MEMORANDUM

Via E-Mail

DATE: November 5, 2009

TO: Clients and Friends

FROM: The Acta Group, L.L.C.

RE: Summary of Ninth Antimicrobial Workshop

On October 27-28, 2009, the Ninth Antimicrobial Workshop was held in Arlington, Virginia. The American Chemistry Council (ACC) Biocides Panel, the Consumer Specialty Products Association (CSPA), and ISSA sponsored the Workshop, which was conducted in coordination with the U.S. Environmental Protection Agency (EPA) Antimicrobials Division. The Workshop included presentations on the following topics:

- Eco-Claims for Disinfectants and Sanitizers;
- Current Activities/Future Directions for the EPA Antimicrobials Division;
- Inerts Regulation;
- Proposed Part 158W Antimicrobial Data Requirements;
- Antimicrobial Testing Program;
- EPA/Industry Issues Updates;
- Perspectives on Implementing the EPA Container Regulations;
- PRIA 2 Update;
- Thresholds of Toxicological Concerns for Antimicrobials;

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- EPA Policy on Emerging Pathogens;
- End Users' Perspectives on Antimicrobials;
- Canadian Antimicrobial Regulatory Issues;
- European Antimicrobial Regulatory Issues: BPD and REACH;
- Update from Antimicrobial Exposure Industry Groups; and
- Antimicrobial Reregistration and Registration Review Update.

According to the Workshop organizers, the presentations will be available by the end of this week on the sponsoring organizations' websites; a copy also is available upon request from The Acta Group, L.L.C. (Acta).

The following summary briefly discusses some of the key points made during these presentations.

Eco-Claims for Disinfectants and Sanitizers

William (Bill) Balek, ISSA, and Michael Hardy, EPA Antimicrobials Division (AD) gave successive presentations discussing two upcoming AD pilot projects related to permissible environmentally-friendly product claims. Hardy stated there would be a formal announcement about these pilot projects in **November 2009**. Balek discussed the market demand for environmentally preferable products and guidance on their selection.

The first pilot project will allow the addition of the EPA Office of Pollution Prevention and Toxics (OPPT) Design for the Environment (DfE) logo and website on pesticide labels for products that have completed successfully the DfE program review. Hardy stated that AD will begin accepting applications to add the DfE logo in **May 2010**, but registrants may apply to the existing DfE program at any time. More information about OPPT's DfE program is available at http://www.epa.gov/oppt/dfe/pubs/about/index.htm.

The second pilot project will allow registrants to add the following limited factual statements to their labels as applicable: dye- and/or fragrance-free, and a reference to the registrant's company website for a discussion of the company's commitment to the environment and sustainability. Hardy emphasized the company's website must be consistent with product labeling, and this pilot project is not authorizing cause marketing or generic "green" statements.

Among the statements that EPA considered but is not including in the pilot at this time are statements concerning ready biodegradability. Hardy stated that EPA is continuing to review the availability of study protocols that demonstrate ready biodegradability in formulated mixtures. Hardy also stated that this pilot project would begin in **January 2010**. Finally, Hardy stated that AD had determined that another set of statements -- concerning the recycled content of product packaging -- could be included on the label now, outside of the pilot, and be added via notification.

Current Activities/Future Directions for the EPA Antimicrobials Division

Joan Harrigan-Farrelly, Director, AD, reflected in her remarks on her first year in the AD Director position, AD's activities during this period, and AD's objectives moving forward. Included in her remarks were the following points:

- ***Personnel and Organizational Changes***: Harrigan-Farrelly listed retirements (*e.g.*, Adam Heyward), notice of upcoming retirements (*e.g.*, Norm Cook) and other changes (*e.g.*, Michael Hardy leaving AD to become Special Assistant to Marty Monell, OPP Deputy Office Director for Management). She also stated AD is considering dividing the Risk Assessment and Science Support Branch into two parts, one addressing human health and one addressing ecological effects.

