

STEPTOE & JOHNSON^{LLP}

ATTORNEYS AT LAW

Seth Goldberg
202.429.6213
sgoldberg@steptoe.com

1330 Connecticut Avenue, NW
Washington, DC 20036-1795
Tel 202.429.3000
Fax 202.429.3902
steptoe.com

July 6, 2007

Via HAND DELIVERY

Information Quality Guidelines Staff
US EPA - Room M1200
1300 Pennsylvania Ave. NW
Washington, DC 20008

Re: **Information Quality Act Request for Correction**

To Whom it Concerns:

This request for the correction of information is submitted on behalf of the Efficacy Working Group under the Information Quality Act¹ and the implementing guidelines issued, respectively, by the Office of Management and Budget (OMB)² and the U.S. Environmental Protection Agency (EPA).³ The Efficacy Working Group is composed of seven registrants of disinfectant products, Clorox, Ecolab, Lonza, Mason Chemical Company, Reckitt Benckiser, SC Johnson, and Stepan Company, all of which are impacted by the information quality issue set forth below.

EPA's Guidelines implementing the Information Quality Act expressly contemplate the correction of information disseminated by EPA that falls short of the "basic standard of quality, including objectivity, utility, and integrity," established either by EPA's own Guidelines or those issued by OMB. The Efficacy Working Group seeks the correction of EPA's required use of the Association of Official Analytical Chemists (AOAC) Use-Dilution Test (UDT) method for the bacterium *Pseudomonas aeruginosa*.⁴ The UDT is a qualitative, carrier-based laboratory test which EPA's Office of Pesticide Programs Antimicrobial Division imposes on all registrants of certain products.

¹ Section 515(a) of the Treasury and General Government Appropriations Act for Fiscal Year 2001, P.L. 106-554; 44 U.S.C. § 3516 (notes).

² OMB Guidelines for Ensuring and Maximizing the Quality, Objectivity, Utility, and Integrity of Information Disseminated by Federal Agencies (hereinafter "OMB Guidelines"), 67 Fed. Reg. 8452 (Feb. 22, 2002).

³ Guidelines for Ensuring and Maximizing the Quality, Objectivity, Utility, and Integrity, of Information Disseminated by the Environmental Protection Agency, EPA/260R-02-008 (October 2002) (hereinafter "EPA Information Quality Guidelines").

⁴ AOAC Official Method 964.02, Testing Disinfectants against *Pseudomonas aeruginosa*, Use-Dilution Method, First Action 1964, Revised 2006.

The data requirements prerequisite to making a disinfectant claim are set forth in EPA's DSS/TSS documents. DSS/TSS-1⁵ states that to make a hospital disinfectant claim on the product label, the disinfectant must be tested against three different species of bacteria: *Salmonella choleraesuis* (ATCC 10708)⁶, *Staphylococcus aureus* (ATCC 6538), and *Pseudomonas aeruginosa* (ATCC 15442). The required performance criteria for the test stipulates that a disinfectant must kill "...59 out of each set of 60 carriers...to provide effectiveness at the 95% confidence level."⁷ The UDT is also used by EPA to perform enforcement testing. If a product fails EPA's UDT testing, EPA can impose penalties for "misbranding" under FIFRA or force withdrawal of products from the market. Thus, EPA clearly disseminated the information requiring the use of the UDT to demonstrate the efficacy of disinfectants, including the performance criteria for the test.⁸

The UDT Constitutes Influential Information

Under EPA's Information Quality Guidelines, information is considered influential if "...the Agency can reasonably determine that dissemination of the information will have or does have a clear and substantial impact (i.e., potential change or effect) on important public policies or private sector decisions". EPA Information Quality Guidelines at 19. EPA's long-standing requirement for UDT results to demonstrate the efficacy of hospital disinfectants has "clear and substantial" impacts on the hospital disinfectant industry. The UDT is required for companies seeking initial registration or re-registration of hospital disinfectants. Enforcement actions based upon the UDT can result in removal of disinfectant products from the market, disrupting supply, limiting hospitals' and the public's options, and reducing confidence in these essential products. Thus, the Agency's reliance on the UDT impacts the availability and perception of hospital disinfectants in the marketplace, and involves substantial economic impacts.

