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# Data Quality Objectives Supporting U.S. Transuranium and Uranium Registries Mission

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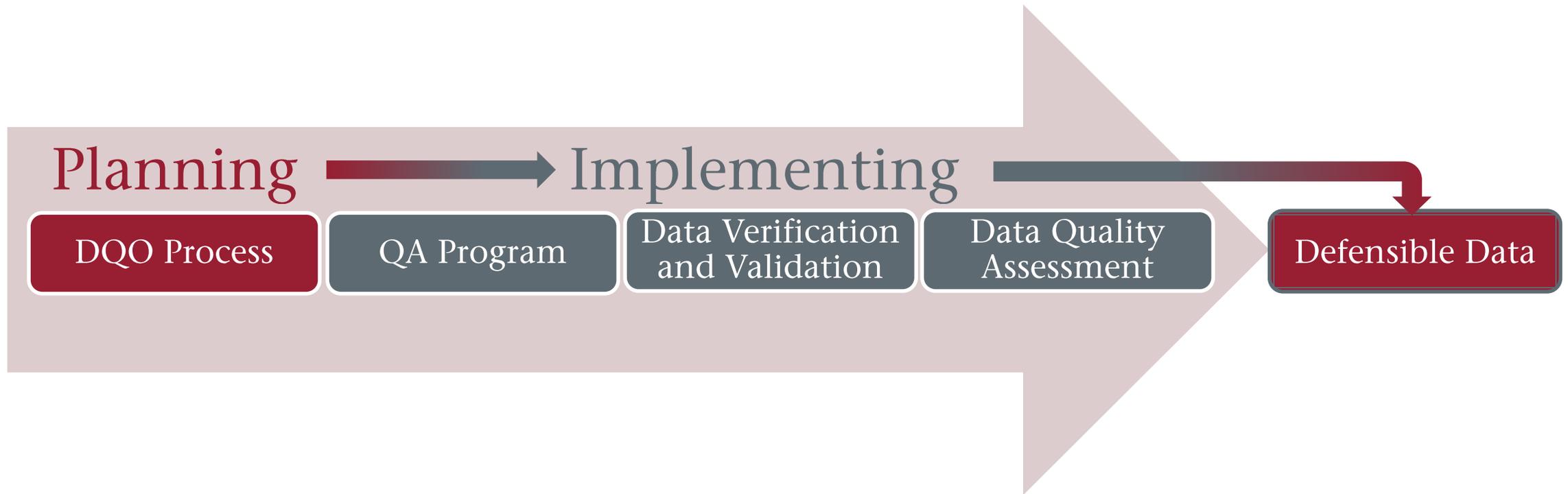
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# USTUR Quality Assurance Planning for Data Collection

Data collection and Data Quality Objectives in support of the U.S. Transuranium and Uranium Registries Mission:

- Tools necessary to ensure project mission and objectives are achieved





# USTUR Mission

The USTUR's mission is to:

- Follow up occupationally-exposed individuals (volunteer Registrants) by studying the biokinetics (deposition, translocation, retention, and excretion) and tissue dosimetry of uranium and transuranium elements, such as plutonium, americium, curium, and neptunium
- Obtain, analyze, preserve, and make available for future research, materials from individuals who had documented intakes of uranium and transuranium elements
- Apply USTUR data to refine dose assessment methods in support of reliable epidemiological studies, radiation risk assessment, and regulatory standards for radiological protection of workers and the general public

*The objective of the DQO document is to determine an optimal sample collection and data analysis techniques to meet mission statement objectives*

