

ISO 11138: 2017 SERIES OF GUIDANCE DOCUMENTS RECENTLY REVISED

Published in March 2017, the ISO 11138 documents have undergone an update. While most of the changes made to the documents relate to verbiage and reformatting, there were several changes which required review specific to how they relate to Crosstex' Biological Indicators (BIs) and manufacturing processes. Below is a summary of the significant changes and the impact they have or potentially have related to our biological based products.

ISO 11138-1:2017 Sterilization of healthcare products – Biological indicators Part 1: General requirements

This document is applicable to all biological indicator and inoculated carrier products manufactured by Crosstex.

Section 6 – *Determination of Population and Resistance* underwent the largest change. The changes included:

- 6.1.2 now references ISO 14937 Sterilization of health care products – General requirements for characterization of a sterilizing agent and the development, validation and routine control of a sterilization process for medical devices. Where the resistance characteristics of a BI intended for a sterilization process are not specified in any subsequent part of ISO 11138, ISO 14937 shall apply for the specific critical variables of that sterilization process.
- 6.3.2 was expanded to include clarification associated with verification results obtained for the population of BIs. Confirmatory testing which results in a population which is within 50% to 300% of the manufacturer's stated nominal population is considered acceptable. Further, the verbiage includes the confirmatory population yielding a count below the minimum population specification as defined in the subsequent documents is acceptable if within the range of 50% to 300% of the manufacturer's certified value.

For example, ISO 11138-2: 2017 Sterilization of health care products – Biological indicators – Part 2: Biological indicators for ethylene oxide sterilization processes outlines a minimum population of 1.0×10^6 . If the certified population of a lot is 1.8×10^6 , the acceptable range for confirmatory population results would be 0.9×10^6 to 5.4×10^6 as this is 50% to 300% of the certified value. Thus, while a population of 0.9×10^6 does not meet the minimum population outlined in ISO 11138-2, the count is acceptable as it is within the range of 50% to 300%.

- 6.4.3 was revised in a similar manner to 6.3.2, whereas, the *D* value shall be within $\pm 20\%$ of the certified *D* value. Confirmatory testing which results in a *D* value which is within $\pm 20\%$ is considered acceptable. Additional verbiage indicates a confirmatory test which results in a *D* value which is below the minimum *D* value outlined in the subsequent documents is acceptable if the obtained value is within $\pm 20\%$ of the stated value.

For example, ISO 11138-3: 2017 Sterilization of health care products – Biological indicators – Part 3: Biological indicators for moist heat sterilization processes outlines a *D* value equal to or greater than

1.5 minutes. If the certified *D* value of a lot is 1.7 minutes, the acceptable range for confirmatory results would be 1.4 to 2.0 minutes. Thus, while the *D* value of 1.4 minutes does not meet the minimum requirement outlined in ISO 11138-3, the *D* value is acceptable as it is within the range of $\pm 20\%$.

For sections 6.3.2 and 6.4.3, Crosstex interprets the verbiage to clearly outline that the confirmatory test results should not be considered a re-certification of the manufacturer's labeled claims but rather verification of said claims.

Section 7 – Culture conditions

- 7.4 – *Software validation* and 7.5 – *Incubation time using detection system* are new to the document and reflect current practice associated with incubators with software and/or use of detection systems.

Annexes

- Annex B – *Determination of growth inhibition by carriers and primary packaging materials exposed to sterilization processes* – The number of samples was increased to eighteen (18).
- Annex E – *Survival-kill response characteristics* – Verbiage was included relating to allowance of testing an additional 100 samples should a single negative in a survival test or single positive in a kill test be obtained. The document now outlines “If no additional unexpected results are obtained, the survival and kill times are confirmed”. This change better aligns with the language previously outlined in the USP where an allowance for additional testing had been historically included.

ISO 11138-2: 2017 Sterilization of health care products – Part 2: Biological indicators for ethylene oxide sterilization processes

This guidance document applies to the following product codes: BG-106, BG-506, STN-062xy, DS-100, BG-106D, DN18-06, SWN-06, THN-06(P), SCE-06, SCA-100, VBA-106/SUN-06 and higher population levels.

