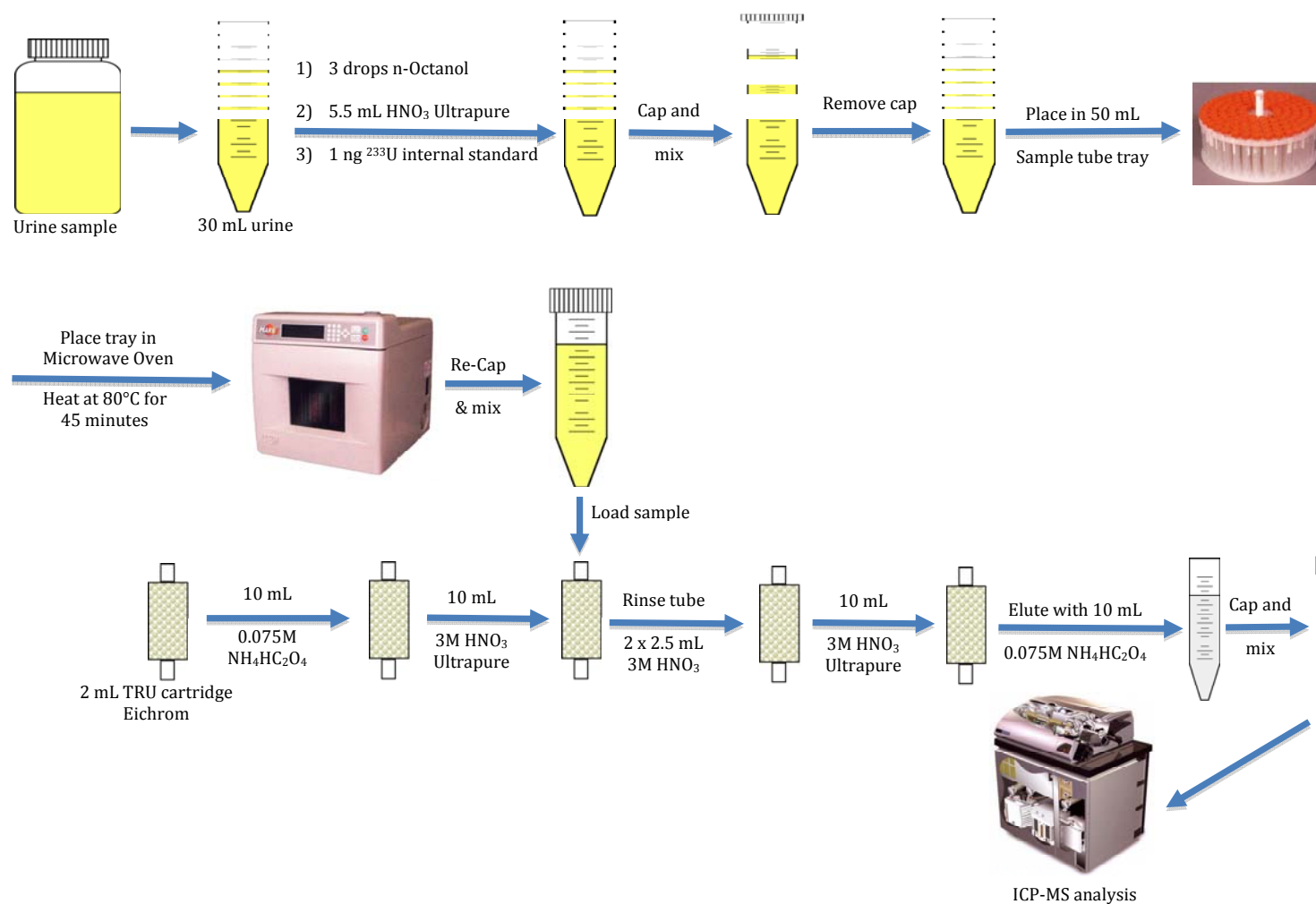
# Designing the New $^{235}\text{U}/^{238}\text{U}$ Ratio Method

## Advantages of New $^{235}\text{U}/^{238}\text{U}$ Ratio Method

- 30 mL of urine used.  
*(30 times more sample than old method)*
- $^{233}\text{U}$  internal standard added in the beginning.  
*(can estimate combined chemical and measurement recovery)*
- Microwave digested in 3M nitric acid.  
*(isotope equilibrium is guaranteed)*
- After Microwave digestion, sample is ready to be loaded onto TRU cartridge.  
*(less reagents used .... no  $\text{Al}(\text{NO}_3)_3$  added)*
- Eluted with 10 mL of Ammonium bi-oxalate.  
*(3 times sample pre-concentration is achieved)*
- 0.075M Ammonium bi-oxalate is compatible with ICP-MS (< 0.5% solids).  
*(optimum concentration to elute TRU cartridge and does not clog up the ICP-MS injector and cones)*



