

Risk analysis approaches for microbial ingredients in microbial-based cleaning products

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Abstract

Microbial-based cleaning products (MBCPs) are an emerging class of cleaning products that contain viable microorganisms, often bacteria or bacterial endospores, as intentionally added formulation ingredients for cleaning and/or odor control. Although several well-established methodologies exist to support risk analysis for conventional chemical-based cleaning products, at present there are no widely recognized methods or commonly utilized frameworks to support risk analysis for use of microbial ingredients present in MBCPs, specifically. The purpose of this work is to provide information to MBCP manufacturers and regulators that can be used to assist in developing their own approaches to MBCP risk assessment. As part of this assessment, potential hazards associated with use of bacterial or bacterial endospore ingredients of MBCPs can be adequately characterized, assessed, and managed as part of both product development and ongoing product stewardship. Accordingly, this document summarizes potential approaches to support strain-level identification of microbial ingredient(s), evaluate their hazards and potential for human exposure, and assess their potential effects following such exposures to different human populations. Recommendations for both hazard and risk characterization are discussed. Additionally, guidance is provided to support decision-making by risk managers, including guidance for the development of risk communication strategies, where appropriate, to mitigate the identified risks. Properly applied, the conceptual approaches described herein may facilitate the standardization and more consistent application of appropriate risk analysis procedures tailored to suit microbial ingredients present in MBCPs. Beyond their utility in assessing microbial ingredients commonly used in MBCPs today, these same approaches may help companies and regulators consider and manage risks for new microbial ingredients that may be utilized in future MBCP formulations.

KEYWORDS

microbial cleaning products, microbiological hazards, product safety, risk analysis

1 | INTRODUCTION

Microbial-based cleaning products (MBCPs) are cleaning products that contain one or more viable microorganisms as an intentionally added formulation ingredient. Unlike similar type products intended to exhibit antimicrobial properties,

MBCPs are intended to be used for aesthetic cleaning and/or odor control purposes only. Microbe-containing products intended for biocidal uses are regulated by the pertinent regulatory authorities as biocides (or as pesticides in the United States), which have their own regulatory requirements, inclusive of an evaluation of risk. As such, risk analysis approaches for biocides will not be covered here.

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Microorganisms have long been used successfully in consumer cleaning products such as drain cleaners and septic tank treatment products. However, in recent years there has been increasing commercial and consumer interest in the use of microbially based technologies in household, professional, and industrial cleaning applications as well. Much, though not all, of this interest is focused on products that can clean environmental hard surfaces such as floors and countertops, as well as carpets and upholstery. As with standard chemical-based cleaning products, MBCPs come in various formulation types (e.g., liquids, powders, granules, foams, etc.) and can be applied via different application approaches (e.g., trigger spray, wipe, pour, sponge, cloth, mop, pod, etc.). Market innovation in this evolving sector may spur additional innovation regarding MBCP formulation types and application approaches. Regardless of formulation type or application approach, the increasing use of such products for surface cleaning applications has the potential to increase overall human exposure to their intentionally added microbial ingredients, therefore necessitating an evaluation of risk through employment of hazard and risk assessments.

Following their application, the microbial ingredients in MBCPs are commonly intended to perform functions such as the degradation of organic matter on surfaces and/or the mitigation of odors associated with microbial degradation of organic matter. Such functions are typically accomplished through metabolic activity of the subject microbe and/or the production of extracellular enzymes that facilitate the degradation of organic soil. The use of microbial ingredients for this purpose can potentially lend other desirable qualities to a given cleaning product, such as the ability to facilitate cleaning in otherwise inaccessible places (e.g., deep pores, cracks, and crevices) where mechanical cleaning is difficult to accomplish. Additionally, some MBCPs can potentially sustain cleaning activity over extended periods of time in between product applications, as the viable microbial ingredients can provide cleaning benefits for as long as they remain viable and/or metabolically active on a treated surface.

Although the term “microbial” in MBCP could refer to a variety of different biological entities (i.e., bacteria and fungi), most MBCPs currently on the market contain bacteria as the intentionally added microbial ingredient(s) (Razenberg et al., 2020; Spök et al., 2018). Bacteria commonly used in MBCP formulations include various members of the *Bacillus* genera (e.g., *B. subtilis*, *B. licheniformis*, and *B. pumilus*), as well as *Bifidobacterium* spp., *Lactobacillus* spp., and *Rhodospseudomonas* spp. (Jeżewska-Fraćkowiak, Joanna et al., 2019; Razenberg et al., 2020; Spök et al., 2018). Although some currently marketed MBCP formulations include non-endospore-forming bacteria (e.g., *Lactobacillus* spp.); in practice, most currently marketed MBCPs contain endospore-forming bacteria or bacterial endospores themselves (Razenberg et al., 2020; Spök et al., 2018). Bacterial endospores are a metabolically dormant and nonreplicating form of a bacterial cell and are exclusively produced by bacteria within the Firmicutes phylum (Egan et al., 2021; Galperin, 2013). Bacterial endospores are quite robust and much more

resistant to adverse factors such as nutrient deprivation, temperature and pH extremes, desiccation, and chemical- or UV-based inactivation than vegetative bacteria. Therefore, they tend to be more stable in an end-use formulation. These characteristics make endospore-forming bacteria, or bacterial endospores themselves, particularly advantageous from a product manufacturing perspective. Likewise, these characteristics can also help ensure that bacterial concentrations within an MBCP remain at acceptable levels both during product storage and after product application.

MBCPs using endospores as formulation ingredients rely on them to germinate, imparting a cleaning benefit to a treated surface after application. Notably, favorable conditions for endospore germination often correspond to those where cleaning may be desired (e.g., the presence of excess moisture, nutrient sources in the form of organic soil, etc.). When unfavorable conditions for vegetative growth return (i.e., when the substrate had been metabolized), vegetative microbial ingredients can sporulate, leaving behind endospores, which are then available for future germination and renewed activity when the application location again becomes “dirty.”

As a general class of cleaning products, MBCPs offer a promising area of innovation for cleaning technology and are often perceived by consumers as being more environmentally friendly (i.e., greener) than their chemical alternatives. It is likewise tempting to assume that such products are “safe” given their “natural” bacterial ingredients. There are several examples in the literature of surface treatment products containing *Bacillus* species or their endospores (i.e., *B. subtilis*, *B. pumilus*, *B. megaterium*, *B. licheniformis*, and *B. amyloliquefaciens*) being tested in hospitals and other healthcare settings) to assess their cleaning and/or biocidal properties (Al-Marzooq et al., 2018; Caselli et al., 2016, 2018; Leistner et al., 2023; Vandini et al., 2014). When evaluated, these studies have generally found that the use of these surface treatment products does not adversely impact hospital-acquired infection (HAI) incident rates (Caselli et al., 2018; Leistner et al., 2023). Likewise, there is evidence to suggest that HAIs that do occur following the use of such products are not generally attributable to intentionally added microbial ingredients present in the surface treatment product (Caselli et al., 2016, 2018). Overall, these data are supportive of the idea that MBCPs can be safely used, provided that appropriate microorganisms, product use patterns, and risk mitigation measures are employed. Nevertheless, the responsible stewardship of household, professional, and industrial cleaning product manufacturers calls for a holistic analysis and mitigation of the potential risks that such products may pose to their users and/or other individuals who may be exposed to microbial ingredients following product use.

