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Status of Microbial Based Cleaning Products in Statutory Regulations and Ecolabelling in Europe, the USA, and Canada

Armin Spök[1,*], **George Arvanitakis**[2], **Gwendolyn McClung**[3,†]

[1)]Graz Technical University and Alpen-Adria Universität Klagenfurt | Wien-Graz, Schlögelgasse 2, A-8010 Graz, Austria

[2)]New Substances Assessment and Control Bureau, Health Canada, 269 Laurier Ave. West123 Slater Street, A.L. 4905B 3505A, K1A 0K9 Ottawa, Ontario, Canada

[3)]Office of Pollution Prevention and Toxics, US Environmental Protection Agency, 1200 Pennsylvania Ave., Washington DC 20460, USA

Abstract

Cleaning products containing living microorganisms as active ingredients are increasingly being used in household, professional and industrial cleaning applications. Microorganisms can degrade soiling associated with dirt, food residues, and grease by enzymatic and metabolic action and out-compete microorganisms associated with odor problems. Their potential for odor control seems to result in a competitive advantage over conventional chemically-based cleaning products. Moreover, producers of microbial-based cleaning products (MBCPs) claim that their products are less harmful to the environment. These promising prospects have triggered interest from consumer and environmental organizations, professional users, and regulators in understanding if there are also possible negative health and environmental impacts which require attention and how the safety of these products is ensured. Unfortunately, there is little information on these issues in the public domain. Moreover, regulatory oversight in Europe is essentially limited to pathogenic properties in the context of worker protection. Canada, in contrast, has a regulatory framework in place to assess risks to human health and the environment from the manufacture, import and/or use of new microorganisms contained in MBCPs. In the absence of mandatory standards, safety assessment and hygienic practices seem to vary considerably across companies. Recently developed ecolabelling standards are – for the time being - the only option for transparent compliance to minimum standards in terms of safety as well as assessments of manufacturer information by third parties. These standards highlight in particular the need for precise taxonomic information for assessing the pathogenic properties and the need to ensure the absence of potentially harmful microorganisms as contaminants. Ecolabelling standards are, however, voluntary and do not cover all relevant safety issues. In order to develop a more comprehensive set of mandatory standards for health and safety, a number of areas would benefit from further research (e.g. the role in plant pathogenicity and other environmental properties of the

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[*]Corresponding author armin.spoek@tugraz.at/ armin.spoek@aau.at.

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microorganisms used; the relevance of chronic exposure to dusts and aerosols containing vegetative cells and spores; the relevance of strains which belong to species known to include opportunistic pathogens and possible hazards for particularly sensitive risk groups). Improved knowledge in these areas will contribute to a predictable level of product safety.

Keywords

Microbial based cleaning products; MBCPs; microbial cleaner; probiotic cleaner; risk assessment; safety assessment; risk management; ecolabelling

1 Introduction

In recent years, a novel type of cleaning product containing living microorganisms or spores as active ingredients has been gaining the attention of professional users, consumer organisations, and regulators. These products are sometimes referred to as ‘biological’ cleaners, ‘probiotic’ cleaners, or microbial cleaners. A more recently emerging term, ‘microbial-based cleaning products’ (MBCPs) is used in this paper.

Given the limited availability of both general information on MBCPs in the public domain and product specific information from developers, consumer and environmental organisations highlight difficulties in assessing the efficacy and safety of these products, e.g., when asked for recommendations by the public and private sectors for green procurement. Information is particularly scarce on environmental properties, health risks and efficacy of the cleaning products. In many jurisdictions, it is also not clear which regulations and standards govern the safety and efficacy of these products.

Against this backdrop this paper sets out to review the status of MBCPs in statutory regulations and ecolabelling schemes in different countries and jurisdictions. This paper: (i) briefly describes what are MBCPs and the range of cleaning applications, (ii) discusses possible environmental and health issues, (iii) discusses health and environmental legislation potentially applicable to MBCPs, (iv), describes MBCP-specific and safety relevant criteria in ecolabelling standards, and (v) draws conclusions.

The core of this analysis is based on a study conducted in 2009 which included a survey of the scientific literature, “grey literature”, patents, company documents, regulatory and policy documents, web-based information and on interviews and consultations with representatives of manufacturers, blenders, professional cleaning service operators, governmental authorities, consumer and environmental organisations, and scientists (Spök and Klade 2009). The results of this survey were subsequently updated and further explored (Thomas and Versteeg 2013; OECD 2015).

A particular difficulty arose from the overall lack of information in the public domain, from the fact that manufacturers and blenders are not well represented in professional associations and, therefore, are difficult to identify, and lastly, from the reluctance of these business operators to share information which they consider as confidential business information with users and researchers.

2 Technical concept and applications

The technical concept for using microbes is similar for all types of products. Living microbes are capable of enzymatically degrading substances associated with dirt, food residues, grease and other objectionable matter (known in cleaning terminology as ‘soil’). Microbial action is aimed at controlling odour and to support the cleaning action of detergents.

Some microorganisms produce a broad range of extracellular enzymes including proteases, cellulases, amylases, and ureases which can degrade organic high molecular weight substances in soil. As opposed to cleaners with added enzymes, microbes can further metabolise (some of) these degradation products. Substances creating odour problems such as NH_3 can be metabolised, or the formation of H_2S may be avoided by transforming SO_4^{-2} into S_2. Some cleaning products include microbes claimed to out-compete unwanted microorganisms in colonising surfaces by using up the nutrients provided in the soil and from polluted surfaces, or can directly inhibit the growth of unwanted microbes, for example, by lowering pH. Some producers claim a long-term effect because microorganisms will stay on the treated surface (often as spores; many formulations contain spore forming bacteria, e.g. Bacillus spp.) and hinder re-colonisation by unwanted microorganisms.

