SC&A Summary Position on Observed Trivalent Bioassay Variability

Bob Barton
Patrick Kelly
Joyce Lipsztein

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Background on co-exposure implementation guidelines

- Core tenet of co-exposure implementation guidelines is data adequacy (NIOSH, 2020)
  - Does the monitoring method used adequately reflect the exposure to be reconstructed?
  - "When paired measurements are available, the precision between measurements should be examined. **If widely different results from the same aliquot are observed, the effect this might have on the usefulness of the data should be considered.**" [Emphasis added.]

Background on SRS-specific issue

- **September 2013:** SC&A first expressed concern over observed variability among aliquots (discs) of the same sample
- **February 2014:** SC&A provides 188 individual examples from among samples that were above the detection limit (SC&A, 2014a)
- **December 2019:** Joint SRS and SEC Issues work groups requested SC&A formalize position

Updated analysis

- SC&A revisited 188 samples:
  - Assure sample was taken from a single voiding
  - Verify sample was not invalidated (e.g., contaminated or “lost in process”)
  - 145 valid examples above detection limit
  - Average variability approximately +/- 50%

Dosimetric significance

- What does this matter in terms of dose?
- Table 12 of SC&A (2014b) provides a scoping calculation of potential doses to the critical organ (bone surface)
  - Refer to extract from table 12 on the next slide
  - Calculations based on an assumed chronic intake of 1 year
  - Urinalysis performed at the end of the intake period

Committed dose to critical organ

Bioassay result (dpm/1.5L)	30-year dose to the bone surface (rem)	50-year dose to the bone surface (rem)
0.3	20	28
0.6	39	56
0.9	59	84
1.2	79	110
1.5	98	140

Additional documentation provided by NIOSH in 2019

- Two technical reports in response to SC&A points:
  - "Determination of Actinides in Biological Samples with Bidentate Organophosphorus Extractant" (Butler & Hall, 1970)
  - "Two Californium-252 Inhalation Cases" (Poda & Hall, 1975)
- SC&A position:
  - Documents are general methodologies illustrative of process
  - Technical questions are not adequately answered without additional information

SC&A specific technical questions

- Are the multiple aliquots from the same sample correlated with a specific void?
- Were multiple aliquots taken from what appeared to be different fractions on a sample based on observable attributes or anticipated chemical difficulties attributed to nonhomogeneous samples in the interest of representativeness?
- If multiple aliquots were taken, can we assume that they are of the same or equivalent volumes?
- What is the technical basis for this approach, and where is this aspect referenced in an analytical protocol (e.g., SRS, 1987, 1993)?
- Whatever the multiple counts represent, is this approach adequately represented in the determination of the method's measurement uncertainty?
- How much variation between discs is acceptable such that a simple average of all values is considered representative?
- Is there an acceptance criterion for the degree of variability (e.g., not to exceed 50% at a given disintegration rate)?

Examples of additional information required

- Example of formal SRS or laboratory calculations with all terms identified:
  - values used for volume
  - counting efficiency (counts per disintegration)
  - chemical yield (target analyte percent recovery based on tracer yields or another technical reason)
  - measurement uncertainty
- Written instructions explaining the technical basis, practice, and procedural controls regarding multiple counts
- Prospectively determined acceptance criteria for the performance samples analyzed with each batch (blanks and spikes)
- Objective evidence that the laboratory had predetermined acceptance criteria for the performance samples and that these criteria were technically appropriate and were, in fact, applied to routine bioassays

Concerns about batch spike samples

- Spike samples are a routine aspect of the analytical process
  - Provide evidence of laboratory ability to quantify target analyte
  - Identify potential systematic biases in the analytical protocols
- SC&A observed spike recovery samples varying from 6% to 116% (in some cases, 0% recovery)
- Samples were still deemed “OK to report” by SRS

Standard practices on sample variability

- Information on precision at SRS not identified until 1987 (+/- 19% at 13.6 dpm/1.5L)
- SC&A (2014a) identified aliquot examples above 13 dpm/1.5L to range 16–246% of the average value

Guidance from the National Council on Radiation Protection & Measurements

- NCRP Report No. 164, “Uncertainties in Internal Radiation Dose Assessment” (2009)
  - 18 individual laboratories performing actinide analyses
  - Optimum conditions determined to be <25% variability at 0.06 dpm/1.5L
  - Average uncertainty of +/- 30% at 0.006 dpm/1.5L
  - SRS detection limit 0.3 dpm/1.5L
  - “In addition to the normal counting uncertainties due to counting time, detector efficiency, and counting background, the parameters influencing the uncertainty of the results include heterogeneity of the material being analyzed, reagent blanks, and chemical yield (tracer recovery). The uncertainty due to the heterogeneity of the material is calculated as SD of the results from repetitive measurements of several subsamples randomly taken from the bottle and analyzed under the same experimental conditions. It has been estimated to be equal to 5 %.” (NCRP, 2009, p. 562)

SC&A conclusions

- Sufficient explanation has not been provided to explain the observed variability at SRS
- Observed variability outside the scope of analytical precision reported at SRS in 1987 (+/- 19%) and at other analytical laboratories
- SC&A finds a lack of documentation and/or objective evidence to understand what the trivalent bioassay represent and verify that they are technically adequate

Suggested path forward in SC&A (2020)

- Capture of any benchtop procedures in use at the SRS analytical laboratory
- Documentation of quality assurance criteria at SRS
- Interviews with analytical chemistry workers specifically performing the trivalent bioassay analysis
  - Note: SC&A has since identified 11 potential candidates who worked in the analytical laboratory performing bioassay analysis from among the claimant population

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Questions?