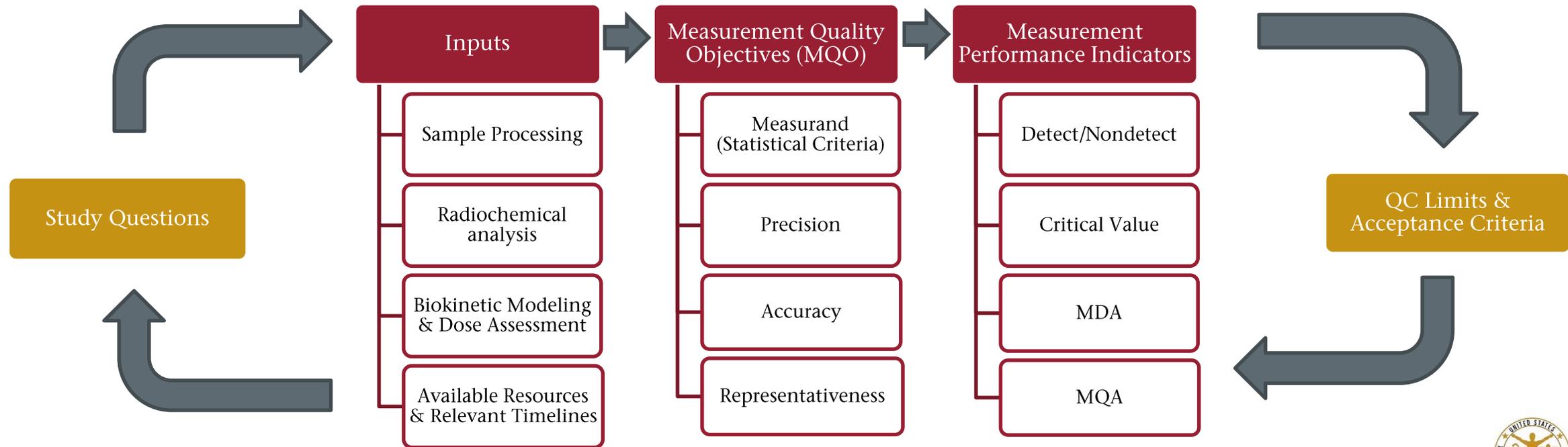




# Goals of the DQO

Study questions:

- What tissue samples are collected at the autopsy?
- What are the activities in dosimetrically important organs and tissues?
- What is the activity distribution of actinides in the whole body?





# New Document Details Radiochemistry Equations

Adopts Multi-Agency Radiological Laboratory Analytical Protocols Manual (MARLAP) notation where possible and appropriate

- Relies on MARLAP chapters 19, 20, and 20A (low level counting)
- Describes all calculations in detail
- Emphasizes quantitative propagation of uncertainty
- Includes statistics for decisions and measurement capabilities:
  - ✓ critical value of the net count rate,  $S'_c$
  - ✓ minimum detectable activity,  $MDA$
  - ✓  $p$ -value
  - ✓ minimum quantifiable activity,  $MQA$



# A Data Dictionary Is Now Available

- 8 distinct masses are used in calculations
- Over 25 distinct activity or activity-like quantities are used

Time-Dependent Quantities Intended to Be Measured (Measurands) Are Activities (Bq) Identified by Isotope, Destination, Origin	Unique Symbol	$t_{ref}$	Date/Time for sample	dissolved tissue, solution, acid solution	aliquot of solution	aliquot of solution with added tracer(s)	solution containing an elemental fraction				planchet with electrodeposited elemental fraction			
							Th fraction	U fraction	Pu fraction	Am fraction	Th fraction	U fraction	Pu fraction	Am fraction
$^{228}\text{Th}$ in the thorium fraction from the prepared tissue sample	$A_{T8,Th,prep}(t)$		$t_D$	✓	✓	✓	$t_{sep}$				$t_{c,Th}$			
$^{228}\text{Th}$ in the thorium fraction from the $^{232}\text{U}$ tracer	$A_{T8,Th,U2tr}(t)$	$t_{ref,U2}$				✓	$t_{sep}$				$t_{c,Th}$			
$^{228}\text{Th}$ in the uranium fraction from the $^{232}\text{U}$ tracer	$A_{T8,U,U2tr}(t \geq t_{sep})$	$t_{ref,U2}$				✓		$t_{sep}$				$t_{c,U}$		
$^{229}\text{Th}$ in the thorium fraction from the $^{229}\text{Th}$ tracer	$A_{T9,Th,T9tr}(t)$	$t_{ref,T9}$				✓	$t_{sep}$				$t_{c,Th}$			
$^{230}\text{Th}$ in the thorium fraction from the prepared tissue sample	$A_{T0,Th,prep}(t)$		$t_D$	✓	✓	✓	$t_{sep}$				$t_{c,Th}$			
$^{232}\text{Th}$ in the thorium fraction from the prepared tissue sample	$A_{T2,Th,prep}(t)$		$t_D$	✓	✓	✓	$t_{sep}$				$t_{c,Th}$			
$^{232}\text{U}$ in the uranium fraction from the $^{232}\text{U}$ tracer	$A_{U2,U,U2tr}(t)$	$t_{ref,U2}$				✓		$t_{sep}$				$t_{c,U}$		
$^{234}\text{U}$ in the uranium fraction from the prepared tissue sample	$A_{U4,U,prep}(t)$		$t_D$	✓	✓	✓		$t_{sep}$				$t_{c,U}$		
$^{235}\text{U}$ in the uranium fraction from the prepared tissue sample	$A_{U5,U,prep}(t)$		$t_D$	✓	✓	✓		$t_{sep}$				$t_{c,U}$		
$^{238}\text{U}$ in the uranium fraction from the prepared tissue sample	$A_{U8,U,prep}(t)$		$t_D$	✓	✓	✓		$t_{sep}$				$t_{c,U}$		
$^{238}\text{Pu}$ in the plutonium fraction from the prepared tissue sample	$A_{P8,Pu,prep}(t)$		$t_D$	✓	✓	✓			$t_{sep}$				$t_{c,Pu}$	





# Variables Identified: *Over Forty-five*

Table 16. Data dictionary for other variables, in alphabetical order by variable name

