White Paper

1979 "AAMI ^{60}Co Dose Setting Intercompany Studies"

5/11/17

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Introduction

In 1979, I was extremely fortunate to participate in the "AAMI ^{60}Co Dose Setting Intercompany Studies". In going through some old files, I came across a set of original typed and handwritten documents from the Phase I, Phase II and Phase III studies. I don't believe these studies were widely published so I thought I'd document them as best as I could from the old files and what I remember.

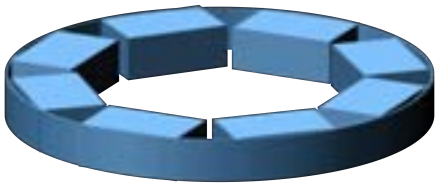
These studies were conducted by the "Dose Setting Working Group" under the auspices of the Association for the Advancement of Medical Instrumentation (AAMI). This working group had members from industry and academia that were interested in and driving the development of methods to set a product-specific radiation sterilization dose. The participating organizations, according to the documents I have, were: Becton-Dickinson, Converters, Ethicon, Isomedix, Johnson & Johnson Products, and University Hospital.

At this time, a radiation dose of 25 kGy was commonly used; it was clear, however, that products with low average bioburden would likely attain a sterility assurance level (SAL) of 10^{-6} at a lesser radiation dose and some products might require a dose higher than 25 kGy to meet this SAL. The goal of the working group was to investigate, develop, test, and codify methods to set product-specific radiation sterilization doses. The ultimate outcome of this and other work was the first AAMI radiation sterilization standard, AAMI RS, in 1984.

During the course of these discussions and activities, a question was raised concerning the reproducibility of microbiological testing and dosimetry from one laboratory to the next. To address this question, the following studies were performed:

- In Phase I, seven sets of inoculated carriers (ICs, 6.9×10^4 colony-forming units of *Bacillus pumilus* spores), Red Perspex, and Amber Perspex dosimeters were irradiated at a single facility in a controlled and highly uniform manner and distributed to the six laboratories for testing/reading. Each set included 13 small (Ceco) boxes each of which contained 20 ICs sealed in foil packages, three Red Perspex, and three Amber Perspex dosimeters. One of the sets also included thin-film dosimeters from the then National Bureau of Standards (NBS). For each set, one box was irradiated at 0.2, 0.4, 0.6, 0.8, 1.0, 1.2, 1.4, and 1.6 Mrad (as in the incremental dose experiment of Method 2 of ISO 11137-2). Five boxes were each irradiated at 1.0 Mrad (as in the Method 2 verification dose experiment).

  To help ensure box-to-box uniformity with respect to delivered dose, the boxes were arranged in layers a cylindrical container, along the inside edge forming a chimney-like structure, and spun on a turntable in the corner of the irradiation cell, a significant distance from the source rack (one layer shown).



The irradiated sets of boxes were then distributed to the participating laboratories for testing of the ICs and reading of the dosimeters. The thin-film dosimeters were returned to NBS for reading.

- In Phase II, the same sets of boxes were prepared at a single facility but, in this phase, the irradiations were performed at different facilities as was the testing of the ICs and the reading of the dosimeters. Each set of boxes contained NBS thin-film dosimeters.

- In Phase III, the participants subjected medical products with their naturally occurring bioburden to the irradiation regimen.

Phase I

A scan of the Phase I microbiology and dosimetry protocols from 1979 are shown in Attachments 1 and 2.

Scans of the results worksheets for the Phase I study are shown in Attachment 3. One of the participants (A) performed two separate incremental dose studies; the second used Inolex Medicase medium for the tests of sterility performed on the irradiated ICs. Participant E performed the irradiations in a Gammacell 220.

The results of the microbiological testing are shown in Table 1. For this and subsequent tables, a "-" entry indicates results that were not reported.

The lab-to-lab reproducibility for the sterility testing results for the irradiated ICs was excellent; five of the seven laboratories had either one or two positive tests of sterility at the 0.8-Mrad target dose.

The results of the Red Perspex dosimetry, Table 2, showed very good agreement amongst the laboratories and also with the results of the NBS thin-film dosimeters.

The results of the Amber Perspex dosimetry are shown in Table 3. The results of each laboratory were a significant underestimation of the delivered dose. Because there was a significant delay between irradiation and reading of the dosimeter, this outcome was felt to be related to dosimeter fading. One laboratory reread the Amber Perspex 12 days after their initial reading and found a further 7% decline in dose.

