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Irradiation Studies of *Cryptococcus* Isolated from Devices

To the Editor:

The article in *MD&DI* by Ed Arscott et al. ("Validating Radiation Sterilization in a Global Marketplace," February 1999) discussed the model population of Whitby and Gelda in reference to the validation procedure known as AAMI method 1 (ANSI/AAMI/ISO 11137). Examination of the log-reduction values in kilogray as set forth in AAMI method 1 (Table 7) reveals that, within limits, the Whitby and Gelda model population is based on levels of radiation traditionally required for bacterial spores—doses far above what is normally expected from non-spore-forming organisms. Although identification of bioburden isolates is not routinely performed, any bioburden count generally assumes the presence of the spores of the genus *Bacillus*—for example, spores of such species as *Bacillus pumilus*, the original biological indicator for radiation resistance. Thus, the appearance of nonsporulating vegetative organisms (gram-positive cocci, gram-negative rods, yeasts) recovered during AAMI quarterly verification audits are often suggestive of laboratory contamination. During an out-of-specification investigation involving approximately 60 out of 100 positive sterility tests, it occurred to us that there is a lack of published data on radiation resistivity for the organisms found during our investigation.

In this regard, we have isolated from verification audits species of the genus *Cryptococcus*, an organism that was not recovered as part of classical bioburden-detection techniques. Reference data on yeasts are limited and widely variable. For example, the D-10 value of the yeast *Saccharomyces cerevesiae* has been given as 0.5 kGy (S.S. Block, *Disinfection, Sterilization, and Preservation* [Philadelphia, Lea & Febiger, 4th ed., 1990]). To learn more about the radioresistance of the cryptococci that we have isolated, we performed irradiation experiments with pure culture suspensions at doses ranging from 1.0 to 10.0 kGy. D-values were calculated by the method of Prince (HN Prince, *Applied Microbiology* 36 (1978): 392). Bacillus isolates from dose-audit sterility tests in our laboratory are included for comparison. The data appear below:

Organism	D-Value (kGy)
C. laurentii (strain 1305)	3.1
C. laurentii (strain 1306)	2.7
C. albidus (strain 4157)	2.0
C. uniguttilans (strain 4460)	1.4
B. megaterium (strain 1289)	2.9
B. subtilis (strain 1289)	2.2
B. pumilus (strain 1299)	1.8
B. pumilus (strain 1300)	1.0
B. macerans (strain 1290)	0.6
Control	
B. pumilus (strain E-601) (ATCC No. 27142) (USP 19; literature)	1.5–1.8

Other studies in our lab with the genus *Cryptococcus* have revealed variations in growth rate from 3 to 7 days (bioburden test) to ≥10 days (outgrowth in the 14-day sterility test). It also appears that recovery is improved in broth culture relative to agar plating techniques. It is inferred that the recovery of cryptococci is enhanced by elimination of mixed flora by sublethal irradiation, thereby explaining why such organisms were detected during the sterility verification test phase of the validation.

The habitats for members of the genus *Cryptococcus* include air, soil, bird feathers, animal dung, fruit, water, tropical plants, decaying plant material, insects, surface-coating components, and fermenting fruit juice. Manufacturing, storage, and packaging areas must have a microbial control program that is alert to the possibility of *Cryptococci* spp. as well as other relevant organisms.

We have learned that the genus *Cryptococcus* must be considered a radioresistant organism when found in medical device bioburden isolates. Additional microbiological, biochemical, disinfectant, and ecological studies are warranted on these and other strains. These findings further emphasize that bioburden methods must be optimized for isolating yeasts in the presence of the normal bacillary and fungal mixed flora of typical device bioburden. Recent data suggest that cryptococci are

an important source of environmental contamination that may lead to failure of irradiation verification experiments.

Daniel L. Prince and J. Chris Knutsen
Gibraltar Laboratories Inc.
Fairfield, NJ
Rodney Parker, Stryker Instruments Inc.
Kalamazoo, MI

Penetrating GPOs Requires Time, Effort

To the Editor:

Richard S. Cohen's article, "The Narrowing Distribution Funnel: How to Get Your Medical Device to Market" (*MD&DI*, February 1999), was informative but incomplete in its suggested strategies.

Group purchasing organizations (GPOs) are increasingly awarding contracts to major suppliers and virtually shutting out medium- to smaller-sized manufacturers. In addition to Cohen's thoughtful recommendations, companies must have a focused national account strategy or else chances of success are very limited.

They must also realistically identify which of the several hundred healthcare GPOs to target, and be certain that their national account representation can penetrate those specific GPOs. Understand, it will require six months to a year to finalize an agreement with most GPOs—provided they have the right representation. Be prepared to invest the time.

As a former manager of two of healthcare's largest proprietary GPOs, I can testify that unless a small company had representatives who knew me or members of my staff personally or professionally, the odds of ever gaining an audience were extremely limited.

That was 10 years ago. In today's "narrowing distribution funnel," as Richard Cohen so accurately describes it, the window of opportunity is much narrower.

For a company that cannot underwrite a full-time position (reporting directly to senior management), there are a number of effective "outsourcing" national accounts representatives to consider.

Dick Ambrose, The Ambrose Group Inc.
San Juan Capistrano, CA