



Response to Comments

Revisions to Criteria for Microbial-Based Cleaning Products

November 11, 2021

Overview

Microbial-based cleaning products, sometimes referred to as “probiotic cleaning products,” are formulated with non-pathogenic microbes as functional ingredients. Well-characterized, commercially produced microbes are included in cleaning products due to their ability to produce specific enzymes that target and breakdown common contaminants such as fats, oils, greases, and odor-causing chemicals such as ammonia.

In 2012, Green Seal issued the health protective requirements for microbial-based cleaning products, including requirements for microbial-based products sold in or designed for use in spray packaging. Between 2012 and 2017, Green Seal attempted to certify these products. It became clear that the requirements for spray-applied products were infeasible. One of the barriers was that the required inhalation exposure test was not offered as a service by most or any product testing laboratories. Therefore, in 2017, Green Seal clarified the standards by stating that spray-applied products were not eligible for certification, with the intention of revising these requirements for feasibility in the future.

In 2019 and 2020, Green Seal conducted extensive literature reviews on microbial-based cleaning products, focusing on scientific studies that were published between 2010 and 2020. In 2020 and 2021, Green Seal conducted rigorous stakeholder outreach to microbe suppliers, final manufacturers, scientists in academic and commercial laboratories, end users, and companies with certified (non-spray) microbial-based cleaning products. The intention of the research and outreach was to identify any new or emerging information on health risks and environmental risks of these products, evaluate barriers to certification for these products, and design a feasible, health-protective compliance pathway for the certification of these products. Green Seal’s literature reviews did not identify any new or emerging information on health risks and environmental risks.

In the fall of 2021, Green Seal finalized our determination: there continues to be a sufficient track record of safe use of these products; these products are now widely available for purchase on both the professional and household markets; therefore, Green Seal is now again offering Green Seal certification to spray-applied microbial-based cleaning products.

Stakeholder Input and Green Seal Response

The majority of participating stakeholders shared support for the objective of the proposal and the final proposed criteria (proposed in July 2021) for spray-applied microbial cleaning products. Additionally, Green Seal appreciated receiving statements of concern from a minority of stakeholders. Green Seal hosted several discussions to address stakeholder concerns and discuss their recommendations in detail. In Section 4, herein, we detail how Green Seal considered all concerns, addressed certain concerns, and acknowledged certain concerns while providing justification for not incorporating the recommendations into the final criteria.

Stakeholder Participants

The following stakeholders provided recommendations, shared technical expertise, and submitted statements of approval and substantive objections. Green Seal greatly appreciates the participation of more than 30 stakeholder groups and individuals that volunteered time and shared expertise to co-develop the criteria for spray-applied microbial-based cleaning products.

American Cleaning Institute (ACI)

EcoQuality Solutions

Genesis Biosciences

Household & Commercial Products Association (HCPA)

International Flavors and Fragrances (IFF)

Novozymes

ProBioTec international

Document Guide

This document contains the comments that were submitted by stakeholders during the two public comment periods: April 2021 and July 2021, and also contains Green Seal's responses to those comments. To review the proposals and other revision documentation, visit Green Seal's website.

Section 1. Summary of Stakeholder Input

Section 2. Comments Submitted During the April 2021 Public Comment Period

Section 3. Comments Submitted During the July 2021 Public Comment Period

Section 4. Green Seal's Response to Comments

Section 1. Summary of Stakeholder Input

Stakeholder Support

A majority of the participating stakeholders expressed strong support for the two major proposed changes to Green Seal's criteria for microbial-based cleaning products:

- Support for extending eligibility to spray-applied microbial cleaning products
- Support for including additional requirements for spray-applied microbial cleaning products
- Support for deleting most of the requirements for product label statements for both non-spray and spray-applied microbial-based cleaning products.

For product label requirements: All stakeholders with a focus on the household cleaning product market supported the proposed deletion of most of the product label statements.

For spray-applied products: Most stakeholders supported a flexible approach to verifying health protections – either via ingredient restriction that aligns with the requirements set by the EU Ecolabel (only QPS list microorganisms) or that the product must undergo inhalation exposure testing.

Summary of Stakeholder Concern and/or Opposition

A minority of stakeholders recommended requiring an exposure assessment to address the uncertainty regarding health risks of inhalation exposure to these products, as noted in the written comment submitted by the American Cleaning Institute, included in Section 3, herein. Additionally, certain stakeholders encouraged that Green Seal maintain the product label instructions to avoid using the product around immunocompromised individuals.