Phase II

The results of the tests of sterility for the ICs and dosimeter readings are summarized in Tables 4 and 5.

As in Phase I, the results of the tests of sterility were in excellent agreement, nearly identical. This outcome was not expected because of the irradiations being performed at six different facilities with the associated differing irradiation conditions.

As observed previously, the dose values seen with the Amber Perspex dosimetry were generally lower than found with the Red Perspex and NBS thin-film dosimeters. This was not

universally the case, however. Facility E had excellent agreement of all three dosimetry systems.

Phase III

The protocol for the Phase III studies is shown in Attachment 4.

Unfortunately, I have only one record of the Phase III studies; it has the test of sterility results for the incremental dose experiment for a cotton stockinette product. The results are shown in Table 6. As can be seen, the results are very different from those found previously with the irradiated ICs; they indicate a higher number and/or more resistant microorganisms compared to the *B. pumilus* spores on the ICs.

Discussion

The AAMI Intercompany Studies gave great insight into the reproducibility of sterility testing and dosimetry results for uniformly prepared boxes of test items either irradiated at one facility and then distributed for analysis or distributed and then irradiated and analyzed at different facilities. As I remember, the group was rather surprised (pleasantly) at the excellent reproducibility of the IC sterility testing results. The dosimetry results raised some questions that required follow-up; I do not recall what was done or the outcome of this work. It was interesting to see the very different sterility testing results for the stockinette product subjected to the incremental dose experiment.

Table 1. Phase I test of sterility results.

Target Dose (Mrad)	A1	A2	B	C	D	E	F
	Number Positive for Growth Out of 20 Tested						
0.2	20	20	20	20	20	20	20
0.4	20	20	20	20	20	20	20
0.6	19	20	20	20	20	20	20
0.8	8	4	1	2	2	2	1
1.0	0	0	0	0	0	0	0
1.2	0	0	0	0	0	0	0
1.4	0	0	0	0	0	0	0
1.6	0	0	0	0	0	0	0
1.0	0	-	0	0	0	0	0
1.0	0	-	0	0	0	0	0
1.0	0	-	0	0	0	0	0
1.0	0	-	0	0	0	0	0
1.0	0	-	0	0	0	0	0

Table 2. Phase I Red Perspex results.

Target Dose (Mrad)	Mrad Dose - Median of Three Red Perspex							
	A1	**A2**	**B**	**C**	**D**	**E**	**F**	***NBS***
0.2	0.11	0.14	0.11	0.12	-	0.09	0.11	***0.20***
0.4	0.37	0.40	0.37	0.36	-	0.35	0.35	***0.44***
0.6	0.62	0.62	0.63	0.65	0.58	0.63	0.60	***0.68***
0.8	0.89	0.85	0.87	0.90	0.85	0.87	0.88	***0.85***
1.0	1.08	1.08	1.06	1.10	1.04	1.03	1.05	***1.05***
1.2	1.29	1.25	1.28	1.32	1.23	1.32	1.26	***1.28***
1.4	1.50	1.48	1.52	1.57	1.48	1.47	1.55	***1.47***
1.6	1.80	1.70	1.79	1.88	1.72	1.88	1.77	***1.79***
1.0	1.07	-	1.02	1.04	1.00	1.08	1.04	***1.06***
1.0	1.05	-	1.05	1.04	0.98	1.02	1.02	***1.04***
1.0	1.03	-	0.88	1.06	1.04	1.06	1.03	***-***
1.0	1.07	-	1.01	1.07	1.00	1.05	1.01	***1.03***
1.0	1.01	-	1.06	1.04	1.01	1.04	1.01	***1.05***

Table 3. Phase I Amber Perspex results.