⁵ EPA, Disinfectant Technical Science Section, Efficacy Data Requirements, Disinfectants for Use on Hard Surfaces EPA DIS/TSS-1 (January 22, 1982), downloaded on April 13, 2007 from: <http://www.epa.gov/oppad001/sciencepolicy.htm> (hereinafter, "EPA DIS/TSS-1"). Disinfectant Technical Science Section guidance documents provide a summary of current efficacy-related requirements and/or policy for a category of antimicrobial pesticide products, claims, or patterns of use. The efficacy performance standards in DIS/TSS-1 are based on the testing requirements in 40 CFR 158.

It should be noted that EPA's website (<http://www.epa.gov/oppad001/>) indicates the Agency has proposed to create a new subpart (Subpart W Sections 156.440-156.458) in 40 CFR entitled "Public Health Claims for Antimicrobial Pesticides". Subpart W would establish labeling requirements for antimicrobial pesticides that make public health claims based upon the level and type of efficacy demonstrated by testing. The efficacy performance standards upon which the proposed requirements are based are derived from the testing requirements in 40 CFR 158, and the test methods and standards provided in Subdivision G of the Pesticide Assessment Guidelines. The proposed performance standards and labeling requirements are consistent with longstanding EPA policies and requirements. As proposed, Subpart W references the latest draft of the Harmonized Guidelines for Antimicrobial Performance (810 series). The current draft of 810.2100 recommends the use of the AOAC UDT, as outlined in EPA DIS/TSS-1, to demonstrate the efficacy of hospital or healthcare disinfectants.

⁶ EPA's draft 810.2100 guidelines, dated November 21, 2005, indicate that *Salmonella choleraesuis* (ATCC 10708) will no longer be required to support hospital disinfectant claims. Although still draft, the Agency has already implemented this change.

⁷ EPA DIS/TSS-1.

⁸ *Id.*

Moreover, as set forth more fully below, the Agency's use and reliance on the UDT has been criticized by academia, industry, and the Government Accountability Office (GAO). Thus, the UDT also constitutes controversial scientific information, which is another category of "influential information." See EPA Guidelines at 20 (influential information "...may also include precedent-setting or controversial scientific or economic issues.").

The UDT Is Not Reliable and Therefore Does Not Meet the Standards for Information Quality

The OMB Data Quality Guidelines define quality as an encompassing term comprising utility, objectivity, and integrity.⁹ Of these four statutory terms, EPA's definition of objectivity is most relevant to the issues surrounding EPA's required use of the UDT. EPA's Data Quality Guidelines state that objectivity refers to information that "...as a matter of substance, is accurate, reliable, and unbiased." EPA Guidelines at 15. As discussed below, published studies have demonstrated the UDT to be a highly unreliable and inaccurate test method.

Numerous peer-reviewed scientific studies published in the 1980s¹⁰ and funded under a cooperative agreement between EPA and researchers at the University of North Carolina (UNC) demonstrated the extreme variability of the UDT, especially for the *Pseudomonas* organism¹¹. Between October 1983 and October 1989, EPA spent about \$384,000 on two cooperative agreements with the UNC researchers.¹² Among other tasks, these researchers were charged with updating the UDT method and improving its widely-recognized variability problems.

The UNC researchers investigated numerous presumed deficiencies with the UDT and conducted two large collaborative studies to evaluate variability in the published method and in a slightly modified version. On the basis of their work, the UNC researchers concluded that the UDT (and the slightly modified version) were subject to extreme inter-laboratory variability and should not be used for registration or enforcement purposes, and recommended the development of a reproducible method for

⁹ OMB Guidelines, 67 Fed. Reg. at 8459.

¹⁰ Rutala, WA and Cole, EC. 1987. Ineffectiveness of Hospital Disinfectants Against Bacteria: A Collaborative Study. *Infection Control*, 8(12): 501-506. Cole, EC; Rutala, WA; Samsa, GP. 1988. Disinfectant Testing Using a Modified Use-Dilution Method: Collaborative Study. *Journal of AOAC*, 71(6): 1187-1194. Cole, EC; Rutala, WA; Carson, JL. 1987. Evaluation of Penicylinders Used in Disinfectant Testing: Bacterial Attachment and Surface Texture. *Journal of AOAC*, 70(5): 903-906.

¹¹ Cole, EC; Rutala, WA; Samsa, GP. 1987. Standardization of Bacterial Numbers on Penicylinders Used in Disinfectant Testing: Interlaboratory Study. *Journal of AOAC*, 70(4): 635-637. Cole, EC; Rutala, WA; Carson, JL; Alfano, EM. 1989. *Pseudomonas* Pellicle in Disinfectant Testing: Electron Microscopy, Pellicle Removal, and Effect on Test Results. *Applied and Environmental Microbiology*, 55(2): 511-513.