In commercial contexts, MBCPs are mainly applied for odour control in cases where conventional cleaners are considered less efficient and in surface cleaning in sanitary facilities. MBPCs are also used as surface cleaners in buildings with high traffic areas (e.g., public buildings, schools, restaurants, canteens, hotels) and particular odour problems (e.g. sanitary facilities, production facilities, nursing homes, animal shelters, veterinary facilities). Products for hospitals have been tested for health and efficacy (Vandini et al. 2014, La Fauci et al. 2015, Caselli et al. 2016). Here, the rationale is that microbial cleaners seem to be more effective in the long-term lowering of the number of health care related microorganisms on surfaces, when compared to conventional cleaning products, even those containing disinfectant molecules such as chlorine (Vandini et al. 2014).Besides hard surface cleaning these products are also used for cleaning carpets and upholstery. Specialty products are used for cleaning drains, pipes, and grease traps in order to remove deposits, and also in industrial production in the washing of machine parts, as well as for oil spills on masonry or concrete.

3 Potential Health and Environmental Issues

Microorganisms can be harmless to human health and the environment and many microorganisms have been used for thousands of years in the processing of food and feed. Other microorganisms are pathogenic and/or toxic to humans, animals or plants. With some microorganisms certain strains of the same species are pathogenic, while others are not. A familiar example for this is *Escherichia* coli - strain O157:H7 is a well-known cause of food-borne illness, whereas strain K12 is not pathogenic at all, and, therefore, frequently used in laboratory research and for technical purposes. For assessing health or environmental hazards it is, therefore, essential to have a precise taxonomic identification of the microorganisms contained in the cleaners.

Another relevant issue is the lack of data in the public sphere on real-world exposures of cleaning personnel and consumers to microbes and spores in MBCPs.

Third party verification of microbial identification represents a significant challenge. According to a product survey conducted in 2009 (Spök and Klade 2009), producers usually considered the precise identity (species, strain) as confidential business information. Only the taxonomic genus was declared if such information was given at all. In that survey few producers provided more detailed information.

What is clear at this time:

1) MBCPs differ in the particular combination of microorganisms used. The survey noted above identified more than 30 different species, mostly bacteria and a few yeast and fungal species, though, in practice, the range of microorganisms might be much broader as indicated in patent literature and other documents. The most frequently used microbes are members of the genus *Bacillus, Bifidobacterium, Lactobacillus, Rhodopseudomonas*, and *Saccharomyces*. Some producers specialize in utilizing combinations of different *Bacillus* spp. spores instead of using vegetative cells as spores allow for a longer shelf-life, i.e. one year (for details see Spök and Klade 2009) and even up to four years (Chrisal, pers. communication).

2) Producers in that survey (Spök and Klade 2009) claimed that all of their microbes belong to risk group 1 and, therefore, did not pose any health concerns. Moreover, 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).

While this suggests that there is no immediate concern for human health or the environment, several issues identified in the survey require more thorough examination.

3.1 Taxonomic identification of microorganisms used

The classification in the risk group scheme, the assessment of potential hazardous properties, and the existence of relevant experience in safe handling (history of safe use) reported in the scientific literature and regulatory documents are based on a reliable taxonomic identification of the microorganism. Strains can, however, be easily misidentified without the use of appropriate identification methods (OECD 2003). This was, for instance, an issue in the context of probiotic supplements where it was found that ingredient lists occasionally

do not correspond to the microorganisms present in the products (e.g. Lewis et al. 2016, Blandino et al. 2016).

Reliable identification of the microorganism is important, as sometimes even taxonomically closely related species or strains can differ considerably in their hazardous properties. For instance, some strains within the same *Bacillus* species (including some species used in MBCPs) can produce enterotoxins whereas other strains are not capable of doing so. Differentiation between such strains is also important for the QPS status; toxin producing strains are explicitly excluded from the QPS status (EFSA 2008; EFSA 2017). Therefore, any erroneous identification could, thus lead to entirely different results in the hazard assessment. Furthermore, microbial phylogeny and taxonomy have changed considerably over the past 30 years - mainly due to insights from microbial genetics. These difficulties have also been recognised by the OECD which, in response, issued a guidance document for taxonomic identification of bacteria (OECD 2003).

Little information was obtained in the survey on the taxonomic identification methods used by MBCP producers or their microorganisms suppliers. The available information suggests different practices. Some of the organisms used came from widely acknowledged national microbial strain collections (e.g., American Type Culture Collection) where state-of-the-art methods for strain identification are used. Other microorganisms used in MBCPs were isolated by MBCP producers from natural environments. Especially in the latter case and in the absence of detailed information on the identification method the reliability of the identification remains a potential concern. Sometimes, the taxonomic identification is done by the MBCP producer, in other cases by an accredited microbiological laboratory. In-house expertise in microbiology varies among producers. In a few cases vendors provide instructions to consumers on how to breed their own microorganisms using an inoculum as starter (e.g. https://www.multikraft.com) which could lead to inconsistent product composition, quality and safety.

What is said above applies to microorganisms intentionally added to a cleaning formulation to fulfil a specific purpose. However, – it potentially applies also to microorganisms present in MBCPs as contaminants.

3.2 Unintended presence of microorganisms

The maintenance of a culture collection and production of sufficient quantities of microorganisms for a MBCP is done by standard microbiological cultivation methods. Any cultivation process has the potential to result in unwanted microorganisms being present in addition to the desired microbes. These unwanted or contaminating microbes might include pathogens and/or toxin producers some of which might even be non-cultivable and not detectable by methods based on cultivable cells. Moreover, they could also interfere with the intended microbial action. This is widely acknowledged (OECD 2011) and operators of biotechnological processes have therefore established process controls and quality assurance systems aimed at both avoidance of and checking for contaminants.