Target Dose (Mrad)	Mrad Dose - Median of Three Amber Perspex							
	A1	**A2**	**B**	**C**	**D**	**E**	**F**	***NBS***
0.2	0.15	0.17	0.15	0.13	0.13	0.13	0.12	***0.20***
0.4	0.30	0.35	0.32	0.27	0.29	0.30	0.28	***0.44***
0.6	0.50	0.52	0.49	0.45	0.47	0.44	0.51	***0.68***
0.8	0.67	0.72	0.66	0.65	0.62	0.59	0.70	***0.85***
1.0	0.82	0.86	0.81	0.72	0.75	0.71	0.88	***1.05***
1.2	0.96	1.02	0.97	0.86	0.89	0.85	1.05	***1.28***
1.4	1.11	1.18	-	0.95	1.08	1.07	1.20	***1.47***
1.6	1.21	1.36	-	1.15	1.21	1.17	1.39	***1.79***
1.0	0.77	-	0.80	0.69	0.70	0.73	0.86	***1.06***
1.0	0.74	-	0.82	0.67	0.71	0.75	0.82	***1.04***
1.0	0.77	-	0.77	0.70	0.72	0.74	0.81	***-***
1.0	0.76	-	0.78	0.73	0.74	0.72	0.80	***1.03***
1.0	0.75	-	0.80	0.68	0.74	0.67	0.81	***1.05***

Table 4. Phase II IC test of sterility results.

Target Dose (Mrad)	A	B	C	D	E	F
	Number Positive for Growth Out of 20 Tested					
0.2	19[a]	20	20	20	20	20
0.4	20	20	20	20	20	20
0.6	19	20	20	20	20	19
0.8	1	1	2	1	1	0
1.0	0	0	0	0	0	0
1.2	0	0	0	0	0	0
1.4	0	0	0	0	0	0
1.6	0	0	0	0	0	0
1.0	0	0	0	0	0	1
1.0	0	0	0	0	0	0
1.0	1	0	0	0	0	0
1.0	0	0	0	0	0	0
1.0	0	0	0	0	0	0

[a] Only 19 ICs incubated, one dropped during sterility testing.

Table 5. Phase II dosimetry results; values are the median of three readings.

Target Dose (Mrad)	A			B			C			D			E			F		
	Red	**Amb**	**NBS**	**Red**	**Amb**	**NBS**	**Red**	**Amb**	**NBS**	**Red**	**Amb**	**NBS**	**Red**	**Amb**	**NBS**	**Red**	**Amb**	**NBS**
0.2	0.18	0.21	0.22	0.12	0.18	0.21	0.27	0.17	0.20	0.09	0.14	-	-	0.21	0.22	0.18	0.21	0.23
0.4	0.45	0.41	0.43	0.37	0.37	0.40	0.45	0.33	0.40	0.36	0.31	-	-	0.40	0.44	0.43	0.41	0.43
0.6	0.70	0.61	0.65	0.58	0.54	0.60	0.67	0.62	0.60	0.58	0.49	-	0.60	0.61	0.64	0.70	0.61	0.64
0.8	0.96	0.84	0.85	0.90	0.79	0.81	0.88	0.85	0.80	0.82	0.66	-	0.84	0.80	0.92	0.98	0.82	0.87
1.0	1.17	0.99	0.99	0.97	0.84	0.98	1.02	0.86	0.96	1.05	0.83	-	1.03	0.97	1.06	1.20	0.98	1.09
1.2	1.40	1.17	1.19	1.17	1.08	1.17	1.18	1.09	1.16	1.27	0.98	-	1.22	1.13	1.22	1.44	1.14	1.30
1.4	1.65	1.34	1.39	1.37	-	1.37	1.40	1.44	1.36	1.56	1.12	-	1.43	1.34	1.44	1.66	-	1.50
1.6	1.86	1.46	1.58	1.55	-	1.55	1.56	1.55	1.57	1.75	1.29	-	1.62	1.51	1.63	1.91	-	1.73
1.0	1.00	0.86	0.93	1.08	0.95	0.92	1.28	1.20	1.17	1.06	0.85	-	1.02	1.00	1.04	0.97	0.78	0.92
1.0	0.98	0.86	0.95	1.04	0.94	0.94	1.25	1.13	1.14	0.99	0.86	-	1.05	1.00	1.02	0.94	0.81	0.94
1.0	0.99	0.88	0.94	1.05	0.96	0.98	1.28	1.16	1.18	1.02	0.85	-	1.08	1.03	1.08	0.96	0.79	0.93
1.0	0.98	0.86	0.95	1.07	0.95	0.97	1.09	1.12	1.15	1.01	0.88	-	1.07	1.01	1.07	0.96	0.79	0.92
1.0	0.98	0.86	0.96	1.04	0.96	0.96	1.22	1.01	1.12	1.01	0.87	-	1.04	1.00	1.04	0.96	0.75	0.93

Table 6. Phase III product test of sterility results.