Although such risk analysis and mitigation approaches are well-established for cleaning products that exclusively contain chemical ingredients (EPA, 2016), microbial ingredients pose unique challenges to risk analysis and mitigation. Relative to conventional cleaning products and their ingredients, there is less overall experience in both industry and the regulatory community regarding how risk analysis can

appropriately be applied to MBCPs and ultimately used for product development, business decision-making, regulatory oversight, or other purposes. This reality, combined with the expectation that MBCPs may become more common in the household, professional, and industrial sectors in coming years, highlights the need to establish more robust approaches to assess and manage potential risks associated with MBCP ingredients. This need has been emphasized by several recent publications relevant to both microbial MBCP ingredients and microorganisms used in other types of products (Arjmand, 2019; Arvanitakis et al., 2018; Chokesajjawatee et al., 2020; La Maestra et al., 2021; Todorov et al., 2022; Velazquez et al., 2019).

The widespread use of risk assessment and risk management practices in gauging and managing risk for conventional cleaning products suggests that a similar framework could be beneficial for identifying, evaluating, managing, and mitigating risks associated with MBCPs. Accordingly, this document builds on existing work done by others regarding how certain risk assessment procedures and analysis practices can be adapted to suit MBCPs (Berg et al., 2018; Bernatchez et al., 2018; La Maestra et al., 2021; Razenberg et al., 2020; Skaar et al., 2016; Teasdale & Kademi, 2018). In service of this goal, an overview of risk analysis is provided along with a discussion of how a risk assessment process and its attendant steps (i.e., hazard identification, exposure assessment, hazard characterization, and risk characterization) can be applied to microbial ingredients present in MBCPs. The role of risk management in the risk analysis of microbial MBCP ingredients is considered. Finally, this document closes with a discussion of risk communication as a critical step in managing any identified risks associated with microbial ingredients of commercial cleaning products.

This document is not intended to establish a final risk analysis framework for MBCPs. Rather, this document is intended to serve as a reference that governmental authorities (e.g., regulators), manufacturers, and formulators can consult, along with references cited herein, as they develop their own practices and procedures to support the risk analysis for MBCPs. This may not only assist with the development of suitable risk analysis approaches by individual regulatory authorities and companies but also may be used with the standardization of these approaches between organizations and the development of industry-facing guidance. This, in turn, may help to promote more standardized risk assessment approaches and a level regulatory playing field that supports the maturation of the MBCP industry and helps ensure the ongoing safe use of these products.

2 | OVERVIEW OF RISK ANALYSIS FOR MICROBIAL INGREDIENTS

Broadly speaking, the term “risk analysis” refers to an iterative and systemic process by which to understand and express the nature of risk associated with a given article, activity, or process and subsequently manage and communicate informa-

tion regarding that risk (Aven et al., 2018). For the purpose of this document, the term “hazard” refers to the potential for a microbial ingredient to cause adverse effects (e.g., infection, dermal sensitization, etc.), although the term “risk” represents the probability of occurrence and anticipated severity of a human health adverse effect resulting from exposure to the hazard. The concept of risk analysis can be conceived of and presented in different ways. For this discussion, risk analysis includes the following general components: risk assessment, risk management, and risk communication. This approach to risk analysis is largely derived from that developed by the Codex Alimentarius Commission for assessing microbial risks in food (Codex Alimentarius, 1999).

Risk Assessment. Similar to what has been discussed elsewhere for enzyme-containing products, “risk assessment” for MBCP products encompasses identifying the hazard profile of a given microbial ingredient and gauging the likelihood and severity of adverse effects that could potentially result from manufacturing, handling, or use of the MBCP (American Cleanings Institute, 2019). Risk assessment can be viewed as having four different elements (hazard identification, exposure assessment, hazard characterization, and risk characterization), which are further defined in Table 1:

Although the same elements of risk assessment summarized in Table 1 are also appropriate for assessing risk associated with chemical ingredients in cleaning products, unique considerations are required for microbial ingredients, specifically. For example, hazard identification for microbial ingredients needs to account for hazards associated with the use of living microbiological agents (e.g., potential for causing infections), while the exposure assessment needs to account for the potential of microbial ingredients to persist, or even proliferate, following product application. As discussed in more detail below, hazard and risk characterization can be particularly challenging for microbial ingredients, as robust dose–response relationships are either limitedly or not at all available in the scientific literature for many microbiological hazards, and because limited quantitative information generally exists for risks associated with those hazards. Nevertheless, adapting these elements to suit microbiological ingredients, combined with an acknowledgment of and accounting for the uncertainty that may exist for microbiological hazards, can assist risk assessors in developing information that can support downstream risk management and risk communication activities for microbial ingredients in MBCPs.

Risk Management: “Risk management” refers to the process of defining the scope and parameters used for the risk assessment, and after the risk assessment is completed, making decisions to protect the health of consumers and workers. As such, risk management includes activities both upstream and downstream of the risk assessment process described above.

Although the role of risk management for microbial ingredients in MBCPs is similar to that for typical chemical ingredients, risk managers must also adapt their process and responsibilities to account for the unique risk, hazards,

TABLE 1 Risk assessment elements.

Hazard identification	Identification of potential sources of risks associated with a microbial ingredient that could result in harm
Exposure assessment	Identification and characterization of potential routes and nature of exposure to a microbial ingredient
Hazard characterization	Determination of the relationship between exposure to a specified number of microorganisms and the corresponding probability of a specific adverse effect occurring for different subpopulations
Risk characterization	Examination of the relationship between the human exposure and the assessment of the likelihood of occurrence and the severity of an adverse effect

and uncertainties that apply to microbiological ingredients, specifically.

Risk Communication. Risk communication refers to the process by which the risks identified during the risk assessment, as well as appropriate mitigation measures to manage those risks, are communicated to stakeholders. As described in more detail below, risk communication takes different forms. Although the specific nature or form of risk communication can differ between the target audience (e.g., workers, producers, household or professional users, regulators) or with the intent of the communication (e.g., labeling prescriptions, regulatory submissions), in all cases risk communication should be informed by the risk assessment and risk management elements defined above.