Information from the survey indicates huge variations in terms of process controls and quality assurance. In some cases this raises doubts on the hygiene, quality and consistency of

the products. Similar doubts were raised in a study conducted by the Netherlands Food and Consumer Product Safety Authority (NVWA) (VWA 2004). Their microbiological analysis of MBCPs identified striking variations in total viable counts indicating problems with consistency and shelf life. They also found microbial contaminants including - in one case - a risk group 2 microorganism associated with human infections. These hygienic problems and the fact that some of the strains being used belong to microbial species known as either opportunistic pathogens or food contaminants resulted in a NVWA recommendation not to use MBCPs in areas of food processing and preparation and also not where exposure to a particular susceptible population (YOPI – young, old, pregnant, immunocompromised) is likely. Other applications, e.g., for sanitary purposes, were considered acceptable by the NVWA.

Recent ecolabel criteria specifically developed for MBCPs (see Section 5) might have changed this picture and motivated manufacturer to establish proper quality control procedures.

A similar issue emerged from microbiological analyses of probiotic food supplements, which revealed the presence of microorganism in shelf-products that were not indicated on the labels (Toscano et al. 2013, Drago et al. 2010).

3.3 Sensitization – allergenic properties

Some MBCPs are intended to be applied as a spray which inevitably leads to aerosol formation. Assuming routine application and in closed rooms (e.g. sanitary rooms) this can result in chronic respiratory exposure – in particular in the case of professional cleaning personnel.

There is some evidence in the scientific literature of sensitizing properties and of hypersensitivity pneumonitis associated with microorganisms (Simonian et al. 2006). In its Office of Pesticide Programs, the US Environmental Protection Agency (EPA) generally recognizes that microorganisms may be respiratory sensitizers (The Federal Register 2007). Allergenic properties are also described for the mould species *Aspergillus oryzae* (Green and Beezhold 2011), the use of which was described for some cleaners.

It is not clear whether and to what extent these hypersensitivities are caused by the microbial enzymes and/or other components of microbial cells and spores.

In household or professional cleaning settings, the use of detergents containing enzymes rarely appears to be an issue. Cases of worker sensitization and work-related allergies to microbial enzymes and microorganisms are, however, well documented in context where enzymes are being produced and handled.. The difficulty is that there is no agreed upon test for respiratory sensitization. In the EU, microbial enzymes are therefore voluntarily considered by industry as respiratory sensitizers and labelled and handled accordingly (for review see Basketter et al. 2016, Kimber and Basketter 2014, Federal Environment Agency/ Inter-University Research Center for Technology Work, and Culture, 2002).

While there seems to be agreement on the use of this approach, the precautionary labelling of microorganisms as potential respiratory sensitizers has recently come under critical

scrutiny: a workshop of the Netherland's Board for the Authorisation of Plant Protection Products and Biocides (Ctgb) concluded that "it is not considered a general feature of bacteria to express sensitising properties [….]. The warning phrase should be applied for fungi, however viruses, yeast and possibly bacteria may be excluded. The conclusion on the fact that bacteria/viruses/yeast are not potential sensitizers should be further investigated" (Ctgb 2015: 8). Similar conclusions came from a recent OECD Seminar (OECD 2017).

Still, the European Chemical Agency (ECHA) advises in its 2017 guidance that "all micro-organisms should be regarded as potential sensitizers until adequate methods or further guidance are available". A precautionary warning that microorganisms may have the potential to provoke sensitizing reactions should be displayed on the label. Professional users are expected to have access to personal protective equipment (PPE) such as gloves, protective clothing, face mask and other respiratory protection, if necessary. Therefore, the risk can be reduced if the protection provided by PPE is taken into consideration in the exposure assessment (ECHA 2017). While this recommendation clearly applies to situations where microorganisms are being produced and handled in relevant amounts, the relevance of PPE for producing and handling MBCPs remains to be clarified.

3.4 Potential environmental issues

Existing risk group schemes for classifying microorganisms typically address only potential human pathogenicity to healthy adults and do not specifically consider pathogenicity to immunocompromised individuals or plant or animal pathogenicity/toxicity. As a notable exception, the Public Health Agency of Canada and the Canadian Food Inspection Agency take into account pathogenicity to terrestrial animals as well (Government of Canada 2016). Similarly, the EU QPS status of microorganisms does not address environmental issues - as recently concluded in a Ctgb workshop (Ctgb 2015).

Some MBCP producers provided additional information (results of OECD oral toxicity tests on rodents as well as eco-toxicity tests with *Bacillus* strains). According to these producers, these tests did not identify any risks (Spök and Klade 2009). This type of information does not seem to be available from all manufacturers or for all microbes. These issues and the absence of information on environmental impacts have recently been highlighted in a review by the Norwegian Scientific Committee on Food Safety (VKM 2016).

4 MBCP status in environmental and health regulation

There is no specific legislation on MBCPs in any of the jurisdictions investigated in this section. However, other legislation clearly does apply or might apply. Typically, legislation on occupational health risks of biological agents covers MBCPs. With respect to sectoral legislation the picture is less clear. Chemical legislation and detergent legislation is potentially applicable. Considering some of the claims of manufacturers and the properties of MBCPs, biocide legislation might apply to some of these products.

4.1 European Union

In the European Union (EU) detergents, chemicals, and biocides are regulated for all Member States by harmonised legislation specifying in great detail pre-market safety

requirements (ECP 2012). MBCPs, however, seem to be a borderline case with most of them not being covered by harmonised environmental legislation.

However, harmonised regulations on worker's health and general provisions for consumer safety of products still apply and require a certain safety assessment and risk-related information be provided to consumers by manufacturers and importers of these products.

Detergent legislation—Regulation 648/2004 regulates the placing on the market of detergents, labelling and information requirements and sets standards in terms of biodegradability (EPC 2004).