Target Dose (Mrad)	Number Positive Out of 20 Tested
0.2	20
0.4	20
0.6	20
0.8	20
1.0	16
1.2	0
1.4	6
1.6	1

Attachment 1

AAMI PROJECT LEADER

PROTOCOL

AAMI PHASE I EXPERIMENT

For the Phase I experiment, each laboratory has received a total of 260 samples for sterility testing. The samples are inoculated paper strips (1.0 x 5.0 cm) which are sealed in foil packets. The foil packets are supplied in 13 boxes, each of which contains 20 packets. One box of packets was irradiated at each of the following target doses: 0.2, 0.4, 0.6, 0.8, 1.0, 1.2, 1.4, and 1.6 Mrads. The remaining five boxes (D1, D2, D3, D4, D5) were irradiated at D_{*}. For the Phase I experiment, the target D_{*} dose was 1.0 Mrads. Each box also contains six dosimeters, three Red Perspex and three Amber Perspex. All dosimeter packages are labelled to indicate the target dose of their respective boxes.

Materials required for sterility testing:

1. Samples (13 boxes)
2. Two pairs of sterile scissors
3. Two pairs of sterile forceps (or hemostats)
4. Sterility test medium, minimum of 260 tubes. Trypticase Soy Broth (BBL) has been chosen as the sterility test medium. Prepare the medium according to package directions and dispense in an appropriate size screw-cap tube. The depth of the medium should be adjusted so that the paper strip is completely submersed (ca. 7 to 8 cm of medium).
5. Container to place dosimeters (78 total)

Sterility test procedure:

1. Assemble the sample boxes and the materials described above and place in the testing room or facility. Do not remove any wrapping from the boxes prior to sterility testing. The sterility testing is most easily accomplished by two operators; one operator to remove the paper strip from the packets and the other to handle the tubes of medium. The operators should be appropriately dressed for sterility testing.

2. Unwrap the sample boxes and remove the top covers. Each box is labelled as to its target dose on the top cover as well as on its side.

3. Begin the sterility testing with the samples that received 1.6 Mrads. To recover the paper strips, cut approximately 1.0 cm from the "notched" end of the packet. (See the demonstration packet. Open this packet prior to the sterility testing.) Remove the paper strip from the packet with the forceps and drop into the tube of test medium. Repeat this procedure for the remaining packets from the "1.6 Mrad" box. It is recommended that the scissors and forceps be flamed between packets. Remove the dosimeters from the box and place in the designated container. Do not open or disrupt the dosimeter packages in any manner.

4. Repeat the sterility test procedure with the samples from the box that had the target dose of 1.4 Mrad. Continue in this manner (1.2, 1.0, 0.8 etc.) until the "0.2 Mrad" box is completed. At this time, test the packets from the boxes labeled D1, D2, D3, D4, and D5. As each box is completed, place the respective dosimeters in the designated container.

5. When the sterility testing is completed, incubate the tubes at 32°C. Give the container of dosimeters to the person(s) in charge of the dosimetry measurements.

6. Observe the tubes daily and record for each dose the date of the first and last growth. After 14 days of incubation, observe the tubes and record on the data sheet the number of tubes exhibiting growth as well as the number of tubes incubated. Forward the sterility test data to the project leader for the AAMI studies.

Attachment 2

PROTOCOL

DOSIMETRY MEASUREMENTS

I. EQUIPMENT

1. Spectrophotometer (visible), preferably with a 2-nm spectral band width. Please indicate on the data sheet the band width of your instrument.

2. Metric thickness gauge with a 4-mm range (± 0.01mm)

3. Lens tissue

II. PROCEDURE

A. Set Up

1. Turn on the spectrophotometer and, after the appropriate warmup period, verify the wavelength accuracy using the hydrogen lamp (UV - visible models) or a holmium oxide filter or equivalent.

2. Verify optical density (OD) scale linearity using NBS #390b neutral density filters or equivalent (check OD ca. 0.1 and 1.0).

3. Set wavelength; for the Red Perspex dosimeters use 640 nm, for the Amber Perspex use 603 nm.

4. Zero the thickness gauge and verify 3 mm using a gauge block or equivalent.

B. Reading Dosimeters

1. Remove the dosimeter from the packet.

2. Wipe the dosimeter with lens tissue to remove any water spots or dust.

3. Measure optical density using the appropriate wavelength setting.

4. Measure the thickness of the dosimeter (optical path length) in the area of the dosimeter through which the light beam passes.

