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The Gas Plasma Sterilization

Hideharu Shintani*

Faculty of Science and Engineering, Chuo University, Tokyo, Japan

The gas plasma sterilization is now keenly interested among mainly engineering researchers, however their papers have significant mistakes because their background is outside of microbiology and sterilization. They are insufficient knowledge of microbiology and sterilization. Many mistakes can be seen in their papers, books and presentations. The microbiological and chemical researchers are not so many involved in the gas plasma sterilization research. In 2011, Sakudo and Shintani have published entitled Sterilization and Disinfection by Plasma, Sterilization Mechanisms, Biological and Medical Applications from NOVA Science Publishers and remarked in the book that the published books until now have many mistakes in their understanding and interpretation of microbiology and sterilization. In the NOVA Book, Shintani remarked one chapter entitled Several Points to Consider When Conducting Plasma Experiments for their benefit. But no consideration and correction can be made since then.

One example of the mistaken interpretation of the engineering researchers is 6log. They misunderstand 6-6=0. Six log reduction does not mean zero,but 10°=1 and the possibility of survival at SAL of 10° is 63%.

Six log reduction is the requirement of absolute bioburden method in ISO 14161, which address to BI (biological indicator) user only. According to the absolute bioburden method in ISO 14161, the initial population of 10°CFU/carrier reduces 6 log reduction and it attains SAL of 10^{-6}. SAL (sterility assurance level) of 10^{-6} is so-called 6 log reduction. The reason of initial population is 10°CFU/carrier level and it is a bioburden level of a few CFU level (10°CFU/carrier level). In sterilization validation the real target to sterilize is not BI, but biooburden and no 10^{6} CFU/carrier of bioburden is existed in the real status. Following the absolute bioburden method it is required 6 log reduction to BI user in ISO i4i61 because initial population is 10°CFU (colony forming unit) level and SAL of 10^{-6}, so this is 6 log reduction requirement. SAL of 10^{-6} is definitely defined. Bioburden has a few CFU/carrier, so 10°CFU/carrier is defined as a bioburdeen level and SAL of 10^{-6}, thus this is an absolute bioburden method and 6 log reduction can be attained. Bioburden is the sort and number of viable microorganisms in/on the products. From 10°CFU/carrier to SAL of 10^{-6} is 6 log reduction. 10^{-6} is the closest number to zero, which defined from the stochastics in ISO 11137-1.

To achieve 6 log or 12 log reduction, survivor curve must be straight line. BI manufacturers are required an initial population of 10^{6} CFU/carrier, so 10^{6} CFU down to SAL of 10^{-6} as a whole 12 log reduction is required in ISO 11138-1 as an overkill method and sterilization validation. Initial population of 10^{6} CFU/carrier to SAL of 10° is not recognized as 6 log reduction in ISO 14161. ISO 11138-1 is for BI manufacturer and ISO 14161 is for the BI user and most of researcher must obey ISO 14161, BI user requirement and sterilization validation. In ISO 14161, overkill method is described together with another method, but in ISO 11138-1, only overkill method is described, which is the difference between ISO 1138-1 (BI manufacturer) and ISO 14161 (BI user).

Stacking is mistaken as clumping (Figure 1 and 2). And existence of clumping in BI (biological indicator) is a serious problem. It should not be free from any clumping to attain a straight survivor curve from an initial population of 10^{6} CFU/carrier to SAL of 10^{-6}.This means 12 log reduction and this is required in ISO 14161, ISO 11138-1 and sterilization validation. Twelve log reduction is required to BI manufacturer in ISO 11138-1, and it is not always required to BI user in ISO 14161. To attain 12 log reduction, it is necessary to avoid clumping in BI, otherwise obtained only curved (tailing) survivor curve (Figure 3) and cannot attain even SAL 10^{0}, indicating sterilization validation was