In 2009 following a company request, the European Commission (EC) and the EU Members States agreed that MBCPs - even if containing surfactants - do "not seem to have a cleaning action within the meaning of ISO definition (i.e. 'the process by which soil is dislodged from the substrate and brought into a state of solution or dispersion') and are, therefore, out of the scope of the EU Regulation on detergents (EC 2009). However, this decision was based on an inquiry for one specific product where the cleaning action is claimed to result from bacteria feeding on the excrement of dust mites. It was not clear if the rationale of this decision would also apply to all microbial products, e.g. to surface cleaner in sanitary facilities. In a recent 2015 clarification the EC, argued that "there are other products on the market (like certain drain cleaners) which work through a combined action of surfactants, enzymes and bacteria. As the cleaning process of these products is not based solely on the action of bacteria, they do fall within the scope of the Detergents Regulation (EC 2015). As the Regulation does not include any specific labelling and information provisions with respect to microorganisms it remains unclear how it should be implemented in case of MBCPs. In the course of an upcoming evaluation of Regulation 648/2004 the EC intends to look into these types of products (https://infoeuropa.eurocid.pt/files/database/000072001–000073000/000072957_2.pdf).

Chemical legislation—All chemical compounds used in MBCPs are covered by the EU chemical legislation REACH (Registration, Evaluation, Authorisation and Restriction of Chemicals) Regulation (EC) No 1907/2006; EPC 2006). Living microorganisms and spores, however, do not meet the definition of 'substance' as they can neither be classified as 'well defined substances' nor as UVCB substances (Substances of Unknown, Variable composition, Complex reaction Products or Biological Materials) (ECHA 2016). Manufacturers claim that this view has been confirmed by the Dutch and the Finnish national competent authorities. Still, some uncertainty remains. The Manual of Decisions of the EU chemical legislation prior to REACH explicitly excluded living (micro)organisms from the scope of the legislation (European Chemicals Bureau 2006, EC 2008) whereas the REACH guidance document does not (ECHA 2016). It also remains unclear if the enzymes produced by the microbes present in MBCPs and secreted outside the cells during microbial action can be considered as UVCBs under REACH in analogy to enzyme (mixtures) added to cleaners. Enzymes sometimes added to MBCPs in addition to the microbes are covered by REACH whereas enzymes produced by the microbes do not seem to be covered. Despite the absence of a legal requirement, some manufacturers mention microbes in the REACH governed Material Safety Data Sheets (MSDS), but not all manufacturers, and not in a

consistent manner. Occasionally, it is stated that the product contains microorganisms, sometimes only the genus is specified, and sometimes the microorganisms are revealed to the strain level (Spök and Klade 2009). Consistency and transparency cannot be readily assumed in the context of REACH. The provisions of the CLP (Classification, Labelling and Packaging) Regulation cannot be used for microorganisms and thus they cannot be classified or labelled under the current classification and labelling system (EPC 2009, ECHA 2017).

Biocide legislation—Regulation 528/2012 (EPC 2012), which came fully into force in Oct 2015, explicitly includes microorganisms in its scope (ibid: Article 3). Microorganisms registered as active biocide ingredients are specified at the strain level. Similar to safety aspects, potential biocidal activity is strain dependent.

Certain microorganisms were in fact used and registered as biocides (*Bacillus subtilis* and other spp.) under the previous EU harmonised legislation on biocides. *B. subtilis* is also used in MBCPs. Guidance on the specific information and assessment requirements for microorganisms was published very recently (ECHA 2017).

In certain cases manufacturers are making claims which could be interpreted as claiming biocidal effects, in particular in the case of MBCPs used in hospitals, but also for sanitary facilities, for cleaning carpets and upholstery when claiming deodorization or odour control (Spök and Klade 2009). Vandini et al. (2014) describe the efficient application of commercially available MBCPs to reduce problematic microorganisms in hospital surfaces. These products are described by the manufacturer as not having “any direct biocidal action towards other organisms” instead the mechanism of action is vaguely described to be “based on the principle of ‘competitive exclusion’, combined with an influence on the ‘quorum sensing’ communication between organisms” (Chrisal 2014).

The legislation defines biocidal action as “destroying, deterring, rendering harmless, preventing the action of, or otherwise exerting a controlling effect on, any harmful organism by any means other than mere physical or mechanical action” (EPC 2012: Article 3). If the mode of action would solely be based on nutrient competition and ‘overgrowing’, it might fall under ‘physical or mechanical action’ and not constitute biocidal action.

For many microorganisms, however, including some species applied in MBCPs, it is described in the scientific literature that they can inhibit cell growth or even kill other microbes by producing and releasing bactericides or fungicides. Other microbes can inhibit growth by other means, e.g. lactic acid bacteria by lowering the pH. This type of mechanism could potentially be considered a biocidal activity.

So, the question here is, whether these mechanisms would also apply to some of the strains used in MBCPs. An answer to this question cannot readily be provided as more comprehensive descriptions of all the mechanisms of action for each microorganism used are still lacking.

According to the best knowledge of the authors, no MBCP was authorised under this legislation and no application for authorisation filed. Consequently, the applicability of the EU biocide legislation remains to be fully clarified..

In the light of the recent clarification of the EC (EC 2015), however, it can be assumed that MBCPs will typically be considered to fall under EU detergent legislation. If, however, biocidal claims are being made, biocide legislation applies.