C. Reporting Results

1. On the dosimetry raw data sheets (pages 2 and 3), record the optical density and thickness for each dosimeter.

2. For the Red Perspex dosimeters, calculate the induced absorbance coefficient "K" and the absorbed dose by the following equations and record these values on the data sheets. Enter on page 2 of 8 the median of the three dose values.

$$K = \frac{OD - (mt + b)}{t}$$

where OD = Optical density (640 nm) of the exposed dosimeter

t = Thickness of the exposed dosimeter in centimeters

m = 0.10916

b = 0.03527

$$\text{Dose (Mrads)} = A - \sqrt{B + KC}$$

where K = Induced absorbance coefficient

A = 6.708092583

B = 46.09062881

C = -15.03902218

3. For the Amber Perspex dosimeters, calculate the induced absorbance by the following equation and record these values on the data sheets.

$$\text{Induced absorbance} = \frac{OD}{t} - 0.444$$

where OD = Optical density (603 nm) of the exposed dosimeter

t = Thickness of the exposed dosimeter in centimeters

Using the graph relating induced absorbance to dose (Mrads) find the dose that corresponds to the induced absorbance value and record these values on the data sheets. Record the median of the three dose values on page 2 of 8.

Note: The graph supplied will cover dose values up to approximately 1.2 Mrads. For higher doses, calculate only the induced absorbance.

Attachment 3

AAMI ^{60}Co DOSE SETTING WORKSHEET
INTERLAB STUDY PHASE I

Company Name [redacted] Prepared by [redacted] Date 5/10/79

Product I.D. AAMI-Phase I Sample Number #1 X #2 #3

Date Samples Rec'd. ----- Date Samples Place in Incubation 4/19/79

Date Sample Irradiated 4/10/79 Culture Medium: Type T Soy Broth

Spectrometer: Make Bausch & Lomb Manufacturer BBL

Model 100 Period of incubation 14 days

Date last calibration 3/27/79 Incubation Temperature 32°C

STAGE I - DOSE SETTING DATA

	DOSIMETRY DATA			INCUBATION DATA			
TARGET DOSE (MRAD)	(C1) MEDIAN OF 3 RED PERSPEX	(C2) MEDIAN OF 3 AMBER PERSPEX	(C3) MEDIAN OF 3 NAT'L. BUREAU OF STD's	(C4) NO. OF TUBES INCUB-ATED	(C5) NO.OF POS. TUBES	DATE 1ST GROWTH DAY/MO	DATE LAST GROWTH DAY/MO
0.2	0.11	0.15	0.20	20	20	20/4	20/4
0.4	0.37	0.30	0.44	20	20	20/4	21/4
0.6	0.62	0.50	0.68	20	19	20/4	21/4
0.8	0.89	0.67	0.85	20	8	20/4	22/4
1.0	1.08	0.82	1.05	20	0	---	---
1.2	1.29	0.96	1.28	20	0	---	---
1.4	1.50	1.11	1.47	20	0	---	---
1.6	1.80	1.21	1.79	20	0	---	---
STAGE II - DOSE SETTING DATA							
D*(1)	1.07	0.77	1.06	20	0	---	---
D*(2)	1.05	0.74	1.04	20	0	---	---
D*(3)	1.03	0.77	---	20	0	---	---
D*(4)	1.07	0.76	1.03	20	0	---	---
D*(5)	1.01	0.75	1.05	20	0	---	---
AVERAGES	(A1) 1.05	(A2) 0.76	(A3) 1.05	(T4) 100	(T5) 0	TOTALS	

(d#5-t#40--3-13-79)