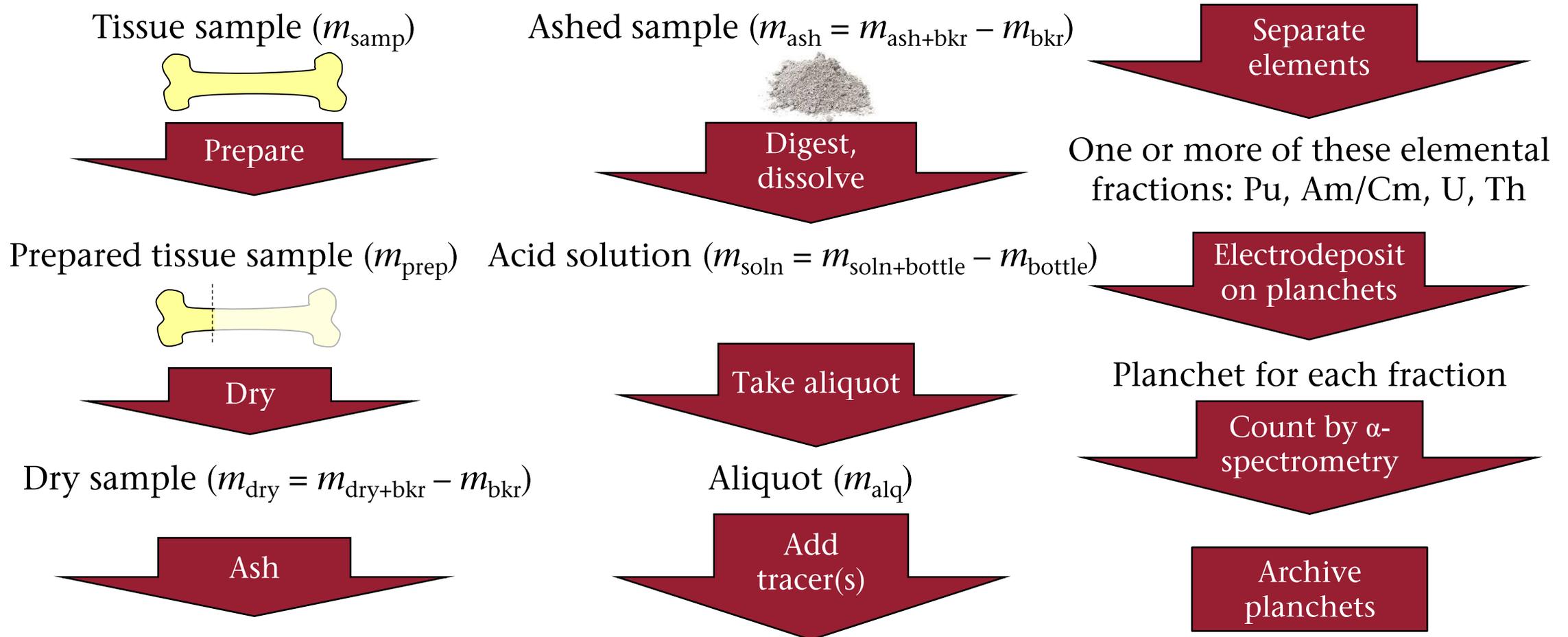
Symbol	Quantity	Unit	RadChem Database	RadChem Summary	Sample Analysis
$A_{\text{isotope,destination,origin}}(t)$	Many activity variables are defined in Table 6, identified by isotope, the chemical fraction Z it is ultimately found in, and its origin ( <u>samp</u> = whole tissue sample; prep = prepared tissue sample, dry, ash, <u>soln</u> = solution, <u>alig</u> = aliquot, <u>tr</u> = tracer).				
$A_{A1,Am,A1inA3tr}(t_{C,Am})$	activity of $^{241}\text{Am}$ in <u>Am</u> fraction from $^{243}\text{Am}$ tracer as of count date	Bq			1
$A_{A1,Am,alig}(t_{C,Am})$	Activity of $^{241}\text{Am}$ on Am-fraction <u>planchet</u> at count date, corrected for $^{241}\text{Am}$ contamination	Bq			1
$A_{A1,Am,P1inP2tr}(t_{C,Am})$	activity of $^{241}\text{Am}$ in <u>Am</u> fraction that has grown in from decay of $^{241}\text{Pu}$ in Pu tracer as of count date	Bq			1
$A_{A1,Pu,alig}(t_{C,Pu})$	Activity of $^{238}\text{Pu}$ on Pu- <u>planchet</u> at count date, corrected for $^{241}\text{Am}$ contamination that produces counts in the same ROI as $^{238}\text{Pu}$				

## Appendix B





# Stages of Radiochemical Process: *Mass Measurements*





# Radiochemistry Process: *Sequence of Events*

- USTUR radiochemistry processing for Pu+Am analyses
- Beginning with the donation of registrant samples through processing, including tracer issues and  $^{241}\text{Am}$  ingrowth issues