- ***Activities in 2009***: Harrigan-Farrelly stated that AD had been working to improve the way AD conducts daily business, including: reviewing and requiring improvements to currently approved labels as they are submitted for amendment; encouraging electronic label submissions and laying the foundation for eventual electronic submissions; increasing the adequacy of supporting data through continued work on the proposed Part 158W requirements, including preparation of responses to robust public comment; and preparing and posting guidance to facilitate H1N1 product claims.

- ***Activities in 2010 and Beyond:*** Harrigan-Farrelly described a broad range of initiatives, including: the pilot programs discussed above, as well as a non-animal testing pilot program; development of the fragrance database; participation in OPP-wide increased transparency through posting of risk assessments and initial decisions in public dockets for certain registration actions; focus on nanotechnology issues, including the four-day Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) Scientific Advisory

Panel (SAP) meeting this week; test method development with the regulated community; and consideration of how to include EPA Administrator Lisa Jackson's priority of environmental justice into AD risk assessment.

Inerts Regulation

Kerry Leifer, Team Leader, OPP Inert Ingredient Assessment Branch, Registration Division, addressed several inert-ingredient related topics, including the following:

- A brief overview of definitions and requirements applicable to inert (or "other") ingredients;
- An explanation of the inert ingredients review and approval process;
- A discussion of the inerts screening process that occurs when a pesticide product registration application is first submitted to EPA;
- An update of the ongoing fragrance component review/evaluation project; and
- A discussion of EPA's upcoming initiative concerning inert ingredient disclosure. In particular, Leifer stated that EPA will publish an advanced notice of proposed rulemaking to solicit public comment concerning inerts disclosure before the end of 2009.

Proposed Part 158W Antimicrobial Data Requirements

John Wood, Ecolab, Inc., and Adrian Krygsman, Troy Corporation, gave successive presentations concerning the proposed Part 158W Antimicrobial Data Requirements. The speakers acknowledged that the complexity of the proposed requirements did not permit a detailed discussion in the time allotted, so each addressed select issues.[1] Krygsman provided a historical overview for the development of the proposed Part 158W requirements. He also cited the following cost estimates for the new data requirements in the proposed rule: EPA -- $61,000 per firm annually; NERA Economic Consulting -- $3.2 million per firm annually. Wood

[1] EPA published the proposed rule on October 8, 2008 (73 Fed. Reg. 59382). For a discussion of the proposed rule, see Acta's October 17, 2008, memorandum, which is available at http://www.actagroup.com/us/fifra.shtml.

emphasized the need for guidance and clarification concerning several aspects of the proposed rule, including: the use of potential exposure levels vs. use patterns to specify data requirements; criteria for the tiering of data requirements; and how the rule, when finalized, will be applied to pending applications. He also commented on the need for additional test guidelines.

Antimicrobial Testing Program

Harrigan-Farrelly discussed AD's Antimicrobial Testing Program, which tests registered products to evaluate and confirm product efficacy, with a focus on hospital disinfectants and tuberculocides. According to Harrigan-Farrelly, EPA has tested more than 300 products and many have failed to demonstrate claimed levels of efficacy. Pass/fail test results are posted on the program's website.[2] As stated in the presentation, the testing program has been in existence since 1991. Various means have been used to obtain products for testing; most recently, EPA sent letters to registrants in December 2008 requesting samples, which resulted in approximately 100 submissions. Harrigan-Farrelly stated a second letter would be sent soon to registrants who did not respond to the first letter. She also stated that AD is considering how to make the program more efficient prospectively, including possibly requiring confirmatory testing before registration approval.

Harrigan-Farrelly stated that when a product does not meet the efficacy standards for which it is registered, AD's resulting course of action depends on the failure rate. For a high failure rate, AD will make an enforcement referral. For a lower failure rate, she stated that AD would seek a correction through regulatory action, such as an amendment to remove the pest from the product label.

