November 25, 2015

Mr. Eliot Harrison
Sanosil International, LLC
c/o Lewis & Harrison, LLC
122 C Street NW, Suite 505
Washington, DC 20001

Dear Mr. Harrison:

Re: **Registration of HaloMist (EPA Reg. No. 84526-6) which Represents a Major Change in Labeling for the Active Ingredients Silver and Hydrogen Peroxide**

The New York State Department of Environmental Conservation (Department) has reviewed the application and all supporting information from Lewis & Harrison, LLC on behalf of Sanosil International, LLC to register the new product HaloMist (EPA Reg. No. 84526-6) in New York State. The product is labeled for use as a total room fogging disinfectant on non-porous surfaces in healthcare facilities using a “HaloFogger” apparatus to disperse a mist of the HaloMist solution. The HaloFogger apparatus is a free standing, portable machine that dispenses a mist of the formulated product.

HaloMist contains hydrogen peroxide and silver that is derived from silver nitrate and not nanosilver. These active ingredients together are currently registered for use as a spray disinfectant. Hydrogen peroxide is also registered for use in a fogging apparatus. However, the proposed use of a total room disinfectant in healthcare facilities by fogging has been determined to be a major change in label for both of these active ingredients.

The application package was deemed complete for purposes of technical review on August 25, 2014. Pursuant to the review time frame specified in Environmental Conservation Law §33-0704.2, a registration decision date of January 22, 2015 had been established.

The Department and the New York State Department of Health (NYSDOH) evaluated the application and all supporting documents and several concerns were identified. The registration decision date was waived in order to address the concerns.

The NYSDOH completed a risk assessment for human health and had identified concerns regarding the potential effects to applicators employing the fogging use disinfection directions. The complete NYSDOH review is located in the Appendix. In addition, concerns were identified regarding whether or not the product would be used
in accordance with the extensive directions and precautions outlined in the directions and application manual. Concerns were raised regarding the need to strictly adhere to the extensive directions in order for the product to be effective against the only labeled organism, *Clostridium difficile*. The application directions for the use of this product with the fogging apparatus are very involved and have a high potential for misuse by untrained healthcare facility staff, which could lead to exposure to the active ingredients. The proper operation of the HaloFogger to ensure targeted disinfection requires complex room preparation, air exchanges, adequate application and ventilation times, as well as monitoring (of hydrogen peroxide air concentration) before re-entry to the treated room. Also, hydrogen peroxide is a respiratory tract irritant and can cause severe eye and skin damage, and long-term exposure to silver can lead to a gradual accumulation of silver compounds in the body.

Mandatory applicator training before purchase or use of the HaloMist product in the HaloFogger apparatus was not required for federal registration. The HaloFogger User Manual states that “Prior to use, applicators must be adequately trained and certified by Sanosil International or its authorized distributor or reseller on the hazards and label directions for HaloMist, on the use and operation of the DMHP application equipment, Sanosil HaloMist monitoring procedures and when appropriate, validation procedures.” However, the training materials and certification process were not provided with the registration package and they were not readily available online.

Concerns were also raised regarding the available marketing materials for the HaloMist product and HaloFogger apparatus. The product label for HaloMist only contains kill claims against *C. difficile*, but appeared to be marketed as a whole room surface disinfection system. Marketing this product as a broad spectrum control system could lead to misuse or overuse of an already complicated product and application process. It could also lead to the perception that a setting has been disinfected from all pathogens when this is not the case – potentially creating an infectious disease risk.

The Department and the NYSDOH met with representatives of Sanosil International regarding the numerous concerns identified. In response to concerns, additional information regarding available training materials and the certification process were submitted for review. Also, changes were made to marketing materials, and the information presented on the product’s website was updated in order to clarify the use and utility of the fogging of the HaloMist product.