Activity notation is  $A_{\text{isotope,destination,origin}}(t)$

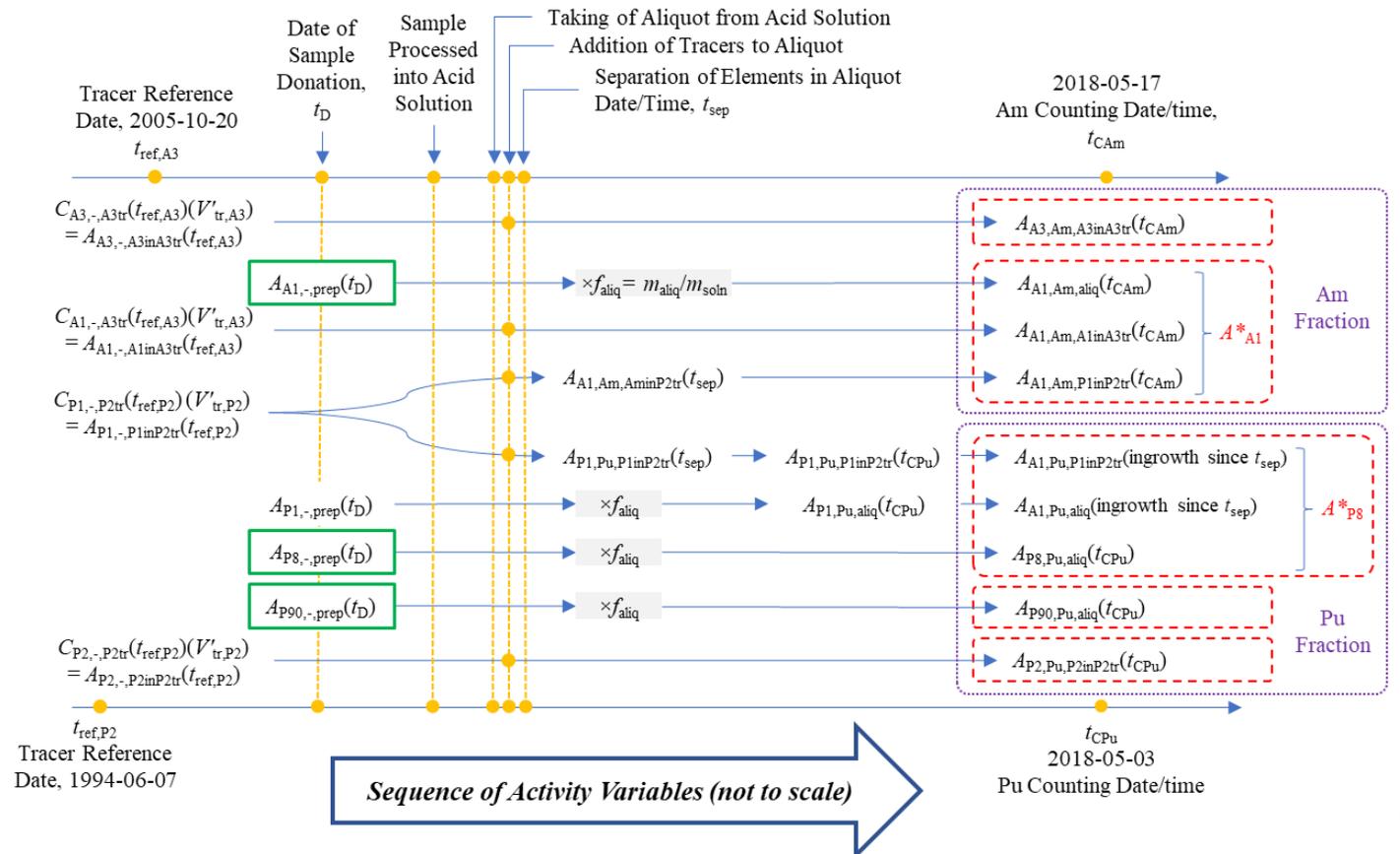
Green boxes are the desired measurands.

Dashed red boxes are measurement results in an ROI.

Dotted purple boxes indicate element fractions (element plachets).

$A^*$  indicates an “apparent activity” inferred from counts in a region-of-interest (ROI) in alpha spectrometry.

Corrections to  $A^*$  must be made to infer values of desired measurands.