# Determination of $^{235}\text{U}/^{238}\text{U}$ Ratio in Urine by ELAN DRC-e ICPMS



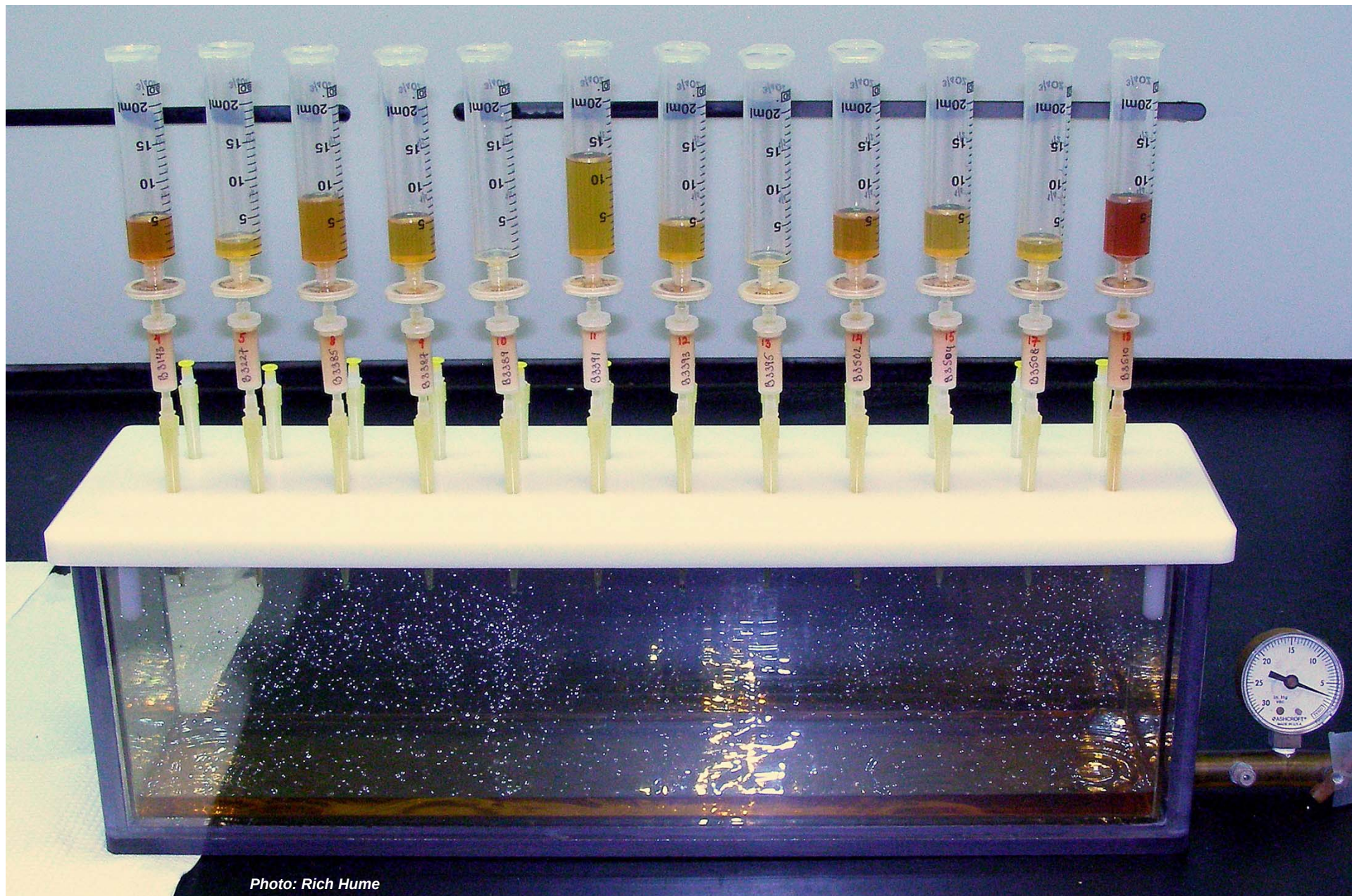


Photo: Rich Hume



## Custom Designed Vacuum Box Rack

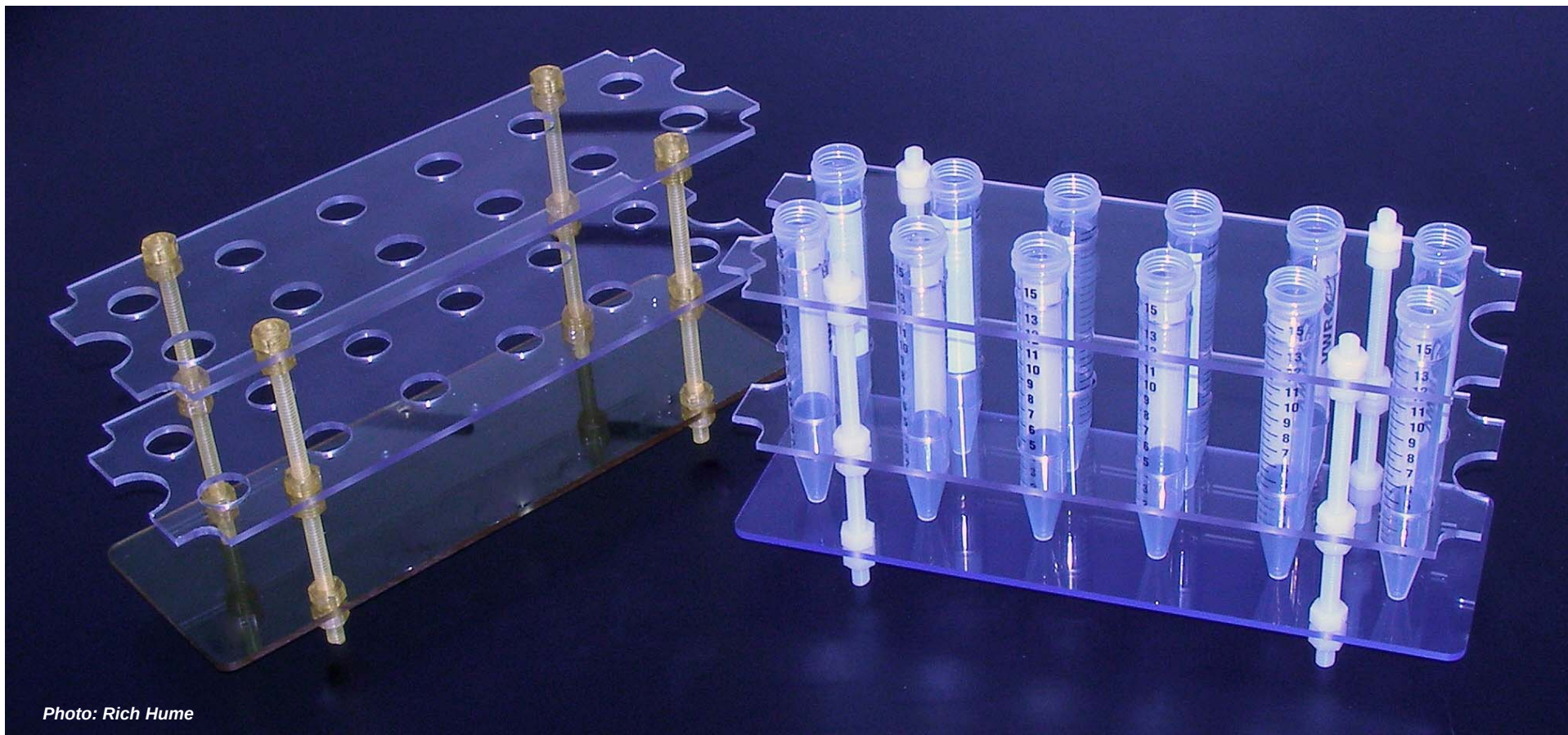


Photo: Rich Hume



# Determination of Method Detection Limit (MDL)

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## Designing MDL Experiments

- Collected urine samples from individuals not occupationally exposed to uranium.
- Samples were spiked with varying amounts of natural U-238.
- 7 replicates prepared for each concentration.
- Each series of spikes was analyzed separately.  
*(shut down instrument and restarted next day)*



## Determination of MDL<sub>99</sub>, MDA<sub>95</sub> and L<sub>C95</sub> for <sup>235</sup>U

| Spike Value (ng/L) | 0.00    | 0.00   | 0.07   | 0.14   | 0.36   | 0.72   | 1.44   | 3.60   | 7.20   |
|--------------------|---------|--------|--------|--------|--------|--------|--------|--------|--------|
|                    | DI      | Urine  | Urine  | Urine  | Urine  | Urine  | Urine  | Urine  | Urine  |
| 1                  | 0.00981 | 0.0359 | 0.115  | 0.183  | 0.402  | 0.763  | 1.50   | 3.64   | 7.29   |
| 2                  | 0.00819 | 0.0353 | 0.106  | 0.179  | 0.413  | 0.744  | 1.49   | 3.61   | 7.23   |
| 3                  | 0.01550 | 0.0409 | 0.104  | 0.181  | 0.402  | 0.756  | 1.45   | 3.67   | 7.24   |
| 4                  | 0.01370 | 0.0357 | 0.113  | 0.185  | 0.428  | 0.779  | 1.49   | 3.63   | 7.24   |
| 5                  | 0.01110 | 0.0356 | 0.110  | 0.187  | 0.404  | 0.750  | 1.46   | 3.68   | 7.25   |
| 6                  | 0.01730 | 0.0403 | 0.107  | 0.183  | 0.400  | 0.758  | 1.42   | 3.70   | 7.19   |
| 7                  | 0.01160 | 0.0381 | 0.110  | 0.187  | 0.419  | 0.757  | 1.49   | 3.58   | 7.24   |