AAMI ^{60}Co DOSE SETTING WORKSHEET
INTERLAB STUDY PHASE I

Company Name [redacted] Prepared by [redacted] Date 5/10/79

Product I.D. AAMI-Phase I Sample Number #1 #2 X #3

Date Samples Rec'd. ----- Date Samples Place in Incubation 4/19/79

Date Sample Irradiated 4/18/79 Culture Medium: Type Medicase Soy Broth

Spectrometer: Make Bausch & Lomb Manufacturer Inolex

Model 100 Period of incubation 14 days

Date last calibration 3/27/79 Incubation Temperature 32°C

STAGE I - DOSE SETTING DATA

	DOSIMETRY DATA			INCUBATION DATA			
TARGET DOSE (MRAD)	(C1) MEDIAN OF 3 RED PERSPEX	(C2) MEDIAN OF 3 AMBER PERSPEX	(C3) MEDIAN OF 3 NAT'L. BUREAU OF STD's	(C4) NO. OF TUBES INCUB-ATED	(C5) NO.OF POS. TUBES	DATE 1ST GROWTH DAY/MO	DATE LAST GROWTH DAY/MO
0.2	0.14	0.17	----	20	20	20/4	20/4
0.4	0.40	0.35	----	20	20	20/4	20/4
0.6	0.62	0.52	----	20	20	20/4	21/4
0.8	0.85	0.72	----	20	4	20/4	21/4
1.0	1.08	0.86	----	20	0	---	---
1.2	1.25	1.02	----	20	0	---	---
1.4	1.48	1.18	----	20	0	---	---
1.6	1.70	1.36	----	20	0	---	---
STAGE II - DOSE SETTING DATA							
D*(1)	----	----	----	----	----	---	---
D*(2)	----	----	----	----	----	---	---
D*(3)	----	----	----	----	----	---	---
D*(4)	----	----	----	----	----	---	---
D*(5)	----	----	----	----	----	---	---
AVERAGES	(A1)	(A2)	(A3)	(T4)	(T5)	TOTALS	

(d#5-t#40--3-13-79)

AAMI ^{60}Co DOSE SETTING WORKSHEET
INTERLAB STUDY (PHASE I)

Company Name [redacted] Prepared by [redacted] Date 5/17/79

Product I.D. AAMI Phase I Sample Number #1 ____ #2 ____ #3 ____

Date Samples Rec'd. 4/23/79 Date Samples Place in Incubation 4/30/79

Date Sample Irradiated 4/10/79 Culture Medium: Type Trypticase Soy Broth

Spectrometer: Make Coleman Manufacturer BBL

Model 124 D Period of incubation 14 days

Date last calibration 4/17/79 Incubation Temperature 30-35C

STAGE I - DOSE SETTING DATA

	DOSIMETRY DATA			INCUBATION DATA			
TARGET DOSE (MRAD)	(C1) MEDIAN OF 3 RED PERSPEX	(C2) MEDIAN OF 3 AMBER PERSPEX	(C3) MEDIAN OF 3 NAT'L. BUREAU OF STD's	(C4) NO. OF TUBES INCUB-ATED	(C5) NO. OF POS. TUBES	DATE 1ST GROWTH DAY/MO	DATE LAST GROWTH DAY/MO
0.2	0.11	0.15		20	20	5/2/79	5/2/79
0.4	0.37	0.32		20	20	5/2/79	5/2/79
0.6	0.63	0.49		20	20	5/2/79	5/2/79
0.8	0.87	0.66		20	1	5/2/79	5/2/79
1.0	1.06	0.81		20	0		
1.2	1.28	0.97		20	0		
1.4	1.52			20	0		
1.6	1.79			20	0		
STAGE II - DOSE SETTING DATA							
D*(1)	1.02	0.80		20	0		
D*(2)	1.05	0.82		20	0		
D*(3)	0.88	0.77		20	0		
D*(4)	1.01	0.78		20	0		
D*(5)	1.06	0.80		20	1	5/2/79	5/2/79
AVERAGES	(A1)	(A2)	(A3)	(T4)	(T5)	TOTALS	

(d#5-t#40--3-13-79)

AAMI ^{60}Co DOSE SETTING WORKSHEET
INTERLAB STUDY (PHASE I)