Finally, Harrigan-Farrelly stated that the Office of Inspector General (OIG) recently had investigated the program based on a complaint that the program was not notifying registrants of the test results. According to Harrigan-Farrelly, the OIG concluded that AD had met the applicable standards for sharing information.

[2] The Antimicrobial Test Program website is accessible at http://www.epa.gov/oppad001/antimicrobial-testing-program.html.

EPA/Industry Issues Updates

Three short updates were presented on the following topics.

AD Label Quality Improvement Program

Mark Hartman, Branch Chief, Regulatory Management Branch II, discussed AD's efforts to address consistency issues for currently approved as well as new products. Hartman acknowledged challenges that have thwarted consistency historically, including the broad range of antimicrobial products regulated by AD, market pressure for consumer products, and competitive "they have it, we want it" pressures that compound errors. Hartman described the processes AD has developed and implemented since early 2009 to improve label quality, which include the following:

- ***Label Quality Peer Review Process***: All label reviewers, Product Managers (PM) and Branch Chiefs discuss labels in weekly peer review meetings. Labels discussed are randomly chosen from a pool of pending actions, though reviewers are encouraged to bring challenging labels up for discussion.

- ***Branch-level Quality Assurance***: AD Branch Chiefs review multiple labels completed by each reviewer each month, with a goal of reviewing at least 10 percent of completed actions.

- Development of a label review checklist and other tools, and integration of label quality into staff performance evaluations.

Hartman acknowledged that the new processes had had the unanticipated consequence of delaying updates to label storage and disposal language, as submissions to adopt Pesticide Registration (PR) Notice 2007-4 language have been caught up in label reviews. Hartman also stated that if a change to an existing label would have a big impact and upset the level playing field among competitors, AD would address the issue more systematically and equitably.

Non-animal Eye Irritation Pilot Project

John Redden, EPA, and Mario Green, Procter & Gamble, discussed a voluntary pilot program to evaluate the use of non-animal testing for eye irritation for certain antimicrobial products with cleaning claims. According to Green, many companies that produce products with

only cleaning claims (*i.e.*, not pesticides) use *in vitro* testing only for eye irritation and have done so for a decade. While the federal Interagency Coordination Committee on the Validation of Alternative Methods (ICCVAM) is considering what *in vitro* assays may be acceptable instead of animal testing, the ICCVAM recommendation to EPA is not expected before **2010**. Accordingly, EPA began a pilot project in Summer 2009 to collect data and experience with three assays: Bovine Corneal Opacity and Permeability (BCOP), Cytosensor Microphysiometer, and EpiOcular. The pilot is open to antimicrobial products with cleaning claims. Submitted data will be considered along with available consumer incident data and existing Draize test results on similar or structurally-related chemicals or products. EPA plans to run the pilot for 18 months and then present data from the pilot and related analyses to OPP's Science Policy Council.

Acute Toxicity Waivers and Bridging

Karen Hicks, AD Product Science Branch, gave a presentation concerning acute toxicity data waivers and bridging for antimicrobial products. Hicks stated that EPA has taken various steps to reduce acute toxicity animal testing, including use of *in vitro* alternative testing and allowing bridging arguments/considering structural activity relationship (SAR) arguments. Hicks stated that AD is preparing procedures and guidance for registrants concerning data waiver requests and EPA's data bridging policy. According to Hicks, EPA will post the guidance on its website along with the Part 870 testing guidelines.

Perspectives on Implementing the EPA Container Regulations

Joanne Ryder, The DOW Chemical Company (DOW), provided comments on lessons learned concerning implementation of EPA's container requirements consistent with PR Notice 2007-4. Ryder outlined the steps DOW followed to implement the label changes, which included: reviewing and updating labels and documenting compliance; coordinating and prioritizing label submission to EPA, with first priority given to products with supplemental distribution and those registered in California; working with supplemental distributors to update labels; submitting labels for state approval; and working through the logistics of producing new labels and relabeling existing inventory.

