



White Paper

Further Enhancements to the Spreadsheet for Automated Calculation of Method VD_{max} Values

2/22/17

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Introduction

In previous White Papers (1,2), a spreadsheet-based method was described to calculate the four VD_{max} values (SIP=1.0 Verification Dose, SIP Verification Dose, SIP Dose Reduction Factor, and Dose Augmentation Value) for a given input average bioburden, sterility assurance level (SAL), and minimum sterilization dose. The purpose of this document is to describe a final set of enhancements to the spreadsheet prior to its discussion at the AAMI WG2 meeting in March.

Spreadsheet Enhancements

The following enhancements have been introduced into the VD_{max} Calculation Spreadsheet (VD_{max} CS):

- The footprint has been changed to a left/right format to more easily see the Calculation Output values; compare Figures 1 and 2.
- The most significant change to the VD_{max} CS is the handling of the calculation of the overall average bioburden value. In the previous version, Figure 1, the overall average bioburden is independently calculated by the user and it or the highest batch average value is then entered into the CS. The overall average bioburden calculation involves determining the three batch average bioburdens and then averaging these three values. Once this overall average bioburden is calculated, it must be compared to the three batch average bioburdens to determine which value is to be taken forward and entered into the CS. If the highest batch average bioburden is greater than 2x the overall average bioburden, this value is taken forward and entered into the CS rather than the overall average bioburden (Clause 9.2.4 of ANSI/AAMI/ISO 11137-2:2013).

In the current version of the CS, the three batch average bioburden values are entered into the CS and the overall average bioburden is automatically calculated and also compared to the three batch average bioburden values. Depending upon the results of the comparison, either the overall average bioburden or the highest batch average bioburden (if more than 2x the overall average) is carried forward to calculate the output VD_{max} values. Compare Figures 2 and 3.

- A provision has been made to use the CS for sterilization dose establishment of either multiple product batches or a single production batch. If "Single" is entered into this input cell, the cells for entry of Batch #2 and Batch #3 average bioburden values are blacked out and the message on the outputs panel changes to "Results Are for a Single Production Batch". See Figure 4.
- A cell has been added for the entry of an optional calculation identifier such as a validation number, batch number(s), etc.
- To avoid confusion and/or possible misuse, the SIP Dose Reduction Factor is no longer shown as a CS output. If an SIP value <1.0 is input, the appropriate SIP <1.0 VD_{max} Verification Dose is automatically calculated and shown.
- When hovering the mouse pointer over a Calculation Input cell, instructions/requirements specific to that cell pop-up. A different approach is now used for these pop-ups to minimized covering other cells in the CS.

- Each time the CS file opens, a specific set of "base case" input values are automatically entered into the Calculation Inputs panel. These inputs then result in a set of "base case" values in the Calculation Outputs panel. Also, a "Welcome" box appears on the screen with a brief instruction. The purpose of this feature is:
 - a) Even though a complete spreadsheet validation will be performed and documented prior to its release, it is desirable to have an easy functional check prior to each use. The base case input values (shown in Figure 2) yield a characteristic set of output values that can be checked prior to use of the CS giving a real-time verification of the correct function of the CS. See Figure 5 for a screenshot of the "Welcome" box and its instruction.
 - b) The base case input values, other than the bioburden, were chosen to represent a set that is commonly used: 10^{-6} SAL, substantiation of a 25 kGy sterilization dose, SIP = 1.0, and 10 product items irradiated in the verification dose experiment.

Conclusions

The VD_{max} Value Calculation Spreadsheet described in this White Paper has been incrementally improved compared to the previous version. The addition of the automated calculation of the overall average bioburden increases capability of the CS and ensures that the proper average bioburden value is used for subsequent calculations. This spreadsheet-based approach to calculation of Method VD_{max} values remains a work in progress and its final embodiment in the US will be defined by the AAMI Radiation Sterilization Working Group - ST/WG 02.