Occupational health—MBCPs are covered by Directive 2000/54/EC (EPC 2000) which regulates the minimum requirements for the protection of workers from risks related to biological agents. Employers (e.g., manufacturers and blenders of MBCPs, professional cleaning service providers) are required to conduct a risk assessment, including the classification of the microorganisms used into one of four risk groups based on the pathogenic potential (ibid, Annex III). Potential allergenic or toxigenic effects (especially the former), are not reflected by the risk group scheme but these effects also have to be considered (ibid Art 3, 3(d)). Only microbes which belong to risk group 1 are not considered pathogenic to healthy adults. The use of microbes classified in risk group 2 or higher requires notification to the national competent authorities and preventive measures by the employer. The type of risk mitigation measures largely depends on the particular risk group and exposure scenario. Manufacturers frequently claim that microbes classified into risk group 2 or higher are neither used nor considered for application in MBCPs and this was essentially confirmed in the 2009 product survey (Spök and Klade 2009). However, many manufacturers do not provide information on the microorganisms used or specify the genus only. Therefore, it is not possible to verify the risk group.

Food safety—In 2007 the European Food Safety Authority (EFSA) established a list of microorganisms which have a long history of safe use in food and feed context (EFSA Scientific Committee 2007). For these micro-organisms a qualified presumption of safety applies (QPS). The QPS list has been regularly updated ever since – most recently in 2016 (EFSA Panel on Biological Hazards 2017). Microorganisms which are included in this list do not need to undergo a risk assessment – though certain assessment needs exist for specific species.

While the QPS status was established in the context of food and feed safety and focuses on pathogenicity and oral toxicity aspects it has recently been also considered in the context of microbial biocides (e.g. Ctgb 2015). Also, some manufacturers of MBCPs refer to the QPS status of the micro-organisms used (e.g. Spök and Klade 2009, Chrisal no publication year indicated).

General Product Safety Directive—The Directive 2001/95/EC (EPC 2001) on general product safety applies in the absence of other EU legislation, national standards, EC recommendations or codes of practice relating to safety of products. It also complements sector specific legislation.

The Directive establishes obligations to both businesses and Member States' authorities. Businesses should place only products which are safe on the market, and inform consumers of any risks associated with the products they supply. They also have to make sure any dangerous products present on the market can be traced so they can be removed to avoid any risks to consumers.

Member States, through their appointed national authorities are responsible for market surveillance. They check whether products available on the market are safe, ensure product safety legislation and rules are applied by manufacturers and business chains and apply sanctions when necessary.

As there are no specific requirements or standards for MBCPs in the context of this Directive it is up to the producer or seller to ensure safety since no harmonised safety standards for these products appear to exist in the EU.

4.2 Norway

Norway is not a member of the EU but of the European Economic Area. As such EU legislation does apply to a certain extent. Still, Norway has its own statutory regulations applicable to MBCPs. MBCPs are regulated – as any other product - by the Product Control Act (1976) and – more specifically - by the Regulations on Microbial Products (Miljøverndepartementet 1998). The latter regulation requires importers, distributers, and manufacturers of MBCPs to declare any information necessary to assess health and environmental risks. The Norwegian Environment Agency recently sought advice of Norwegian Scientific Committee for Food Safety on the need to update the guidance document in order to be fully appropriate for MBCPs. The Scientific Panel on Microbial Ecology together with the Working Group on Health and Environmental Risk Assessment of Microorganisms Used in Bioremediations assessed the issue and developed recommendations how to update the guidance document (VKM 2016).

In its recommendations, the Scientific Committee frequently referred to and reiterated the Nordic Swan requirements for MBCPs (Nordic Swan 2016; see also Tables 1 and 2). Some recommendations go further than the Nordic Swan criteria (VKM 2016):

- Concentration of microorganism in the product: to use more appropriate tools than total plate count
- Pathogenic properties of the microorganisms added: should have more emphasis on animal and plant pathogenicity; reference lists used should also consider potential hazards to the environment; any taxonomic relation to pathogenic organisms should be described; ability to act as opportunistic pathogens. Available studies in the literature and by applicants on toxic and pathogenic effects in humans, animals (including aquatic animals, insects, arthropods), on microbial ecology, and persistence in the environment. Knowledge on exchange of possible virulence and resistance factors with other microbes
- Contaminants: by employing a molecular approach to check also the presence of animal and plant pathogens, as well as antibiotic resistance genes.
- To provide more detailed information to users – similar to the requirements in Table 1.

4.3 USA

In the USA, there is currently no regulatory oversight of naturally occurring microorganisms used in cleaning products. The Food and Drug Administration is responsible for

microorganisms in food, feed and pharmaceuticals. The US Department of Agriculture regulates microorganisms that are plant pests, and the EPA's Office of Pesticide Programs regulates those microorganisms used as pesticides. The Toxic Substances Control Act (TSCA) regulates the manufacture, import, processing, distribution in commerce, use, and disposal of "new" chemicals (including certain genetically engineered microorganisms) used for commercial purposes. However, TSCA does not regulate naturally occurring microorganisms as they are considered to be implicitly listed on the TSCA Chemical Substances Inventory, and therefore, are not "new". Thus, MBCPs containing naturally occurring microorganisms are not regulated under TSCA. While TSCA does not regulate naturally occurring organisms, it does regulate "new" intergeneric microorganisms which it defines as those formed by combining genetic material from microorganisms in different genera or constructed with synthetic genes that are not identical to DNA (deoxyribonucleic acid) sequences that would be derived from the same genus as the recipient microorganism. If MBCPs were to contain intergeneric microorganisms, they would be subject to regulatory oversight under TSCA.

The only program that may evaluate microbial-based cleaning products is the EPA's Safer Choice program. It is a voluntary program whereby EPA enters into partnership with companies that make products having an acceptable human health and environmental profile. In return, the products can display the Safer Choice logo on their labels. There is an extensive list of environmental and human health criteria against which products are evaluated before entering into a partnership with Safer Choice, including criteria related to product efficacy and quality control / assurance measures used in manufacturing processes.