# Measurand at USTUR

- The measurand is “the quantity intended to be measured”
  - ✓ measurand is the true but unknown activity in a tissue, organ or other sample
  - ✓ distinction between measurands and measurement results
- The goal of radiochemical measurements at USTUR is to make probabilistic statements of the likely values the measurand could have given the measurement results and their combined standard uncertainty



# Measurement Results at USTUR

For its measurements, USTUR records:

- the numbers of counts for sample, background, and tracer in the regions of interest (ROI)
- the counting times, real and live
- dates of measurements
- mass of total wet samples, prepared samples, dry samples and ash
- solution aliquots size, mass/fraction
- QC and QA sample measurement results
- all the additional data and metadata that the counting lab can supply

From these data, a future researcher can determine everything that is needed for their analysis





# USTUR Measurements: *Uncertainty Evaluation*

- When considered in an ensemble of data, it is important to record and report each of the radiochemical analysis results in a measurement result and its combined standard uncertainty: *no need to do a comparison with statistical criteria (critical values)*
- Uncertainties have been evaluated throughout the radiochemical analysis process



$$u(C_{X,\text{ash}}(t_D)) = \frac{u(A_{X,-\text{prep}}(t_D))}{m_{\text{ash}}} \left( \frac{1000 \text{ g}}{1 \text{ kg}} \right)$$

$$u(C_{X,\text{wet}}(t_D)) = \frac{u(A_{X,-\text{prep}}(t_D))}{m_{\text{prep}}} \left( \frac{1000 \text{ g}}{1 \text{ kg}} \right)$$

$$u_c^2(y) = \sum_{i=1}^N \left( \frac{\partial f}{\partial x_i} \right)^2 u^2(x_i) + 2 \sum_{i=1}^{N-1} \sum_{j=i+1}^N \frac{\partial f}{\partial x_i} \frac{\partial f}{\partial x_j} u(x_i, x_j)$$

= Sum of variance terms and covariance terms

$$u(A_{A1,Am,\text{aliqu}}) = \sqrt{u^2(A_{Am\text{-ROI},Am,3\text{sources}}) + u^2(A_{A1,Am,A1\text{in}A3\text{tr}}) + u^2(A_{A1,Am,A1\text{in}P2\text{tr}})}$$

$$u_R(A_{P8+A1\text{-ROI},Pu,3\text{sources}}^*) = \sqrt{\left( \frac{N_S + N_B}{t_S + t_B} \right)^2 + u_R^2(\varepsilon)}$$





# Performance Evaluation: *Statistical Criteria*

	Is anything there? Yes, if measurement result $\geq$ Criterion 1		What's the smallest measurand that will usually give a measurement result $\geq$ Criterion 1?		What's the smallest measurand that can be measured with fairly small uncertainty  ( $u_r \leq 10\%$ )?	
Author	Criterion 1	Symbol	Criterion 2	Symbol	Criterion 3	Symbol
Currie (1968)	critical level	$L_C$	detection limit	$L_D$	determination limit	$L_Q$
ANSI N13.30-1996	decision level	$DL$	minimum detectable activity	$MDA$	-	-
ISO-11929-2010	decision threshold	$y^*$	detection limit	$y^\#$	-	-
VIM (2012) §4.16, 4.18	discrimination threshold	-	detection limit $\equiv$ <u>limit of detection<sup>a</sup></u>	$LOD$	-	-
MARLAP (2004)	critical value of the net counts	$S_C$	minimum detectable value of the net counts	$S_D$	minimum quantifiable value	$x_Q$
This document	critical value of the net count rate	$S'_C$	minimum detectable activity	$MDA$	minimum quantifiable activity	$MQA$





# Performance Evaluation: *Critical Value (I)*

- The smallest value of that variable that “can be reliably distinguished from zero” (MARLAP p. 20.1)
- Demarcation line between the decision “analyte is probably present” and “analyte is probably not present”
- < 5% chance of making “Type I error”
- Stapleton approximation:

$$S_{C,X}(N_B, d, t_S, t_B, z_{1-\alpha}) = d \left( \frac{t_S}{t_B} - 1 \right) + \frac{z_{1-\alpha}^2}{4} \left( 1 + \frac{t_S}{t_B} \right) + z_{1-\alpha} \sqrt{(N_B + d) \frac{t_S}{t_B} \left( 1 + \frac{t_S}{t_B} \right)} \quad S'_{C,X} = \frac{S_{C,X}}{t_S}$$

if the net count rate does not exceed the critical value, there is no point in calculating the activity



## Performance Evaluation: *Critical Value (II)*

### Legitimate but rare uses of the critical value at USTUR

- The critical value of the net count rate statistic may be needed for deciding whether activity is present for:
  - ✓ studies of specific tissues
  - ✓ measurements of radionuclides not known a priori to be present
  - ✓ intercomparisons and Data Quality Objectives (DQO)



# Performance Evaluation: *MDA (I)*

In radiochemistry the minimum detectable concentration (*MDC*) is usually obtained from the **minimum detectable value of the net instrument signal**,  $S_D$ , which is the smallest mean value of the net signal at which the probability that the response variable will exceed its critical value is  $1-\beta$  (MARLAP Section 20.2)

