



## White Paper

*1979 "AAMI <sup>60</sup>Co Dose Setting Intercompany Studies" -  
The Beginnings of Method 2*

*5/18/17*

John B. Kowalski, Ph.D.  
Independent Consultant of Sterigenics/SteriPro  
President & Principal Consultant  
microGAMMA, LLC

## Introduction

In the first White Paper on the 1979 "AAMI <sup>60</sup>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<sup>-6</sup>, 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<sup>-6</sup> 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:

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

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<sup>-6</sup> dose:

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

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

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

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

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<sup>-6</sup> 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.



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