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Risks and new challenges in the food chain

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Risks and new challenges in the food chain: Viral contamination and decontamination from a global perspective, guidelines, and cleaning

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Abstract

Even during the continuing world pandemic of severe acute respiratory syndrome coronavirus 2 (SARS CoV-2), consumers remain exposed to the risk of getting infected by existing, emerging, or re-emerging foodborne and waterborne viruses. SARS-CoV-2 is different in that it is transmitted directly via the airborne route (droplets and aerosols) or indirect contact (surfaces contaminated with SARS-CoV-2). International food and health organizations and national regulatory bodies have provided guidance to protect individuals active in food premises from potential occupational exposure to SARS-CoV-2, and have recommended chemicals effective in controlling the virus. Additionally, to exclude transmission of foodborne and waterborne viruses, hygiene practices to remove viral contaminants from surfaces are applied in different stages of the food chain (e.g., food plants, food distribution, storage, retail sector, etc.), while new and enhanced measures effective in the control of all types of viruses are under development. This comprehensive review aims to analyze and compare efficacies of existing cleaning practices currently used in the food industry to remove pathogenic viruses from air, nonfood, and food contact surfaces, as well as from food surfaces. In addition, the classification, modes of transmission, and survival of food and waterborne viruses, as well as SARS-CoV-2 will be presented. The international guidelines and national regulations are summarized in terms of virucidal chemical agents and their applications.

KEYWORDS
cleaning, food contact surfaces, food surfaces, international legislations, SARS-CoV2-, viral food pathogens, virucidal chemical agent

1 | INTRODUCTION

1.1 | Risks and new challenges in the food chain during a world pandemic

In the past, humanity has been faced with the challenges and risks of different epidemics. The most well-known is the Black-death, a bubonic plague pandemic occurring in Afro-Eurasia from 1346 to 1353. The Yersinia pestis bacterium carried by black rats was responsible for this medieval pest. It was transmitted from the rats to humans as a result from the bite of Oriental rat fleas infected after feeding on infected rodents. The epidemic could spread because humans colonized and built cities in the rodents' territories, with traveling to distant places further catalyzing the spread of the plague (Lugo-Morin, 2020). Many epidemics were and are also caused by viruses transmitted from infected animals (e.g., birds and pigs) to humans. The Spanish flu pandemic of 1918−1919 wherein one-third of the world was infected and around 50 million people died was caused by influenza virus A subtype H1N1 (Taubenberger & Morens, 2006).

In late 2019, China reported a cluster of pneumonia cases of unknown cause that would later be identified as severe acute respiratory syndrome caused by coronavirus 2 (SARS-CoV-2) (Emami et al., 2020). Due to the widespread global transmission of SARS-CoV-2, the World Health Organization (WHO) declared COVID-19 to be a pandemic on March 11, 2020 (Cucinotta & Vanelli, 2020; Hu et al., 2021).

New diseases caused by viruses may thus originate from wildlife and livestock, either acting as amplifier hosts or connectors. A virus is one of the smallest biological agents that affects our health, with most viruses pathogenic to humans varying in diameter from 20 up to 400 nm (Roos, 2020). Transmission to humans may occur from primates (human immunodeficiency virus, responsible for acquired immune deficiency syndrome, AIDS), bats (Ebola virus, responsible for Ebola hemorrhagic fever), rats (Lassa mammarenavirus, responsible for Lassa hemorrhagic fever), birds, and even mosquitos. Other existing examples of transmission to humans include: Middle East respiratory syndrome coronavirus (MERS-CoV), originally coming from bats and transmitted from camels; SARS-CoV-1 and SARS-CoV-2 spread from bats through wildlife species and then to humans (Zhou et al., 2021); Nipah virus originating from bats, and multiplied in pigs; influenza viruses mixing between human, pig, and poultry populations in East and Southeast Asia (Bett et al., 2020).

Humankind is faced with the challenges of expanding agricultural frontiers, intensification of agricultural activities, climate change, and the colonization of new rural territories that are displacing animals. In addition, the threats to biodiversity and human health by new pathogens is growing (Daszak et al., 2000). These challenges are having pronounced effects on the global food system. Certain food systems in which wild animals, domestic animals, and humans come in close proximity to each other such as in wet markets are vulnerable to zoonotic emergence (Bett et al., 2020). The concept of "One Health" recognizes our increasing interdependence with animals and animal origin products as a critical risk factor to our health and wellbeing with regard to infectious diseases (AVMA, 2008). In tackling these new challenges as part of the "One Health" concept, the interconnection between humans, animals, and the environment will require a holistic, collaborative, and multidisciplinary approach. The gaps in the current food system that allow the transmission of pathogenic organisms from animals to humans, as well as cross contamination (Galanakis, 2020), need to be closed to ensure that these emerging pathogenic microbial and viral threats are reduced.

Foodborne or waterborne viral outbreaks are caused by consuming contaminated water or food sources, resulting in digestive complaints (e.g., vomiting and diarrhea) and in a worse case death (CDNA, 2010). Although viruses cannot grow in foodstuffs and water, they can survive in food and water.

Nowadays, food manufacturers and food suppliers have predominantly focused on prokaryotic and eukaryotic food spoilage microorganisms and bacterial foodborne pathogens, while comparatively less attention is given to infective waterborne and foodborne viruses. In 2019, 27 EU member states reported a total of 5175 foodborne and 43 waterborne outbreaks of disease, resulting in 49,463 illnesses, 3859 hospitalizations, and 60 deaths (EFSA-ECDC, 2021). Considering foodborne outbreaks with a known causative agent (3101 in total), 17.9% were attributed to viruses, while the other outbreaks were due to bacteria (44.0%), bacterial toxins (32.1%), parasites (1.0%), and other causative agents (5%) (EFSA-ECDC, 2021). In 2019, Salmonella, Listeria monocytogenes, norovirus, and hepatitis A virus were responsible for, respectively, 49.6%, 6.1%, 7.2%, and 2.6% of all outbreak-related hospitalizations (EFSA-ECDC, 2021). Looking at food commodities, viruses account for 30% of the foodborne outbreaks in fruits and vegetables, while 75–80% of the foodborne outbreaks connected with the consumption of seafood, including shellfish, molluscs, and their products, were attributed to viruses (EFSA-ECDC, 2021), especially norovirus and HAV (Bélanger et al., 2015). In its annual report, Surveillance for Foodborne Disease Outbreaks 2017, the U.S. Centers for Disease Control and Prevention (CDC, 2019) mentioned 841 outbreaks of foodborne disease, from which 37.5% were caused by viruses. Norovirus and HAV were responsible for 98% and 2% of the total viral foodborne

outbreaks. Canada reported a total of 115 foodborne outbreaks over the period 2008–2014, from which 14.8% were caused by viruses.