A minority of stakeholders stated that Green Seal should continue to find a more health protective limit for inhalation exposure testing. These stakeholders did not recommend any specific thresholds in lieu of Green Seal's proposed 10^4 CFU maximum airborne threshold.

Green Seal's Full Response to stakeholders can be found in Section 4, herein.

Other Input

Several stakeholders encouraged Green Seal to develop a Best Practices guidance document that could set a foundation for future criteria for these products including verification of Quality Control, stability testing, more detailed performance testing protocols for these products, and on-label disclosure of the microbial species.

Green Seal's General Response to All Stakeholder Input

We appreciate the input, recommendations provided by all participating stakeholders. The technical and market expertise and insight shared has been critical to carrying out evidence-based decision-making for the purposes of defining products that are better for people and our planet. Green Seal standards are designed to reflect today's environmental leadership on the North American market. Green Seal remains vigilant to address any new or emerging health and environmental risks determined by scientific studies and occupational health reports. And as new information arises and as products evolve to be safer, healthier, and greener, Green Seal moves to update our standards in order to continue to encourage market transformation that is increasingly protective of human health and our environment.

Section 2. Comments Submitted During April 2021 Public Comment Period

During the April 2021 Public Comment Period, Green Seal received two written comments from:

- American Cleaning Institute (ACI)
- Household and Commercial Products Association (HCPA)

Comment 1, American Cleaning Institute

I write on behalf of the American Cleaning Institute¹ (ACI) to Green Seal, to provide comment on Green Seal's Proposed Revisions to Criteria for Microbial-Based Cleaning Products.

ACI is an industry leader in serving the cleaning products industry, advancing the health and quality of life of people and protecting our planet. We focus on the advancement, promotion, and utilization of science to drive informed dialogue and decision making. We are pleased to have the opportunity to provide comment to the proposed revisions to Green Seal Standards GS-8, GS-37, GS-48, GS-51, GS-52, and GS-53, as relevant.

Green Seal Proposed Revision: Deletion of Prohibition on Spray Packaging.

ACI offers the following response on Green Seal's proposed revision on the *Deletion of Prohibition on Spray Packaging*:

In review of the proposed standard revision of deleting the prohibition of "microorganisms" that are sold in spray packaging, ACI seeks to provide additional input for consideration. Biosafety level 1 (BSL-1) organisms can be diverse, and some may present health hazards through inhalation, including risks to immunocompromised and sensitive populations, as noted in multiple references to the proposal for revision to the Standard presented by Green Seal. ACI recommends a risk and safety assessment be conducted on spray products before commercialization. Referencing the Panel on Microbial Ecology of the Norwegian Scientific Committee for Food and Environment report provided by Green Seal² there are important considerations when

- o Identification of species and strains
- o Characterization of species and strains
- o Pathogenic potential- cytotoxin production profiles, virulence genes
- o Resistance profiles (AMR—anti-microbial resistance)
- o Application/intended use- exposure assessment of product during use (considering frequency, duration, and dose) determining hazardous properties or risk factors of viable microorganisms and their inclusion in cleaning products.

Recommendations may include but are not limited to:

Green Seal Proposed Revision: Deletion of Burdensome and Unnecessary Labeling requirements

ACI offers the following response on Green Seal's proposed revision on the *Deletion of Unnecessary and Burdensome Labeling Requirements*:

ACI proposes that if a product risk assessment is conducted that supports product safety, then reduced labeling requirements may be appropriate for those products. While this reduction in burden on formulators will be appreciated, ACI emphasizes that the consideration of human health effects, in particular sensitive populations (e.g. immunocompromised individuals), are essential as it concerns product application and use. As the organisms employed in microbial based cleaning products will differ between manufacturers, it is important to recognize that certain organisms though normally considered non-pathogenic, may opportunistically infect individuals with compromised immune systems. These items are important to consider for consumer awareness and safety.

ACI thanks you for consideration of our input during this public comment period. We are happy to provide more clarity or input on any additional questions you may have as you revise your standards. Please contact me at aqueen@cleaninginstitute.org or 202.441.0617 if I can be of further assistance.