Although it is tempting to view risk assessment, risk management, and risk communication as discrete, stepwise events, the reality is that each of these components informs the others when properly implemented. Furthermore, the overall process of risk analysis is an iterative one that is responsive to factors such as (a) the changing risk tolerance profile for the developers, manufacturers, and marketers of MBCPs, (b) the evolving regulatory environment, (c) the current state-of-the-science as it relates to microbiological risk and hazards, as well as exposure assessment, (d) customer expectations and viewpoints, and (e) the availability and nature of post-marketing surveillance data. It is likewise assumed that risk managers will help to define the cadence by which the risk analysis is reexamined, which should be determined individually for each microbial ingredient and MBCP, as appropriate. More information on each risk analysis component applicable to MBCP risk analysis is provided below.

3 | Risk Assessment

The scope and parameters evaluated as part of risk assessment are the responsibility of an organization's risk managers. However, risk assessors are generally responsible for identifying and assembling the relevant data to support the risk assessment, calculating any scenarios or mitigations, and communicating the results appropriately to risk managers and other stakeholders such that appropriate hazard mitigation and communication responses can be levied. An overview of the risk assessment process as applied to microbial ingredients of MBCPs is provided below. Reexamination of a risk

assessment over time and with any changes to a formulation is important for microbial ingredients in MBCPs since it helps ensure the continued safe use of currently marketed products especially given the emergence of new scientific studies and is a basis for determining the safe use of potential new products undergoing commercial development where learnings from currently marketed products may be applied.

3.1 | Hazard identification

For microbial ingredients in MBCPs, hazard identification includes identifying potential hazards associated with the intentionally added microorganisms. This is largely a descriptive (qualitative) process that summarizes valuable information that will be used in the risk assessment and helps determine the exposure pathways and endpoints to focus on during hazard and risk characterization. Hazard identification should focus on three areas: (a) the microorganism's taxonomic identity, (b) the user and any effects to the user that could be caused by the microorganism (e.g., pathogenicity, irritation, sensitization, and toxin production), and (c) formulation type, use sites, and corresponding potential for exposure (Razenberg et al., 2020). Broadly speaking, hazards particularly relevant to the microbial ingredients of MBCPs are related to the microorganism itself (e.g., pathogenicity), compounds produced by the microorganism (e.g., toxic secondary metabolites), and/or the interactions between the microorganism in question and other microorganisms (e.g., impacts on the microbiome). Hazard identification is generally performed without regard for dose–response relationships and is inclusive of all potential exposure routes. The factors considered in hazard identification can be divided into intrinsic and extrinsic factors as described below.

3.1.1 | Intrinsic factors

Microbial Identity. It is well-recognized that an appropriate level of taxonomic identification, generally to the strain level, must underpin risk analysis for MBCPs (Bernatchez et al., 2018; Deckers et al., 2020; La Maestra et al., 2021; Teasdale & Kademi, 2018). Establishing the strain-specific microbial identity of the microbial ingredient is a critical component of the hazard identification process as it under-

pins the gathering and evaluation of data associated with the risk analysis and risk assessment and may inform whether a particular microorganism should be used in an MBCP. Furthermore, hazard identification at the strain level is advisable to distinguish the hazard profile of a given microbial ingredient from the hazard profile of the species overall. Historically, microorganisms have been taxonomically identified and characterized using many methodologies ranging from genetic analyses (e.g., 16S ribosomal gene sequencing) to various physiological tests (e.g., for certain physiological characteristics or metabolic capabilities) or analytical methodologies (e.g., lipid profiling). These methodologies and their advantages and disadvantages have been extensively reviewed in the literature (Franco-Duarte et al., 2019).

Genetic analyses are a common means of identification in the modern era; however, nuances in this regard should be considered on a case-by-case basis. For example, while 16S ribosomal gene sequencing is commonly used for species identification, this sequencing technique alone may be insufficient to distinguish between clades of genetically similar bacteria which may have vastly different risk profiles. In such cases, whole-genome sequencing (WGS) or the sequencing and evaluation of specific distinguishing genetic markers (e.g., housekeeping genes such as those encoding for gyrase enzyme subunits) can and should be used to help establish strain identity more firmly (Chun & Bae, 2000; Wang et al., 2007).

Although genetic approaches to taxonomic classification are undeniably powerful, in some cases additional approaches are necessary to appropriately discriminate a given MBCP ingredient from other, closely related microorganisms and round out the classification determination. In such cases, polyphasic approaches to microbial identification which encompass genetic comparisons as well as the tested metabolic and/or phenotypic characteristics of the microorganism(s) in question may be appropriate to achieve sufficient taxonomic resolution and/or ascertain important characteristics of a given microbial strain which can be used to appropriately assess risk (OECD, 2003; Ramasamy et al., 2014; Vandamme & Peeters, 2014). It has been suggested that a tiered framework for taxonomic classification of MBCP ingredients, including polyphasic approaches where appropriate, may help support science-based decision-making regarding the amount and type of data appropriate to adequately and efficiently identify microbial ingredients of MBCPs (Bernatchez et al., 2018).

The need to take a thoughtful and considered approach to microbial identification is particularly important for certain groups of microorganisms. For example, members of the *Bacillus* genera, which have a long and complicated history with respect to their phylogeny, inclusive of multiple species and strains that have been reclassified over the years. It is important that a scientifically suitable approach to microbial identification be taken as this can help to clarify or narrow scientific literature searches and may help to make important distinctions between microbial strains (e.g., presence of toxin genes), which can, in turn, inform and improve

the overall hazard identification process. In addition to the above, during literature reviews, one should be aware of species identification limitations for older studies that rely solely on nongenetic data to ascribe genera and/or species identifications, which may reflect outdated taxonomy.

Once identity is established, a search should be conducted to determine if the microbial ingredient has a history of safe use and under what conditions. It is also important to understand characteristics of the life cycle of the strain, such as the growth rate of vegetative cells, resistance to desiccation, and capacity for endospore formation.

Potential for Pathogenicity. Hazard identification should include information regarding the pathogenicity and virulence potential of the microbial ingredient in question to humans. Potential adverse effects on animals and plants should also be considered, particularly for MBCPs that may be used outdoors or in indoor environments where animals and/or plants may be present. Both frank and opportunistic pathogenicity should be considered. Although hazard identification does not typically encompass a formal exposure assessment, an evaluation of pathogenic potential associated with different types of exposures, (e.g., dermal, ocular, oral/ingestion, inhalation), both direct and indirect, should be conducted. Likewise, the severity and scope of typical infections associated with the microbial species in question (e.g., local vs. systemic infection) should be identified and considered.