| n                  | 7       | 7      | 7      | 7      | 7      | 7      | 7      | 7      | 7      |
| Average            | 0.01246 | 0.0374 | 0.109  | 0.184  | 0.410  | 0.758  | 1.47   | 3.64   | 7.24   |
| Std. Dev.          | 0.0032  | 0.0024 | 0.0039 | 0.0030 | 0.0106 | 0.0110 | 0.0291 | 0.0420 | 0.0294 |
| RSD                | 26%     | 6.4%   | 3.6%   | 1.6%   | 2.6%   | 1.5%   | 2.0%   | 1.2%   | 0.4%   |



## Determination of MDL<sub>99</sub>, MDA<sub>95</sub> and L<sub>C95</sub> for <sup>238</sup>U

| Spike Value (ng/L) | 0.00  | 0.00  | 9.93  | 19.85 | 49.64 | 99.27 | 198.54 | 496.35 | 992.70 |
|--------------------|-------|-------|-------|-------|-------|-------|--------|--------|--------|
|                    | DI    | Urine | Urine | Urine | Urine | Urine | Urine  | Urine  | Urine  |
| 1                  | 1.63  | 4.73  | 14.2  | 23.3  | 52.4  | 101.4 | 200.2  | 501.0  | 1026   |
| 2                  | 0.98  | 4.71  | 14.2  | 23.9  | 53.4  | 100.5 | 198.4  | 496.8  | 1022   |
| 3                  | 2.33  | 5.09  | 14.2  | 23.7  | 51.9  | 100.8 | 196.7  | 495.7  | 998    |
| 4                  | 1.46  | 4.81  | 14.4  | 23.7  | 52.9  | 101.4 | 199.3  | 501.6  | 1006   |
| 5                  | 1.24  | 4.80  | 14.2  | 23.8  | 52.6  | 100.3 | 198.0  | 504.1  | 1014   |
| 6                  | 1.66  | 4.82  | 14.5  | 23.8  | 52.1  | 101.1 | 195.8  | 501.4  | 1008   |
| 7                  | 1.69  | 4.66  | 14.2  | 24.0  | 53.4  | 100.6 | 198.8  | 496.0  | 1012   |
| n                  | 7     | 7     | 7     | 7     | 7     | 7     | 7      | 7      | 7      |
| Average            | 1.57  | 4.80  | 14.3  | 23.7  | 52.7  | 100.9 | 198.2  | 499.5  | 1012   |
| Std. Dev.          | 0.423 | 0.140 | 0.116 | 0.213 | 0.594 | 0.454 | 1.481  | 3.273  | 9.635  |
| RSD                | 27%   | 2.9%  | 0.8%  | 0.9%  | 1.1%  | 0.5%  | 0.7%   | 0.7%   | 1.0%   |