Best regards,
Ashley Queen, Ph.D.
Director, Microbiology and Public Health

¹ The American Cleaning Institute® (ACI – www.cleaninginstitute.org) is the Home of the U.S. Cleaning Products Industry® and its members include the manufacturers and formulators of soaps, detergents, and general cleaning products used in household, commercial, industrial and institutional settings; companies that supply ingredients and finished packaging for these products; and chemical distributors.

² Current knowledge of the health and environmental risks of microbial-based cleaning products:
<https://www.vkm.no/english/riskassessments/allpublications/healthandenvironmentalassessmentofmicrobialbasedcleaningproducts.4.1aaadf0516963f003a25dde5.html>

Comment 1 Submitted by the Household and Commercial Products Association

Date: April 26, 2021

To: Green Seals Standards (standards@greenseal.org)

From: Andrea Mojica, Vice President, Regulatory Affairs at the Household & Commercial Products Association (HCPA)

Re: Comments on Proposed Revisions to Criteria for Microbial-Based Cleaning Products

The Household & Commercial Products Association (HCPA) appreciates the opportunity to provide comment on Green Seal's proposed revisions to the standards for microbial-based cleaning products¹. HCPA is the premier trade association representing the interests of companies engaged in the manufacture, formulation, distribution, and sale of more than \$180 billion annually in the U.S. of familiar and trusted consumer products that help household and institutional customers create cleaner and healthier environments. Our membership manufactures, supplies, and incorporates microorganisms into end-use products.

HCPA supports Green Seal for allowing products containing bacterial spores of class 1 organisms to be approved under the following standards: GS-8 / GS-37 – Green Seal Standards for General Purpose Cleaners; GS-48 / GS-51 – Green Seal Standards for Laundry Care Products; and GS-52 / GS-53 – Green Seal Standards for Specialty Cleaners. However, HCPA would urge that microbes that are sprayed would have a completed risk assessment evaluating this application method to ensure that they will not cause negative effects in a respirable form. HCPA members are particularly encouraged by the changes to labeling requirements which will reduce consumer confusion and allow products to be better received in the market. These changes to the Standard will continue to bolster support for these products.

Thank you for the opportunity to provide comment on this topic.

Section 3. Comments Submitted During July 2021 Public Comment Period

Comment 2 Submitted by the American Cleaning Institute

I write on behalf of the American Cleaning Institute¹ (ACI) Microbial Cleaning Products Task Force to Green Seal, to provide comment on Green Seal's Proposed Revisions to Criteria for Microbial-Based Cleaning Products. ACI is an industry leader in serving the cleaning products industry; advancing the health and quality of life of people and protecting our planet. We focus on the advancement, promotion, and utilization of science to drive informed dialogue and decision making. We are pleased to have the opportunity to provide comment to the proposed revisions to Green Seal Standards GS-8, GS-37, GS-48, GS-51, GS-52, and GS-53, as relevant.

Below are Green Seal's proposed revisions regarding microbial based cleaning products in spray packaging:

July 2021 Update: Products sold in or designed for use in spray packaging must meet at least one of three requirements:

- (1) Include precautionary statements on the product label
- (2) Formulate only with microbes listed on the European Food Safety Authority's Qualified Presumption of Safety list
- (3) Undergo inhalation exposure testing and meet a maximum threshold of airborne microbes.

Additional Requirements for Products in Spray Packaging. For products formulated with microorganisms and designed for use in, or sold in, spray packaging, at least one of the following requirements must be met:

- The microbial ingredients in the product shall be restricted to those included in the European Food Safety Authority's (EFSA) Qualified Presumption of Safety (QPS) List.
- The product label shall state the following precautionary statements*
 - o Product should not be sprayed into the air.
 - o Avoid inhalation of the product.
 - o Repeated and prolonged exposure may cause sensitization of the respiratory system.
- The product shall demonstrate, via inhalation exposure testing, an airborne concentration of microbes at or below 1 x 10⁴ CFU/m³. Testing parameters shall be in alignment the A.I.S.E. spray protocol (2020) 2.

ACI offers the following response on Green Seal's proposed revision to criteria for microbial based cleaning products (July 21, 2021 update):

Option one (1) of the proposed requirements indicates inclusion of precautionary statements on the product label as a single option. A recommended statement would be to more specifically emphasize that the "*Product is intended for use on surfaces and should not be sprayed into the air.*" ACI recommends that the precautionary labeling requirements remain as they stand in currently adopted version of the Standards, as eight (8) required options. Precautionary labeling is likely not sufficient to protect consumers from exposure, while the other options outlined will be more likely to provide consumer protections.