"The Safer Choice program evaluates and labels certain products that contain naturally occurring microorganisms. To earn Safer Choice recognition, a microbial-based product must have its microorganism content assessed for risk and its chemical content reviewed for potential human health or environmental concerns. The risk assessment must show that the microorganism is non-pathogenic to plant or animal life and the chemistry review that the ingredients meet Safer Choice safer chemical criteria. The product must also meet other quality elements depending on product type. For more information on the review elements for microbial-based products, see the Considerations for Microorganism-based Products at https://www.epa.gov/saferchoice/safer-choice-criteria-formulations-containing-microorganisms" (DiFiore 2017).

While the Safer Choice program considers products containing microorganisms including MBCPs, as previously stated, it currently does not consider microbial products for use in indoor applications such as carpet or hard surface cleaners except for down-the-drain products (e.g., drain cleaners, grease trap treatments, septic system treatments) because of the lack of safety information on the potential effects of chronic long-term or high exposures to the microorganisms and / or spores.

4.4 Canada

In Canada, microorganisms can be regulated under product-specific statutes for pesticides, fertilizers, animal feeds and veterinary biologics, depending on their intended use. New living organisms contained in products, such as MBCPs, that are not regulated under these

other federal Acts and Regulations fall under the Canadian Environmental Protection Act 1999 (CEPA).

CEPA 1999 assesses substances against criteria to determine whether they are “toxic” as defined by the Act[1]. Both genetically modified organisms and naturally occurring organisms applied to a purpose are regulated under CEPA (Government of Canada, Environment Canada, Health Canada 2010). Currently, there are two streams for assessing microorganisms under CEPA.

One stream applies to the 68 existing organisms that are on the Domestic Substances List (DSL, see http://www.ec.gc.ca/subsnouvelles-newsubs/default.asp?lang=En&n=C4E09AE7–1). These include strains of several species known to be used in MBCPs. Organisms on the DSL can be used in any way and in any quantity without notifying the government unless risk management measures are imposed following their risk assessment. As of July 2017, the risk assessment of these 68 microorganisms is almost complete and the reports, fact sheets and descriptions of proposed risk mitigation measures, where applicable, are provided at the following webpage: (https://www.canada.ca/en/health-canada/services/chemical-substances/micro-organisms.html).

Organisms that are not on the DSL are considered to be new. CEPA requires that the government be notified before new organisms are manufactured or imported into Canada and that it be provided with information to allow it to conduct risk assessments. The New Substance Notification Regulations (Organisms) specify the information that must be submitted by proponents to support the assessment of these microorganisms http://laws-lois.justice.gc.ca/eng/regulations/SOR-2005–248/. For new substances notified in Canada, there is a time limit imposed for completing the assessments. Once the assessment period has expired, the manufacturer/importer may proceed subject to any control measures that may be specified. There may be other means for recalling the organism, however. The *Canada Consumer Product Safety Act* (CCPSA) also has oversight over microbial-based cleaning products through their general safety provision. Should health/safety issues arise with any such product, then Health Canada can take any number of actions such as imposing prohibitions/restrictions, propose labelling, issue advisories (examples found here: (http://www.hc-sc.gc.ca/cps-spc/advisories-avis/index-eng.php), or providing guidance.. Completed risk assessments of microorganisms on the DSL are published in *Canada Gazette,* Part I, and on the Government of Canada’s Chemical Substances website (http://www.chemicalsubstanceschimiques.gc.ca/index-eng.php). Risk assessment summaries of selected new microorganisms arising from new substances notifications are also published on Environment and Climate Change Canada’s New Substances website (http://www.ec.gc.ca/subsnouvelles-newsubs/default.asp?lang=En&n=8AD6A8C1–1).

[1]Resulting in risk-based decisions incorporating both hazard and exposure. The assessment considers both the potential to harm the environment and human health.

5 MBCP standards in ecolabelling regimes

5.1 Potential environmental and health benefits

Producers of MBCPs are frequently claiming their products to be more environmentally sound than conventional chemical cleaners because they contain ingredients that are less harmful than chemical ingredients typically found in these cleaners. A comparison of product ingredients for selected MBCPs showed that most MBCP products contain much lower levels of acids and surfactants. Microbial products used in commercial and industrial contexts for cleaning drains, pipes and grease traps are less alkaline, and seem to suggest a potential for reducing the amount of organic solvents used. This is also true for solvent-free microbial degreasing of parts in industrial manufacturing (Spök and Klade 2009).

According to manufacturer claims, the preventive character of microbial action is also potentially beneficial for the environment as microorganisms – once applied onto a surface – continue to be active as long as there is sufficient nutrients and water. When lacking nutrients or water, certain microorganisms can survive as spores which can germinate and become physiologically active again if nutrients and water become available. If used on a regular basis, for instance, in grease traps and drain pipes the formation of sediments and odour is reduced, which renders the need to use environmentally harmful cleaning products unnecessary.

Third-party verification of producer claims is largely missing. Still, the claims appear plausible and MBCPs are marketed as a specific group of “green” cleaning products.

In addition to environmental benefits, evidence from third party studies on health benefits has also been accumulating in recent years (Vandini et al. 2014, La Fauci et al. 2015, Caselli et al. 2016a). These studies essentially confirmed that routinely applied microbial cleaning regimes could significantly and stably reduce pathogenic microorganism population in hospitals.

5.2 The different roles of ecolabelling regimes for MBCPs

The plausible promises and growing evidence on health and environmental benefits seem to have triggered the development of MBCP-specific standards for voluntary ecolabelling. These standards mainly consider the safety for humans/user health, the efficacy of the product, and user information. In the absence of specific legislation in most jurisdictions setting specific and mandatory standards for environmental and health safety of MBCPs, ecolabelling is currently the only mechanism for ensuring minimum safety (and efficacy) standards. Both users/consumers and producers are therefore welcoming this development.