In addition to scientific literature, various regulatory tools and documents are available to assist with evaluating the pathogenic potential of some microorganisms. For example, per Directive 2000/54/EC on protecting workers from risks related to exposure to biological agents at work, microorganisms in Risk Group 1 demonstrate low pathogenic potential (Directive 2000/54/EC, 2000). In addition, publicly available resources, such as the US Food and Drug Administration's (FDA) General Recognized as Safe (GRAS) substances database (the SCOGS database) and the Qualified Presumption of Safety list issued by the European Food Safety Authority, can be helpful since microorganisms included in these resources have already been reviewed for pathogenic potential (and potentially other risks and hazards) by authoritative regulatory bodies. For species and strains that are less known, it becomes important to conduct a thorough investigation of the strain (e.g., using data from WGS) to understand whether genes of public health concern are present and could be expressed before, during, or after use of the cleaning product for its intended purpose.

Irritation and Sensitization Potential. The potential for MBCPs to cause irritation and sensitization should be considered as part of the risk assessment both in general and with respect to specific exposure patterns and tissues pertinent to a given product (i.e., dermal, ocular, and inhalation exposures). The potential for irritation and sensitization should also consider possible exposures to any given population (e.g., healthy, immunocompromised, children, etc.). This is especially important for products that may be in contact with vulnerable tissues (e.g., eyes, broken skin, etc.) for lengthy

periods of time (e.g., laundry detergents). Concern exists that since MBCPs are not always forthcoming with their ingredients on their labeling and/or may contain unintended microorganisms, the cause of an adverse irritation event, should one occur, may not be evident (La Maestra et al., 2021). Additionally, it may be unclear if irritation was caused by exposure to the microorganisms, its enzymes, or secondary metabolites, metabolic end products or intermediates, and/or from a chemical-based ingredient (e.g., surfactant) contained in the product (La Maestra et al., 2021). Irritation potential also depends on the susceptibility of the host (Aven et al., 2018).

Allergenicity Potential. The potential development of allergenicity to MBCPs should be considered as well, as for some organisms, including microorganisms commonly regarded as “safe,” allergic reactions can be a relevant toxicological concern (EPA, 1997). Notably, several publicly available bioinformatics resources exist that are intended to help predict the allergenic potential for a given microorganism using genetic or amino acid sequence information (Garcia-Moreno & Gutiérrez-Naranjo, 2022; Maurer-Stroh et al., 2019; Goodman et al., 2016; Nguyen et al., 2022). Use of such resources, in conjunction with standard literature reviews, available test data, etc., can help understand whether there is a potential for irritation and sensitization hazards, and can also help inform what mitigation measures, if any, are appropriate to address those hazards and mitigate risk.

Toxin Production. Some microorganisms can produce toxins capable of adversely impacting human beings or other living organisms. Potential bacterial toxins include both exotoxins (which are secreted from the cell into the local environment) and endotoxins (which are associated with certain bacterial membrane components). Such toxins can be important virulence factors determinative of a microorganism’s ability to establish infection and/or cause disease. Toxins can also impact the severity and symptoms of an infection, disease, or other adverse condition caused by microorganisms. The ability of a given microbial species to produce toxins is strain-specific and does not necessarily track with species identification or common genetic sequences used for speciation (e.g., 16S gene sequence). It is therefore important to consider if there are genes present that could be involved in toxin production on a strain-by-strain basis. Given strain-to-strain variability and the inability of speciation information alone to predict toxin production, it is advisable that, where practicable, WGS be conducted to support the evaluation of a given microorganism’s toxigenic potential, particularly for those microorganisms that do not have a long track record of safe use in MBCPs.

In addition to reviews of existing data, certain analyses can help determine the potential for toxin production by a given microorganism. For example, many laboratories can screen for the production of certain toxins in growth cultures or in tissue cultures. A variety of genetic and bioinformatic tools are also available to screen for the presence of genes that could be involved in toxin production, and frameworks exist to help consider the genetic identity/similarity thresh-

olds of unknown genetic sequences to known toxins (Negi et al., 2017).

Antibiotic Resistance. The antibiotic resistance characteristics of a microbial ingredient can impact treatability and overall hazards resulting from potential infections due to exposure to MBCPs especially with sensitive populations (e.g., immunocompromised). Furthermore, the spread of antibiotic resistance in bacteria is a public health concern, and it is well understood that antibiotic resistance genes in one bacterium can be spread throughout a wider microbial population. Therefore, it is important that hazard identification for microbial ingredients includes an assessment of antibiotic resistance characteristics and whether a resistance phenotype is expressed. Antibiotic resistance can be assessed through susceptibility testing (against the minimum inhibitory concentration (MIC)). Antimicrobial resistance can also be evaluated by conducting a genetic analysis, such as following a WGS approach and conducting a bioinformatics analysis for the presence of antimicrobial-resistance genes. Such genetic approaches currently contain several limitations (e.g., difficulty in identifying novel or multivariant mechanisms of resistance, requirement for high genome quality, etc.) (Davis et al., 2016; Jeukens et al., 2019; McDermott & Davis, 2021; Su et al., 2019). As such, genetic analyses may be most useful when paired with susceptibility testing for antibiotic resistance. Should a given bacterium exhibit actual or potential antibiotic resistance, it is likewise important to consider the potential mechanism(s) of that resistance, its clinical relevance, and how that resistance may be encoded in the bacterium’s genetic information (see Mobile Genetic Elements (MGE) below). The nature of the resistance to specific antimicrobial compounds and whether that resistance is intrinsic or transferrable should be considered when evaluating the risk from the resistance gene.

When identifying hazards associated with antibiotic resistance, it is important to draw a distinction between acquired and intrinsic antibiotic resistance, as the genetic basis of resistance has different implications, such as the likelihood of a given antibiotic resistance gene being transferred to an unintended, nontarget microorganism. Acquired resistance occurs through gene exchange either within (intracellular, vertical) or between (intercellular, horizontal) bacteria. Vertical gene transfer is often synonymous with mutation and the propagation of genetic information when bacterial cell division occurs, while horizontal gene transfer (HGT) occurs through the mechanisms of transduction, conjugation, and transformation (see the following section on MGE). Transduction involves a virus that infects bacteria, otherwise known as a bacteriophage, while conjugation is through direct contact between bacterium using pili. Transformation refers to the direct uptake of exogenous genetic material from the environment. In contrast, intrinsic resistance to antibiotics is typically chromosomally encoded and is often due to structural or functional characteristics inherent to that microorganism, for example, the physical structure of bacterial spores makes them more survivable and has reduced cell membrane permeability. Intrinsic resistance is essentially more predictable,

given that it is characteristic to the bacterial species and not unique to a strain. In addition to the above, it is also important to consider the identity of the antibiotics against which resistance is observed or anticipated and the roles of those specific antibiotics in typical clinical treatment.