- **Minimum detectable value** of the net counts for isotope  $X$ :

$$S_{D,X}(S_{C,X}, R_B, t_S, t_B, z_{1-\beta}) = S_{C,X} + \frac{z_{1-\beta}^2}{2} + z_{1-\beta} \sqrt{\frac{z_{1-\beta}^2}{4} + S_{C,X} + R_B t_S \left(1 + \frac{t_S}{t_B}\right)} \quad S'_{D,X} = \frac{S_{D,X}}{t_S}$$

- Sample-specific **minimum detectable activity** (Bq) for isotope  $X$ :

$$MDA_X = \frac{S'_{D,X}}{\varepsilon f_{X,ROI} y_{RR}} = \frac{S_{D,X}}{t_S \varepsilon f_{X,ROI} y_{RR}} = \frac{S_{C,X} + \frac{z_{1-\beta}^2}{2} + z_{1-\beta} \sqrt{\frac{z_{1-\beta}^2}{4} + S_{C,X} + R_B t_S \left(1 + \frac{t_S}{t_B}\right)}}{t_S \varepsilon f_{X,ROI} y_{RR}}$$





## Performance Evaluation: *MDA* (II)

- The *MDA* statistic can be used at USTUR to:
  - ✓ characterize the detection capability of a system comprising both radiochemical processing and radioactivity measurements
  - ✓ determine how long to count a sample to achieve a chosen degree of precision in measurement results
- If the *MDA* is too high, that is, the measurements are not sensitive enough
- Potential Registrants may not provide usable data if their intake was so low that the range of measurands, that is, expected quantities in tissues, will be less than the *MDA*
- Larger samples or longer counting times may be needed if the *MDA* is too high



# Performance Evaluation: MQA

- The minimum quantifiable activity (MQA) is the value of a theoretical measurand activity that can be measured with a specified statistical precision
- USTUR chooses to specify MQA at a precision of  $u_R(A^*) = 10\%$

$N_B$	$N_S$	MQA using $\epsilon$ , $f_{X,ROI}$ and $\gamma_{RR}$			
		(Bq)	(mBq)	(Ci)	(fCi)
0	113	3.72E-03	3.72	1.01E-13	100.5
1	114	3.74E-03	3.74	1.01E-13	101.0
2	115	3.75E-03	3.75	1.01E-13	101.4
3	117	3.80E-03	3.80	1.03E-13	102.8
4	118	3.82E-03	3.82	1.03E-13	103.2
5	119	3.84E-03	3.84	1.04E-13	103.7
6	120	3.85E-03	3.85	1.04E-13	104.1
7	121	3.87E-03	3.87	1.05E-13	104.5
8	123	3.92E-03	3.92	1.06E-13	105.9
9	124	3.93E-03	3.93	1.06E-13	106.3
10	125	3.95E-03	3.95	1.07E-13	106.8

For  $N_B \leq 10$  counts,  
MQA  $\leq 4.0$  mBq (110 fCi),  
 $u_R(A^*) \leq 10\%$ .



# USTUR Radiochemistry Measurements: *Practical Considerations (I)*

- The critical value of the net count rate,  $S'_C$ , is the smallest count rate that has only a 5% chance of being due to background noise
- For some applications, these are recorded as “nondetects” or “less-than” values
- USTUR does not censor its measurement results by changing numbers to *nondetects*
- USTUR is not determining whether activity is present in autopsy samples – we know it’s there, so it’s only a question of how much
- USTUR records and reports values less than  $S'_C$  along with their uncertainties
- Highly uncertain measurements (rather than *nondetects* or *less-thans*) contain information that can be used for calculating intake and dose



# USTUR Radiochemistry Measurements: *Practical Considerations (II)*

- Usually adds 2 dpm (0.033 Bq) of each tracer to aliquots
- Samples are counted for 150,000 s (2,500 min or  $\approx$  42 hours)
- With about 20% of  $\alpha$ -particles ultimately producing counts, this is:
  - ✓ about 1,000 counts
  - ✓ about  $\pm 3\%$  uncertainty in radiochemical recovery yield
- Counting longer would reduce uncertainty but is impractical
- Adding more tracer would reduce uncertainty but is:
  - ✓ likely to cause spillover of tracer counts into ROIs of measurand isotopes
  - ✓ more likely to result in detector contamination
  - ✓ expensive



# USTUR Radiochemistry Measurements: *Practical Considerations (III)*

- Stapleton's formula is used for the critical value of the net count rate
- *MDA* is calculated based on the Stapleton formula
- *MQA* as a function of number of background counts in 300,000 s is calculated by determining the number of sample (gross) counts required to produce a relative uncertainty  $u_R \leq 10\%$
- Typically,  $MQA \leq 4.0$  mBq ( $\leq 110$  fCi) for typical counting parameters and background counts up to 10
- The *MQA* is achieved when roughly 120 or more sample counts are observed



# Quality Control Limits & Acceptance Criteria: *Future Work*

Quality control limits are set for all USTUR performance indicators based on the specified acceptance criteria