Company Name [redacted] Prepared by [redacted] Date 6/12/79

Product I.D. AAMI - Phase I B. pumilus I.C. Sample Number #1 ✓ #2 _____ #3 _____

Date Samples Rec'd. 4/20/79 Date Samples Place in Incubation 4/23/79

Date Sample Irradiated 4/10/79 Culture Medium: Type Trypticase Soy Broth

Spectrometer: Make Beckman Manufacturer BBL

Model 35 Period of incubation 14 days

Date last calibration 5/7/79 Incubation Temperature 32°C

STAGE I - DOSE SETTING DATA

	DOSIMETRY DATA			INCUBATION DATA			
TARGET DOSE (MRAD)	(C1) MEDIAN OF 3 RED PERSPEX	(C2) MEDIAN OF 3 AMBER PERSPEX	(C3) MEDIAN OF 3 NAT'L. BUREAU OF STD's	(C4) NO. OF TUBES INCUB-ATED	(C5) NO. OF POS. TUBES	DATE 1ST GROWTH DAY/MO	DATE LAST GROWTH DAY/MO
0.2	.120	.13		20	20	24/4	24/4
0.4	.361	.27		20	20	24/4	26/4
0.6	.645	.45		20	20	24/4	26/4
0.8	.901	.65		20	2	26/4	30/4
1.0	1.10	.72		20	0	—	—
1.2	1.32	.86		20	0	—	—
1.4	1.57	.95		20	0	—	—
1.6	1.88	1.15		20	0	—	—
STAGE II - DOSE SETTING DATA							
D*(1)	1.04	.69		20	0	—	—
D*(2)	1.04	.67		20	0	—	—
D*(3)	1.06	.70		20	0	—	—
D*(4)	1.07	.73		20	0	—	—
D*(5)	1.04	.68		20	0	—	—
AVERAGES	(A1) 1.05	(A2) .69	(A3)	(T4) 100	(T5) 0	TOTALS	

(d#5-t#40—3-13-79)

AAMI ^{60}Co DOSE SETTING WORKSHEET .
INTERLAB STUDY (PHASE I)

Company Name [redacted] Prepared by [redacted] Date 5/15/79

Product I.D. _____ Sample Number #1 x #2 _____ #3 _____

Date Samples Rec'd. 4/18/79 Date Samples Place in Incubation 4/21/79

Date Sample Irradiated 4/10/79 Culture Medium: Type BBL TSB

Spectrometer: Make Bausch & Lomb Manufacturer BBL

Model 710 Period of incubation 14 DAYS

Date last calibration 4/17/79 Incubation Temperature 32°C

STAGE I - DOSE SETTING DATA

	DOSIMETRY DATA			INCUBATION DATA			
TARGET DOSE (MRAD)	(C1) MEDIAN OF 3 RED PERSPEX	(C2) MEDIAN OF 3 AMBER PERSPEX	(C3) MEDIAN OF 3 NAT'L. BUREAU OF STD's	(C4) NO. OF TUBES INCUB-ATED	(C5) NO. OF POS. TUBES	DATE 1ST GROWTH DAY/MO	DATE LAST GROWTH DAY/MO
0.2	--	.13		20	20	22/4	--
0.4	--	.29		20	20	22/4	--
0.6	.58	.47		20	20	23/4	
0.8	.85	.62		20	2	24/4	25/4
1.0	1.04	.75		20	--	--	--
1.2	1.23	.89		20	--	--	--
1.4	1.48	1.08		20	--	--	--
1.6	1.72	1.21		20	--	--	--
STAGE II - DOSE SETTING DATA							
D*(1)	1.0032	.70		20	0	--	--
D*(2)	.9826	.71		20	0	--	--
D*(3)	1.0354	.72		20	0	--	--
D*(4)	.9983	.74		20	0	--	--
D*(5)	1.0116	.74		20	0	--	--
AVERAGES	(A1) 1,0062	(A2) .72	(A3)	(T4) 100	(T5) 0	TOTALS	

(d#5-t#40--3-13-79)

AAMI ^{60}Co DOSE SETTING WORKSHEET
INTERLAB STUDY (PHASE I)