Antibiotic Production. Some microorganisms can produce antibiotics which should be considered during hazard identification because some antibiotics can be allergens, and the production of antibiotics can negatively impact beneficial microorganisms or microbial communities in MBCP products themselves or on intentionally or unintentionally treated surfaces. Under some circumstances, secondary metabolites produced by microbial ingredients of MBCPs may likewise promote the development of antimicrobial drug cross-resistance in other microorganisms. Both genetic and physiological screening tools can be used to assess the potential for antibiotic and secondary metabolite production by a given microorganism. Note that the inclusion of microorganisms capable of producing antibiotics in an MBCP does not necessarily imply that the MBCP has an intended or practical biocidal effect under its labeled conditions for use. Regardless, for regulatory purposes, a consideration of potential biocidal effects from antibiotic production, in combination with an MBCP's intended use and labeling claims, should ensure that the MBCP is appropriately positioned by the manufacturer as a cleaning product rather than as a biocide. Different regulatory authorities may come to different conclusions on the regulatory positioning of such products. This possibility should be accounted for and addressed by MBCP product manufacturers prior to product marketing.

Known Virulence Factors. Here, the term “virulence factor” refers to compounds, structures, or elements that contribute to a microorganism's pathogenicity. Although many of the items discussed above can also be classified as virulence factors (e.g., toxins), virulence factors can also refer to various other aspects of microbial physiology that are less intuitively related to pathogenicity (e.g., ability to adhere to epithelial cells, form biofilms, presence of quorum sensing systems, etc.). Virulence factors important for pathogenicity have been identified and characterized for different microbial genera and species. As such, an evaluation of the presence or absence of such known genes encoding potential virulence factors is a prudent step to take when identifying the hazards associated with a given microbial ingredient. As mentioned above, such evaluations can be conducted through targeted testing and/or through assessing a given microorganism's genome and conducting a bioinformatics review against databases, such as the Virulence Factors Database (VFDB; as one example).

Mobile Genetic Elements. MGEs are genetic material that can move within a genome or between bacteria. MGEs include plasmids, prophages, and transposons. Plasmids replicate independently from the bacterial chromosome and can be passed from one cell to another through HGT. In contrast, prophages integrate into a host cell's genome and may carry genetic cassettes that have the potential to code for toxins, antibiotics, virulence factors, etc. Under

certain conditions, lysogenic bacteriophages that present as prophages in a host genome can enter a lytic phase, which results in the expression of bacteriophage genes, bacteriophage replication within the host bacterium, and cell lysis resulting in the release of bacteriophage progeny outside the cell. This process can generate particles that possess genes containing virulence factors that are subsequently transferred to other bacteria via the bacteriophage's lysogenic lifecycle.

An evaluation of the presence or absence of MGEs is important because a variety of genes containing virulence factors, including those for the production of some toxins, resistance to antibiotics, etc., can be spread through these elements. Accounting for MGE helps ensure that relevant genes encoding virulence factors are assessed during hazard identification. This accounting also provides information regarding the likelihood that virulence features potentially present in one microbial ingredient could be spread to other microorganisms that are more likely to exhibit pathogenic potential.

Lifecycle. Because microbial ingredients of MBCPs are living organisms, the anticipated lifecycle of these organisms in a given use case should be assessed in order to contextualize how hazards may be actualized or changed (a) when formulated into a microbial cleaning product, (b) within the product's package during storage, and (c) following application and reapplication of the product to surfaces. For example, the potential for toxin production may change for a given bacterium over different phases of its lifecycle.

3.1.2 | Extrinsic factors

Impacts on Microbial Communities. In addition to the intrinsic factors discussed above, hazard identification should include an evaluation of how the assessed microbe may interact with or otherwise impact other microbial communities. Unlike the chemical ingredients present in conventional cleaning products, the microbial ingredients of MBCPs can persist in the environment after application and grow and proliferate. This could lead to changes in the microbial community structure at the treatment site due to factors such as the introduction of previously absent microorganisms, competition for limited resources, or the production of secondary metabolites including antimicrobial compounds (e.g., antibiotics).

Potential impacts to endogenous microbial communities associated with human beings or other animals (e.g., normal skin flora or gut microbiota) should also be considered (Klassert et al., 2022). This is especially true for products whose delivery mechanisms may realistically allow for exposure to skin or eyes, ingestion (e.g., via the hand-to-mouth pathway), or inhalation, although indirect transfer of microorganisms from a treated surface to the body should also be considered. When evaluating potential impacts in this respect, it is important to note that even nonpathogenic microorganisms may have the capacity to adversely impact other beneficial microbial communities in or on the body.

Contamination. MBCPs have the potential to become contaminated with unintended microorganisms during their manufacture and use, and historic surveys of MBCPs have occasionally found potentially pathogenic microorganisms present in product formulations (Jeżewska-Fraćkowiak et al., 2019; Subasinghe et al., 2018; Teasdale & Kademi, 2018). Accordingly, the potential for contamination with pathogenic microorganisms should be considered as part of hazard identification and controlled. Assessments for the production facility's environmental bioburden should account for the possibility of introducing contamination during the manufacturing of both microbial ingredient(s) and final, finished products. This should include the identification of manufacturing and quality controls at all relevant facilities to mitigate contamination and the inclusion of a methodology for rapid identification of contamination, should it occur. Furthermore, the potential for an end-use product to be contaminated following manufacturing due to product storage and/or use conditions should be considered, with appropriate controls identified and implemented.

3.2 | Exposure assessment

The exposure assessment component of risk assessment for a microbial ingredient evaluates the potential routes of exposure for the microorganism(s) in question, and the number and type of microorganisms that the user may be exposed to resulting from manufacturing and handling processes during production, intended product use, and foreseeable product misuse. Considerations when assessing exposure include the manufacturing process for the product and its microbial ingredient(s), product composition, product use pattern and application method, concentration of the microbial ingredient, changes during storage over product shelf life, and frequency of exposure. The contribution of manufacturing processes, usage characteristics, and application method(s) to exposure should consider inadvertent direct and indirect contact by skin (e.g., for pourable, spray, and wipe products), eyes and airways (e.g., for intended and inadvertent aerosols resulting from product use), and introduction to the gastrointestinal tract (e.g., hand-to-mouth transfer). If the product is intended to remain for an extended time on a surface, then the survival, regrowth, and exposure to the user by various routes following product application need to be considered, as does the potential for reapplication. In addition to direct manufacturer and user exposures, potential indirect exposures to individuals not directly involved in product manufacturing or use should also be considered. High levels of uncertainty in an exposure assessment may require measuring exposure under simulated use conditions or during manufacturing or actual consumer use to learn about potential microbial exposure that may be associated with a given MBCP.