DQO document

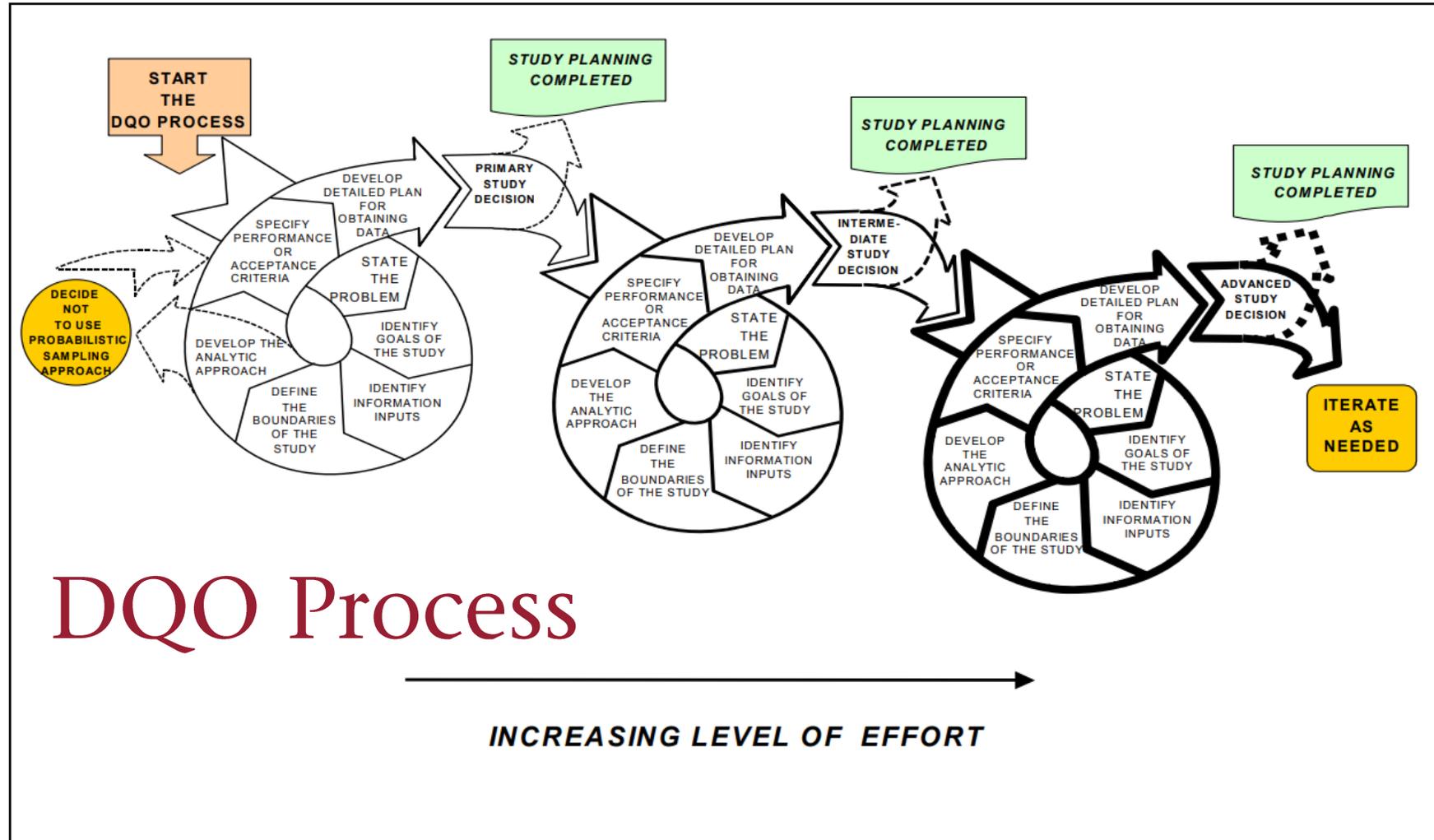
- Chapter 7

Data Quality Indicator (DQI)	QC Measure for Sampling (S) analytical (A) or (S&A)	QC Sample or Activity	Frequency/ Number	QC Acceptance Limits (Measurement Performance Criteria)	Corrective Action (CA)	Person(s) Responsible for CA
Accuracy	A	Energy & Efficiency Calibration	Monthly	Control limits within $\pm 2$ standard deviations (SD) of the mean efficiency or 1% tolerance limit	Warning within $\pm 3$ SD, recount until in range. If over 2 SD, Re-optimize instrument and re-calibrate, repeat until successful	Analyst
Accuracy & Sensitivity	A	Background Calibration	Monthly	Control limits within $\pm 2$ standard deviations (SD) of MDA	Warning within $\pm 3$ SD, recount until in range. If over 2 SD, Re-optimize instrument and re-calibrate, repeat until successful	Analyst
Precision	A	Reagent Blank (RB)	1 of every 20 samples	Check against MQA at $\mu_r(A^*) = 10\%$ . $t_s = 150,000s$	N/A	Analyst