For a number of years, international and national food safety bodies are looking at means to tackle viral foodborne and waterborne outbreaks. The enhanced practices to clean and disinfect surfaces to exclude indirect contact transmission of SARS-CoV-2 may trigger food manufacturers and suppliers to extend these approaches in the post-COVID-19 era to put up a hurdle against the abovementioned viruses. Although standardized detection methods for the two most important viral food pathogens (human norovirus [HuNoV] and HAV) exist, the inability to reliably discriminate between infectious and noninfectious virus particles makes the control of these food- and waterborne viruses more challenging. The main challenge, however, is preventing fecal contamination of food, in particular because the implementation of preventive measures is difficult.

This review aims to analyze and compare efficacies of existing cleaning practices that are currently used in the food chain to remove viruses pathogenic to humans from air, contact, and food surfaces. Classification, modes of transmissions, and survival of airborne, foodborne, and waterborne viruses will be discussed along with recent knowledge on contamination and transmission of emerging viruses, such as SARS-CoV-2. The international guidelines and national regulations are summarized in terms of virucidal chemical agents and their recommended applications.

1.2 | Current knowledge on transmission, survival, and control of SARS-CoV-2

The most common modes of transmission of emerging and re-emerging viruses are contact with infected body secretions/excretions and contaminated fomites (especially high-touch surfaces) and inhalation of respiratory droplets/aerosols that contain infectious virus (Ijaz et al., 2020). Similarly, the main routes of human-to-human transmission of SARS-CoV-2 are through aerosols and respiratory droplets when an infected person is in close contact with a noninfected person (Greenhalgh et al., 2021). Still uncertainties exist around additional modes of transmission, such as transmission via contaminated surfaces (Zuber & Brüssow, 2020). Existing information supports knowledge that food has not been implicated in the direct transmission of SARS-CoV-2, because viruses cannot grow on food products–they need living host cells to replicate–the chance that it can ever happen is very low. However, there is a risk that workers in the food industry can get

infected and transmit SARS-CoV-2 to their noninfected colleagues (Ceylan et al., 2020; Zuber & Brüssow, 2020). During the pandemic, large outbreaks of COVID-19 have been registered in meat processing plants in the United States, Canada, Germany, France, Spain, Portugal, and the United Kingdom due to close contacts of workers (Middleton et al., 2020). In most cases, this transmission among workers in the food industry correlates quite well with their working conditions and living standards, since they often live and commute in close contact.

Although some investigations have shown that the SARS-CoV-2 virus can be detected within hours in human stool of an infected person, there is no evidence for fecal–oral transmission of the virus (WHO, 2020). There are reports on the presence of viral RNA (SARS-CoV-2) in the gastrointestinal tracts of COVID-19 patients; however, it must be stressed that further studies are necessary on the specific transmission mechanism (Guo et al., 2021).

It is known that wastewater-based epidemiology may provide interesting information on health, disease, and pathogens. Waste water can be used as an early warning or as a surveillance that lacks the biases of the traditional indicators used to understand where the disease transmission is occurring, increasing, or decreasing. Detection of pathogens in waste water is more cost-effective as compared to more invasive methods (Larsen & Wiggiton, 2020; Richardson, 2021).

Testing wastewater for SARS-CoV-2 has also proven to be effective in predicting the spread of this infection, especially because biomarkers typically for the virus (e.g., SARS-CoV-2 RNA) could be found in drain systems. It is known that SARS-CoV-2 can survive in appropriate environment days after being excreted from the human body via feces and urine (Yang et al., 2015; Mao et al., 2020). So, wastewater data can be used to check the reliability of epidemiological trends calculated from diagnosed cases (Larsen & Wigginton, 2020).

Several surveys on other coronaviruses, such as SARS-CoV-1 and MERS-CoV, have indicated that fomites, along with airborne routes, contribute to the widespread transmission of coronaviruses (Tseng & Li, 2007; Otter et al., 2016; Xiao et al., 2017). Shortly after COVID-19 was declared as a pandemic, several governmental and international bodies (CDC, WHO, US FDA, etc.) have recommended the disinfection of surfaces to avoid or reduce the risk of indirect contact transmission of SARS-CoV-2. The underlying reason was that other respiratory viruses are spread through indirect contact transmission as the predominant transmission route (Otter et al., 2016; Asadi et al., 2020). In comparison to SARS-CoV-1 (2003 outbreak in China), SARS-CoV-2 was shown to be more stable on plastic and stainless steel than on copper and cardboard, and viable virus was detected up to 72 h after

contamination of these surfaces (Van Doremalen et al., 2020). A number of authors, such as Kumar et al. (2020) and Ceylan, Meral, and Cetinkaya (2020), allegedly suggested the risk of SARS-CoV-2 being present on food contact surfaces and packing materials because infected individuals (e.g., staff)–albeit asymptomatic–could possibly contaminate food contact surfaces or packaging throughout the food supply chain via indirect contact transmission. However, Goldman (2020) emphasized that the chance of transmission through inanimate surfaces is very small, and only in instances where an infected person coughs or sneezes on the surface, and someone else touches that surface soon after the cough or sneeze (within 1−2 h). In all survival studies of SARS-CoV-2 on different surfaces, large initial virus titer samples (10^4–10^7 infectious virus particles) were placed on these surfaces, resulting in long survival times on diverse fomites. These results have given rise to a misplaced obsession with surface hygiene and deep cleaning, what some people describe with the terminology "hygiene theater." In other words: a "COVID-19 risk-reduction ritual that make us feel safer, but doesn't actually do much to reduce risk, even as more dangerous activities are still allowed" (Lewis, 2021). The studies of Dowell et al. (2004) and Mondelli, Colaneri, Seminari, Baldanti, and Raffaele (2021) better presented real-life situations (hospital settings) with the amount of virus actually and naturally deposited on surfaces being several orders of magnitude smaller. No viable virus was found on fomites. The U.S. Centers for Disease Control and Prevention (CDC, 2021) and the WHO (Lewis, 2021) followed the opinion that there is limited evidence of SARS-CoV-2 transmission through fomites.

Even though SARS-CoV-2 is a nonfoodborne virus, it may spread among workers active in the food chain (e.g., food plants, food distribution, retail sector, etc.) through the respiratory droplets of infected individuals. Overcrowding and lack of ventilation are associated with respiratory infection outbreaks, including COVID-19, in many food handling areas. Increasing the distance from an infection source and removing aerosols and droplets by adequate ventilation are means to reduce airborne transmission of SARS-CoV-2 among employees active in the food chain (NCIRD, 2021; Li, 2021). A high ventilation flow-rate will reduce the contribution of airborne transmission to a low level, whereas a low ventilation flow-rate leads to a relatively high contribution of aerosols to transmission (Li, 2021).

Key to limiting the spread of SARS-CoV-2 is to follow the recommendations of the WHO and guidelines of national health agencies. US FDA-OSHA (2020), WHO (2020), EC (2020), and many other national and international bodies have provided guidance to protect food workers from potential occupational exposures to SARS-CoV-2. These guidelines are based on improved understanding of the virus and its variants, their survival, and the overall effects of environmental, physical, and chemical factors on them.