Determining the extent of potential exposure to the microbial ingredient in the MBCP is essential. In the absence of good quality exposure data, conservative worst-case assumptions and uncertainty factors should be employed, which may lead to an overestimation of exposure levels and thereby

unnecessarily limit the type or quantity of microorganisms that can be used in a product. Therefore, additional studies to reduce the uncertainties may be initiated by the risk managers to help reduce this overestimation, as has been demonstrated elsewhere in the literature (Aven et al., 2018).

3.2.1 | Product formulation and delivery mechanism

Exposure to a given microbial ingredient can be impacted by the nature of the MBCP itself and how that product is delivered under recommended conditions of use. The following product formulation and delivery mechanism information should be considered.

Product Formulation. The physical and chemical properties of a formulation influence the potential for exposure (e.g., respiratory tract, skin, eyes). The potential for aerosolization of liquids (sprays), powders, and foams leading to inhalation and contact with mucosal membranes should be evaluated. This can be affected by the delivery mechanism, rate, particle size, pattern, and viscosity of the product. Aerosols should be characterized in terms of their droplet or particle size and/or distribution (pattern), density, and settling rates, as these factors influence the concentration and respirability of microorganisms in the air during and after product use. Large droplets or particles have the advantage of settling out of the air quickly; however, droplet and particle size can change during application and may be dependent on the application method. For example, liquid droplet size can decrease after impact on a surface during spray application, potentially leading to a higher percentage of particles that are of respirable size. An assessment of the particle size and distribution should be included in the product formulation evaluation to determine if inhalation risks exist. An assessment of the potential for exposure to skin and eyes should also be evaluated, especially for those with active skin conditions or where the potential exists for surface-to-eye transfer (American Cleanings Institute, 2019).

Delivery System. When formulating a product, consideration should be given to how the design of a delivery system can affect user exposure upon application. Unit dose delivery systems provide an inherent reduction of exposure by design. A spray delivery system has the highest potential for inhalation exposure and should be designed carefully to minimize the production of inhalable mist.

3.2.2 | Use conditions

Normal Product Use. For product use under normal conditions, the amount of product used per application, duration of usage, and frequency of use are factors that affect the exposure to the product. Knowledge of the habits and practices of product users is important for a thorough understanding of potential exposure during a product's use. These data can be obtained by conducting both pre- and post-launch market surveys. With prelaunch surveys, manufacturers can obtain

information from potential consumers with questionnaires about potential product claims and a product's usage and perform consumer in-use tests to determine and potentially experience how the product will be used in real-use situations. Equally as important are for companies to conduct post-launch market surveillance such as follow-up in-market surveys, evaluation of consumer complaints and analysis of data from poison control centers. Information obtained from consumer feedback, whether it be pre- or post-launch, can help a manufacturer refine language regarding product directions for use and identify uses leading to exposure levels that were not considered in the initial exposure assessment for foreseeable misuse, thereby warranting a reassessment of exposure. For example, data from resources such as poison control centers are valuable to assess trends, misuse, or accidental exposures to MBCPs. In the United States, summarized poison control center data are published in the "Toxic Exposure Surveillance System." These data can be obtained by contacting the American Association of Poison Control Centers via email (aapcc@poison.org) or through their website (www.aapcc.org). Reevaluation of a risk assessment for a product already on the market can help to continue to refine exposure potential and be used for future product development (American Cleanings Institute, 2019). Reevaluation of a risk assessment for a product already on the market can help to continue to refine exposure potential and be used for future product development.

Potential Misuse. In addition to the intended applications, the potential for intentional or unintentional product misuse should be considered during an assessment of potential exposures. Misuses may result in higher exposures than can be anticipated during recommended product use. These differences should be considered before extrapolating the results of any exposure assessment from one user group or geography to another. These differences should be investigated carefully to ensure proper characterization of exposures in all parts of the world where the product will be marketed. If appropriate, advisory statements could be applied to a particular product label to guard against misuse.

Use Sites. Products on the market today have varying use sites ranging from household and professional cleaners, animal housing products, drain and sewer cleaners, etc. The physical environment in which the product is used also influences the extent of exposure. For example, factors such as room size and ventilation will affect aerosol exposure as will the use of a product indoors as compared with outdoors. The orientation of the consumer relative to the product during use (i.e., breathing zone relative to the source of microbial aerosols) will also influence exposure.

3.2.3 | Exposure routes

The most common routes of exposure are listed below. Mitigating the route of exposure can be achieved by the inclusion of personal protective equipment (PPE) (e.g., masks, gloves, protective clothing, etc.). The use of PPE can be enhanced through appropriate product labeling.

Inhalation. A major route of exposure to consider is inhalation. Inhalation exposure potential will be determined by factors such as the product's formulation ingredients, formulation type (e.g., liquid vs. granular), application method (e.g., spray vs. pre-wetted wipe), use directions, and use sites. Exposure may arise from the intentional pouring of powdered or liquid products, stirring or agitating product solutions (e.g., hand laundering), spray applications, vacuuming powder products or liquid products that have dried (e.g., carpet cleaning), or via other means.

Dermal. Skin exposure may occur during product use (e.g., hand laundering or surface cleaning) or from incidental exposure. Dermal exposures will also occur post-application for products applied to and remain on surfaces.

Oral Exposure/Ingestion. Direct oral exposure and potential ingestion of the product during its application may occur. Indirect oral exposure/ingestion may also result from touching or other interactions with previously treated surfaces through various mechanisms including the treatment of food-contact surfaces, children mouthing previously treated surfaces (e.g., textiles), and hand-to-mouth activity following dermal exposures.

Ocular. Direct ocular exposures of the product during its application may occur due to splashing, spray dispersal, absent or ineffective eye protection, etc. Indirect ocular exposure may also occur through various mechanisms, including dermal exposures on hands or the treatment of certain surfaces that may be touched prior to interactions with the eye (e.g., putting in contact lenses).

3.2.4 | Product dilution

Some MBCPs may be sold as concentrates that require dilution prior to use. Exposures to concentrated products may increase total exposure due to the presence of higher microbial concentrations in the concentrated form. Furthermore, the potential for intentional or unintentional misuse of a concentrated product exists. With concentrated products, the process of product dilution for the purposes of refilling a smaller container (e.g., trigger spray) may furthermore offer an opportunity for accidental exposures due to spilling, splashing, etc., which may lead to increased exposure potential.