The Department and the NYSDOH are very concerned about the proliferation of antimicrobial products on the market which contain claims of increased efficacy without the necessary directions and contact times. This is particularly troubling because the actual efficacy of antimicrobial products is not apparent to the naked eye. Unlike insecticides, herbicides and rodenticides, antimicrobial products do not have visible results. People may buy and use a product which claims to be effective, however, they do not know if it actually works, unless specific tests are performed. In addition, overuse of ineffective products can lead to the proliferation of resistant microbial species.
Efficacy data for the HaloMist product exists for the use of the product in controlled, healthcare settings. The label use directions and sites are limited to such areas. If the HaloMist product is used in strict accordance with the label directions and use manual for the HaloFogger apparatus, the product should be effective and there should be no adverse impacts to the applicator or the general public. Therefore, the Department hereby registers HaloMist (EPA Reg. No. 84526-6) in New York State.

Enclosed is a copy of the Certificate of Pesticide Registration and stamped “Accepted for Registration” label for HaloMist (EPA Reg. No. 84526-6). Please note that a proposal by Sanosil International, LLC or any other registrant to register a product that contains hydrogen peroxide and silver, and whose labeled uses are likely to increase the potential for significant impact on humans, non-target organisms, or the environment, would constitute a major change in labeling. Such an application must be accompanied by a new application fee and meet the requirements listed for major change in labeling applications as listed on our website.

Please contact Jeanine Broughel, Chief of the Pesticide Product Registration Section, at (518) 402-8768, if you have any questions regarding this letter.

Sincerely,

Scott Menrath

Scott Menrath, P.E.
Director
Bureau of Pest Management

Enclosures
Appendix

The following is the NYSDOH review:

**Toxicity Review**
The U.S. Environmental Protection Agency (U.S. EPA) required very limited toxicity data for federal registration of both hydrogen peroxide and silver. The NYSDOH previously reviewed the toxicological properties of the active ingredient hydrogen peroxide for registration of the pesticide product ZeroTol Algaecide/Fungicide. Hydrogen peroxide is a volatile, but relatively short-lived chemical (half-life in air approximately thirty minutes) that breaks down into oxygen and water. This chemical is a respiratory tract irritant and can cause severe eye and skin damage due to its strong oxidizing potential. As part of the registration review process for peroxy compounds, the U.S. EPA required inhalation toxicity studies on hydrogen peroxide to better characterize potential human health risks from inhalation exposure. In a recently conducted 28-day inhalation toxicity study in rats, pathological findings in the respiratory tract were observed at 3 milligrams per cubic meter (mg/m$^3$), the lowest concentration tested.

Although the NYSDOH has not formally reviewed silver as part of the pesticide registration program, it has been used for centuries for medical and personal use. As part of the recent federal registration review of silver (and silver salts), the U.S. EPA assessed the potential risks for human exposure to silver based on studies available in the open scientific literature. The U.S. EPA established an oral reference dose (RfD) of 0.005 milligrams per kilogram body weight per day (mg/kg/day) for silver based on observed argyria (gradual accumulation of silver compounds in various parts of the body) at 0.014 mg/kg/day (1 gram total dose) in people intravenously injected with organic and colloidal silver medication.

**Occupational Risk Assessment**

The U.S. EPA reported the results of a post-application bystander risk assessment for inhalation exposures to hydrogen peroxide and silver from application via the Sanosil HaloFogger apparatus. The U.S. EPA estimated exposures to hospital staff and patients assuming a properly sealed room with a volume of 1,100 cubic feet (ft$^3$) was treated for 10 minutes at an application rate of 1 ounce per minute as per label instructions. Occupational risks for applicators of the Sanosil HaloMist product were not estimated because the applicator does not remain in the room during the fogging application. For determining margins of exposure (MOEs), the U.S. EPA compared estimated short- (1−30 days)/intermediate-term (1−6 months) inhalation exposures to hydrogen peroxide to the lowest-observed-effect level (LOEL) of 3 mg/m$^3$ from a 28-day inhalation toxicity study in rats (pathological findings in the respiratory tract). The inhalation MOE for exposure of hospital staff and patients to hydrogen peroxide from entering a room 75 minutes after treatment was 310. For this scenario, the U.S. EPA considered MOEs of 300-fold or greater to provide adequate protection from exposure to hydrogen peroxide.
The U.S. EPA also estimated exposures to silver for patients (child and adult), as well as hospital staff using the same application assumptions mentioned above. Estimated short-/intermediate-term inhalation exposures to silver for child and adult patients were compared to a no-observed-effect-level (NOEL) of 65 mg/kg/day (the highest dose tested) from a developmental toxicity study in rats. Estimated long-term inhalation exposures to silver for hospital staff were compared to a U.S. EPA estimated point-of-departure of 0.001 mg/kg/day, which was derived from the Occupational Safety and Health Administration’s permissible exposure limit for silver of 0.01 mg/m3 (argyria in previously mentioned human observational study). The short-/intermediate-term inhalation MOEs for exposure to silver for a child and adult patient (entering the room 60 minutes after treatment) were 42,000 and 280,000, respectively. The long-term inhalation MOE for exposure of hospital staff to silver was 3.3, assuming an 80 minute ventilation time after treatment. For short-/intermediate-term inhalation exposures of patients to silver, the U.S. EPA considered MOEs of 1,000 or greater (10 for intraspecies variability, 10 for interspecies extrapolation, 3 for an incomplete toxicity database and 3 for extrapolating an inhalation endpoint from an oral study) to be adequately protective. The U.S. EPA considered MOEs of 3 or greater (1 because the endpoint was derived from a human study and 3 for an incomplete toxicity database) to be adequately protective of long-term exposures to hospital staff.