It was indicated by Green Seal in response to ACI's previous comments, that in their literature search no sources were identified that indicated instances of negative health effects associated with application of microbial based cleaning products. Based on this literature evaluation Green Seal determined that consideration of respiratory health hazards in immunocompromised individuals is not warranted [in summary]. ACI highly recommends cautioning against that approach and recommends a thorough review of the following references which do indicate the potential for negative health effects.

- <https://doi.org/10.2903/sp.efsa.2010.EN-75>
- <https://doi.org/10.1080/17476348.2018.1473036>

- <https://doi.org/10.1186/1471-2180-10-233>

ACI emphasizes that the consideration of sensitive populations (e.g. immunocompromised individuals) is essential as it concerns product application and safety.

ACI still strongly supports the comments made on April 26, 2021 regarding recommendations to determine hazardous properties and risk factors of spray cleaning with viable microorganisms. In addition, consideration of quality control processes to identify contaminants should be included in the Standards. Many of these recommendations were also supported by the Panel on Microbial Ecology of the Norwegian Scientific Committee for Food and Environment report (VKM) provided as reference by Green Seal during the previous revision comment period.
(<https://www.vkm.no/english/riskassessments/allpublications/healthandenvironmentalassessmentofmicrobialbasedcleaningproducts.4.1aaadf0516963f003a25dde5.html>)

Item two (2) of the proposed revision suggests *formulating products only with microbes listed on the European Food Safety Authority's Qualified Presumption of Safety list*. ACI recommends that any organisms not within this list be demonstrated to also minimally meet the same strain safety evaluation and requirements as those organisms listed in the QPS. Further, note that the EFSA evaluation is likely to pertain to primarily ingestion and would not necessarily evaluate inhalation hazards. A thorough review and evaluation of strain characteristics as per VKM guidance could be an alternative approach to demonstrate safety, in addition to an appropriate and robust exposure-based approach to assess safety for the specific use application.

Item three (3) of the proposed revision indicates *products should undergo inhalation exposure testing and meet a maximum threshold of airborne microbes*. ACI recommends that Green Seal continues to identify additional sources to support the limit of 1×10^4 CFU/m³. In a literature review, a reference was identified in a 1989 Dutch provisional recommendation. The Dutch Health Council ultimately stated that an exposure level cannot be established for microorganisms. In addition, the original Dutch provisional recommendation limit of 1×10^4 CFU/m³ was for a combination of environmental organisms (bacteria, fungi) and limited single microorganism type at 500 CFU/m³. There are other references that indicate potentially appropriate ranges and ACI recommends that Green Seal considers additionally reviewing these sources before settling on a proposed limit; links to such sources are listed below. These references are for workplace exposures and additional consideration may be needed in applying to consumer exposure.

Fungal spores: a critical review of the toxicological and epidemiological evidence as a basis for occupational exposure limit setting - PubMed (nih.gov)
Guide on respiratory protection against bioaerosols (irsst.qc.ca)
Bioaerosols and OSH - OSHWiki

ACI encourages Green Seal to continue their efforts to identify testing laboratories by specifically holding a call for comment to industry for labs capable of conducting these proposed risk assessments (in addition to capabilities of airborne microbial sampling). This product category requires much consideration in assurance of product integrity, application, and safety. We look forward to the opportunity for continued communication regarding this product category.

ACI thanks you for consideration of our input during this public comment period. We are happy to provide more clarity or input on any additional questions you may have as you revise your standards.

Best regards,
Ashley Queen, Ph.D.
Director, Microbiology and Public Health

¹ The American Cleaning Institute® (ACI – www.cleaninginstitute.org) is the Home of the U.S. Cleaning Products Industry® and its members include the manufacturers and formulators of soaps, detergents, and general cleaning products

used in household, commercial, industrial and institutional settings; companies that supply ingredients and finished packaging for these products; and chemical distributors.

² Safety assessment of the use of Bacillus-based cleaning products:
<https://www.sciencedirect.com/science/article/abs/pii/S0278691517306968>

Comment 2 Submitted by the Household and Commercial Products Association

The Household & Commercial Products Association¹ (HCPA) appreciates the opportunity to provide input on the updated criteria for the microbial-based cleaning products. We value the collaborative discussions with Green Seal and appreciate the chance to review the updated proposal.