PRIA 2 Update

Elizabeth Leovey, Senior Advisor for PRIA Implementation, and Dennis Edwards, Branch Chief, Regulatory Management Branch I, gave successive presentations concerning Pesticide Registration Improvement Renewal Act (PRIA 2) issues. Leovey reviewed the changes for antimicrobial products introduced by PRIA 2, including seven new fee categories. Leovey discussed the availability on EPA's website of updated guidance concerning

the scope of the fee categories. Leovey stated that in Fiscal Year (FY) 2009, 29 percent of AD completed/withdrawn actions required due date extensions, and emphasized that extensions require at least two weeks for review and approval. Finally, Leovey reminded the audience that PRIA 2 is scheduled for renewal consideration in **2012** and invited comment on improvements that could be incorporated into PRIA 3.

Edwards discussed the 21-day initial content screen that transpires upon EPA's initial receipt of an application. Edwards commented that in FY 2009, many AD applications required corrections during the 21-day screen for a range of reasons, including: PR Notice 86-5 formatting deficiencies; use of inert ingredients not approved by EPA; missing forms; and omission of required data. Edwards also stated that as applications are received, EPA will be asking for all silver products whether the silver is nanoscale, and that EPA may extend this inquiry to other metals such as copper and zinc.

Thresholds of Toxicological Concerns for Antimicrobials

Elizabeth Brown, Steptoe & Johnson, LLC, on behalf of the ACC Biocides Panel, stated that antimicrobial pesticides are different than conventional pesticides and different approaches in risk assessment are appropriate. As stated by Brown in her presentation, Threshold of Toxicological Concern (TTC) is a risk assessment approach that uses an exposure-driven model to identify "safe" levels based on chemical structure and related chemical toxicity information. Brown provided several examples in which regulators or other authoritative bodies have adopted the TTC approach, including specific types of assessments by the U.S. Food and Drug Administration (FDA), the World Health Organization/Joint Expert Committee on Food Additives, and European authorities.

Brown explained that current TTC models are not appropriate for antimicrobial pesticides, *e.g.*, they only address long-term exposure by the oral route -- not shorter or dermal or inhalation exposures -- and associated databases do not contain antimicrobial-related information. Accordingly, Brown stated the ACC Biocides Panel has proposed to work with the ILSI Research Foundation to consider whether a TTC-type risk assessment approach could be developed for antimicrobial pesticides; OPP has concurred with this proposal. Brown stated that preliminary steering committee and scoping committee meetings have been held; working groups are expected to include experts from EPA, FDA, industry, academia, and international organizations. Among the issues that the working groups may consider are: reconsideration of hazard identification; development of a policy regarding how to identify and evaluate compounds without systemic toxicity endpoints of concern, including applicability of uncertainty factors; evaluation of relevant exposure models and when specific models are applicable; and consideration of which exposures should be evaluated. According to Brown, the effort is

expected to take one to two years (or more) and will produce a white paper with a proposed approach, supported by documentation and case studies. The white paper will be presented to OPP for its consideration.

EPA Policy on Emerging Pathogens

Tajah Blackburn, AD, and William McCormick, Clorox Company, presented successively on EPA's activities related to emerging pathogens and related issues. Blackburn first defined and provided examples of emerging pathogens in recent history, including H1N1 Influenza and Severe Acute Respiratory Syndrome (SARS). Blackburn then discussed EPA's emerging pathogen guidance, available at http://www.epa.gov/oppad001/disinfection_hier.htm, which uses a disinfection hierarchy scheme to allow claims for which there is no specific efficacy testing. According to Blackburn, EPA departed from its disinfection hierarchy design, as the organism was not considered new, to take timely action to address the H1N1 virus. As a result, registrants of products registered for use against Influenza A may add H1N1 to the product labels. Blackburn listed the specific claims against H1N1 that registrants may add to their labels by notification and provided the website for EPA's new H1N1 guidance: http://www.epa.gov/oppad001/influenza-disinfectants.html. In his presentation, McCormick discussed the many Clorox initiatives that address a range of human and environmental emerging pathogens.