# Determination of MDL<sub>99</sub>, MDA<sub>95</sub> and L<sub>C95</sub>

<sup>235</sup>U

$$\text{MDL}_{99} = (t_{n-1, 0.99}) (S) \\ = 0.0000075 \mu\text{g/L}$$

$$0.0000092 \mu\text{g/L}$$

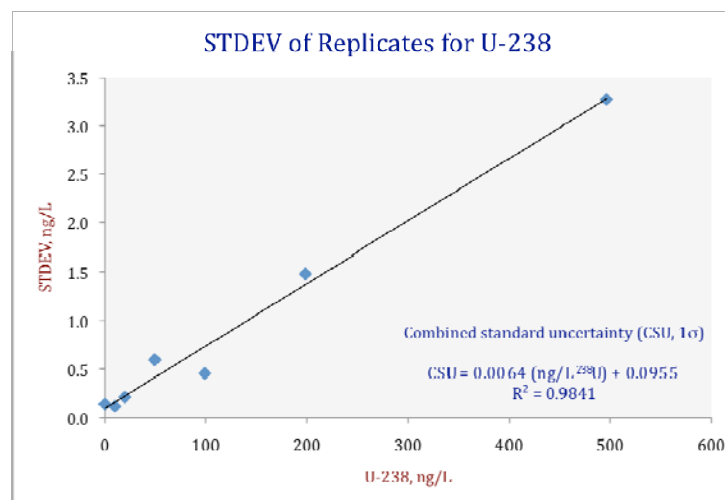
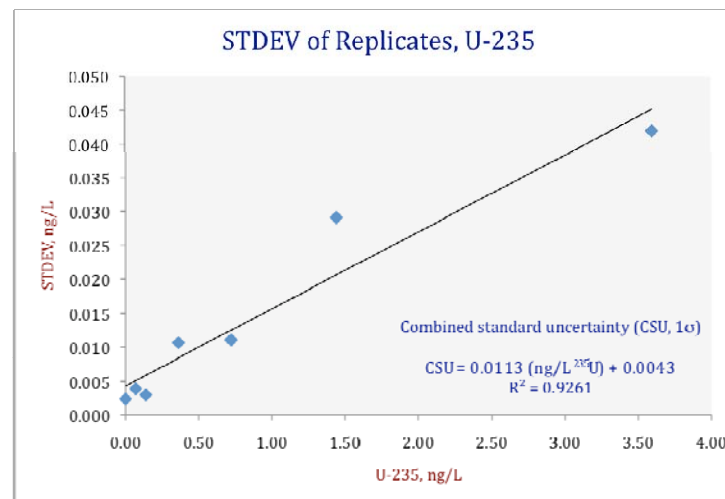
$$\text{L}_{\text{C95}} = (t_{n-1, 0.95}) (S) \\ = 0.0000046 \mu\text{g/L}$$

<sup>238</sup>U

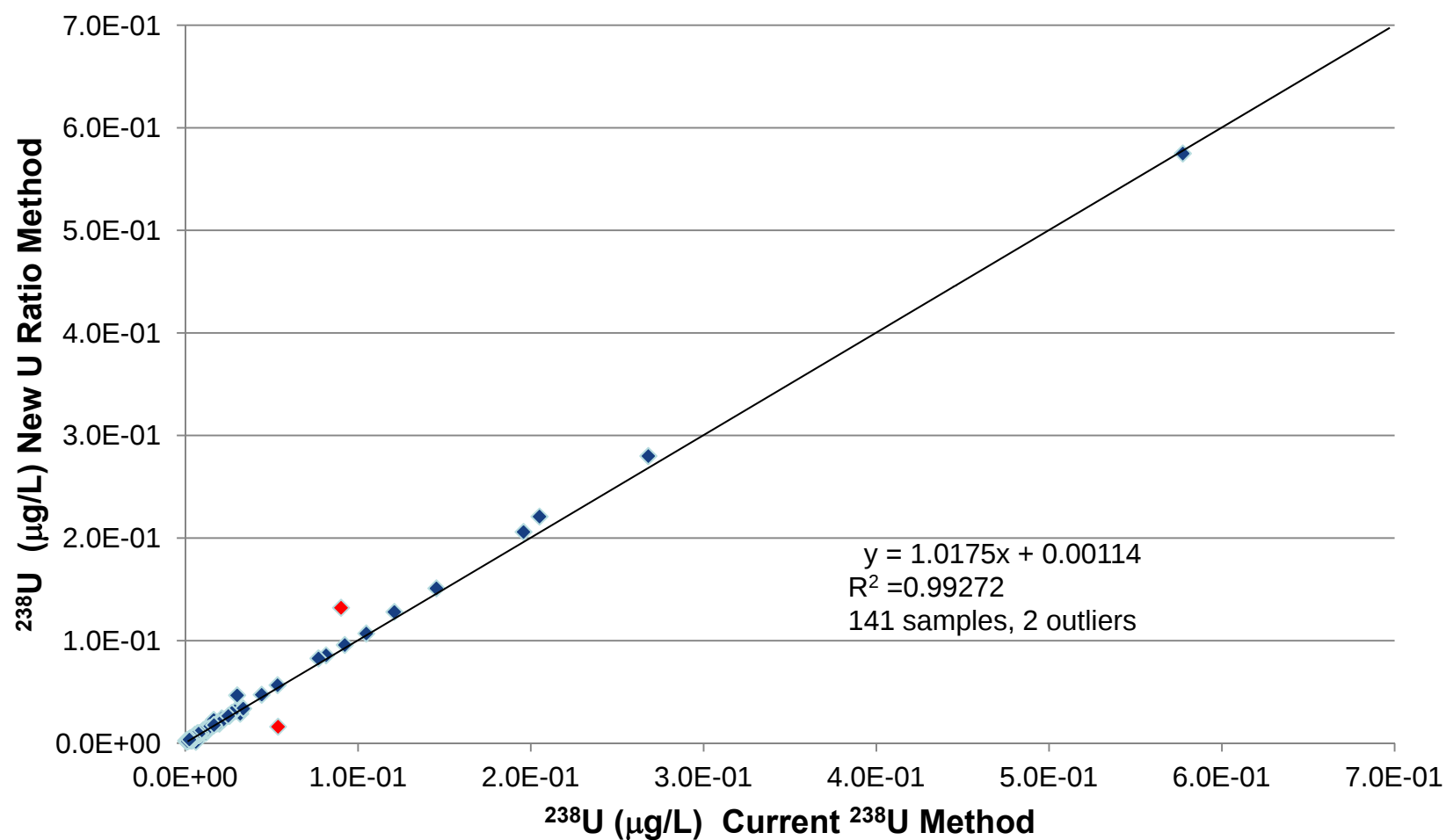
$$\text{MDL}_{99} = (t_{n-1, 0.99}) (S) \\ = 0.00044 \mu\text{g/L}$$