Efficacy Data
The U.S. EPA reported the results of several efficacy studies conducted against bacteria (Pseudomonas aeruginosa, Staphylococcus aureus and Clostridium difficile) with fogging applications of the formulated product Sanosil HaloMist. These efficacy studies were conducted at room temperature on pre-cleaned, hard, non-porous surfaces in sealed rooms (including sealed HVAC vents) with a volume of 3663.7 ft³ (104 m³). Rooms were fogged with undiluted formulated product at an application rate of 1 ounce per minute for 22-24 minutes followed by a 143-150 minute ventilation time, according to label directions. Sanosil HaloMist was effective at disinfecting (i.e., adequate reduction in the number of colony forming units of each bacteria) pre-cleaned, hard, non-porous surfaces by fogging application. The U.S. EPA concluded that the efficacy data adequately supports claims against P. aeruginosa, S. aureus and C. difficile (in rooms no larger than 104 m³).

Summary/Recommendation
The NYSDOH has concerns for the use of the Sanosil HaloMist product as a disinfecting fogger in healthcare facilities. Hydrogen peroxide is a respiratory tract irritant and can cause severe eye and skin damage, and long-term exposure to silver can lead to a gradual accumulation of silver compounds in the body. The application directions for the use of this product with the fogging apparatus are very involved and have a high potential for misuse by healthcare facility staff, which could lead to exposure to the active ingredients. The proper operation of Sanosil HaloFogger to ensure targeted disinfection requires complex room preparation, air exchanges, adequate application and ventilation times, as well as monitoring (of hydrogen peroxide air concentration) before re-entry to the treated room. It does not appear that a mandatory applicator training program before purchase or use of the Sanosil
HaloFogger apparatus was required for federal registration. The Sanosil HaloFogger User Manual provided in the registration package states that “Prior to use, applicators must be adequately trained and certified by Sanosil International or its authorized distributor or reseller on the hazards and label directions for Sanosil HaloMist, on the use and operation of the DMHP application equipment, Sanosil HaloMist monitoring procedures and when appropriate, validation procedures.” However, the training materials and certification process were not provided with the registration package and they are not readily available online. Consequently, the NYSDOH is not able to adequately assess whether the training program would mitigate concerns about the proper operation of the fogging apparatus at healthcare facilities.

The NYSDOH also has some concerns with the available marketing materials for the Sanosil HaloMist and HaloFogger apparatus. A marketing video available online shows the HaloFogger apparatus being used in an office’s breakroom, which would violate the HaloMist label in two ways: 1) use outside of a healthcare facility and 2) use on food-contact surfaces. Although the video does not specify which formulated product is being used, it’s possible the HaloMist formulated product could be used in this manner. In addition, the submitted product label for Sanosil HaloMist only makes kill claims against C. difficile, but is marketed as a whole room surface disinfection system. Marketing this product as a broad spectrum control system when efficacy has only been evaluated for the aforementioned three microbes could lead to misuse or overuse of an already complicated product and application process. It could also lead to the perception that a setting has been disinfected from all pathogens when this is not the case – potentially creating an infectious disease risk.