1. Development of a Spreadsheet for Automated Calculation of Method VD_{max} Verification Dose, SIP Dose Reduction Factor, and Dose Augmentation Values. 11/14/16
[White Paper #1](#)
2. Refinement and Performance Testing of the Spreadsheet for Automated Calculation of Method VD_{max} Values. 12/7/16
[White Paper #2](#)

Figure 1. Screenshot of the previous revision of the VD_{max} CS.

Spreadsheet for Calculation of VD_{max} Values	
Calculation Inputs	
Average Bioburden	1,000.00
Sterility Assurance Level	-6.0
Minimum Sterilization Dose (kGy)	25.0
SIP	1.00
Number of Product Items for Irradiation	10
Calculation Outputs	
Calculation Bioburden Value	1,000.00
Number of Product Items for Irradiation	10
SIP=1.0 VD_{max} Verification Dose (kGy)	8.1
SIP VD_{max} Verification Dose (kGy)	NA - SIP=1.00 Input
SIP Dose Reduction Factor	2.02
Dose Augmentation Value (kGy)	3.4
Draft Version - For Evaluation Only - Validation in Progress	
12/1/16 2:58 PM	
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/Users/jbk/Google Drive/VDmax Spreadsheet/[VDmax_Calc_Rev6_multi_120116.xlsx]VDmax Values Calculator	

Figure 2. Screenshot of the current version of the VD_{max} CS.

Calculation Spreadsheet (CS) for Method VD_{max}^{SD-S} Values			
Hover mouse pointer over green-highlighted cells for instructions. Select cell to enter a value. The "Arrow Down" and "Enter" keys cycle through the cells that require an entry. A Calculation Identifier is optional.		Verify entries in the green-highlighted Calculation Input cells prior to recording, printing, or saving Calculation Outputs.	
Calculation Identifier (Optional):		Results Are For Multiple Production Batches	
Validation Type - Multiple or Single Production Batch?	Multiple		
Calculation Inputs		Calculation Outputs	
Batch #1 or Single Batch Average Bioburden	1,000.0	Calculation Bioburden Value	1,000.0
Batch #2 Average Bioburden	1,000.0	Number of Product Items for Irradiation	10
Batch #3 Average Bioburden	1,000.0	SIP = 1.0 Verification Dose (kGy)	8.1
Overall Average Bioburden	1,000.0	SIP < 1.0 Verification Dose (kGy)	NA - SIP = 1.0 Input
Sterility Assurance Level (SAL)	6.0	Dose Augmentation Value (kGy)	3.4
Calculated Minimum Sterilization Dose (kGy)	24.9	Draft Version - For Evaluation Only - Validation in Progress	
Selected Sterilization Dose (kGy)	25.0	2/22/17 10:49 AM	
SIP	1.00	/Users/jbk/Google Drive/VDmax Spreadsheet/VDmax CS/[VDmax_CS_021917_macro_PC.xlsm]VDmax CS	
Number of Product Items for Irradiation	10	©2016 John B. Kowalski Ph.D. and SteriPro™ Advanced Consulting	

Figure 3. Screenshot of the version of the VD_{max} CS showing the situation where the average bioburden of one production batch is greater than 2x the overall average bioburden. Note that the batch average of 1000 is used for the calculation rather than the overall average of 466.7.

Calculation Spreadsheet (CS) for Method VD_{max}^{SD-S} Values			
Hover mouse pointer over green-highlighted cells for instructions. Select cell to enter a value. The "Arrow Down" and "Enter" keys cycle through the cells that require an entry. A Calculation Identifier is optional.		Verify entries in the green-highlighted Calculation Input cells prior to recording, printing, or saving Calculation Outputs.	
Calculation Identifier (Optional):		Results Are For Multiple Production Batches	
Validation Type - Multiple or Single Production Batch?	Multiple		
Calculation Inputs		Calculation Outputs	
Batch #1 or Single Batch Average Bioburden	150.0	Calculation Bioburden Value	1,000.0
Batch #2 Average Bioburden	250.0	Number of Product Items for Irradiation	10
Batch #3 Average Bioburden	1,000.0	SIP = 1.0 Verification Dose (kGy)	8.1
Overall Average Bioburden	466.7	SIP < 1.0 Verification Dose (kGy)	NA - SIP = 1.0 Input
Sterility Assurance Level (SAL)	6.0	Dose Augmentation Value (kGy)	3.4
Calculated Minimum Sterilization Dose (kGy)	24.9	Draft Version - For Evaluation Only - Validation in Progress	
Selected Sterilization Dose (kGy)	25.0	2/22/17 10:48 AM	
SIP	1.00	/Users/jbk/Google Drive/VDmax Spreadsheet/VDmax CS/[VDmax_CS_021917_macro_PC.xism]VDmax CS	
Number of Product Items for Irradiation	10	©2016 John B. Kowalski Ph.D. and SteriPro™ Advanced Consulting	