3.2.5 | Microorganism lifecycle and fate

Because microbial ingredients of MBCPs are living microorganisms, the anticipated fate, persistence, and lifecycle of these organisms both within the product's package during storage and following application of the product to treated surfaces can influence exposure. The potential for the microorganisms to be in a steady state (e.g., spore form) or in a growth phase (e.g., vegetative cells) needs to be considered during the formulation process and assessed as part of the risk analysis.

3.2.6 | Estimating exposure

A comprehensive risk assessment encompassing all potential exposures would require the evaluation of numerous individual exposure scenarios, which may have radically different outcomes. For example, the scenarios of a child mouthing an article of treated clothing or an elderly person treating a kitchen counter are quite different, requiring independent consideration, and likely yielding very different results. Furthermore, globally marketed products may differ in exposure potential between countries or geographies based upon factors such as different use site characteristics (e.g., typical room size or manufacturing practices), cultural practices (e.g., typical number of daily working hours), and user behaviors (e.g., frequency of cleaning). Likewise, different assessment practices, procedures, or parameter assumptions may be necessitated between geographical regions or countries to account for local regulatory requirements or commonly accepted industry practices. Accordingly, the scenarios selected for exposure assessment, as well as the methods to conduct that assessment, should be selected carefully to ensure they are protective for the purposes of general product use in the geographies of interest.

Each scenario needs to be separated into a series of individual steps from manufacture to human exposure and the changes in microbial populations need to be estimated at each step. For example, the concentration of microorganisms as contained in the packaging will be different from what is put onto and remains on a surface post-application, therefore, influencing exposure and risk. For each of these steps, estimates of the relevant parameters (e.g., microorganism concentration, exposure type, risk, etc.) need to be considered in the exposure assessment. Different evaluations within a use scenario in which various input values are evaluated can be used to calculate quantitative levels of exposure or provide relative exposures between use scenarios that can be compared. The assumptions used in the estimation should be based on consumer habits and practices and the other factors referred to in the preceding paragraphs.

The first step in estimating exposure usually involves a conservative theoretical calculation using reasonable worst-case assumptions (e.g., using the entire packaged product at one time) while employing uncertainty factors. Exposure can be estimated initially from available data. If there are insufficient data to allow a reliable estimate of exposure to be developed, then actual exposure measurements should be obtained before making a final risk characterization.

3.3 | Hazard characterization

Also termed the dose–response relationship, hazard characterization determines the relationship between exposure to a specified number of microorganisms (i.e., level of exposure or delivered dose), and the corresponding probability of a specific adverse effect occurring for different subpopulations,

such as healthy adults, children, neonates, or immunocompromised individuals. Included in this relationship are the duration of use, how often use is repeated over time, and route(s) of exposure (e.g., dermal, oral, inhalation, etc.).

3.3.1 | Dose–response relationships

Dose–response estimation for populations is inherently a statistical process. Ideally, a quantitative mathematical model is/has been developed that relates exposure to the likelihood of adverse effects. However, for microorganisms, there are often little data on the dose–response, so oftentimes a benchmark approach must be used to assess risk. A benchmark dose is a value derived from a study or studies generally considered safe by scientific and medical experts and can be used as a pass/fail criterion. Given the lack of data overall, a benchmark may be inferred from a closely related microorganism. In the risk assessment process, the exposure level estimated for a use application is compared with benchmark values to assess risk.

3.3.2 | Caution in use of benchmarks

Caution should be used in the application of benchmarks. Exposure data need to be relevant to a particular use or misuse for comparison with a newly derived exposure value. Furthermore, measurement at the point of exposure may or may not relate to the actual internal body dose. As discussed previously, the actual dose is nearly impossible to obtain with current methodologies. Care should also be taken when extrapolating from one product type to another since the exposure conditions may be too different to be comparable.

3.4 | Risk characterization

Risk characterization is the examination of the relationship between human exposure, the assessed likelihood of an adverse effect occurring, and the potential severity of that adverse effect. This step integrates the outcome of hazard identification, exposure assessment, and hazard characterization associated with the use and foreseeable misuse of a product (American Cleanings Institute, 2019).

Overall risk is characterized in microbial risk assessments either qualitatively or quantitatively. The risk estimate is based upon exposure levels and frequency for the general population (e.g., non-immunocompromised) and sensitive subpopulations (e.g., immunocompromised, elderly, infants/children) for specific adverse health outcomes, such as a specific illness, allergic reaction, hospitalization, or death. For qualitative risk characterization, a risk estimate is typically expressed with a scale that ranges from 0 to 4: (0) negligible likelihood of occurrence, (1) very low, (2)

low, (3) medium, or (4) high. This could be developed into a semiquantitative estimate, such as “low” equals 1 illness per 10,000 exposures. Quantitative risk estimates are more probabilistic and expressed for a given exposure as either the individual risk (probability of illness/number of exposures) or at a population level, such as the number of adverse outcomes per population size (e.g., 1.3 illnesses/100,000 users).

Current knowledge generally does not allow for quantifying hazards associated with microorganisms, for example, the production of a toxin or an allergen, in MBCP scenarios. Instead, for microbial ingredients of MBCPs the risk characterization process typically relies on comparing potential exposure to benchmark values or resorting to determining the presence/absence of a hazard. Here, a benchmark can be defined as the maximum hazard exposure considered to be safe by scientific and medical experts and used as a pass/fail criterion. In the latter case, the hazard identification where the presence of virulence factors, toxin genes, allergens, etc., is determined is the critical component in the risk characterization.

4 | RISK MANAGEMENT

Risk management involves the overall control of the risk assessment process, the identification and selection of risk management options, the implementation of these options, and the monitoring and review of the process to determine whether the product is achieving the desired level of safety. There is also a role in Risk Communication described in that section of this paper.

Risk management has been described in the related context of microorganisms in foods by the Food and Agriculture Organization and the World Health Organization of the United Nations (FAO/WHO, 2000, 2006). The overall control by risk management includes, in part, (1) identification of the safety issues, (2) establishing the objectives of the risk assessment (processes and scenarios to be evaluated, metrics for describing the results), and (3) commissioning the risk assessment. Following completion of the risk assessment, risk managers (4) identify, evaluate, and select the risk management control options characterized in the risk assessment. These options are then (5) implicated in the process, validated, and verified. (6) After production, the process is monitored and reviewed to ensure the safety objectives are achieved.

Risk managers are responsible for making decisions to protect the health of consumers and workers. Because the risk assessment process does not define an acceptable level of risk and it is impossible to eliminate all risks, risk managers need to articulate and defend what exposure to the hazard, if any, is acceptable in each individual scenario. Safety is a nonscientific judgment to be made by risk managers with communication and input from stakeholders, described in the Risk Communication section.