¹² In response to a request by the U.S. House Committee on Government Operations, the US General Accounting Office (GAO) (subsequently renamed the Government Accountability Office) undertook a review of EPA's regulation of disinfectant efficacy. In 1990 the GAO published the following report regarding EPA's disinfectant efficacy program: US General Accounting Office. 1990. Report to Congressional Requesters, "Disinfectants, EPA Lacks Assurance They Work". GAO/RCED-90-139. August (hereinafter "GAO Report"). GAO reported that "[m]ethods recommended by EPA for testing disinfectant efficacy have been widely criticized by industry, academia, and others for producing highly variable results." *Id.* at 21.

use in pre- and post-registration testing.¹³ The UNC researchers also noted that the UDT for *Pseudomonas aeruginosa* was never collaboratively studied using the AOAC test method and recommended that all three AOAC UDT methods be downgraded to official First Action status¹⁴; the *Pseudomonas* UDT has been a First Action since 1964¹⁵. The original 1953 AOAC collaborative study of the UDT was not statistically analyzed.¹⁶ Examination of these original data by the UNC researchers showed that the UDT did not have any better reproducibility in 1953 than it did in their current collaborative study. Thus, the UDT was never statistically validated, and based on the UNC findings, remains too variable a method to be validated.

Based largely on the results of the UNC studies, the AOAC actively considered repealing both the UDT and the Tuberculocidal Activity Method (TAM), another AOAC hard surface carrier test, in the late 1980s because of inconsistent results with both test methods.¹⁷ In fact the AOAC repealed the TAM during its September 1988 meeting; however, this method was reinstated in March 1989 by AOAC following an objection raised by EPA that the Association acted on erroneous information presented during the September 1988 meeting.¹⁸

A joint research effort in 2006 conducted by two registrants, Lonza and Ecolab, at a cost of over one million dollars, focused on the variability problems with the UDT for *Pseudomonas* and confirmed the variability in test results for this organism that were first published by the UNC researchers in the 1980s.¹⁹ In addition, this research effort centered on ways to more thoroughly remove or mitigate the effect of residual *Pseudomonas* pellicle (a biofilm substance naturally secreted by the organism) in the culture before the disinfectant challenge step in the test procedure. The AOAC UDT method specifically states that the pellicle "...must be removed from the broth..." for the test to be valid.²⁰ The

¹³ Cole, EC; Rutala, WA; Samsa, GP. 1988. Disinfectant Testing Using a Modified Use-Dilution Method: Collaborative Study. *Journal of AOAC*, 71(6): 1187-1194.

¹⁴ The AOAC Review and Approval Process document indicates that after 2 years of use as a First Action (the current status of the UDT for *Pseudomonas*), if the AOAC has not received any information indicating significant problems with the performance of a method, the method should be adopted as a Final Action. Furthermore, First Action methods that are not recommended for Final Action after 2 years of eligibility will be automatically recommended for repeal. Refer to "Part 5 Official Methods Review and Approval Process, AOAC International, OMA Program Manual, January 2002".

¹⁵ AOAC Official Method 964.02, Testing Disinfectants against *Pseudomonas aeruginosa*, Use-Dilution Method.

¹⁶ Disinfectant Testing Using a Modified Use-Dilution Method: Collaborative Study. *Journal of AOAC*, 71(6): 1187-1194.

¹⁷ GAO Report at 21.

¹⁸ *Id.*

¹⁹ Joint Research Program to Assess and Improve Reliability of AOAC Use Dilution Test Method with *Pseudomonas aeruginosa*. Ecolab Inc. and Lonza Inc, October 24, 2006; attached as Attachment 1.

²⁰ AOAC Official Method 964.02, Testing Disinfectants against *Pseudomonas aeruginosa*, Use-Dilution Method.