To reiterate our April 26th comments, HCPA supports Green Seal for allowing products containing bacterial spores of class 1 organisms to be approved under the following standards: GS-8 / GS-37 – Green Seal Standards for General Purpose Cleaners; GS-48 / GS-51 – Green Seal Standards for Laundry Care Products; and GS-52 / GS-53 – Green Seal Standards for Specialty Cleaners.

HCPA supports the following additional criteria for microbial cleaning products sold in spray packaging: (1) that microbial ingredients in the product shall be restricted to those included in the European Food Safety Authority's (EFSA) Qualified Presumption of Safety (QPS) List or (2) that the product shall demonstrate, via inhalation exposure testing, an airborne concentration of microbes at or below 1×10^4 CFU/m³. Testing parameters shall be in alignment with the A.I.S.E. spray protocol (2020).

HCPA recommends that the option to only put precautionary language on the label be removed. The addition of precautionary language, absent of other requirements, could potentially lead to unintended health consequences.

Thank you for the opportunity to provide additional comment on this topic.

Section 4. Green Seal's Responses to Written Comments

Product Label Requirements:

- 1.) **ACI recommends that Green Seal maintain the requirement that product labels must include instructions to “not spray the product into the air. (Noted in ACI’s Comment 2)**

Green Seal Response: We appreciate this recommendation. After consideration and discussion with product users and marketing teams of household and professional-care cleaning products, Green Seal confirmed that this statement is appropriate, clear to users, and is feasible and non-problematic. Therefore,

Outcome: Green Seal criteria for spray-applied microbial products includes this product label statement.

- 2.) **ACI states preference for maintaining the original eight required precautionary statements, but notes that precautionary statements are not likely to provide consumer protections. “ACI recommends that the precautionary labeling requirements remain as they stand in currently adopted version of the Standards, as eight (8) required options. Precautionary labeling is likely not sufficient to protect consumers from exposure, while the other options outlined will be more likely to provide consumer protections.”**

Green Seal Response: We appreciate this recommendation, however, we maintain that eight precautionary statements on product labels are not feasible or appropriate for household product labels, and are not relevant to professional product applications where product data sheets are common tools for conveying detailed user information. Green Seal agrees with ACI’s statement that precautionary statements are insufficient and less likely to result in health protections for product users in comparison to other possible requirements, such as verifications of safer formulas and verified low potential of user inhalation of microorganisms. In Green Seal’s final criteria for these products, we have established an additional verification for safer formulas (QPS list microorganisms, noted below) and verified low potential of user inhalation of microorganisms (inhalation exposure testing, noted below).

Outcome: For feasibility and because we have confirmed a sufficient track record of safe use of these products, Green Seal has deleted most of the previous requirements for precautionary statements on product labels.

- 3.) **HCPA recommends that the option to only put precautionary language on the label be removed. The addition of precautionary language, absent of other requirements, could potentially lead to unintended health consequences.**

Green Seal Response: We appreciate this input and agree that this compliance pathway does not sufficiently address uncertainties regarding inhalation exposure to microorganisms. Therefore, Green Seal did not include the compliance pathway that was proposed in July 2021, which allowed spray-applied products to be certified if they included specific precautionary statements on the product label. With support from stakeholders, Green Seal has opted to set only two compliance pathways for spray-applied products: formula restrictions or an inhalation exposure test demonstrating a low level of bioaerosols generated from product application. Also, Green Seal maintains one additional precautionary statement for spray-applied products: the product label must state that users should not spray the product into the air.

Outcome: Green Seal’s criteria for spray-applied cleaning products is now designed to be more restrictive and health-protective; the product label statement compliance pathway was not enacted into the final criteria.

Safety and Risks Assessments

- 4.) **ACI and HCPA recommend a Safety and Risk Assessment.** In ACI’s two comments and HCPA’s initial comment submitted in April 2021, these two organizations encouraged Green Seal to require a full safety and risk assessment for spray-applied cleaning products. Below is an excerpt from ACI’s comments:
- o Identification of species and strains
 - o Characterization of species and strains
 - o Pathogenic potential- cytotoxin production profiles, virulence genes
 - o Resistance profiles (AMR—anti-microbial resistance)
 - o Application/intended use- exposure assessment of product during use (considering frequency, duration, and dose) determining hazardous properties or risk factors of viable microorganisms and their inclusion in cleaning products.