Ecolabelling standards also consider efficacy of the products. Manufacturers of MBCPs admit that MBCPs are still less efficient than conventional chemical products in terms of surface cleaning (ibid). In terms of odour control, however, these products are claimed to be superior. Also in this respect third-party evaluation is largely missing. The absence of agreed upon and standardised methods for comparing the efficacy of cleaning products might be one reason for this.

The following section briefly describes ecolabelling schemes which have developed MBCP-specific criteria: two governmental (EU-Ecolabel, Nordic Swan) and two private ecolabelling standards (Green Seal, EcoLogo/UL).

EU Ecolabel—In 2011 MBCPs were excluded from the EU Ecolabel and some national ecolabelling programmes in the EU followed suit. The rationale for excluding MBCPs was that there was little documentation on their performance benefits and safety. For example, the Austrian Ecolabel for All-Purpose and Sanitary Cleaners states that products "must not contain micro-organisms which have been deliberately added by the manufacturer." (Österreichisches Umweltzeichen 2011). Following a thorough evaluation of the ecolabelling criteria for all-purpose cleaners by the European Commission Joint Research Centers (Medina et al. 2015) and a clarification that MBCPs will normally fall within the scope of the EU detergent legislation (EC 2015), the EU Ecolabel criteria were updated and MBCPs were included again in one product category in 2016. The updated criteria includes for the first time specific requirements for MBPCs (EC 2017). The EU Ecolabel also seems to be the first governmental ecolabelling scheme which included specific criteria for MBCPs.

Nordic countries - Nordic Swan—The Nordic Ecolabelling Program ("Nordic Swan") is the most widely used ecolabel in the Nordic countries in Europe. Although not mandatory, the Nordic Swan carries a lot of marketing clout in the Nordic countries, and companies have a difficult time marketing products without it. The exclusion of MBCPs was reviewed from 2012 onwards and in 2016 updated standards for cleaning products were published which included criteria for MBCPs (Nordic Swan 2016).

USA – Safer Choice—As previously mentioned, Safer Choice is a voluntary program (formerly the Design for the Environment (DfE) program) whereby the US EPA enters into partnerships with companies that make products having "a more positive human health and environmental profile" than other products with the same use. In return, the products can use the Safer Choice logo on their labels. Companies with products that contain naturally occurring microorganisms need only submit information if they are seeking the Safer Choice partnership (US EPA 2013). At the present time, EPA's Safer Choice program considers only down-the-drain microbial-based products (e.g., drain cleaners, grease trap treatments, septic systems) that pose limited human exposure.

USA – Green Seal—Green Seal is a non-profit organization that develops sustainability standards for a broad range of product categories including cleaning products. Their criteria for MBCPs published in 2012 (Green Seal 2012) were meanwhile incorporated in broad range of general and specialty cleaning product (Green Seal 2013, 2014, 2015a, 2015b).

Canada/USA-Underwriters Laboratories (UL)—Eco Logo - a Canadian ecolabelling certification scheme originally launched by Environment Canada, developed standards for MBCPs (e.g. Eco Logo 2011). Following acquisition of Eco Logo by UL, the Eco Logo MBCP criteria were further developed as UL standards for odour control, carpet and upholstery care, cleaning and degreasing compounds (UL 2012a, b, 2013).

5.3 Ecolabelling criteria

Table 1 provides a simplified comparison of the MBCP-specific criteria of the ecolabelling schemes described above. Some of these standards focus on very specific groups of cleaning products (e.g. hard surface cleaner for consumer use) others are deemed to be more broadly applicable to general purpose and speciality cleaning products for consumer and professional products.

Overall, the criteria for human health and safety are similar in all cases. Three of the four ecolabelling standards also include user information discouraging use as sprays and on surfaces in contact with food. Efficacy-relevant criteria include in all cases a specification of a minimum number of microorganisms per ml or g and in case of the European standards – also requirements related to shelf life, performance and other aspects (see also Table 2 in the Supplementary Content). A more detailed comparison also showing how criteria are sometimes slightly different e.g., in terms of referring to recognised methods is shown in Table 2 (Supplementary Content).

Some of the criteria seem to be of a precautionary nature - either because evidence is lacking or inconsistent. One example is the exclusion of spray applications, another one the exclusion from use in food preparation or processing context (in case of the EU Ecolabel even in case of microorganisms having a QPS status (EC/JRC/IPTS 2016).Interestingly, the MBCP-specific criteria do not consider environmental properties. This seems to suggest that microorganisms are environmentally benign or at least neutral. Given the fact some microorganisms can be pathogenic to plants and animals and that such properties may also exist in risk group 1 microorganisms, additional criteria might be considered in the revisions of these eco-labelling schemes.

The lack of evidence on environmental properties has also been highlighted by the European Environmental Bureau and by BEUC (Bureau Européen des Unions de Consommateurs), the European umbrella organisation for consumer protection (EEB/BEUC 2016).

6 Conclusions and Recommendations

MBCPs represent a novel type of cleaning product which does not smoothly fit into existing legislation ensuring standards for environmental and health safety. This seems to be particularly true for the EU context.

The absence of regulatory oversight might be an important reason that MBCPs on the market can differ markedly in terms of safety assessment and efficacy (Spök and Klade 2009, VWA 2004). Regulatory oversight needs minimum standards that require developers to provide safety-relevant information in a harmonised and systematic way for governmental scrutiny. This would be in the interest of producers and users as this would provide reassurance to both of them.

For the EU, further clarification is required as to which of the candidate EU legislations could and should be adapted to provide a framework which is both appropriate and

proportionate for MBCP safety assessment. Alternatively, a specific regulation could be established – but the law-making process in the EU usually takes a long time.

As previously stated, there is no regulatory oversight of MBCPs using naturally occurring microorganisms in the USA. If companies are interested in partnering with US EPA's Safer Choice program to display the Safer Choice logo on their product, then there are rigorous criteria involved. Of primary consideration is that the risk assessment must conclude that the microorganism(s) in a product is not pathogenic to any species with which it will come into contact and will not cause any other adverse human health or ecological effects. Although the safety of the microbial species is most important, non-microorganism ingredients must have acceptable health and environmental profiles as well.