$$\text{MDA}_{95} = (2) (t_{n-1, 0.95}) (S) \\ = 0.00054 \mu\text{g/L}$$

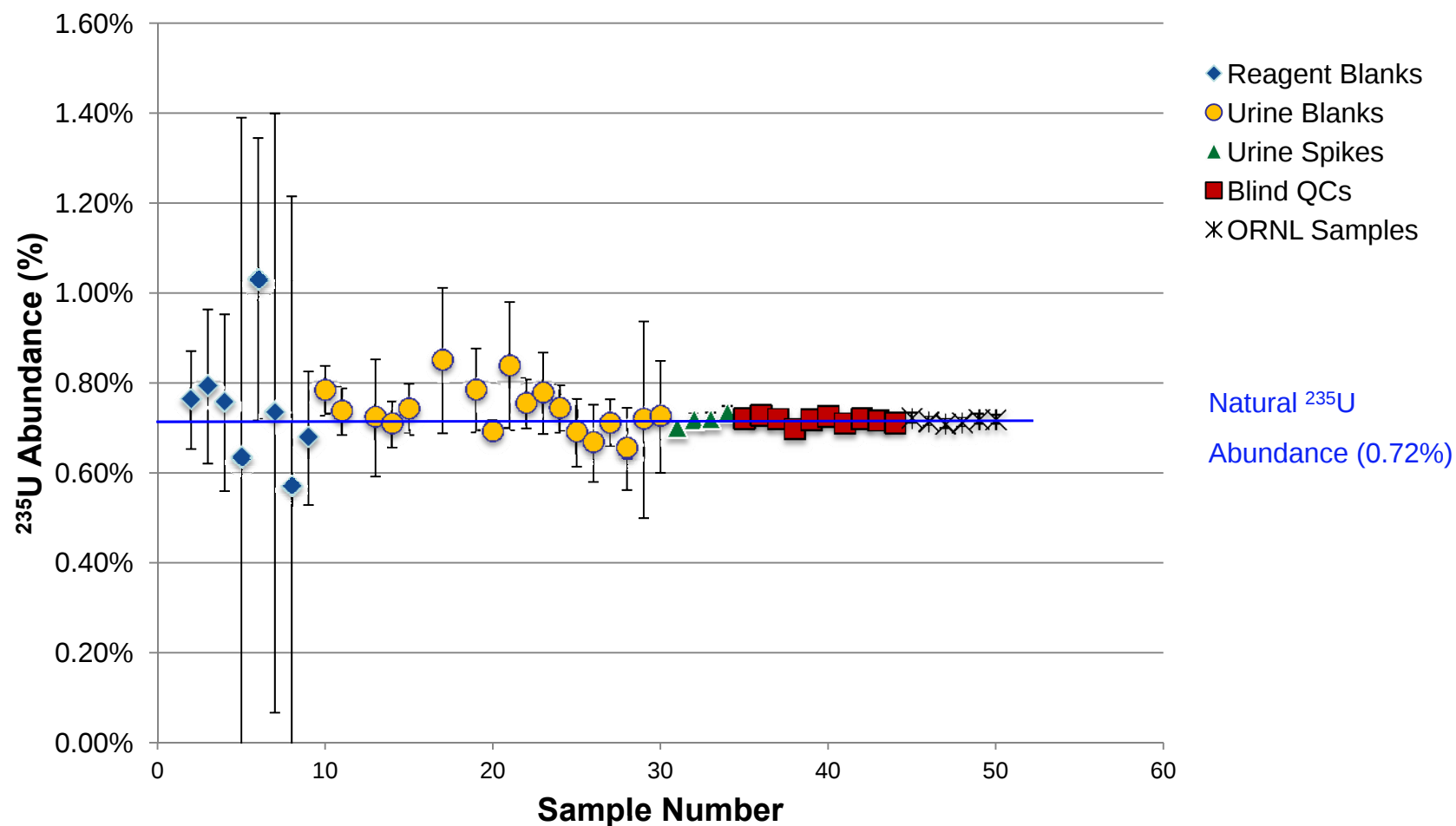
$$\text{L}_{\text{C95}} = (t_{n-1, 0.95}) (S) \\ = 0.00027 \mu\text{g/L}$$