Figure 4. Screenshot of the current version of the VD_{max} CS showing its use for a single production batch.

Calculation Spreadsheet (CS) for Method VD_{max}^{SD-S} Values			
Hover mouse pointer over green-highlighted cells for instructions. Select cell to enter a value. The "Arrow Down" and "Enter" keys cycle through the cells that require an entry. A Calculation Identifier is optional.		Verify entries in the green-highlighted Calculation Input cells prior to recording, printing, or saving Calculation Outputs.	
Calculation Identifier (Optional):		Results are For A Single Production Batch	
Validation Type - Multiple or Single Production Batch?	Single		
Calculation Inputs		Calculation Outputs	
Batch #1 or Single Batch Average Bioburden	1,000.0	Calculation Bioburden Value	1,000.0
		Number of Product Items for Irradiation	10
Overall Average Bioburden	1,000.0	SIP = 1.0 Verification Dose (kGy)	8.1
Sterility Assurance Level (SAL)	6.0	SIP < 1.0 Verification Dose (kGy)	NA - SIP = 1.0 Input
Calculated Minimum Sterilization Dose (kGy)	24.9	Dose Augmentation Value (kGy)	3.4
Selected Sterilization Dose (kGy)	25.0	Draft Version - For Evaluation Only - Validation in Progress	
SIP	1.00	2/22/17 10:50 AM	
Number of Product Items for Irradiation	10	/Users/jbk/Google Drive/VDmax Spreadsheet/VDmax CS/[VDmax_CS_021917_macro_PC.xlsm]VDmax CS	
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Figure 5. Screenshot of the "Welcome" box and its instruction.

Calculation Spreadsheet	
Hover mouse pointer over green-highlighted cells for instructions. Select cell to enter a value. The "Arrow Down" and "Enter" keys cycle through the cells that require an entry. A Calculation Identifier is optional.	
Calculation Identifier (Optional):	
Validation Type - Multiple or Single Production Batch?	Multiple

Welcome to the Method Vdmax Calculation Spreadsheet

Before proceeding, verify that the Calculation Outputs are from top to bottom: 1000.0, 10, 8.1, NA - SIP = 1.0 Input, and 3.4. If one or more of these outputs are different or missing, do not use the Calculation Spreadsheet.

Calculation Inputs		Calculation Outputs	
Batch #1 or Single Batch Average Bioburden	1,000.0	Calculation Bioburden Value	1,000.0
Batch #2 Average Bioburden	1,000.0	Number of Product Items for Irradiation	10
Batch #3 Average Bioburden	1,000.0	SIP = 1.0 Verification Dose (kGy)	8.1
Overall Average Bioburden	1,000.0	SIP < 1.0 Verification Dose (kGy)	NA - SIP = 1.0 Input
Sterility Assurance Level (SAL)	6.0	Dose Augmentation Value (kGy)	3.4
Calculated Minimum Sterilization Dose (kGy)	24.9	Draft Version - For Evaluation Only - Validation in Progress	
Selected Sterilization Dose (kGy)	25.0	2/22/17 12:20 PM	
SIP	1.00	/Users/jbk/Google Drive/Vdmax Spreadsheet/Vdmax CS/[Vdmax_CS_022217_macro_PC.xism]Vdmax CS	
Number of Product Items for Irradiation	10	©2016 John B. Kowalski Ph.D. and SteriPro™ Advanced Consulting	