Company Name [redacted] Prepared by [redacted] Date 5/23/79

Product I.D. AAMIPHASE I Sample Number #1 — #2 — #3 —

Date Samples Rec'd. 4/23/79 Date Samples Place in Incubation 4/26/79

Date Sample Irradiated 4/10/79 Culture Medium: Type TSB

Spectrometer: Make BAUSCH & LOMB Manufacturer BBL

Model 700 2nm Band width Period of incubation 140A15

Date last calibration 5/4/79 Incubation Temperature 32°C

STAGE I - DOSE SETTING DATA

	DOSIMETRY DATA			INCUBATION DATA			
TARGET DOSE (MRAD)	(C1) MEDIAN OF 3 RED PERSPEX	(C2) MEDIAN OF 3 AMBER PERSPEX	(C3) MEDIAN OF 3 NAT'L. BUREAU OF STD's	(C4) NO. OF TUBES INCUB-ATED	(C5) NO. OF POS. TUBES	DATE 1ST GROWTH DAY/MO	DATE LAST GROWTH DAY/MO
0.2	.089	.126	Na	20	20	27/4	30/4
0.4	.347	.301		20	20	30/4	30/4
0.6	.631	.441		20	20	30/4	30/4
0.8	.874	.589		20	2	30/4	30/4
1.0	1.029	.710		20	0	—	—
1.2	1.320	.845		20	0	—	—
1.4	1.468	1.071		20	0	—	—
1.6	1.882	1.168		20	0	—	—
STAGE II - DOSE SETTING DATA							
D*(1)	1.076	.726	Na	20	0	—	—
D*(2)	1.023	.752		20	0	—	—
D*(3)	1.056	.742		20	0	—	—
D*(4)	1.052	.722		20	0	—	—
D*(5)	1.036	.672		20	0	—	—
AVERAGES	(A1) 1.049	(A2) .723	(A3)	(T4) 100	(T5) "1"	TOTALS	

(d#5-t#40--3-13-79)

AAMI ^{60}Co DOSE SETTING WORKSHEET
INTERLAB STUDY (PHASE I)

Company Name [redacted] Prepared by [redacted] Date 24 MAY 1979

Product I.D. PHASE I - IC Sample Number #1 ____ #2 ____ #3 ____

Date Samples Rec'd. 27 April 1979 Date Samples Place in Incubation 2 May 1979

Date Sample Irradiated 4/16/79 Culture Medium: Type T.S.B

Spectrometer: Make Unicam Manufacturer Difco

Model SP 1805 Period of incubation 14 days

Date last calibration April 26th 1979 Incubation Temperature 32°C

STAGE I - DOSE SETTING DATA

	DOSIMETRY DATA			INCUBATION DATA			
TARGET DOSE (MRAD)	(C1) MEDIAN OF 3 RED PERSPEX	(C2) MEDIAN OF 3 AMBER PERSPEX	(C3) MEDIAN OF 3 NAT'L. BUREAU OF STD's	(C4) NO. OF TUBES INCUB-ATED	(C5) NO. OF POS. TUBES	DATE 1ST GROWTH DAY/MO	DATE LAST GROWTH DAY/MO
0.2	0.114	0.123		20	20	3/5	3/5
0.4	0.350	0.283		20	20	3/5	3/5
0.6	0.643	0.507		20	20	3/5	4/5
0.8	0.821	0.703		20	1	3/5	3/5
1.0	1.046	0.876		20	0	-	-
1.2	1.256	1.05		20	0	-	-
1.4	1.548	1.20		20	0	-	-
1.6	1.769	1.39		20	0	-	-
STAGE II - DOSE SETTING DATA							
D*(1)	1.036	0.857		20	0	-	-
D*(2)	1.017	0.820		20	0	-	-
D*(3)	1.032	0.807		20	0	-	-
D*(4)	1.013	0.803		20	0	-	-
D*(5)	1.010	0.807		20	0	-	-
AVERAGES	(A1) 1.0216	(A2) 0.819	(A3)	(T4) 100	(T5) 0	TOTALS	

(d#5-t#40--3-13-79)

Attachment 4

PROTOCOL

AAMI PHASE III EXPERIMENT

The purpose of the Phase III AAMI experiments is to evaluate the proposed dose-setting methodology by determining ^{60}Co sterilizing doses with actual products. The goal of the Phase III experiments is to have each of the participating companies determine a sterilizing dose on three lots of at least one product and, if possible, on three lots of two different products. For the first lot of each product, a Stage I experiment (incremental series) and a Stage II experiment (irradiation at D_*) will be performed. Only Stage II experiments will be performed on the second and third lots. To complete the analysis of the three lots, 360 samples are required.

The Phase III experiments will follow the same general procedures used in the previous studies. The following comments apply to the Phase III experiments.

PACKAGING

Whenever possible, the samples should be irradiated in production packaging. If this is not possible, the packaging method should approximate the density of production material.

DOSIMETRY

Each company will monitor dose delivery with their own dosimetry system(s). The dosimeters should be carefully placed to ensure that the absorbed dose is accurately determined.

IRRADIATION

In most situations, the irradiation procedure used for the Phase II experiment will be applicable to Phase III. The procedure should be thoroughly documented to ensure reproducibility between different experiments.

STERILITY TESTING

The procedure used for sterility testing should follow that used for the Phase I and Phase II experiments. Describe any significant changes on an addendum to the data sheets.