Typical measures to implement include: access ban for infected employees, keeping visitors, contractors, truck drivers, and so on outside of the food premises, obligatory registration of visitors, distance of at least 1.5–2 m (6 feet) between food workers, physical barriers, wearing face masks covering both mouth and nose or shields, good hand hygiene, gloves, testing on SARS-CoV-2 regularly and intermittently for personnel who handle food products or have physical access to food contact surfaces, tests to sample surfaces for SARS-CoV-2 (test kits), separation of raw ingredients from cooked products, and so on. Many of these measures have put particular strain on the different players in the food supply chain during the COVID-19 pandemic (Ceylan et al., 2020; Zuber & Brüssow, 2020). The continuing COVID-19 pandemic may have an impact on the future of the food chain and decontamination approaches.

2 | CLASSIFICATION OF VIRUSES

When looking at the host cells and tissues that support replication of a particular virus, a distinction has been made between: (1) enterotropic viruses causing gastroenteritis (e.g., HuNoV, human sapovirus, human astrovirus, human rotavirus, and human enteric adenovirus), (2) hepatotropic viruses being enterically transmitted and causing hepatitis (e.g., HAV and hepatitis E virus [HEV]), (3) neurotropic viruses replicating in the human intestine and further migrating to the central nervous system to subsequently cause flaccid paralysis, meningitis, fever, and so on (e.g., poliovirus and nonpolio enteroviruses), (4) multitropic viruses affecting several types of cells and tissues and causing a large variety of symptoms, which can often result in death (e.g., ebola virus and human parvovirus), and (5) pneumotropic viruses causing respiratory diseases, fever, myalgia, and sometimes gastroenteritis (Heegaard & Brown, 2002; Halami et al., 2013; Bosch et al., 2016; Roos, 2020).

Besides airborne transmission, transmission of pneumotropic viruses may occur from surfaces and packages contaminated with these viruses. They present a recognized risk for food workers in food handling and food processing facilities (e.g., influenza A virus, Avian influenza virus, 2003 SARS-CoV-1, 2012 MERS-CoV, and 2019 SARS-CoV-2) (Roos, 2020).

On the exception of coronaviruses and influenza viruses which are enveloped viruses, the abovementioned viruses (1–5) are nonenveloped. Naked viruses are usually sensitive to chlorine, heat, and UV-light, while larger enveloped

viruses are even more fragile (Kong et al., 2021). Consumption of food or water contaminated with these nonenveloped viral pathogens is the main route of infection. Food and water may get contaminated by feces or body fluids of potentially infected animals or humans. Viral contamination may also occur via the hands of food workers. Surfaces in general, when contaminated with these virions, may transmit them to susceptible hosts. Surfaces become contaminated with virus particles by direct contact with infected body secretions or fluids, contact with soiled hands, the settling of aerosolized viral particles (large droplet spread) generated via talking, sneezing, coughing, or vomiting (Boone & Gerba, 2007). Oral autoinoculation of these virus particles may occur due to contact with inanimate surfaces or the skin of the upper limbs being contaminated with virions. A number of outbreaks due to indirect contact transmission of HAV, rotavirus, enterovirus, and the 2003 severe acute respiratory syndrome coronavirus (2003 SARS-CoV) have been reported (Tseng & Li, 2007). Numerous respiratory and enteric viruses have been reported to survive for hours to days, depending on the nature of the contaminated surface (e.g., metal, plastics, etc.), the type of virus, the presence of food soil, the temperature, and humidity. Typically, viral presence on fomites may decrease with surface cleanliness, and disinfection of fomites may interrupt viral indirect contact transmission (Boone & Gerba, 2007; Eterpi et al., 2009).

2.1 | Classification of viruses according to Baltimore

The working classification of viruses by David Baltimore that was published in 1971 still has been used today in parallel with official virus taxonomy. Baltimore grouped all viruses into seven disconnected groups without any subdivisions; they are commonly referred to as Baltimore Classes (BCs) (Kuhn, 2021). BCs were established based on the type of nucleic acid incorporated into the virions, and thereby on the type of virus reproduction.

Classifying viruses is the grouping of viruses into progressively more inclusive groups (lower taxa included in higher-ranked taxa) based on common genomic, phylogenetic, and phenotypic properties that, ideally, are proof of evolutionary relationships or descendance. The International Committee on Taxonomy of Viruses recommends complete-genome pairwise sequence comparisons to establish percentage similarity cutoffs for taxon demarcation. The criteria for virus classification and the demarcation criteria that are used to decide whether a virus belongs to an already established taxon or requires the establishment of a new taxon are modified continuously based on improved understanding of virus micro

and macroevolution (Kuhn, 2021). These criteria tend to differ between taxa because distinct virus groups evolve with different speeds depending on their genome types, absence or presence of replication proofreading mechanisms, and propensity to reassort genome segments, which results in gene transfer. Genetic materials can also be interchanged through recombination. As an example, Xu et al. (2020) indicated that SARS-CoV-2 possibly originated from recombination between bat and pangolin coronaviruses.

2.2 | Single- and double-stranded DNA and RNA viruses

Genetic material in viruses can either be DNA or RNA. Looking further at the structure of the genome, this genome may be either single-stranded (ss) or double-stranded (ds), linear or circular. Single- and double-stranded genomes can be found in viruses infecting vertebrates, invertebrates, plants, bacteria, fungi, yeasts, algae, and protozoa. The whole genome may consist of either one nucleic acid molecule (monopartite genome) or several nucleic acid segments (multipartite genome). These differences in genome necessitate different replication strategies (Gelderblom, 1996). A schematic morphological representation of DNA or RNA viruses infecting vertebrates is shown in Figure 1 (King et al., 2012).

Knowing the processes behind viral mutations allows for a better understanding of viral pathogenesis, as well as improved understanding and management of emerging viral diseases, antiviral drug resistance, and immune escape (Sanjuán & Domingo-Calap, 2016). Today, information on spontaneous mutations is easily accessible for various microorganisms. Viruses mutate due to errors during replication. Although most mutations affect the virus negatively, some mutations are beneficial for the virus. Such beneficial mutations may allow viral populations to better adapt to a new environment. As they can better cope with the challenges of this new environment, they can transmit and survive better in this environment (Smith et al., 2014).