4.1 | Accepted levels of risk

Setting a benchmark or evaluating an acceptable level of risk for a product/scenario must be defensible and is typically the risk managers' decision after considering all available data and considering additional data that may need to be generated to make an informed decision. Because the risk assessment process does not define an acceptable level of risk and it is impossible to eliminate all risks, risk managers need to articulate what exposure to the hazard, if any, is acceptable in each individual scenario. Safety is ultimately a nonscientific judgment to be made by risk managers with communication and input from stakeholders.

Companies should diligently evaluate consumer complaints and other indications from users to ensure that the risk assessment was correct and exposure to the microorganism(s) was indeed safe. If the risks associated with the product uses are not acceptable, product modification (e.g., revised labeling to include use restrictions, product modifications, etc.) and reevaluation of the risk characterization including whether the product should remain in the marketplace are recommended.

5 | RISK COMMUNICATION

An integral part of the risk analysis process is to effectively communicate the potential risks to appropriate audiences (American Cleanings Institute, 2019). There are several important audiences to target in designing a risk communication program, including but not limited to: (1) decision-makers within the company, (2) key employees, (3) suppliers, (4) users of the company's products, and (5) other stakeholders, such as the public, public interest groups, and regulatory authorities.

Company decision-makers are important recipients and disseminators of risk communication within their organization. They also play a crucial role in ensuring adequate risk communication outside of their organization. A company's decision-makers will decide whether to market a given MBCP. Therefore, risk communication to these decision-makers is of critical importance to ensure that the risks associated with a given product's marketing can be appropriately weighed against anticipated benefits. Risk communication within a given company is also needed so that decision-makers can appropriately establish the necessary infrastructure to market an MBCP and facilitate surveillance of that product following marketing. Communicating any risks associated with product manufacturing to protect workers and promote safe manufacturing practices within the company itself is necessary. If other products are manufactured in the same facility, the potential for microorganisms (e.g., bacteria and fungi) cross-contamination may need to be determined.

Product labels, printed materials, and digital media communications are the primary means of informing consumers. For MBCPs, as with all consumer and professional products,

many countries require that the label include appropriate warning statements. The consumer products regulatory authority with jurisdiction is driven by the claims, product usage, and where the product is being sold (i.e., the United States, Canada, and the EU). In some cases, there may be more than one jurisdiction within a certain country which needs to be considered to appropriately label a product. In the United States, the regulations of the Consumer Product Safety Commission apply (15 U.S.C. 2079(a)); in Canada, those of the Consumer Chemicals and Containers Regulations (CCCR, 2001) apply; and in the European Union, the Classification Labeling and Packaging (CLP (EC) No 1272/2008) Regulation, and Detergent Regulation ((EC) No 648/2004) apply.

Other stakeholders may be governmental authorities, non-governmental organizations including trade associations, or industry partners. Gaining acceptance of MBCP by these stakeholders is through interaction among experts in the field or industry, government authorities, and other interested parties, such as consumer associations, scientific journalists, and academia. The goal is to build confidence in the company and/or industry for the technology.

An attitude of openness and willingness to share information and data is essential while recognizing the legitimate needs of companies to protect competitively sensitive information. Position papers and dossiers giving details of the product, process, and the microorganisms may be used. In addition to information relevant to consumers, product manufacturers should anticipate requests related to exposure in the workplace.

6 | DISCUSSION

As discussed throughout this document, MBCPs have unique safety considerations given the nature of their microbial ingredients. These factors, combined with the likelihood that MBCPs will be used both more routinely and at higher volumes in the future by household consumers, workers, professional applicators (e.g., cleaners), and others, emphasize the importance of ensuring that MBCPs are formulated and used in a manner that is protective of both human and environmental health. This is particularly true as MBCP manufacturers seek market differentiation regarding microbial ingredients, coformulants, use patterns, and application methodologies.

Microbial risk analysis practices for food and water have long been employed to assist in the protection of public and environmental health, and specific regulatory guidance exists with respect to the assessment of product safety (EPA, 2014; Health Canada, 2018; USDA/FSIS & EPA, 2012). In contrast, microbial risk analysis practices are less well developed for the specific uses and organisms typically employed for MBCPs. Although the risk analysis precedent for microorganisms in food and water can certainly inform how these practices may be applied to MBCPs, the nature of these prod-

ucts and the ways in which their use may lead to microbial exposures warrant their own approaches and considerations. In keeping with this need, considerable work has been done in recent years to identify key safety considerations relevant to MBCPs and develop first principles and methodologies to support the risk analysis of MBCPs and their microbial ingredients (Aven et al., 2018; Bernatchez et al., 2018; La Maestra et al., 2021; Razenberg et al., 2020; Skaar et al., 2016; Teasdale & Kademi, 2018). The information described in this document is intended to contribute to this body of work and to provide additional actionable information to both cleaning product companies and relevant regulators as they develop and implement their own risk analysis approaches for MBCPs.

Despite their recent increase in popularity, MBCPs intended to treat surfaces are still relatively new to the marketplace. Formulators are trending toward using microbial ingredients widely considered to have low risk, such as microorganisms in Risk Group 1 per 2000/54/EC and/or microorganisms that are “GRAS” by the FDA per sections 201(s) and 409 of the Federal Food, Drug, and Cosmetic Act. Data suggest that surface treatment products containing microbial ingredients can, when properly formulated and used, be safely applied in healthcare settings. That said, there are relatively few studies and limited historical context that explicitly speak to the safety of MBCPs, particularly when used by nonprofessional applicators. This reality, combined with the existence of data gaps presently inherent to the evaluation of microbial ingredients (e.g., lack of reliable dose–response information), makes the risk analysis process for MBCPs important even when they are formulated with microorganisms commonly regarded as “safe.” Thoughtful approaches to this risk analysis should therefore be employed to ensure the continued safe manufacturing, development, and use of these products.

The various literature cited here substantiate the assertion that the risks associated with MBCPs can be adequately evaluated and managed; however, the focus, execution, and interpretation of risk analysis differs between the cited literature. This is especially evident considering MBCPs are still considered to be an emerging class of products without well-established and agreed-upon methodologies for risk analysis. Some variation in this respect is expected and necessary for various products and microbial ingredients with different use patterns, hazards, exposure potential, etc. Nevertheless, additional alignment efforts in the MBCP industry may help to increase confidence in the overall risk analysis process, particularly if that process is at least centered around a standardized consensus approach. Beyond building confidence in the risk analysis process itself, such standardization efforts will facilitate comparison between risk analyses conducted for individual MBCPs. When combined with outcome evaluations, such comparisons may improve the predictive power of MBCP risk analysis and/or help identify aspects of risk analysis that require further research, refinement, and/or dialogue within the scientific literature moving forward.

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CONFLICTS OF INTEREST STATEMENT

All authors declare that they have no conflicts of interest.

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