



Memorandum

To: Dr. Henry Anderson, Special Exposure Cohort Issues Workgroup Chair and
Mr. Bradley Clawson, Savannah River Site Workgroup Chair

From: John Cardarelli II, DCAS Research Health Physicist

Subject: Status Update on SC&A Comments on OTIB-0081, Revision 4

Date: October 8, 2020

Status of SC&A Comments Presented in Response Paper Dated March 2020

This memo provides an update on issues presented in SC&A's "Review of ORAUT-OTIB-0081, Revision 04, 'Internal Coworker Dosimetry Data for the Savannah River site' revision 1", dated March 13, 2020. It is worth noting that Finding 3 in SC&A's revision 0 (dated September 2019) was changed to Observation 3 in SC&A's revision 1 (dated March 13, 2020). SC&A's revision 0 finding and observations numbers are referred to in the workgroup and board meeting transcripts. These subtle changes are noted below. The December 5, 2019 Workgroup transcript is located at <https://www.cdc.gov/niosh/ocas/pdfs/abrwh/2019/wgtr120519-508.pdf> and the transcript for the December 11, 2019 Board meeting is at <https://www.cdc.gov/niosh/ocas/pdfs/abrwh/2019/tr121119-508.pdf>

Finding 1 – Chelation and Bioassay Variability (OPEN)

NIOSH agrees with SC&A that chelation therapy is not a source of variability in repeated counts of a given planchet. NIOSH does not agree with SC&A that the observed variability in repeated counts prohibits use of the bioassay data for developing co-exposure models. There is no definition for "high variability"; it is a subjective decision. Research on this issue is currently being performed by NIOSH and will be presented and discussed at the upcoming WG meeting on November 20, 2020.

Finding 2 – Multiple Imputation values less than 1/2 of MDA (Recommend Closing)

NIOSH presented that multiple imputation is more appropriate than the LOD/2 method for estimating censored data. SC&A memo dated June 3, 2020, Review of Multiple Imputation Methods Applied to Censored Bioassay Datasets (SRDB 182225, PDF page 9), concludes "*..the use of multiple imputation in evaluation of bioassay datasets with censored results is technically appropriate, scientifically defensible, and likely of small practical significance when considering its effect on resulting POC calculations.*" As a result of this review, NIOSH recommends closing this finding.

Finding 3 (originally Finding 4) – Claimant Data Cutoff for Data (CLOSED)

NIOSH agrees that additional data normally improves statistical analysis. However, given the large amount of data already available for most of the radionuclides, NIOSH believes that the time to code and validate additional data (many months) is not warranted due to the already limited resources. Per transcripts of the December 5, 2019 Workgroup meeting referenced above (page 165), it was decided not to pursue the inclusion of additional data. Therefore, NIOSH believes this finding is closed.

Finding 4 (originally Finding 5) – Potential Misclassification of Machinist as a Non-Construction Trade Worker (CTW) (CLOSED)

NIOSH stratified between CTW and non-CTW based on routine vs. non-routine work. SC&A noted that in OCAS-PER-014 the job title “machinist” was categorized as a CTW but in OTIB-0081, Rev 4, it was categorized as a non-CTW. During the SRS/SEC Workgroup meeting in Cincinnati, OH on December 5, 2019 (pages 118 – 146) the workgroup discussed this issue at length and concluded that since the misclassification rate is less than 5% it would have minor impact on the co-exposure models. Even though this met the quality assurance criteria, NIOSH is agreeable to designate all machinists as CTW if requested by the Board. Additionally, the Special Exposure Cohort (SEC) Workgroup voted to close Findings 5 and 6 and Observation 6 (now referred to Findings 4 and 5, and Observation 7) on December 5, 2019 (pages 145-146). NIOSH believes this finding is closed.

Finding 5 (originally Finding 6) – CTW Misclassification Evaluation (CLOSED)

NIOSH presented information (December 5, 2019) showing the targeted sampling by SC&A was not appropriate for application to the co-exposure model as a whole and presented data indicating there were less than 5% discrepancy between the original CTW vs. nonCTW designation. As a result, the SEC Workgroup voted to close Findings 5 and 6 and Observation 6 (now referred to Findings 4 and 5, and Observation 7) on December 5, 2019 (pages 145-146). NIOSH believes this finding is closed.

Observation 1 – Multiple Imputation (Recommend Closing)

Similar to Finding 2, NIOSH presented information showing that multiple imputation is more statistically appropriate for estimating censored data than the LOD/2 method. SC&A memo dated June 3, 2020, “Review of Multiple Imputation Methods Applied to Censored Bioassay Datasets”, PDF page 9, states “...*the use of multiple imputation in evaluation of bioassay datasets with censored results is technically appropriate, scientifically defensible, and likely of small practical significance when considering its effect on resulting POC calculations.*” As a result of this review, NIOSH recommends closing this observation.