Drake's rule applies to DNA-viruses and other microbes, such as bacteria and unicellular eukaryotes, which means that the density of accumulated mutations per generation is roughly inversely proportional to genome size. The mutation rate is thus higher in microorganisms (including DNA viruses) with smaller genomes (Drake, 1991). But there has been some skepticism about Drake's conjecture, because it was formulated after an analysis based on just seven taxa, four of which were bacteriophages. However, as genomic information for a wide variety of organisms is now available due to the widespread use of genome analysis techniques, scaling of the mutation
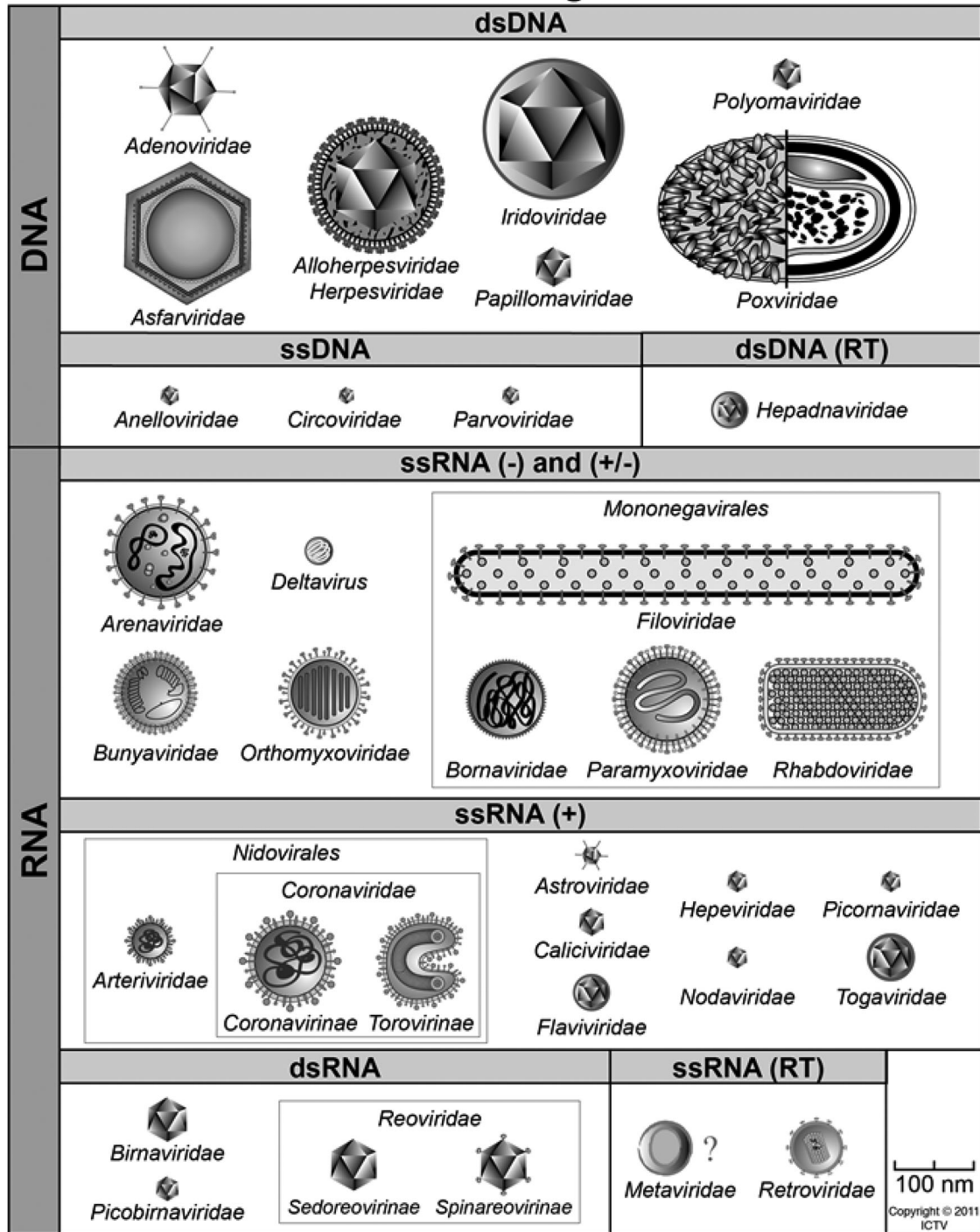
Virus Taxa Infecting Vertebrates

FIGURE 1 A schematic morphological representation of DNA and RNA viruses. Adapted from King, Adams, Carstens, and Lefkowitz (2012)

rate based on genome size and the likely mechanisms driving it becomes more straightforward (Lynch, 2010). Sanjuán et al. (2010) found that single-stranded DNA bacteriophages tend to mutate faster than double-stranded ones. Mutation rates in single-stranded DNA viruses infecting eukaryotes, however, were not considered. In their study, Drake's conjecture "that mutation rate is higher when the amount of genetic material is lower" fits well. The mechanisms responsible for this inverse correlation between mutation rate and genome size are not completely understood. One possible explanation is that single-stranded nucleic acids are more prone to oxidative

deamination and chemical damage. During viral infections, elevated levels of reactive oxygen species and other cellular metabolites can induce mutations in both the host cell and virus (Sanjuán & Domingo-Calap, 2016).

In general, mutation rates in the genome of RNA viruses are larger than mutation rates observed in viral double-stranded DNA genome of comparable size. The same negative relationship between mutation rate and genome size seems to exist in RNA viruses, although the smaller variation in genome size makes it more difficult to detect such a trend (Sanjuán & Domingo-Calap, 2016). Due to this difficulty, little differences in mutation rate in RNA viruses were observed among the BCs. The lack of replication fidelity in many RNA viruses is especially due to the absence of proofreading activity.

A high mutation rate beyond that of the wild-type virus usually decreases the survival chance of viruses, although some beneficial mutations may allow viruses to flourish in a new environment (Domingo et al., 2021). RNA viruses seem to balance between genome stability on one side and generation of sufficient genetic diversity on the other side. To remain fit in their environment, some RNA viruses also possess proofreading capacity, reducing the mutation rate as well as the generation of too many deleterious mutations. Coronaviruses even possess evolved proofreading capacity, making them substantially different from all other RNA viruses. This proofreading capacity allowed them to increase the size and complexity of their genome. As a result, coronaviruses have the largest genomes among the RNA viruses (30−33 kb) (Smith, Sexton, & Denison, 2014).

2.3 | Enveloped/nonenveloped

The stability of viruses strongly depends on whether they are nonenveloped (naked capsid) (e.g., enteroviruses) or enveloped (e.g., influenza and coronaviruses). The structure of nonenveloped and enveloped viruses is shown in Figure 2. Especially infectious nonenveloped viruses are more stable in food and the environment. Factors affecting their stability must be known to develop effective mitigation and control strategies. These factors include the properties, water activity, and storage conditions of foods. In enveloped viruses, water is essential in maintaining the structure of their lipid bilayer, which in turn enhances the retention of water molecules inside the virion. Water molecules are essential in maintaining the viral activity, and protect virions against loss of activity during release from host cells and transmission. In nonenveloped viruses, water is also essential for their viral activity, as shown by the fact that enteroviruses can be inactivated by drying. However, other nonenveloped viruses, such as HAV and norovirus, are not inactivated during drying operations (Roos, 2020).

Where culturing of foodborne viruses outside a human host is hard to manage or even impossible, surrogates may be considered (Miranda, & Schaffner, 2019). Cultivable surrogates that are sufficiently persistent to diverse treatment conditions (e.g., heat, radiation, and chemicals) have demonstrated to be effective in estimating the virucidal effect of a treatment on closely related strains. In contrary, a viral surrogate with a low persistence can provide incorrect information with regard to the efficacy of a treatment or mitigation measures. The effectiveness of this treatment or these implemented mitigation measures then can be overestimated (Leblanc et al., 2019).