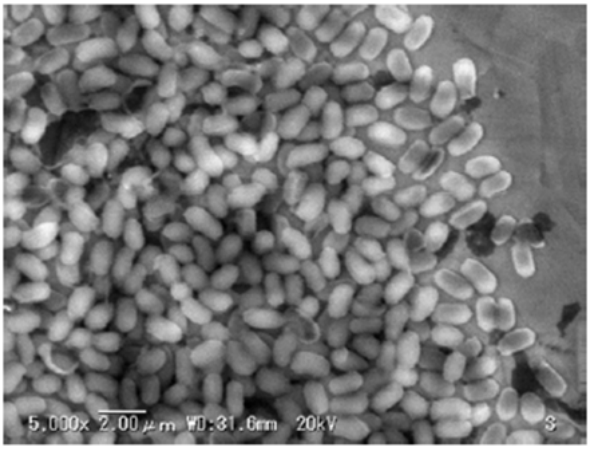

Figure 1: SEM observation of pile of clumping

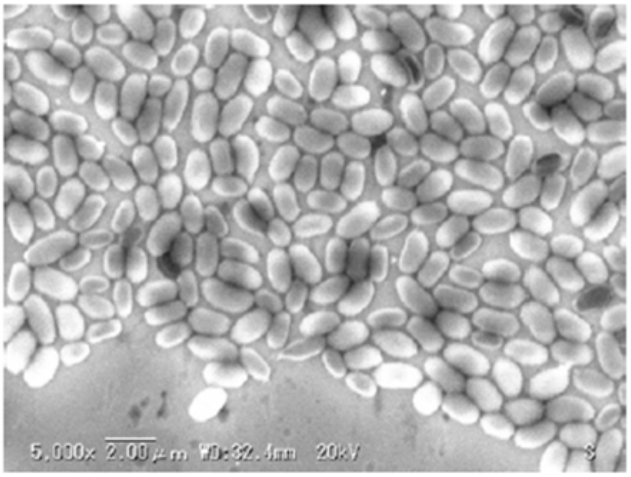

Figure 2: SEM observation free from clumping

***Corresponding author:** Hideharu Shintani, Faculty of Science and Engineering, Chuo University, 1-13-27, Kasuga, Bunkyo, 112-8551, Tokyo, Japan, Tel: +81425922336, Fax: +81425922336, E-mail: shintani@mail.hinocatv.ne.jp

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failed. Sterilization validation is required in an official document and authority requires sterilization validation by conducting inspection. Straight line of survivor curve was presented in Figure 4 and 3 using BI presented in Figure 2 free from clumping. This slope can be attained straight line from 10^6 CFU/carrier to SAL of 10^{-6} (Figure 3 and 4).

It is quite important to note that *D* value (decimal reduction value, the time and dose to decrease 1 log) is only one per one microorganism. So often tailing phenomenon can be explained from the difference of kinetics and put *D* values to each kinetic line indicating more than one *D* value per one microorganism, which is serious mistake. Why clumping causes the tailing? Because penetration depth of gas plasma is quite shallow (10-20 nm) except oxygen gas plasma and if spore has multilayer, only surface of first layer killed at the beginning and the killing of the second or third layer is delayed by the interference of the first layer, therefore tailing curve is observed. Tailed survivor curve is not the exact survivor curve because BI of *Geobacillus stearothermophilus* ATCC 7953 is not the spore presenting the tailed survivor curve. The magnitude of *Geobacillus stearothermophilus* ATCC 7953 is 1 μm X 3 μm [1].

As gas plasma penetration is so shallow, so only bioburdern can be killed and products itself was not damaged in the exact status. To be killed bioburden and no deterioration,of the material is called simultaneous attainment of material/functional compatibility and SAL of 10^{-6}. Bioburden is scattering in the surface of the product and 10-20 CFU/500L [2,3] without clumping is the real estimated bioburden. This amount of bioburden is scattered in larger area of product than BI, so no clumping is observed, thus no tailing phenomenon is observed as far as using bioburden following ISO 14161 (absolute bioburden method).

In order to avoid mistaken interpretation among engineering researcher's papers, we, microbiologist and chemist, need to contribute to convey correct information and correct mechanisms to the engineering researchers. Correct sterilization mechanisms of spores are recently obtained and presented in Pharmaceutical Regulatory Affairs J. Including them the coming book has quite useful information to gas plasma researcher, ISO information and validation study and so on.

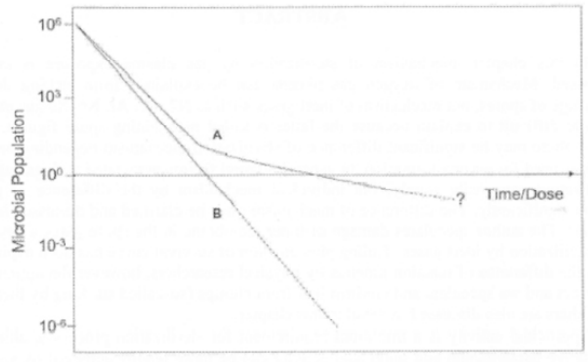
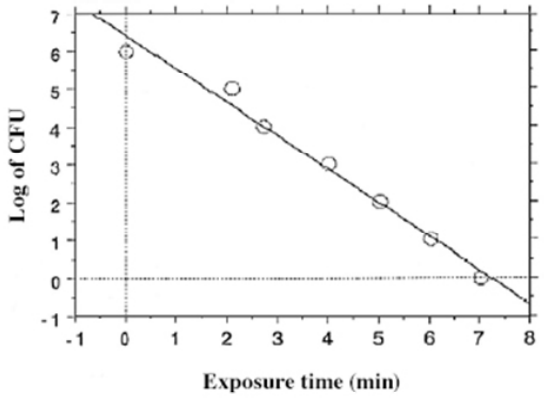


Figure 3: Straight line and curved tailing survivor curve



According to the use of clump free BI (Figure 2), from initial population of 106 CFU/carrier to SAL 10-1 straight line can be experimentally confirmed. For 6 log reduction, it takes 7 min, indicating D value is 1.2 min.

Figure 4: Straight line of survivor curve using BI from Figure 2

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