Green Seal Response: We appreciate this recommendation.

Green Seal’s existing health protective framework for all microbial-based cleaning products already requires the first four of the five steps of the Safety and Risk Assessment (identification, characterization, pathogenic potential, and resistance profiles).

Green Seal did not initially consider setting a requirement for inhalation exposure testing (“Exposure Assessment.” Green Seal agreed with ACI and HCPA’s initial comments and therefore updated our proposed criteria and re-published the proposal in July 2021. The final proposed and now final criteria include an exposure assessment of the product during use as one of two options for compliance. The other option for compliance is that the microorganisms must be included on the European Food Safety Authority’s (EFSA’s) Qualified Presumption of Safety list.

Green Seal agrees that exposure assessments are beneficial for understanding the potential user exposure during product application from these products. However, exposure assessments – specifically inhalation exposure assessments for microbial-based cleaning products – are not widely available on the North American market. Therefore, Green Seal has included this as an option so that we can demonstrate support for this investment, set a feasible bioaerosol threshold, gather data via product certifications to monitor if this test is becoming more common for leadership products in this product category, and continue collaborative work with microbial suppliers and final manufacturers to define a more health protective bioaerosol threshold for these products as we learn more by reviewing laboratory test reports.

Outcome: Inhalation exposure testing and meeting a bioaerosol threshold of 10^4 CFU/m³ is one of two compliance options that are now required for spray-applied microbial-based cleaning products.

Addressing Uncertainties Regarding Inhalation Exposure to Microorganisms

5.) ACI States Concern for Sensitive Populations

ACI proposes that if a product risk assessment is conducted that supports product safety, then reduced labeling requirements may be appropriate for those products. While this reduction in burden on formulators will be appreciated, ACI emphasizes that the consideration of human health effects, in particular sensitive populations (e.g. immunocompromised individuals), are essential as it concerns product application and use. As the organisms employed in microbial based cleaning products will differ between manufacturers, it is important to recognize that certain organisms though normally considered non-pathogenic, may opportunistically infect individuals with compromised immune systems. These items are important to consider for consumer awareness and safety.

Green Seal Response: We appreciate this recommendation and agree that it is important to consider how these products (and conventionally formulated cleaning products) may affect sensitive populations, in particular,

immunocompromised individuals. Green Seal has applied the Precautionary Principle to develop health-protective requirements that far exceed existing US federal and European Union product regulations for microbial-based cleaning products: non-pathogenic (Biosafety Level 1) microorganisms are not classified as hazardous, however, to address uncertainties, Green Seal sets six additional health-protective requirements for microbial-based cleaning products, and now three additional requirements that must be met for spray-applied products. Below are the three lists of health-protective requirements that all microbial-based cleaning products must meet (not including environmentally protective criteria) totaling 18 health-protective requirements.

9 Core Health Protective Requirements for All Products	6 Additional Health-Protective Requirements for Microorganisms in Cleaning Products	3 Additional Requirements for Spray-Applied Microbial-Based Cleaning Products
Cannot be acutely toxic via ingestion Cannot be acutely toxic via inhalation No carcinogens No reproductive toxins No mutagens Cannot cause skin or eye damage Cannot cause skin sensitization Must be low VOC Cannot be combustible	Microorganisms cannot be genetically modified. Microorganisms must be WHO Risk Level 1 or equivalent biosafety designation. Microorganism strains must be identified through a taxonomic review provided by a full-service culture collection. A Certificate of Analysis must demonstrate that there are no pathogenic microorganisms present in the microbial strain, finished product or at the end of the product’s intended shelf life. All microorganisms must be susceptible to antimicrobial agents or one of the five major antibiotic classes. The product ingredient line must include the microbial ingredient.	For spray-applied products, product labels must state that the product should not be sprayed into the air. For spray-applied products, products cannot be formulated with fungal or mold species. For spray-applied products, product can only include microorganisms that are included on the European Food Safety Authority (EFSA)’s Qualified Presumption of Safety (QPS) list or undergo inhalation exposure testing and demonstrate a bioaerosol level of no greater than a 10,000 CFU/m3.