Prussin et al. (2018) studied the transmission of enveloped bacteriophage φ6 (used as a surrogate for influenza viruses and coronaviruses) by droplets and aerosols. Relative humidity, absolute humidity, and temperature were evaluated as predictors of survival of enveloped viruses in droplets. Understanding this relationship may lead to improved disease control strategies related to these enveloped viruses. However, the authors' findings were inconclusive. With respect to virus infectivity, the relation between relative humidity, absolute humidity, and temperature was found to be complex and could not be easily captured by linear or log-linear regressions. But how viruses are transmitted and survive in various environments depends on the physicochemical properties of their viral structure. These properties also determine the effectiveness of disinfection, sterilization, and other control measures against viruses.

3 | PATHOGENIC VIRUSES IN FOOD CHAIN

Consumers may come into contact with a large diversity of pathogenic viruses after oral ingestion of virally contaminated food. *Adenoviridae*, *Astroviridae*, *Caliciviridae*, *Hepeviridae*, *Orthomyxoviridae*, *Paramyxoviridae*, *Parvoviridae*, *Picornaviridae*, and *Reoviridae* are families of viruses that can transmit to human via the foodborne route (Newell et al., 2010). Those resistant to the highly acidic conditions in the stomach, as well as digestive enzymes and bile salts in the intestines, may finally cause infection. However, viral contamination of food usually occurs via infected persons, crops irrigated or food products rinsed with virally contaminated water, pollution of cultivation grounds of bivalve molluscs, and so on. These routes of food contamination have in common that feces are the underlying source of foodborne viruses. Especially raw food, refrigerated food, and bivalve molluscs are involved in viral food infections (Mena, 2017). Because bivalve molluscs are often
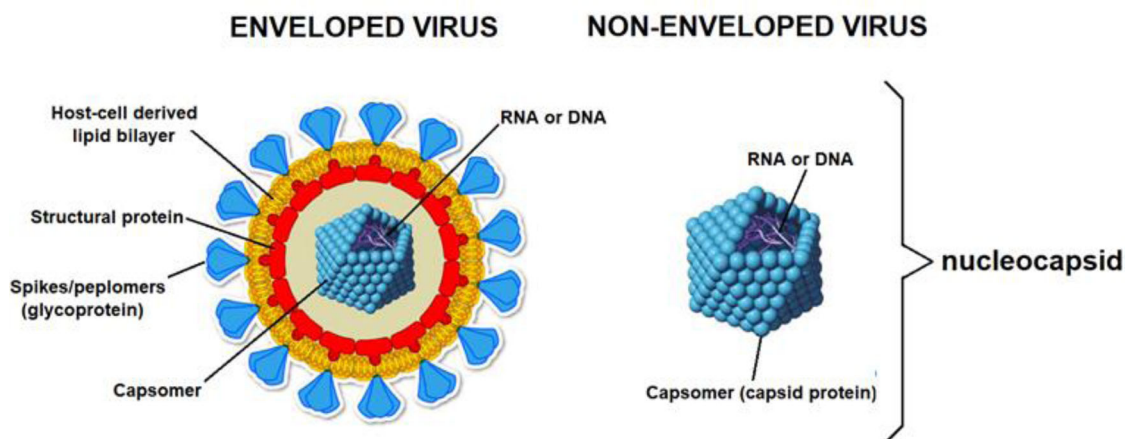
ENVELOPED VIRUS   **NON-ENVELOPED VIRUS**

FIGURE 2 Structure of enveloped and nonenveloped viruses. Adapted from Ijaz et al. (2020)

eaten raw or only slightly heated, fecal viruses can infect consumers. Virus particles are concentrated in bivalve molluscs because they filtrate water to feed. Just because bivalve molluscs may contain fecal indicator organisms, they are often rinsed with pure seawater (International Commission on Microbiological Specifications for Foods, 2011). This practice has proven to be effective in reducing bacterial contamination, but is less successful in reducing viral contamination. Salads, baked goods, desserts, raw cut vegetables and fruits, frozen raspberry, and drinking water are other sources of viral food infection. In general, all types of food that is handled and eaten without (sufficient) heat treatment is of risk. As an example, HEV can also be transmitted during the consumption of undercooked pork and liver (Bosch et al., 2018).

Norovirus, HAV, HEV, rotavirus, enterovirus, adenovirus, astrovirus, and sapovirus are among the most potent food- and waterborne viral pathogens (White et al., 2017). According to Zainazor et al. (2010), norovirus was the main cause of viral gastroenteritis in humans worldwide. Norovirus outbreaks were mostly associated with consuming shellfish, fruits, vegetables, and ready-to-eat foods contaminated by food handlers and consumed without preliminary heat treatment (FSANZ, 2017a). According to NSWG (2019), food and drinks that are not subjected to a rigorous heat treatment afterward also largely contributed to the fecal–oral transmission of HAV.

There are numerous factors that are responsible for the increasing number of viral foodborne infections: (1) increase in the scale of agriculture, (2) globalization of food production, (3) traffic and trade, (4) prepared food contaminated by infected persons (e.g., meat virally contaminated after the transfer of viruses from hands to the food surface) or after contact with critical products, (5) exposure of travelers, refugees, and immigrants to unknown food-related dangers, (6) the vulnerability of a majority of

the population (HIV-infected persons, the elderly, and immuno-compromised people), (7) increased focus on healthy diet (more leafy greens and berries), (8) return to traditional methods of conservation (pickling, etc.), (9) altered food habitudes (ready meals, exotic food, etc.), and (10) changes in food preparation. With respect to the latter, in-sufficient heating of food during cooking, roasting, barbecue, and fondue is to a large extent responsible for a high number of viral foodborne infections (Bosch et al., 2016, 2018).

4 | DEFINITIONS AND GOALS OF CLEANING, DISINFECTION, AND SANITIZING

According to the Codex Alimentarius Commission (CAC), cleaning is the process of removing product residues, contaminants (dirt, dust, and grease), and other objectionable matter from product and splash contact surfaces (CAC, 2009). The cleaning objective is obtaining a surface free of visible matter, clean to touch, and without odors, so that subsequent disinfection will be effective (Middleton & Holah, 2008).

Disinfection is targeted to reduce the number of harmful microorganisms down to a level acceptable for a defined purpose, for example, a level that will not lead to contamination or spoilage of foods and is not harmful to health. This level of microbial reduction is based on a risk assessment, which depends on process and product requirements. Disinfection methods include chemical agents (or disinfectants) and/or physical methods (hot water, steam, hot air, ultraviolet light [UV-C], etc.) that are effective against a majority of microorganisms but not including spores. In the United States, "sanitizing" (sanitization) is used as an alternative for "disinfection," although the

meaning is not completely the same. Sanitizing is the process applied to a cleaned surface to reduce the total vegetative cell population to a level considered safe for public health. In the meaning of sanitizing, the numbers of the most resistant human pathogens are reduced by applying hot water, hot air or steam, or an EPA-registered sanitizer according to label directions. According to this definition, sanitizing does not necessarily involve the destruction of all pathogenic organisms (EHEDG, 2013; Nikoleiski et al., 2021).

