White Paper

1979 "AAMI ^{60}Co Dose Setting Intercompany Studies" - The Beginnings of Method 2

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Introduction

In the first White Paper on the 1979 *"AAMI ^{60}Co Dose Setting Intercompany Studies",* protocols and results of the three study phases of these studies were described and discussed. The original documents also showed calculations that were made to determine an *estimated* sterilization dose, at a sterility assurance level (SAL) of 10^{-6}, based on the results of the microbiological testing of the irradiated inoculated control (IC) samples. The approach used in these calculations shows the beginnings of the development of Method 2 of ISO 11137-2.

Results

A scan of the original worksheet is shown in Figure 1. The calculation had the following inputs:

- A - the desired SAL (10^{-6} in this case)
- B - the proportion (by weight) of the irradiated item or component (1.0 in this case)
- C - the average of the five D* doses
- D - the total of the items tested for sterility (100 in this case)
- E - the number of positive tests of sterility

The estimated SAL dose was calculated as using the following equation:

$$SAL\ Dose\ (Mrad) = C + ([-\log_{10} A + \log_{10} \{E/D\} - \log_{10} B] * [0.3])$$

As can be seen, this early equation for calculation of an estimated sterilization dose is simpler than those found in Method 2 in ISO 11137-2. Operationally, assuming irradiation of the entire item (B = 1.0) and a 1+/100 sterility testing result at 1.0 Mrad, the dose (C) that yielded the 1+/100 result is added to four times 0.3 Mrad, this being an extrapolation factor to calculate the 10^{-6} dose:

$$SAL\ Dose\ (Mrad) = 1.0 + ([-\log_{10} \{10^{-6}\} + \log_{10} \{1/100\} - \log_{10} 1] * [0.3])$$

$$SAL\ Dose\ (Mrad) = 1.0 + ([6 + (-2) - 0] * [0.3])$$

$$SAL\ Dose\ (Mrad) = 1.0 + (4 * [0.3])$$

$$SAL\ Dose\ (Mrad) = 1.0 + 1.2 = 2.2\ Mrad$$

Compared to the current Method 2 procedure, there is no calculation of a First No Positive (FNP) dose that is adjusted for the number of positive tests of sterility nor is there a calculation of a *DS* value. In the 1979 equation, the extrapolation factor, DS, is a fixed 0.3 Mrad (3.0 kGy).

The 10^{-6} dose calculation results for the Phase I and Phase II studies are shown in Table 1.