End Users' Perspectives on Antimicrobials

Three speakers shared their views as part of the user community for antimicrobial products: Lynne Sehulster, Centers for Disease Control and Prevention (CDC); Judene Bartley, Executive Director, Association for Professionals in Infection Control and Epidemiology, Inc. (APIC); and Patti Costello, Executive Director, American Society for Healthcare Environmental Services (ASHES). All three shared some similar themes in their remarks, such as the importance of cleaning and the use of disinfectants as only one part of a multifaceted approach to infection prevention and management. Sehulster reviewed factors that contribute to infection -- a virulent pathogen, present in sufficient concentration; a mode of transmission; a portal of entry; and a susceptible host -- and the importance of considering these factors when devising a strategy to combat infection. Sehulster also cited a 2008 CDC guideline concerning disinfection and sterilization and emphasized that the CDC neither tests nor endorses products. Bartley discussed APIC and ASHES work with the Green Guide for HealthCare to develop practices that reduced the use of antimicrobial products when they are not, in APIC's view, necessary. Bartley stated that many hospitals are adopting approaches that: use products with a less toxic profile; emphasize cleaning; and focus disinfection on high-touch surfaces. All three speakers identified as a user challenged the typical instructions on a hospital disinfectant label for the treated surface

to "remain wet for 10 minutes," which, according to the presenters, requires multiple applications.

Canadian Antimicrobial Regulatory Issues

After a brief introduction by Krygsman regarding this and the remaining presentations, Marion Law, Chief Registrar, Pest Management Regulatory Agency (PMRA), Health Canada, and Jan Wengler, Reckitt Benckiser, Inc. presented successively on the regulation of antimicrobial products in Canada. Law explained that in Canada, jurisdiction over antimicrobial products is divided: some products are regulated by PMRA under the same legislation as agricultural chemicals (Pest Control Products Act), whereas others are regulated as drugs under the Food and Drugs Act by Health Canada's Therapeutic Products Directorate (TPD). Antimicrobials regulated as "drugs" by TPD include hard surface disinfectants and disinfectant/sanitizer combination products, and medical devices making antimicrobial claims.

Law stated that there are initiatives underway under the North American Free Trade Agreement (NAFTA) to, *e.g.*, harmonize antimicrobial data requirements between the United States and Canada, and permit joint reviews for new product applications. Law also briefly reviewed Canada's product registration process and discussed Canada's recent adoption of a new data protection policy.

Wengler in her presentation focused on the jurisdictional divide between TPD and PMRA. She described the change in jurisdiction over disinfectants in 2001, but also stated that the current regulatory paradigm for drugs in TPD is ill suited for disinfectant products. She stated that prospectively, many desire to combine the regulation of sanitizers with disinfectants and develop a regulatory framework more appropriate for both.

European Antimicrobial Regulatory Issues: BPD and REACH

Darren Abrahams, Steptoe & Johnson L.L.P. (U.K.) and Robert Matthews, McKenna, Long & Aldridge L.L.P., gave successive presentations on the European Union (EU) Biocidal Products Directive (BPD) and Registration, Evaluation, Authorization and Restriction of Chemicals (REACH) implementation respectively. Abrahams first provided a brief BPD overview, reminding the audience that the BPD is separate legislation from the Plant Protection Directive under which agricultural chemicals are regulated. Abrahams then discussed the active substance review program, explaining that biocidal products currently on the market may only contain active substances that are either under review and listed in the Review Programme or already included in the BPD Annex I/IA. Abrahams stated this review originally was scheduled to conclude in **May 2010**; as the Review Programme is behind schedule, it has been extended by

four years in Directive 2009/107/EC. Abrahams stated another two-year extension is likely. Abrahams next discussed data protection issues, stating that different protection periods apply in different member states. Abrahams described "free-rider" issues that, according to Abrahams, have been the subject of much litigation, explaining that during the transition period in which biocidal products are reviewed and the BPD fully implemented, product manufacturers that have not supported actives during review may remain on the market. Abrahams also discussed product registration issues and the differences in implementation between EU member states. Finally, Abrahams discussed issues with the current BPD and an upcoming effort to amend the BPD.