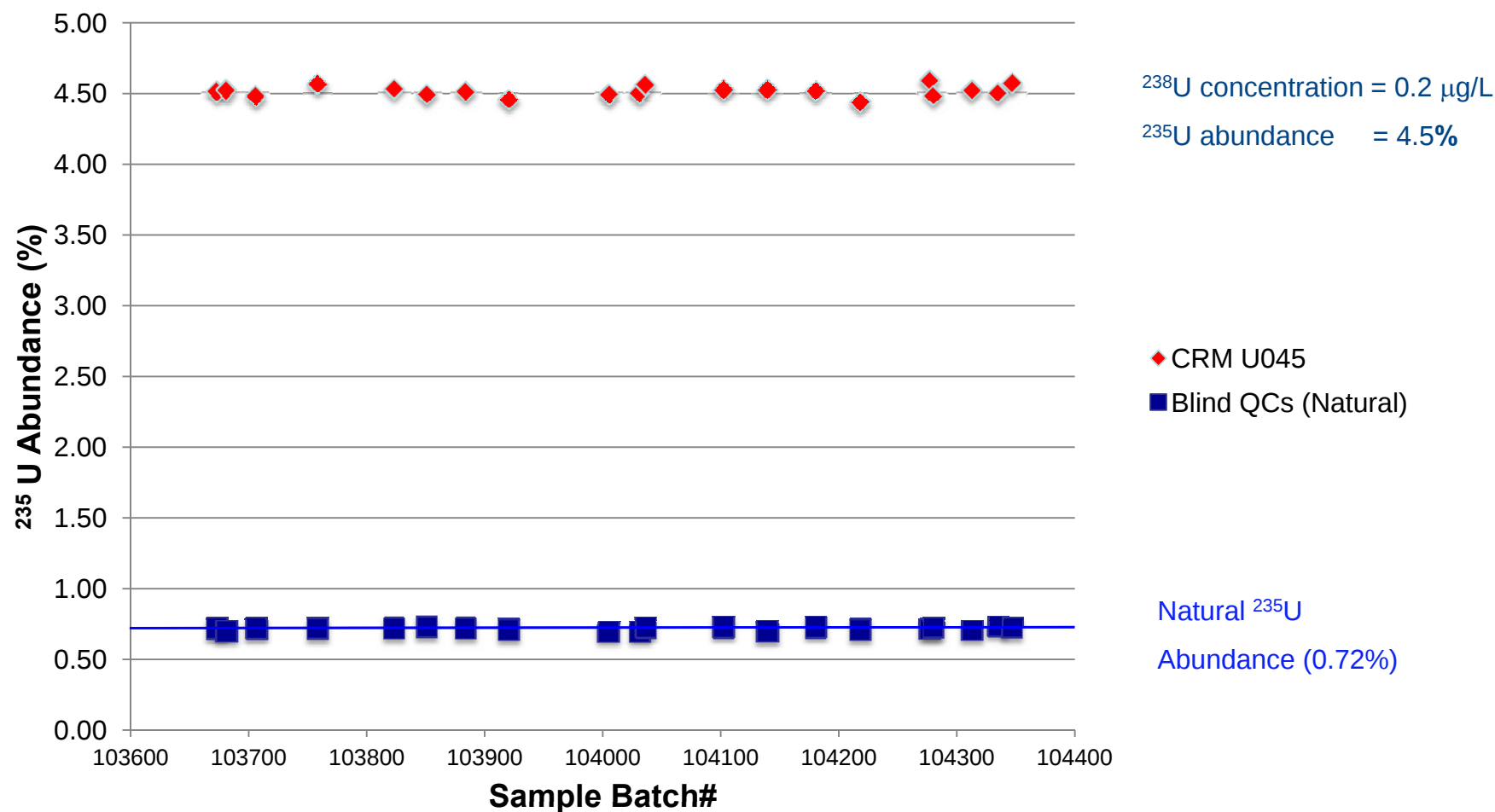
## Comparison of $^{238}\text{U}$ Results between Current $^{238}\text{U}$ Method & New U Ratio Method



# $^{235}\text{U}$ Abundance of Urine Samples from Non-exposed Employees and Quality Control Samples



## Observed $^{235}\text{U}$ Abundances in Natural Uranium Blind QC & CRM U045 Samples



# Typical ELAN DRC-e $^{235}\text{U}/\text{U}^{238}$ Ratio Method Report

## U-235/U-238 Results Summary - Batch 104313

$$^{235}\text{U CSU} = (0.0113 * (^{235}\text{U content in } \mu\text{g/L})) + 0.0000043$$

$$^{238}\text{U CSU} = (0.0064 * (^{238}\text{U content in } \mu\text{g/L})) + 0.0000955$$