Observation 2 – Multiple Imputation: Probability of Causation Scoping Assessment (Recommend Closing)

SC&A noted that the calculated intakes and doses differed between multiple imputation vs. LOD/2 methods, but concluded that the overall effect on the probability of causation (POC) was relatively minor, and in most cases, the co-exposure derived POC bounded the missed dose evaluation. NIOSH

intends to use multiple imputation as the primary method for analysis of censored datasets unless the Board indicates otherwise. Following the December meetings, SC&A released a memo dated June 3, 2020, “Review of Multiple Imputation Methods Applied to Censored Bioassay Datasets”, PDF page 9, stating “...*the use of multiple imputation in evaluation of bioassay datasets with censored results is technically appropriate, scientifically defensible, and likely of small practical significance when considering its effect on resulting POC calculations.*” Therefore, NIOSH recommends closing this observation.

Observation 3 (originally Finding 3) – Differences between ‘multiple imputation’ and ‘missed dose’ methods using uranium bioassay data may introduce inequity between unmonitored and monitored workers (Recommend closing)

SC&A noted that uranium intake calculations based on the multiple imputation method could be a factor of four or more higher than the missed dose method. They suggested that this may lead to inequity between the treatment of unmonitored workers assigned co-exposure intakes and monitored workers with results less than the detection limit. NIOSH acknowledges that in using the multiple imputation method, the censored values can be higher or lower depending on the uncensored data. Further, in the case of uranium, there are multiple censoring levels over time and that the relatively high censoring level for some data explain the increased intake results. In contrast, missed dose is based exclusively on data that are less than the MDA. The resulting intakes use a triangular distribution encompassing the full range of possible missed intakes from zero to the MDA. Following the December meetings, SC&A released a memo dated June 3, 2020, “Review of Multiple Imputation Methods Applied to Censored Bioassay Datasets”, PDF page 9, stating “...*the use of multiple imputation in evaluation of bioassay datasets with censored results is technically appropriate, scientifically defensible, and likely of small practical significance when considering its effect on resulting POC calculations.*” Therefore, NIOSH recommends closing this observation.

Observation 4 (originally Observation 3) – Difference in the # of Trivalent Samples reported in 1980 and 1982 (Recommend closing)

NIOSH provided a detailed explanation to the SRS and SEC Issues Workgroup chairs via a Memorandum dated August 11, 2020 with a subject title “Data Completeness associated with Trivalent Logbooks”. In summary, the mixture of bottle dates, received dates, and analyzed dates prevents a direct comparison on a year by year basis. A more broad timeframe examination showed a difference of <1%. NIOSH recommends closing this Observation.

Observation 5 (originally Observation 4) – Statistical Comparison of Stratified Groups (OPEN)

NIOSH used a qualitative exposure potential difference as a basis for stratification a priori due to there being no single statistical analysis (e.g., quantitative analysis) that could be applied a priori. NIOSH requested Workgroup guidance regarding CTW vs non-CTW stratification. Transcript from the December 11 meeting, page 129, shows SC&A states “*And so the status of this is*

there's really no action required. It's just, it's there to note the fact that the co-exposure guidelines say that you should perform a statistical analysis after you stratify the groups to see if they're truly different.”

**Observation 6 (originally Observation 5) – Quantitative Assessment of Job Plans
(Recommend closing)**

SC&A recommended quantitative assessment be used to determine if DuPont CTW and Subcontractor CTW are part of the same exposure strata. It was discussed during the December 11, 2019 board meeting (p 129-130) and SC&A states that there is “...*really no action required with regard to OTIB-0081*” because this is being addressed through another effort, therefore NIOSH recommends closing this observation.

The other effort is a NIOSH White Paper entitled “Savannah River Site Plutonium Construction Trade Worker Stratification Refinement” dated May 28, 2019 which stated that “...*NIOSH believes it is reasonable to combine all CTWs into a single stratum for assignment of intakes in the SRS internal dose coworker study.*” SC&A disagreed in their review (dated November 12, 2019) and suggested additional analyses. NIOSH’s responses to SC&A comments, dated March 4, 2020 (<https://ftp.cdc.gov/pub/FOIAREQ/179903-508.pdf>) concludes (PDF page 9) that “...*the final conclusions that sub-stratification is not necessary remains unchanged...*” and notes that “...*additional coding and analysis would take many months, if not years to complete.*”

**Observation 7 (originally Observation 6) – Sensitivity Analysis of Misclassification
(CLOSED)**

Due to the limited resources and other significant issues, NIOSH recommended the sensitivity analysis not be conducted. Motion made by Board Member Ziemer, December 5 (transcript pages 144 - 146) that Findings 5 and 6 and Observation 6 be closed (these are now Findings 4 and 5, and Observation 7). On page 146 Mr. Katz states “those two findings and that observation are closed.”

**Observation 8 (originally Observation 7) – Error Rates Dependent on Payroll ID
(Recommend closing)**

This was a data validation issue. The Payroll prefix issues have no effect on the CTW/non-CTW co-exposure distributions. The Workgroup discussion on pages 146 through 150 of the December 5 transcript indicate there was agreement by all this was a non-issue. Although no vote was taken, page 134 of the December 11 transcript has SC&A considering this observation closed and therefore NIOSH recommends closing this observation.