Lonza/Ecolab research showed that residual microscopic pellicle fragments remain in the culture after the pellicle removal steps described in the AOAC test method are employed. Complete pellicle removal is required for testing with all disinfectants because "...any pellicle fragment remaining will result in uneven clumping and layering of organism on the cylinders, allowing unfair exposure to disinfectant and causing false positive results."²¹

EPA has acknowledged the problems with the "repeatability and reproducibility" of the UDT²², yet still requires the same unpredictable test method to demonstrate the efficacy of hospital disinfectants. EPA's continued requirement for registrants to use the UDT for disinfectant registration and re-registration contradicts its Information Quality Guidelines by ignoring the best available, peer reviewed science on the test method. As discussed above, a number of peer-reviewed studies have shown the UDT method to be unreliable and incapable of being validated.²³ Furthermore, the AOAC UDT for *Pseudomonas* expressly states that the pellicle must be removed completely for the test to be valid. The recent work by Lonza and Ecolab clearly show the pellicle removal procedure in the current AOAC test method is insufficient to do this.²⁴ Thus, EPA has adopted and requires the use of a test method that is inaccurate, unreliable and does not function as intended.

Conclusions and Recommendations

The variability problems with the UDT can result in false positive results and unwarranted enforcement actions against registrants. Enforcement actions against registrants can result in removal of effective disinfectant products from the market, disrupting supply, limiting hospitals' and the public's options, and reducing confidence in these essential products.

EPA's reliance on a variable and inaccurate test method to determine the efficacy of disinfectant products, despite a substantial body of peer-reviewed studies that document the reliability and accuracy problems with the test method, is contrary to its Information Quality Guidelines. The test is too variable to reliably and accurately predict the efficacy of hospital disinfectants.

²¹ *Id.*

²² EPA, Office of Prevention, Pesticides and Toxic Substances, Response to Office of Inspector General Report, 2007, at p. 21; available at: <http://www.epa.gov/oig/reports/2007/20070329-2007-P-00018.pdf>.

²³ The data generated by the UNC researchers and the recent Lonza/Ecolab study were based largely on conducting the UDT repeatedly by different operators and in different labs to confirm the variability in results, and to evaluate the effect of modifications to the test procedure. This is a valid and accepted method of test development and is the same approach required by the AOAC for test method approval; refer to "Part 5 Official Methods Review and Approval Process, AOAC International, OMA Program Manual, January 2002".

²⁴ Attachment 1 at 10.

Information Quality Act Request for Correction

July 6, 2007

Page 6

Based on the results of the joint Lonza/Ecolab research effort, the Efficacy Working Group has separately recommended two clarifications to the EPA/OPP Microbiology Laboratory SOPs that implement the AOAC UDT method for *Pseudomonas*. These clarifications²⁵ have been empirically shown in multi-laboratory tests to minimize the variability in the UDT results, and have been presented to Antimicrobials Division and BEAD laboratory staff. They can provide an interim approach until EPA can develop and implement a more reliable disinfectant efficacy test.

The Efficacy Working Group appreciates the Agency's prompt attention to these serious concerns regarding information quality aspects of use of the UDT for *Pseudomonas aeruginosa* to assess the efficacy of hospital disinfectants. This issue is especially urgent now because the Data Call-In (DCI) for the Quaternary Re-registration Eligibility Decision (RED) is expected later this year. Once issued, the DCI will require, among other things, that registrants provide efficacy data to support hospital disinfectant claims. We therefore urge the Agency to act expeditiously to correct the requirement to use the UDT and replace it with a valid, reproducible method. Amending the EPA/OPP Microbiology Laboratory SOPs that implement the AOAC UDT method for *Pseudomonas* in the manner suggested by the Efficacy Working Group is one way to accomplish this expeditiously.

Thank you for your consideration of this request.

Respectfully submitted,



Seth Goldberg

cc: Frank Sanders, EPA OPP

²⁵ The clarifications are: (1) a 1:50 dilution in nutrient broth of the *Pseudomonas* culture is made after the obvious pellicle has been removed. This dilution step aids in solubilizing remaining microscopic pellicle fragments in the culture so they don't interfere with the activity of the disinfectant. This dilution step is implemented in section 10.3.1 of EPA/OPP Microbiology Laboratory SOP No. MB-05-04 for AOAC Use Dilution Method for Testing Disinfectants; and in section 10.3.8 of EPA/OPP Microbiology Laboratory SOP No. MB-06-02 for Testing of Spray Disinfectants; and (2) a sentence is added to section 10.1.1.1 of EPA/OPP Microbiology Laboratory SOP No. MB-04-03 for Determining Carrier Counts that reads "Allow the carrier to remain in the letheen broth for 30-60 minutes". This specified letheen broth soak time optimizes recovery of cells from the surface of the carrier yielding more reliable cell counts.