Although the meaning of "disinfectant" is not specific, a "sanitizer" in the United States is defined as a chemical that reduces the microbial contamination of two standard organisms, *Staphylococcus aureus* and *Escherichia coli*, by 5-$\log_{10}$ in 30 s, at 25°C. Nonfood contact sanitizers must reduce the microbial contamination by 3-$\log_{10}$ in 5 min, at 25°C. Notice that the conditions in which the substances are applied seldom enable to achieve the number of reductions obtained in laboratory tests (EHEDG, 2013).

Sanitizing may not be confused with sanitation, which has as meaning: cleaning, disinfection, if necessary, pest control, and waste management. In Europe, the synonym of sanitation is (food) hygiene, which has as definition: all conditions and measures necessary to ensure the safety and suitability of food at all stages of the food chain (CAC, 2009; EHEDG, 2013). In the United States, industrial hygiene has a completely different meaning, being the control of occupational health hazards. In this review, the term "disinfection" is preferred over "sanitizing," because it is more accepted worldwide, as proven in the publications of the CAC.

5 | INTERNATIONAL GUIDELINES AND NATIONAL REGULATIONS

5.1 | FAO/WHO/Codex

The Codex Alimentarius has addressed the issue of contamination of foods by viruses, proposing guidelines on the application of the general principles of food hygiene (CAC, 2012). The CAC/GL 79–2012 document developed by the CAC in 2012 (CAC, 2012) establishes guidelines focused on different points in the food production process:

(a) The primary production/harvesting area. It recognizes that viral contamination of foods may occur at the primary production stage by soil, contaminated water, contaminated harvesting containers or utensils, as well as by food handlers. The guideline aims to describe the conditions in which the primary production must occur and to identify different aspects of pro-

duction processes that should be controlled to reduce the chance of contamination.

(b) Design of equipment and facilities. The design and construction of equipment and facilities must ensure that they can be properly cleaned and disinfected to avoid persistence of virus contamination that finally could be transferred to foods.

(c) Control of operation. To prevent food contamination, processing operations should be controlled by taking preventive measures against identified hazards or risks.

(d) Maintenance and sanitation of food premises and equipment. It is especially related to procedures to be followed after an event of vomiting, diarrhea, and/or notification of hepatitis. Vomiting/diarrhea events and persons shedding viruses may cause widespread contamination of food production premises. Measures to eliminate this contamination must be taken.

(e) Personal hygiene. It deals with the need for strict personal hygiene of food handlers in order to prevent viral food contamination due to poor personal hygiene.

(f) Product information and consumer awareness. It emphasizes the need to maintain traceability of food and encourages countries to educate consumers in making them more alert to the risk of some ready-to-eat foods, such as raw bivalve molluscs.

(g) Training. Those food handlers that can have contact with foods should be trained in the control of enteric viruses.

The guideline for fresh produce encompasses general hygienic practices for the production, harvesting, processing, packing, and storage of fresh produce since the fresh produce is susceptible to viral contamination along these steps. However, decontamination methods used in the industry to eliminate bacterial pathogens may not be effective for the reduction of norovirus and hepatitis A virus in fresh produce.

In addition, the CAC/GL 79–2012 document (CAC, 2012) provides particular guidance to control HAV and norovirus in bivalve molluscs and fresh produce. The guideline for bivalve molluscs is mainly aimed to prevent the contamination of bivalves at growing and harvesting areas by monitoring water quality and acknowledges the difficulties of guaranteeing a high water quality during the growing and harvesting of these animals. Therefore, it provides advice about how to avoid contamination of water and what to do when it becomes contaminated by events, such as overflow of sewage treatment plants. The use of decontamination methods, such as heating the bivalves at 85–90°C for at least 90 s, and the use of high hydrostatic pressure are also addressed.

5.2 | North America

5.2.1 | Legislation, guidelines, and surveillance in the United States

In the United States, the CDC conducts surveillance of foodborne disease outbreaks through the Foodborne Disease Outbreak Surveillance System. Public health agencies in all 50 states voluntarily report outbreaks investigated by agencies via a web-based reporting platform, the National Outbreak Reporting System (NORS). This NORS was launched in 2009 to report all waterborne, foodborne, and enteric disease outbreaks. There is also a 7-page form "National Outbreak Reporting System–Foodborne Disease Transmission, Person-to-Person Disease Transmission, Animal Contact, Environmental Contamination, Unknown Transmission Mode," bearing number CDC 52.13. Since 2011, CDC also has a web-based system, called SEDRIC (System for Enteric Disease Response, Investigation, and Coordination), to streamline and coordinate multistate outbreak investigation (Hall, 2016).

Furthermore, there is the national norovirus outbreak surveillance network "CaliciNet" of federal, state, and local public health laboratories in the United States. It was launched by CDC in 2009 to collect information on norovirus strains associated with gastroenteritis outbreaks in the United States. In August 2012, CDC also set up the "Norovirus Sentinel Testing and Tracking (NoroSTAT)" network, where 12 state health departments and CDC work together to establish and maintain standard practices for norovirus outbreak reporting to CDC surveillance systems (Hall, 2016).

The U.S. Food & Drug Administration (FDA) recommends the risk-based approach system hazard analysis critical control points (HACCP) to control foodborne pathogens in the production, distribution, and retail of food products. To conduct a risk assessment for foodborne or waterborne viruses, the EPA/100/J-12/001 &USDA/FSIS/2012-001 guideline "Microbial risk assessment–pathogenic microorganisms with focus on food and water" can be used (EPA/USDA-FSIS, 2012). Although HACCP is successful in reducing contamination of food with pathogens, most HACCP systems are designed to control bacterial pathogens. HACCP has not yet proven to be an excellent tool in the control of foodborne viruses (e.g., norovirus). Fecal bacteria are most often used as indicators for control of foodborne viruses but the correlation between fecal contamination and the presence of enteric viruses is rather poor (Jones & Karst, 2013). However, molecular detection assays can assist prevention efforts and be used to monitor the effect of interventions as part of the HACCP program.

The U.S. FDA has published protocols, which have or are soon to become standard methods for virus detection in a variety of food types. Like in Europe, the use of standardized methods for detecting foodborne and waterborne viruses is recommended. The ISO 15216-1:2017 international standard, although developed in Europe, is also used as standardized reference method for molecular detection of norovirus and hepatitis A virus in the United States. It is obvious that the interpretation of monitoring results is prone to the same problems as mentioned in the section EU and UK legislation. The Codex Alimentarius guideline CAC/GL 79–2012 with the title: "Guidelines on the application of general principles of food hygiene to the control of viruses in food" is accepted as a guidance document in the United States. But preventing food products, such as fresh vegetables and fruits, from becoming contaminated with foodborne and waterborne viruses also starts with good agricultural practices (GAPs), such as the use of irrigation water, which is not fecal contaminated, controls for farm pollutants, properly cleaned harvesting and postharvest processing machinery, clean storage containers, and so on (Early, 2009).

