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Deinococcus Detection: Why Relevant Microbial Libraries are Critical for the Medical Device Industry

A contamination event at a sterile pharmaceutical or medical device company could prove to be disastrous for operations, company finances, brand reputation, and of course, the patient. Companies mitigate the risk of contamination by implementing a contamination control strategy which typically includes either aseptic processing or terminal sterilization. According to the FDA (https://datadashboard.fda.gov/ora/cd/recalls.htm), there is an increasing number of medical device recalls, including inadequately sterilized medical devices that pose a risk of transmitting pathogens and resulting in patient infections.

Radiation sterilization has some advantages over other methods as it is very quick and effective, doesn't damage products like heat can, or leave unwanted residues like ethylene oxide. Single-use prepackaged medical devices are primarily sterilized using gamma or electron beam radiation. Gamma radiation can penetrate deep into a box of orthopedics and takes hours to complete, but it can have deleterious effects on some plastics, despite being relatively low temperature. Electron-beam radiation imparts the dose much faster (in seconds) but cannot penetrate dense packaging.

Regardless of the radiation method used, some microorganisms, like the *Deinococcus* genus, may still pose a risk to the final product as they can be resistant to radiation. The type of microorganism is indicative of its resistance to radiation. It becomes critical then to have a complete and accurate understanding of the manufacturing flora. This knowledge is imperative to the validation as the radiation dose will be calculated based on resident bioburden.

Moreover, Health Canada states:
"It is important that the level of microbial quality be critically evaluated first, in order that the use of ionizing radiation may be rationally applied. A knowledge of the microbial quality of the raw materials and the manner in which it was achieved may have significant implications. Reduction of the microbial bioburden of raw materials will, in general, allow a reduction in the radiation dose to the final product. It thus reduces the effects of ionizing radiation on the product. At the same time, attention must be paid to the formulation in order that the most stable form of the product is manufactured. This will allow a greater radiation dose and provide for a greater degree of Sterility Assurance.

It is important to track the species as well as the number of organisms in order that the radiation dose delivered to the product continues to provide the same Sterility Assurance Level.[1]*"*

In 2019, one of the largest global medical device companies experienced a sterility failure caused by *Deinococcus wulumuqiensis*. This is not surprising given that the Deinococcus genus shows remarkable resistance to damage caused by ionizing radiation, desiccation, UV radiation, oxidizing agents, and electrophilic mutagens. Not only can it grow continuously in the presence of chronic radiation, but it can also survive acute exposures to gamma radiation without dying or undergoing induced mutation. *D. wulumuqiensis* is extremely radioresistant, more so than most species in the *Deinococcus* genus, and has been shown to withstand at least 15 kGy. For comparison, *Escherichia coli* is killed by a dose of only 1-2 kGy. Similarly, vegetative cells of *Bacillus* spp. spores show a 5-order-of-magnitude decrease in viability following acute exposure of 2-10 kGy.

There is an increased risk of nonsterile medical devices due to *Deinococcus* because of the difficulty in identifying it with current microbial identification systems and the organism's increased D-value to radiation. D-value in this case refers to the amount of dose required to achieve a 1-log population reduction. How would the Sterility Assurance Level (SAL) or Probability of a Non-sterile Unit (PNSU) be affected by the presence of such an organism? Who is responsible if the SAL/PNSU drops below 10^{-6}?

Moreover, if the microorganism was recovered during routine sterility testing but incorrectly identified, it could interfere with an Out of Specification investigation and delay or entirely derail the root cause determination.

Deinococcus and other radiation-resistant organisms are ubiquitous. *Deinococcus wulumugiensis* has been identified hundreds of times from a total of 55 different global facilities by Charles River's Accugenix® services. Table 1 shows the presence or absence of *Deinococcus wulumugiensis* and other radiation-resistant organisms in the libraries of current microbial ID systems. If the absent organism cannot be correctly identified by that system it will result in either no ID or a wrong ID. There are three organisms, including *D. wulumugiensis*, that only Accugenix® services are able to identify, clearly demonstrating broad library coverage.

Table 1. Presence of radiation-resistant microorganisms in libraries of ID systems

Name	Vitek®2	Vitek®MS	Biolog Gen III	Bruker	MicroSEQ®	Charles River Accugenix®
Methylobacterium radiotolerans		√	√	√	√	√
Acinetobacter radioresistens	√	√	√	√	√	√
Deinococcus wulumuqiensis						√
Deinococcus radiopugnans			√		√	√
Deinococcus radiophilus			√		√	√
Deinococcus radiodurans			√		√	√
Kineococcus radiotolerans						√
Microbacterium radiodurans						√

Microbial identifications by any of Charles River's global Accugenix® laboratories, with our robust and accurate services, can give you the confidence of knowing which microorganisms are present in your facility. Fast and reliable services can speed up your timelines and investigations, allow you to make informed decisions about your operations, decrease contamination risk, and save valuable QC resources. Using Accugenix® services is not only reliable and cost effective, but could save you the catastrophe of non-sterile products and recalls.

Learn more about Accugenix® microbial identification services at www.criver.com/accugenix.

[1]Health Canada. Process Validation: Irradiation Sterilization for Pharmaceuticals [Internet]. aem. 2001 [cited 2019 Oct 1]. Available from: https://www.canada.ca/en/health-canada/services/drugs-health-products/compliance-enforcement/good-manufacturing-practices/validation/irradiation-sterilization-pharmaceuticals.html

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