Section 9 – Population and resistance

- 9.5 continues to specify a *D* value of not less than 2.5 minutes at 54°C; however, now requires this result only where test gas mixtures are utilized. Additionally, the specification for *D* value testing at 30°C was removed from this section.
- 9.6 has been added and specifies a *D* value of not less than 2.0 minutes 54°C where 100% EO gas is utilized.

The rationale for the additional *D* value specification at 54°C and the deletion of the *D* value specification at 30°C are explained in the newly added Annex B (Informative) – *Rationale for the*

inclusion of a second minimum D value specification as a result of changes to the test gas used to evaluate resistance and deletion of the requirement for a minimum D value at 30°C.

This Annex includes reference to a round robin study related to resistance testing performed by three (3) US-based biological indicator manufacturers where *D* values were determined utilizing a gas mixture and 100% EO. The study was conducted as a result of changes to the US EPA Clean Air Act effective December 31, 2014. While both Crosstex and the former NAMSA Products Division (part of Crosstex since 2016) participated in the round robin study, the results were not included as no significant difference in the determined *D* values when utilizing the gas mixture versus 100% EO was noted. NAMSA Products Division had switched from use of a gas mixture to 100% EO in late 2010. Crosstex has historically always utilized 100% EO, thus the change to the Clean Air Act did not impact our BIs or manufacturing process.

ISO 11138-3: 2017 Sterilization of health care products – Biological indicators – Part 3: Biological indicators for moist heat sterilization processes

This guidance document applies to the following product codes: BS-105, BS-106, STS-062xy, DS-100, BS-105D, BS-106D, DS18-06, SWS-06, THS-06(P), SA1-15-05, SA1-15-06, SA1-50-05, SA1-50-06, OS1-50-06, SCS-05, SCS-06, SCS-100, SCS-106, SVT-050, SVT-056, VGS-105/SUS-05 and higher population levels

Two changes to note associated with ISO 11138-3:

- Section 9.5 – The *z* value temperature range was expanded from 110°C to 130°C to 110°C to 138°C.

Crosstex will retain the temperatures historically utilized for the *z* value calculation (118°C, 121°C and 126°C) as these temperatures remain within the expanded range.
- Annex A (normative) – *Method for determination of resistance to moist heat sterilization* – The requirement for the post vacuum to reach 10 kPa or less within 1 minute was changed to 100 kPa within 10 seconds or less. This change did not have an impact as the resistometers utilized by Crosstex are capable of meeting this requirement.

ISO 11138-4: 2017 Sterilization of health care products – Biological indicators – Part 4: Biological indicators for dry heat sterilization processes

This guidance document applies to product code BG-106DH.

Section 9 – Population and resistance

- 9.5 was changed to require a minimum D_{160} value at of not less than 2.0 minutes. The minimum *D* value was previously 2.5 minutes.

This change broadens Crosstex' ability to meet the requirements of this document. Crosstex will continue to offer Product Code BG-106DH which will claim compliance to ISO 11138-4. Product Code

BG-106 will be certified with dry heat resistance data; however, the *D* value at 160°C may be less than 2.0 minutes and hence compliant with ISO 11138-1 and 11138-2 only.

ISO 11138-5: 2017 Sterilization of health care products – Biological indicators – Part 5: Biological indicators for steam and formaldehyde sterilization processes

No significant changes were made to this document. At this time, Crosstex' biological indicators do not meet the requirements of this document in regards to resistance.

Based on the review of the updated ISO 11138 series of documents, the compliance of Crosstex' BIs and inoculated carriers has not changed. The BIs and inoculated carriers manufactured by Crosstex will remain compliant with ISO 11138-1, ISO 11138-2, ISO 11138-3 and ISO 11138-4. If you have any questions regarding the changes to the ISO 11138:2017 documents, our review or compliance status, please do not hesitate to contact us for further information.

Best regards,



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