Green Seal acknowledges that there are documented occurrences of adverse health outcomes for individuals that are exposed to “opportunistic” microorganisms and those who inhale “biological dusts.” In these known cases, the microorganisms are those that are naturally occurring, i.e., are not commercially produced microbial strains that are scrutinized via Whole Genome Testing. Examples of adverse health effects are “farmer’s lung,” (an allergy caused by inhaling mold-contaminated hay), Legionnaire’s Disease (exposure to the pathogenic gram-negative legionella), and bacterially contaminated humidifiers. Green Seal is also aware of rare cases where non-fatal sepsis has occurred in hospitalized or infirm individuals due to the ingestion of prescribed oral probiotics.

The above cases were considered but deemed irrelevant to Green Seal’s considerations regarding spray-applied microbial-based cleaning products. The species of microorganisms in these instances are not those known to be ingredients in cleaning products, and the exposure scenarios are not equivalent to routine cleaning events.

According to Green Seal’s research, there is no known case where a microbial-based cleaning product caused an infection to an individual. These products have been studied for safety and efficacy in hospital settings with particular consideration on the potential for the spray-applied products to result in infections. There were no associated infections or associated adverse health effects in these studies.

Below are excerpts from studies that Green Seal reviewed with outcomes that factored into our final decisions for setting criteria for spray-applied cleaning products.

“Cleaning products made with non-pathogenic *Bacillus* pose a low potential for inhalation and thus minimal risk of adverse effects.” Safety assessment of the use of *Bacillus*-based cleaning products, [Food and Chemical Toxicology](#), June 2018

“The article by Caselli et al.[5] showed that it was safe to use the *Bacillus* species for decontaminating hospital surfaces, and that the probiotic bacteria did not acquire any new drug-resistance qualities. In a study by D’Accolti et al.,[7] it was found that probiotics can be active in decontaminating all kinds of hard surfaces, be effective in eliminating multi-drug resistant hospital isolates, and maintain their antibacterial activity in a detergent solution.[7].” The effect of probiotics for environmental cleaning on hospital-acquired infection in a burn centre: The results of a non-randomised controlled prospective study, *South African Journal of Plastic & Reconstructive Aesthetic Surgery & Burns* 3(2):33 2020

“What is clear at this time...some of the microbes used in cleaners are generally recognised as safe (GRAS) in food and other processing contexts, or as QPS (qualified presumption of safety) in other contexts, indicating that they have a sufficient track record of safe use and handling to be exempted from certain risk assessment requirements. Some producers also referred to additional safety reassurance from various OECD (Organisation for Economic Co-operation and Development) toxicity tests on rodents, although the test data were not publicly accessible. To the best knowledge of the authors there is no report on health incidents resulting from professional or consumer use of MBCPs. Recent evidence suggests that microorganisms in MBCPs used in health-care settings do not contribute in any way to hospital-acquired infections ([Caselli et al. 2016a, b](#)).” Status of Microbial Based Cleaning Products in Statutory Regulations and Ecolabelling in Europe, the USA, and Canada, *Food Chem Toxicol.* 2018 June

Outcome: Green Seal has addressed inhalation exposure via two health-protective compliance pathways: ingredient restriction (QPS list microorganisms, defined herein) and inhalation exposure testing. Green Seal criteria for these products does not include product label statements noting that these products may be more hazardous to individuals who are immunocompromised.

Submission of Additional Evidence Pointing to Potential Adverse Health Effects

6. ACI submitted additional sources of information on potential health risks

It was indicated by Green Seal in response to ACI’s previous comments, that in their literature search no sources were identified that indicated instances of negative health effects associated with application of microbial based cleaning products. Based on this literature evaluation Green Seal determined that consideration of respiratory health hazards in immunocompromised individuals is not warranted [in summary]. ACI highly recommends cautioning against that approach and recommends a thorough review of the following references which do indicate the potential for negative health effects.

- <https://doi.org/10.2903/sp.efsa.2010.EN-75>
- <https://doi.org/10.1080/17476348.2018.1473036>
- <https://doi.org/10.1186/1471-2180-10-233>

Green Seal Response: We appreciate the submission of evidence for our consideration. We reviewed the four links to understand the relevance to Green Seal’s proposal. We did not find definitive conclusions or data presented that related to the impact of microbial spores on immunocompromised individuals or definitive conclusions that exposure to spray-applied microbial-based cleaning products, or similar exposure scenarios, result in adverse health effects to product users or bystanders. Below, we have noted the title of the document and provided excerpts that we deemed relevant to our final decision making.

In response to the Bibliographic review, Green Seal recognized an unacceptable potential risk to product users and therefore Green Seal established that spray-applied cleaning products cannot be formulated with either fungi or mold species. However, yeast species (within the Fungi Kingdom) are acceptable.