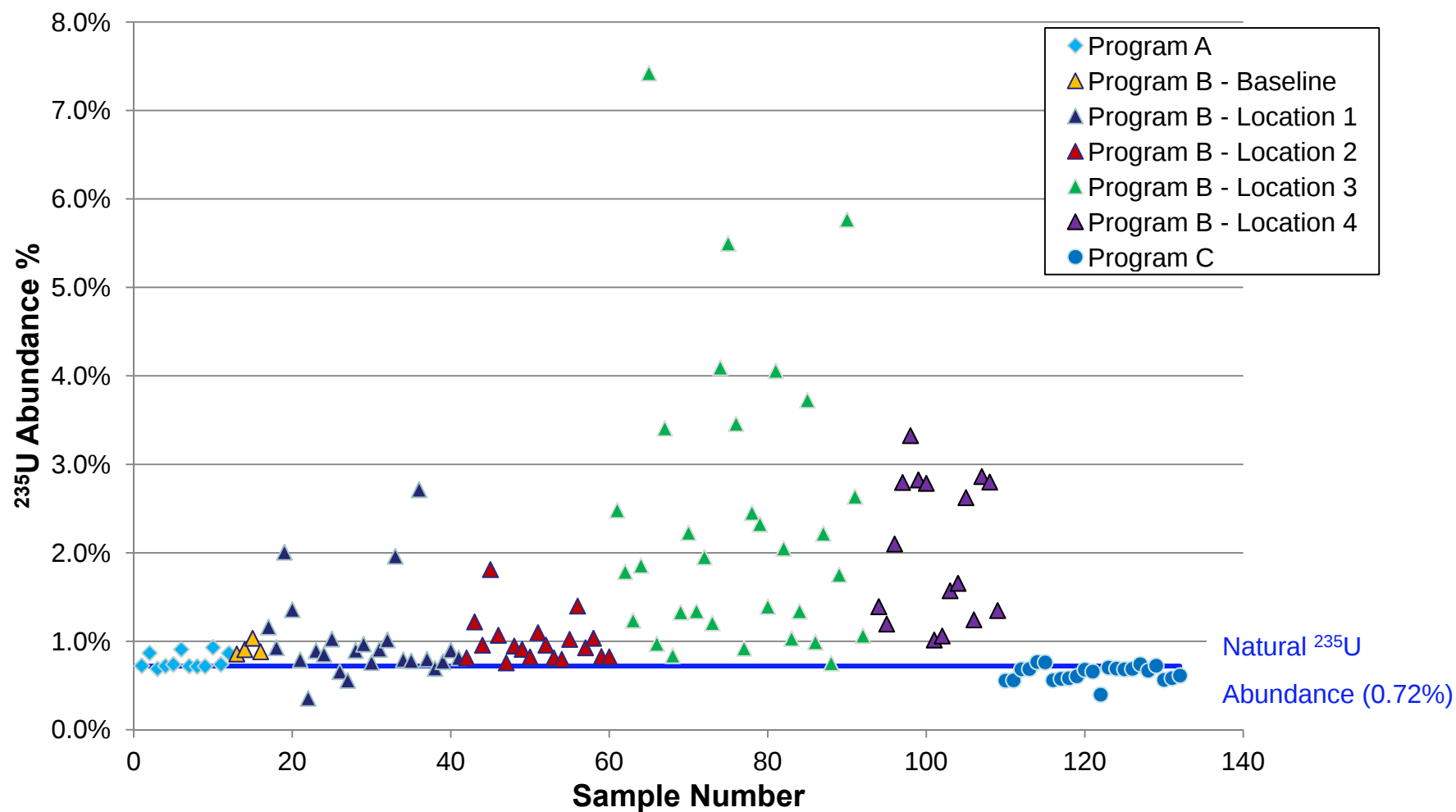
$$^{235}\text{U ratio} = \frac{^{235}\text{U content in } \mu\text{g/L}}{^{235}\text{U content in } \mu\text{g/L} + ^{238}\text{U content in } \mu\text{g/L}}$$

$$\text{U ratio CSU} = {}^{235}\text{U ratio} * \sqrt{({}^{235}\text{U CSU} / {}^{235}\text{U content})^2 + ({}^{238}\text{U CSU} / {}^{238}\text{U content})^2}$$

```
= IF(OR(235U ratio - 1.96 * U ratio CSU >0.0072, 235U ratio + 1.96 * U ratio CSU <0.0072), "**", "")
```

| B20   |          |         |          |         |       |    | 5%    |
|-------|----------|---------|----------|---------|-------|----|-------|
| B2611 | 3.65E-05 | 4.7E-06 | 2.90E-03 | 1.1E-04 | 1.24% | ** | 0.17% |
| B2613 | 2.17E-04 | 6.8E-06 | 7.20E-03 | 1.4E-04 | 2.93% | ** | 0.11% |
| B2615 | 4.73E-05 | 4.8E-06 | 2.74E-03 | 1.1E-04 | 1.70% | ** | 0.19% |
| B2617 | 5.53E-05 | 4.9E-06 | 2.78E-03 | 1.1E-04 | 1.95% | ** | 0.19% |
| B2619 | 7.70E-05 | 5.2E-06 | 3.25E-03 | 1.2E-04 | 2.31% | ** | 0.18% |
| B2647 | 9.47E-05 | 5.4E-06 | 7.34E-03 | 1.4E-04 | 1.27% | ** | 0.08% |

# Observed $^{235}\text{U}$ Abundances in Urine Samples from Different Programs



# Oak Ridge National Laboratory Intercomparison Studies Samples

| BLIMS#  | U-235<br>( $\mu\text{g/L}$ ) | CSU<br>(%) | U-238<br>( $\mu\text{g/L}$ ) | CSU<br>(%) | U-235<br>Abundance<br>(%) | CSU<br>(%) | Known Value<br>U-238 ( $\mu\text{g/L}$ ) | Relative Bias<br>(%) |
|---------|------------------------------|------------|------------------------------|------------|---------------------------|------------|------------------------------------------|----------------------|
| A1306R1 | 1.60E-03                     | 2.2E-05    | 2.21E-01                     | 1.5E-03    | 0.72                      | 0.01       | 0.246                                    | -10.2                |
| A1307R1 | 3.86E-03                     | 4.8E-05    | 5.39E-01                     | 3.5E-03    | 0.71                      | 0.01       | 0.577                                    | -6.6                 |
| A4795   | 1.94E-03                     | 2.6E-05    | 2.73E-01                     | 1.8E-03    | 0.71                      | 0.01       | 0.265                                    | 3.0                  |
| A4797   | 3.44E-03                     | 4.3E-05    | 4.82E-01                     | 3.2E-03    | 0.71                      | 0.01       | 0.474                                    | 1.7                  |
| B2828   | 1.50E-03                     | 2.1E-05    | 2.08E-01                     | 1.4E-03    | 0.72                      | 0.01       | 0.201                                    | 3.5                  |
| B2830   | 4.20E-03                     | 5.2E-05    | 5.83E-01                     | 3.8E-03    | 0.72                      | 0.01       | 0.580                                    | 0.5                  |