In 2018, the U.S. Environmental Protection Agency's Office of Chemical Safety and Pollution Prevention (EPA-OCSPP) published a guideline for testing the efficacy of antimicrobial pesticides. The title of this guideline is "Product performance test guidelines, OCSPP 810.2000: general considerations for testing public health antimicrobial pesticides–guidance for efficacy testing." Furthermore, the OCSPP Test Guideline Series 810.2100 through 810.2700 describe general information regarding product performance testing to meet the requirements of the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) (7 U.S.C. 136, et seq.) and the requirements of the Federal Food, Drug, and Cosmetic Act (FFDCA) (21 U.S.C. 346a). The OCSPP 810 Test Guideline Series is applicable to antimicrobial pesticide products with a public health function. Product performance test data are also required when agents are intended to bear public health claims. These test data must be submitted to EPA to support registration or amended registration, including the requirements of 40 CFR § 158.2220(a). "OCSPP Guideline 810.2200–disinfectants for use on environmental surfaces–guidance for efficacy" and "OCSPP Guideline 810.2300–sanitizers for use on hard surfaces–efficacy data recommendations" are important with regard to the testing of antimicrobials for virucidal activity when applied to surfaces (EPA, 2018a).

To assess the virucidal activity of antimicrobials (water-soluble powder, liquid, aerosolized, sprayed, and towelettes) intended for disinfection of inanimate, nonporous environmental surfaces (as required in the OCSPP 810 Test Guideline Series), the U.S. EPA requires the use of a hard surface carrier test according to the E1053-20 standard practice of ASTM International (ASTM, 2020b). All viruses mentioned on the label should be tested, unless there is a surrogate for the virus that is accepted by EPA. To mimic in-use conditions, the specific virus or its surrogate should be inoculated onto hard, nonporous surfaces (e.g., petri-dishes, glass carriers, or another appropriate test surface). For the same reasons, the efficacy of antimicrobial substances must be tested in the presence of a specific organic soil at an appropriate concentration. Correction for water hardness must be taken into account (EPA, 2018a,b).

The test virus suspension is first allowed to dry, and then overlaid with a known volume of the test formulation for a predetermined contact time ($\leq$10 min, and same or shorter than the contact time identified on the product label) at ambient temperature (according to the directions for use on the product label). The remaining viable virus present should then be assayed by determining the loss in virus titer due to the test formulation's virucidal activity. An appropriate virological technique (e.g., cytopathogenic effect, fluorescent antibody, plaque count, or animal response) must be used for that purpose. EPA requires that the disinfectant achieves $\geq$3-$\log_{10}$ reduction on each surface.

The Technical Committee ISO/TC 61, plastics, subcommittee SC 6–aging, chemical, and environmental resistance has recently published the ISO 21702:2019 standard, with a title: "measurement of antiviral activity on plastics and other nonporous surfaces." As participant in this subcommittee, the American National Standards Institute has made this standard available to interested parties in the United States. When an antimicrobial product is intended to be effective in treating a specific, porous surface (hard or soft), the porous material (as a carrier) is to be specified in the test protocol for the existing standard method. Examples of hard porous surfaces include unglazed ceramic tiles, while the soft porous surfaces include fabrics (e.g., cotton, polyester, etc.). A new protocol review is not needed when replacing the standard method's hard nonporous carrier with a hard-porous carrier (e.g., AOAC use-dilution stainless steel carrier replaced with porcelain pen cylinder). However, applicants should consult with the agency to determine whether the proposed carrier type is representative of the desired claim (EPA, 2018a).

For confirmatory testing, only the hardest or most difficult to kill virus strain on the product label should be tested at the lower certified limit(s) of active ingredient(s) present in the formulation. Testing the virucidal effect against additional viruses must occur at lower certified limit(s) or below nominal concentration (concentration expected to be present in an antimicrobial pesticide as a result of the production or formulation process). The most difficult to kill virus can be determined from the viral disinfection hierarchy groups:

- Group 1, most resistant to biocidal chemicals and hardest to kill, are small and nonenveloped viruses (<50 nm) such as members of the *Picornaviridae* (e.g., enterovirus, HAV, and rhinovirus), *Caliciviridae*, and *Parvoviridae* (e.g., parvovirus) family. The most resistant representative virus (or EPA acceptable surrogate) must be selected. As an example, Feline calicivirus (FCV) is used as surrogate for norovirus.
- Group 2, intermediate level of resistance to inactivation, is the group with large nonenveloped viruses (>50 nm), such as members of the *Adenoviridae* (e.g., adenovirus), *Reoviridae* (e.g., rotavirus), and *Papillomaviridae* (e.g., papillomavirus) family. Again, the most resistant representative virus (or acceptable surrogate) must be selected such as adenovirus.
- Group 3, sensitive to biocidal chemicals and least difficult to kill, is the group of the enveloped viruses with members of the *Voronaviridae* (e.g., coronavirus), *Flaviviridae* (e.g., hepatitis C virus), *Herpesviridae* (e.g., herpes simplex virus), *Poxviridae* (e.g., vaccinia virus), *Hepadnaviridae* (e.g., hepatitis B virus), *Orthomyxoviridae* (e.g., influenza virus), *Paramyxoviridae* (e.g., parainfluenza virus), and *Retroviridae* (e.g., human immuno-deficiency virus) family. The most resistant representative virus (or EPA acceptable surrogate) in this group should be used for testing.

Since 2015, the U.S. EPA requires a reregistration of antimicrobial pesticide products to ensure that they are supported by acceptable efficacy data. Information is given in EPA guidance "Efficacy testing standards for antimicrobial product data call-In responses." For that purpose, the same EPA 810 series standards (product performance testing) can be used. Only the hardest or most difficult to kill virus on a product label should be tested at the lower certified limit(s). For that purpose, the same viral disinfection hierarchy groups can be used as mentioned above (EPA, 2015).

In March 2020, the EPA released a "List N" with disinfectants suitable to inactivate SARS-CoV-2. The disinfectant chemicals are only applicable to surfaces and are not intended for human use, such as hand sanitizers. All products in the list have EPA registration numbers. Various information is included, such as the name of the product and manufacturer, active ingredient(s), formulation base, precautions and instructions to follow, and

application details (contact time, surface type, and on-site use). Since its publication, the list is updated weekly with additional products as needed. Being on this list does not mean EPA approval (EPA, 2021).