# Data Quality Objectives Document





# Thank you!





Tissue Sample ( $m_{\text{samp}}$ )



$$A_{X,Z,\text{alq}}^*(t_{C,Z}) = \frac{\left(\frac{N_S}{t_S} - \frac{N_B}{t_B}\right)}{\varepsilon f_{X,\text{ROI}} y_{\text{RR}}} = \frac{R_S - R_B}{\varepsilon f_{X,\text{ROI}} y_{\text{RR}}} = \frac{R_N}{\varepsilon f_{X,\text{ROI}} y_{\text{RR}}}$$

Dry Sample ( $m_{\text{dry}} = m_{\text{dry+blkr}} - m_{\text{blkr}}$ )

$$u_c^2(y) = \sum_{i=1}^N \left(\frac{\partial f}{\partial x_i}\right)^2 u^2(x_i) + 2 \sum_{i=1}^{N-1} \sum_{j=i+1}^N \frac{\partial f}{\partial x_i} \frac{\partial f}{\partial x_j} u(x_i, x_j)$$

= Sum of variance terms and covariance terms

Acid Solution ( $m_{\text{soln}} = m_{\text{soln+bottle}} - m_{\text{bottle}}$ )

$$u_c^2(A_{X,Z}) = \left(\frac{1}{t_S \varepsilon f_{X,\text{ROI}} y_{\text{RR}}}\right)^2 N_S + \left(\frac{1}{t_B \varepsilon f_{X,\text{ROI}} y_{\text{RR}}}\right)^2 N_B + \left(\frac{-1}{\varepsilon^2} \left(\frac{N_S}{t_S} - \frac{N_B}{t_B}\right) \frac{1}{f_{X,\text{ROI}} y_{\text{RR}}}\right)^2 (\varepsilon u_R(\varepsilon))^2$$

$$+ \left(\frac{-1}{f_{X,\text{ROI}}^2} \left(\frac{N_S}{t_S} - \frac{N_B}{t_B}\right) \frac{1}{\varepsilon y_{\text{RR}}}\right)^2 (f_{X,\text{ROI}} u_R(f_{X,\text{ROI}}))^2 + \left(\frac{-1}{y_{\text{RR}}^2} \left(\frac{N_S}{t_S} - \frac{N_B}{t_B}\right) \frac{1}{\varepsilon f_{X,\text{ROI}}}\right)^2 (y_{\text{RR}} u_R(y_{\text{RR}}))^2$$

$$= \left(\frac{1}{\varepsilon f_{X,\text{ROI}} y_{\text{RR}}}\right)^2 \left(\frac{N_S}{t_S} + \frac{N_B}{t_B}\right) + \left(\frac{N_S - N_B}{\varepsilon f_{X,\text{ROI}} y_{\text{RR}}}\right)^2 (u_R^2(\varepsilon) + u_R^2(f_{X,\text{ROI}}) + u_R^2(y_{\text{RR}}))$$

Taking of Aliquot from Acid Solution  
Addition of Tracers to Aliquot  
Separation of Elements in Aliquot

$$S_{C,X}(N_B, d, t_S, t_B, z_{1-\alpha}) = d \left(\frac{t_S}{t_B} - 1\right) + \frac{z_{1-\alpha}^2}{4} \left(1 + \frac{t_S}{t_B}\right) + z_{1-\alpha} \sqrt{(N_B + d) \frac{t_S}{t_B} \left(1 + \frac{t_S}{t_B}\right)}$$

$$MDA_X = \frac{S'_{D,X}}{\varepsilon f_{X,\text{ROI}} y_{\text{RR}}} = \frac{S_{D,X}}{t_S \varepsilon f_{X,\text{ROI}} y_{\text{RR}}} = \frac{S_{C,X} + \frac{z_{1-\beta}^2}{2} + z_{1-\beta} \sqrt{\frac{z_{1-\beta}^2}{4} + S_{C,X} + R_B t_S \left(1 + \frac{t_S}{t_B}\right)}}{t_S \varepsilon f_{X,\text{ROI}} y_{\text{RR}}}$$

$$A_{X,Z,\text{soln}}(t_{C,Z}) = \frac{A_{X,Z,\text{alq}}(t_{C,Z}) m_{\text{soln}}}{y_{\text{RR}}(Y) m_{\text{aliq}}}$$

$$A_{X,Z,\text{soln}}(t_D) = A_{X,Z,\text{soln}}(t_{C,Z}) e^{-\lambda_X(t_{C,Z} - t_D)}$$

$$C_{X,\text{wet}}(t_D) = \frac{A_{X,\text{-prep}}(t_D) \left(\frac{1000 \text{ g}}{1 \text{ kg}}\right)}{m_{\text{prep}}}$$

# Questions?