## Comparison of Sensitivities (cps) for Current $^{238}\text{U}$ and New $^{235}\text{U}/^{238}\text{U}$ Ratio Methods

| BLAB (LLNL) Uranium                                                               |      |              |                 |     | BLAB (LLNL) U-235/U-238 Analysis                                                    |      |              |                 |            |             |             |
|-----------------------------------------------------------------------------------|------|--------------|-----------------|-----|-------------------------------------------------------------------------------------|------|--------------|-----------------|------------|-------------|-------------|
| Sample Description: B3118                                                         |      |              |                 |     | Sample Description: B3118R1                                                         |      |              |                 |            |             |             |
| Sample Date/Time: Wednesday, September 14, 2011 16:17:08                          |      |              |                 |     | Sample Date/Time: Wednesday, September 28, 2011 16:17:08                            |      |              |                 |            |             |             |
| Sample ID: 10432528                                                               |      |              |                 |     | Sample ID: 10434706                                                                 |      |              |                 |            |             |             |
| Batch ID: 104325                                                                  |      |              |                 |     | Batch ID: 104347                                                                    |      |              |                 |            |             |             |
| Autosampler Position: 65                                                          |      |              |                 |     | Autosampler Position: 43                                                            |      |              |                 |            |             |             |
| Method File: C:\elandata\Method\BLAB Uranium.mth                                  |      |              |                 |     | Method File: C:\elandata\Method\blab u 235.mth                                      |      |              |                 |            |             |             |
| Sample File: C:\elandata\Sample\110914u.sam                                       |      |              |                 |     | Sample File: C:\elandata\Sample\U235_110928.sam                                     |      |              |                 |            |             |             |
| Dataset File: C:\elandata\Dataset\110914u\10432528                                |      |              |                 |     | Dataset File: C:\elandata\Dataset\U_235_110928\10434706.016                         |      |              |                 |            |             |             |
| Aliquot Volume (mL): 1.00                                                         |      |              |                 |     | Aliquot Volume (mL): 30.00                                                          |      |              |                 |            |             |             |
| Diluted To Volume (mL): 10.0                                                      |      |              |                 |     | Diluted To Volume (mL): 10.0                                                        |      |              |                 |            |             |             |
| Replicates                                                                        |      |              |                 |     | Replicates                                                                          |      |              |                 |            |             |             |
|  |      |              |                 |     |  |      |              |                 |            |             |             |
| Summary                                                                           |      |              |                 |     | Summary                                                                             |      |              |                 |            |             |             |
| Analyte                                                                           | Mass | Intens. Mean | Blank Intensity | CPS | Analyte                                                                             | Mass | Intens. Mean | Blank Intensity | Conc. Mean | Report Unit | Intens. RSD |
| > U                                                                               | 233  | 9601.6       | 10395.6         | 103 | > U                                                                                 | 233  | 10153.0      | 11132.6         |            | ug/L        | 1.6         |
| U                                                                                 | 234  | 18.5         | 21.1            | 10  | U                                                                                   | 234  | 22.3         | 22.7            |            | ug/L        | 1.4         |
| U                                                                                 | 235  | 9.7          | 8.8             | 10  | U                                                                                   | 235  | 32.3         | 9.9             | 7.77e-005  | ug/L        | 5.9         |
| U                                                                                 | 237  | 0.1          | 0.7             | 10  | U                                                                                   | 237  | 0.9          | 0.7             |            | ug/L        | 48.0        |
| U                                                                                 | 238  | 163.2        | 35.8            | 10  | U                                                                                   | 238  | 4736.2       | 37.6            | 1.53e-002  | ug/L        | 1.0         |
| U                                                                                 | 239  | 0.3          | 0.8             | 10  | U                                                                                   | 239  | 1.2          | 0.7             |            | ug/L        | 28.9        |
| U                                                                                 | 240  | 0.7          | 0.7             | 10  | U                                                                                   | 240  | 1.2          | 0.8             |            | ug/L        | 16.7        |
| Th                                                                                | 232  | 6.1          | 6.9             | 10  | Th                                                                                  | 232  | 447.8        | 11.1            |            | ug/L        | 4.5         |
| Sample Description: B3118                                                         |      |              |                 |     | Sample Description: B3118R1                                                         |      |              |                 |            |             |             |

# Conclusions

## LLNL Internal Dosimetry Program

- The new procedure satisfies the requirement to determine  $^{235}\text{U}/^{238}\text{U}$  ratio in bioassay urine samples.

## MDA

- The  $L_C$  and  $MDA_{95}$  for  $^{235}\text{U}$  are well below the required detection limit of  $0.00035 \mu\text{g/L}$ .

## Turn Around Time

- Analysis of 10 samples plus 2 QCs can be completed in one working day (8 hours).



**As of October 19, 2011**

**LLNL passed all elements required  
for DOELAP Accreditation for this procedure.**

**The DOELAP Oversight Board has  
recommended accreditation.**