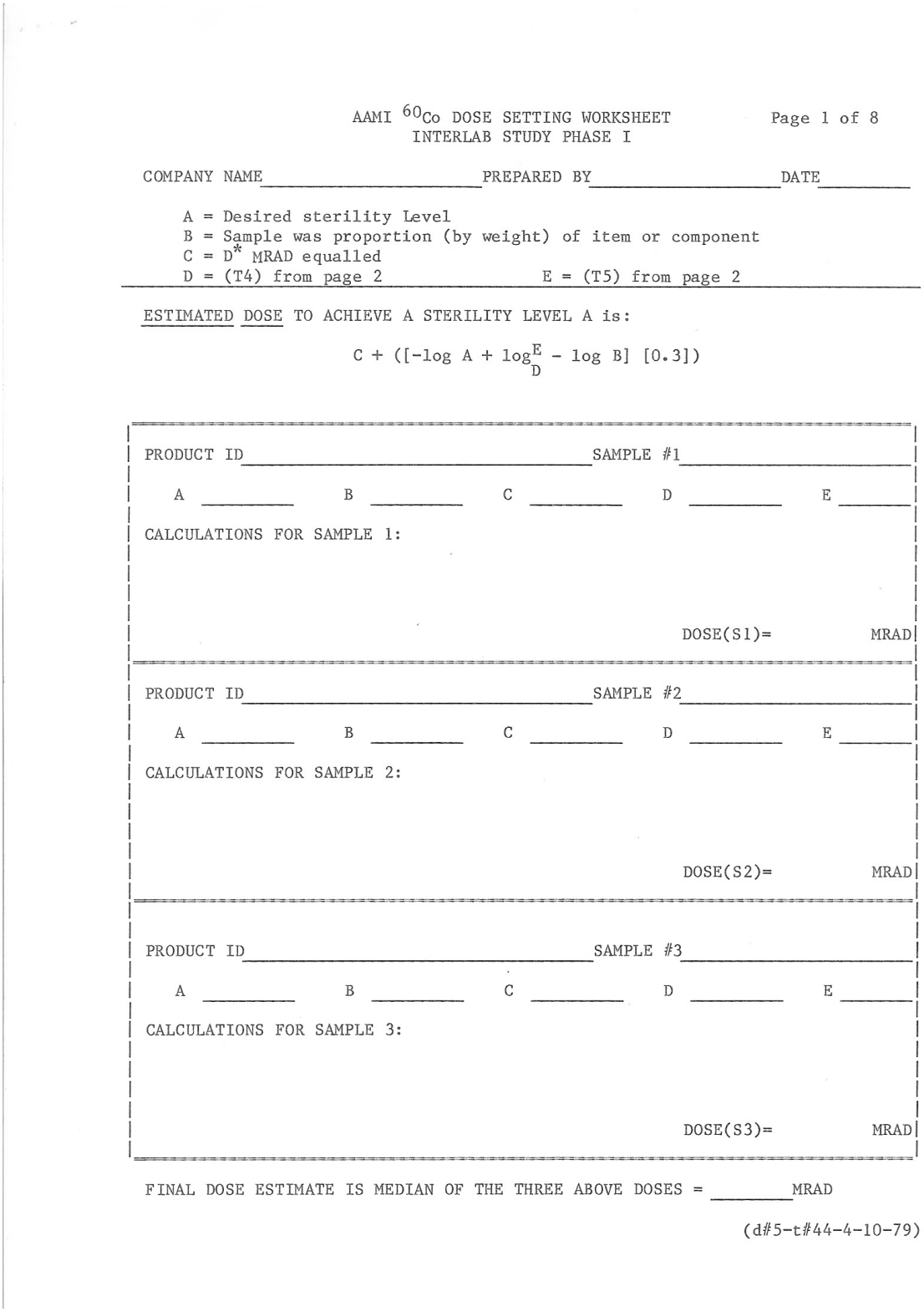
As can be seen for both phases, the results were very similar. In all cases, the sterility testing results were either 0+/100 (1+/100 assumed for the calculation) or 1+/100. The variation in the dose calculation results was solely due to the average D* dose values (C) entered into the equation.

Discussion

The approach used for the calculation of an estimated sterilization dose in the "AAMI Studies" in 1979 are evident today in Method 2 and Method 1 of ISO 11137-2. For the current Method 2, a 10^{-2} dose is calculated and an extrapolation is used to identify a 10^{-6} dose. For the current Method 1, a 10^{-2} dose for a given average bioburden is specified by the radiation response of Population C, the Standard Distribution of Resistances (SDR). If irradiation of 100 product items at this 10^{-2} dose gives an acceptable result on sterility testing, an SDR-based extrapolation identifies the 10^{-6} SAL minimum sterilization dose.

A new dose-setting methodology is under development/evaluation that reflects both current approaches and those used in the 1979 studies.

Figure 1. Scan of original dose calculation worksheet.



AAMI ^{60}Co DOSE SETTING WORKSHEET — Page 1 of 8
INTERLAB STUDY PHASE I

COMPANY NAME _____ PREPARED BY _____ DATE _____

A = Desired sterility Level
B = Sample was proportion (by weight) of item or component
C = D* MRAD equalled
D = (T4) from page 2 E = (T5) from page 2

ESTIMATED DOSE TO ACHIEVE A STERILITY LEVEL A is:

$$C + ([-\log A + \log_D^E - \log B] [0.3])$$

PRODUCT ID _____ SAMPLE #1 _____

A _____ B _____ C _____ D _____ E _____

CALCULATIONS FOR SAMPLE 1:

DOSE(S1)= MRAD

PRODUCT ID _____ SAMPLE #2 _____

A _____ B _____ C _____ D _____ E _____

CALCULATIONS FOR SAMPLE 2:

DOSE(S2)= MRAD

PRODUCT ID _____ SAMPLE #3 _____

A _____ B _____ C _____ D _____ E _____

CALCULATIONS FOR SAMPLE 3:

DOSE(S3)= MRAD

FINAL DOSE ESTIMATE IS MEDIAN OF THE THREE ABOVE DOSES = _____ MRAD

(d#5-t#44-4-10-79)

Table 1. Results of the calculations of the estimated 10^{-6} sterilization dose.

Phase	Facility					
	A	B	C	D	E	F
	Mrad					
I	2.25	2.20	2.20	2.20	2.25	2.22
II	2.19	2.26	2.37	2.22	2.25	2.16