In Canada, new microorganisms manufactured or imported for use in MBCPs are required to undergo notification and assessment for risks to human health and the environment under CEPA. The New Substances Notification Regulations (Organisms) prescribes the information notifiers must submit in order to conduct this assessment. This includes information verifying taxonomic identity, all intended and potential uses, antibiotic susceptibility profiles, and any information or data on pathogenicity in humans and environmental species (animals, plants). In cases where the taxonomic identity of the microorganism indicates that it may be of low pathogenicity to humans, animals and/or plants, waivers for some of the requirements may be granted. A microorganism, whether genetically modified or naturally occurring, is considered to be new if it's not listed on the Domestic Substances List http://www.ec.gc.ca/subsnouvelles-newsubs/default.asp?lang=En&n=C4E09AE7–1. Canada appears to be unique among national jurisdictions in applying this type of regulatory oversight over microorganisms contained in MBCPs.

When developing MBCP-specific requirements it will be important to carefully balance the requirements - otherwise this might be detrimental for developers – almost all of them are small or medium-sized enterprises.

Based on recent reviews (Thomas and Versteeg 2013, VKM 2016) there seem to be a few key issues in terms of assessing and minimising human health risks: (i) precise taxonomic identification of the microorganisms used as the basis of the entire risk assessment ; (ii) use of microorganisms from risk group 1 only; (iii) susceptibility to clinically important antibiotics; (iv) need for process control and monitoring system to avoid unwanted microbes being present in the final product.

These issues are also reflected in the MBCP-specific criteria of eco-labelling standards – most of which have been established fairly recently. In jurisdictions without statutory regulations requiring regulatory oversight and/or clear safety requirements, these standards seem to fill the gap for transparent criteria-based safety assessment and risk mitigation as well as for third-party verification.

Other issues still require clarification and/or research in order to understand if and how additional provisions should be included in such standards, e.g. the role of plant pathogenicity and other environmental properties of the microorganisms used; the magnitude and relevance of chronic exposure to dusts and aerosols of MBCPs containing

vegetative cells or spores; the relevance of strains which belong to species known to include opportunistic pathogens and possible hazards for particular risk groups and the risks associated with particular species, some strains of which are known from cases of food contamination and poisoning.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations (Footnote)

BEUC	Bureau Européen des Unions de Consommateurs
CCPSA	Canada Consumer Product Safety Act
CEPA	Canadian Environmental Protection Act
CLP	Classification, Labelling and Packaging
Ctgb	Netherland’s Board for the Authorisation of Plant Protection Products and Biocides
DfE	Design for the Environment Program
DNA	Deoxyribonucleic Acid
DSL	Domestic Substances List
EC	European Commission
ECHA	European Chemical Agency
EFSA	European Food Safety Authority
EM	Effective Microorganisms
EPA	Environmental Protection Agency
EU	European Union
GRAS	Generally Recognised as Safe
MBCPs	Microbial-Based Cleaning Products

MSDS	Material Safety Data Sheets
NVWA	Netherlands Food and Consumer Product Safety Authority
OECD	Organisation for Economic Co-operation and Development
PPE	Personal Protective Equipment
QPS	Qualified Presumption of Safety
REACH	Registration, Evaluation, Authorisation and Restriction of Chemicals
TSCA	Toxic Substances Control Act
UL	Underwriters Laboratories
UVCB	Unknown, variable composition
YOPI	Young, Old, Pregnant, Immunocompromised

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Highlights

- Cleaning products with living microorganisms as active ingredients (MBCPs) are a relatively novel types of cleaning products
- Production and use as well as the range of application of MBCPs has increased in recent years
- There are possible health and environmental issues associated with MBCPs
- Globally there are few statutory regulations setting health and environmental safety standards
- In the absence of statutory regulations voluntary ecolabelling schemes are providing minimum safety standards

Table 1:

Overview of MBCP-specific criteria ecolabelling standards in Europe, USA, and Canada.

Criteria/Ecolabel	**EU Ecolabel**[a]	**Nordic Swan**[b]	**Green Seal**[c]	**Eco Logo /UL**[d]
Geographical scope	EU	Sweden, Norway, Finnland, Iceland, Denmark	USA	Canada/USA
Risk assessment related information				
Taxonomic identification requirements specified	X	X	X	X
Risk Group 1 microorganism only	X	X	X	X
Susceptibility to five main classes of antibiotics	X	X	X	X
Genetically modified microorganisms not permitted	X	X	X[e]	X
Test for specific contaminants of the MBCP required and specified	X	X	X	X
Restriction for spray use in place	X	X	X[f]	N.sp.
User information				
Product contains microorganisms Product shall not be used as spray Product should not be used on surfaces in contact with food	X[g]	X[g]	X[g, h]	N.sp.
Efficacy				
Minimal microbial content	X	X	X	X
Shelf life	X	X	N.sp.	N.sp.
Other	X[g]	X[g]	N.sp.	N.sp.

N.sp.: not specified

[a] EC (2017)

[b] Nordic Ecolabelling (2016)

[c] Green Seal (2013, 2014, 2015a, b)

[d] UL (2012a, b, 2013)

[e] ≤0.01% in the finished product (deliberate or contaminant) (Green Seal 2013, 2014, 2015a,b)

[f] If intended to be used as spray: airborne enzyme exposure for users <1 ng/m3 (Green Seal 2013, 2014, 2015a, b)

[g] Additional requirements specified – see Table 2 in the Supplementary Content

[h] Products […] should not be sprayed directly into the air (Green Seal 2013, 2014, 2015a, b)