<https://doi.org/10.2903/sp.efsa.2010.EN-75> - **Title:** Bibliographic review on the potential of microorganisms, microbial products and enzymes to induce respiratory sensitization.

Conclusions of Bibliographic Review:

- “Cases of occupational allergy to both fungi and bacteria have been documented, but allergic reactions to microorganisms purportedly introduced in the work environment seem to concern only a limited number of fungi.”
- The abstract and conclusions of this article clearly point to the “apparent lack of role of bacteria in allergic diseases.”
- “...from our survey, it seems that HP has been linked to exposure to *B. pumilis* (machine operator’s lung), *B. subtilis* (wood dust) and *A. globiformis*(agricultural workers). HP remains, however, a very rare disease, and is associated with very specific conditions and high level of exposure. None of the cases described resulted from an intentional use of the bacteria.”

Additional Summary: This article touches on several times of microorganisms that are naturally occurring, unrelated to the products or processes and “ubiquitous in the human environment” - *Mycobacterium* species in metalworking, the naturally high level of thermophilic actinomycetes and molds that exist in soil during the harvesting of mushrooms and emphasized that the humidity of the environments were likely one of the factors in exposures. In the section focused on microorganisms, there is no example where cleaning or facility care occupations or products were identified as the cause or suspected cause of respiratory issues in workers or building occupants. In particular in cases focused on animals and humidifiers and cheese production. Additionally, the strains identified as known for causing respiratory issues were not those that are known to be common in cleaning products and are those that are not included on the EFSA’s list.

- *Arthrobacter globiformis* (found in soil)
- *Aspergillus niger* – a single case found in 1996
- *Bacillus licheniformis* – no human cases – in mice they cause a reaction when in the blood stream, no evidence of inhalation
- *Lactobacillus*, *L. acidophilus*, *L. plantarum*, – “ample evidence indicating that lactobacilli alleviate allergic symptoms. Reduce severity of type 1 allergic reactions in both humans and mice.

<https://doi.org/10.1080/17476348.2018.1473036> -- **Title:** Current and emerging techniques for the diagnosis of hypersensitivity pneumonitis

Excerpt: “We review current diagnostic procedures including antigen detection, high resolution computed tomography, histopathology and provide an overview of emerging techniques.”

Green Seal Response: We did not find this review of diagnosis techniques to be relevant to microbial-based cleaning products.

<https://doi.org/10.1186/1471-2180-10-233> -- **Title:** Sub-chronic lung inflammation after airway exposures to *Bacillus thuringiensis* biopesticides in mice

Excerpt: “The sub-chronic inflammation observed in the present study, was most likely due to the prolonged presence of Bt spores or other product residues in the lungs, triggering and maintaining the inflammatory response. This should be seen in the light that the formulated biopesticides contains only about 2% spores and 98% other ingredients according to manufacturer which makes long term inhalation studies using the final formulated biopesticide important. The list of other ingredients besides water is known to authorities (e.g. the EPA) and approved for other purposes e.g. a "food- carbohydrate" and preservatives [32]. Most of these other ingredients have probably not been subjected to long term inhalation studies in animals as this was not their intended use. Therefore alternative inoculums or controls, including spore free or heat-inactivated biopesticide or specific excipients/additives should also be studied for biological effect.”

Green Seal Response: We did not find this study of biopesticides, using a rodent model, to be relevant as a proxy for exposures to microbial-based cleaning products. Lung inflammation was noted after chronic inhalation exposure to aerosolized biopesticides. The excerpt above expresses uncertainty regarding if the inflammation was caused by inhalation to the bacillus thuringiensis spores or the other ingredients in the product. The type of bacillus species and the modeled levels of exposures, intended to reflect greenhouse applications of the biopesticide, are not relevant to microbial-based cleaning products.

Outcome: No actions were taken in regard to the three sources of information provided by ACI.

Final Note Acknowledging Participating Stakeholders

Green Seal appreciates our stakeholders’ time, expertise, and commitment to constructive collaboration as we pursue common goals: to encourage the production and use of safer, greener cleaning products in household and professional settings. We pledge to remain vigilante regarding newly defined hazards or stronger evidence of health risks noted for any product eligible for Green Seal certification and to continuously raise the bar to reflect today’s sustainable product leaders on the North American market.