Matthews gave a presentation on REACH implementation and related emerging issues. By way of background, Matthews first discussed when pesticidal active ingredients must be registered (dual use) and stated that "co-formulants" (inert ingredients) must be registered under REACH. Matthews also discussed the significance of the December 1, 2008, deadline for phasing-in full registration requirements; EU manufacturers and/or importers of a substance at greater than the 1 tonne threshold must either have preregistered the chemical substance or otherwise submit a complete registration dossier for review. Matthews next discussed enforcement-related issues, stating the consequences of inadvertent omissions and the availability of mitigation for demonstrated due diligence is unclear. Matthews explained that enforcement is the responsibility of the EU member states, some of which are still developing their REACH enforcement provisions and policies; for those with developed policies, there is a range of penalties and actions considered criminal. Matthews described the development of the first list of substances of very high concern (SVHC), and the recommendation by the European Chemicals Agency (ECHA) to the European Commission (EC) to include seven of the SVHC on Annex XIV. If on Annex XIV, Matthews stated, the substance may not be placed on the market after the applicable sunset date, unless the EC has granted a specific use authorization. Finally, Matthews stated that Substance Information Exchange Forums (SIEF) have begun to form, but that the process appears to be slow and that the number of SIEFs currently is very small when compared with the number of substances preregistered.

Update from Antimicrobial Exposure Industry Groups

Has Shah, ACC, and Susan Little, CSPA/Product Ingredient Review (PIR) Program, provided an overview and discussion concerning the activities of two industry groups: the Antimicrobial Exposure Assessment Task Force II (AEATFII) and the Antimicrobial Exposure Joint Venture (AEJV). Shah and Little described the efforts as "complementary," intended to generate compensable antimicrobial exposure data for product registration and reregistration. According to the presentation, the AEJV is a consortium of 14 companies that is collecting information via surveys, facility management tools, and in-home observations. Five

studies have been submitted to EPA, including residential diary data, pool and spa studies, and an amount-used study. Additional studies concerning industrial and institutional exposure and day care exposure are ongoing.

The AEATFII is a successor to earlier efforts dating back to the 1986 EPA Antimicrobial Data Call In; the presentation briefly reviewed the pertinent regulatory history. Established in 2004, the AEATFII currently includes 44 member companies, according to the presentation. The initial scope of effort includes conducting 19 core exposure studies to measure exposure during production (mixer/loaders) and application, as well as during post-application activities; the scope may change as part of ongoing discussions with EPA. To date, reviews by the FIFRA SAP and EPA Human Studies Review Board have been completed. The AEATFII plans on conducting studies through **2014**, and then populating a database for use in risk assessments by **2016**. The anticipated overall cost of the effort is $18 million.

Antimicrobial Reregistration and Registration Review Update

In the final presentation of the Workshop, Hartman provided an update on AD's reregistration and registration review efforts. Regarding reregistration, Hartman stated that active ingredient reregistration was completed in September 2008, and that more than 40 Reregistration Eligibility Decision (RED) documents were published between 2005 and 2008. Hartman stated that AD is now in the process of implementing RED decisions and updating labels, and is awaiting guidance from the Office of Management and Budget on processing related data call-ins. Hartman stated that AD expects to register more than 2,400 end-use products in the upcoming years. Regarding registration review, Hartman stated that the process is underway, and that AD anticipates 18 chemicals to begin the process in **FY 2010**. Finally, Hartman stated that, as EPA anticipated based on an earlier scoping pilot project, the registration review process will result in significant data call-ins for many antimicrobial pesticides and extensive risk assessments based on the new data.

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We hope this information is helpful. As always, please call if you have any questions.