The "ASTM E1052-20–Standard test method to assess the activity of microbicides against viruses in suspension" is used as a first step in determining the virucidal potential of liquid chemical microbicides (ASTM, 2020a). The "ASTM E1053-20–Standard test method to asses virucidal activity of a chemical intended for disinfection of inanimate, nonporous environmental surfaces" can be modified for the formulation type. This test method can be performed with most viruses that can multiply in cell cultures (ASTM, 2020b). However, other host systems (e.g., embryonated eggs) can be used with justification and adequate documentation. The standard lists different viruses with varying degrees of resistance to liquid chemical microbicides: adenoviruses, type-4 or type-5, canine parvovirus, cytomegalovirus, FCV, HAV, herpes simplex virus, influenza A virus, murine norovirus (MNV), respiratory syncytial virus, rhinovirus, rotavirus, and vaccinia virus. The cell culture-adapted HM-175 strain of HAV (ATCC VR-1402), the F9 strain of FCV (American Type Culture Collection, Manassas, VA, ATCC VR-782), and the cell culture-adapted human rotavirus WA strain (ATCC VR-2018) can be used to evaluate microbicides against, respectively, HAV, HuNoV, and human rotavirus. The F9 strain of FCV is especially recommended by the U.S. EPA (EPA, 2002a & 2002b). Cell culture-adapted MNV, type-1 (S99 strain) could be used as an alternative surrogate in the testing of microbicides against HuNoV, especially because FCV has higher sensitivity to acidity. MNV more suitable surrogate in the testing of acid-based formulations (Sattar & Bidawid, 2016). A load of interfering soil may be used in the test, such as fetal bovine serum (except for rotaviruses) at a final concentration of 5%. Tests must occur at three concentrations, with at least one in the nonactive range and one in the active interval of the microbicide. If the product requires dilution in water prior to use, water with a specific level of hardness should be used. In all tests, disinfectants must achieve at least a 4-$\log_{10}$ reduction in infectivity, as well as complete inactivation of the virus (Sattar & Bidawid, 2016; EPA, 2018b).

To assess the virucidal activity of disinfectants for hard nonporous surfaces using towelettes, the AOAC Method 961.02 (germicidal spray disinfectants test modified for towelettes) (AOAC International, 2019) or the ASTM E2362 test (ASTM, 2015) should be applied. The virus claimed on the label or an approved surrogate should be used as a test organism. The F9 strain of FCV is recommended by the U.S. EPA (EPA, 2002c,d).

The "ASTM E2197-17e1–Standard quantitative disk carrier test method for determining the bactericidal, virucidal, fungicidal, mycobactericidal and sporicidal activities of liquid chemical germicides" (QCT-2) can be additionally used to test the activity of microbicidal chemicals against several types of viruses. Flat stainless steel disk carriers (approx. 1 cm diameter) are inoculated with 10 µl of the viral inoculum. Once the inoculum is dry, the contaminated carrier is exposed to 50 µl of the test microbicide at 20°C for a time period considered suitable by the manufacturer. Standard methods exist to determine the titer of the test virus. The test is useful to assess the virucidal activity of microbicidal chemicals against several types of viruses (ASTM, 2017). The Organization for Economic Co-operation and Development has developed its own carrier test method, as well as a "Guidance document on quantitative methods for evaluating the activity of microbicides used on hard nonporous surfaces, section D" (OECD, 2013).

5.2.2 | Legislation and guidelines in Canada

In Canada, chemical products used to clean, sanitize, or disinfect environmental surfaces and inanimate objects are regulated under different regulatory frameworks. Regulation is not only based on their chemical composition, but also on their use or purpose. Two key factors determine which regulatory framework applies to a chemical product: (1) the intended use as claimed, including the level of antimicrobial activity on the label, and (2) the type of surface or object to which the product is intended to be applied. Chemical products used as disinfectants on environmental surfaces and inanimate objects, or for use on noncritical medical devices are regulated under the Food and Drugs Act and Regulations. Before they can be sold in Canada, a premarket assessment is required, as well as a drug identification number (DIN). To receive this DIN and market authorization, applicants must provide evidence of safety, efficacy, and quality. The performance of the product is indicated by the label. A chemical product without any antimicrobial claim on its label is regulated as a cleaner (Health Canada, 2018).

The Natural and Non-prescription Health Products Directorate is the regulatory body within Health Canada which assesses disinfectants for use on "non-critical medical devices, environmental surfaces, inanimate objects in homes, industrial or institutional settings, hospitals, food processing plants and barns" (hard surface disinfectants), and also evaluates the labeling for "hard nonporous food and non-food contact surface sanitizer claims" (disinfectant-sanitizers) (Health Canada, 2018).

Products (hard surface disinfectants and disinfectant-sanitizers) that were registered under both the "Food and Drugs Act" and the "Pest Control Products Act" are now registered under the "Food and Drugs Act." This consolidation took place on April 1, 2020. Three new guidance documents are published by Health Canada to help stakeholders in the interpretation of the legislative and regulatory requirements associated with this new registration process:

- The "Disinfectant drugs" guidance document gives an overview of the regulation of disinfectant drugs and disinfectant-sanitizers in Canada, outlines the information needed to support their safety, efficacy, and quality, and sets out the labeling requirements according to the Act and Regulations.
- The "Safety and efficacy requirements for (hard) surface disinfectant drugs" provides the information needed to support the safety and efficacy of chemical products that meet the regulatory definition of "antimicrobial agent." It applies for use on noncritical medical devices, and on environmental surfaces and inanimate objects (Health Canada, 2014).
- The "Management of disinfectant drug applications" guidance document gives an overview of the application streams that apply to disinfectant drugs, including disinfectant-sanitizers.

To test disinfectants and sanitizers, Health Canada accepts the methods and protocols published by AOAC International, ASTM International, Therapeutic Goods Administration of Australia (ATG), European Committee for Standardization (CEN), Organization for Economic Co-Operation and Development (OECD), and U.S. EPA. Testing for virucidal activity largely follows the United States EPA "OCSPP Guideline 810.2200–disinfectants for use on environmental surfaces–guidance for efficacy."

While Health Canada also accepts the abovementioned surrogates, for a broad spectrum virucidal claim, it requires a given chemical to provide the required level of activity against either Sabin strain of poliovirus, type-1 (ATCC VR1562), human adenovirus, type-5 (ATCC VR-5 or VR-16), bovine parvovirus (ATCC VR-767), or canine parvovirus (ATCC VR-2017). The nonenveloped poliovirus is safe to handle, relatively resistant to microbicides, makes product development easier, and label claims simpler and reliable. However, in view of the anticipated eradication of poliomyelitis, laboratory use of all types of polioviruses will be banned (Mundel & Orenstein, 2013). For any specific virus claims, the specific virus should be used as test organism. The surrogate viruses of HuNoV may be used for any virucidal claims against this virus. Recommended test methods are ASTM E1053-20 and AOAC 961.02.

5.3 | European Union/United Kingdom

5.3.1 | Legislation, guidelines, and surveillance in the European Union

The Zoonoses Directive 2003/99/EC of the European Union (EU, 2003) obliges member states to collect relevant and comparable data on zoonoses, zoonotic agents, antimicrobial resistance, and foodborne outbreaks. List B of Annex I of this Zoonoses Directive also includes calicivirus, HAV, influenza virus, and rabies virus, although in reality, caliciviruses and HAV are not zoonotic agents. Every year, since 2007, reports on trends about and sources of zoonoses, zoonotic agents, and foodborne outbreaks in the European Union are jointly published by European Food Safety Authority (EFSA) and European Centre for Disease Prevention and Control. These reports also contain information on foodborne outbreaks caused by viruses in the EU, although not all countries provide data on viral outbreaks. Routine harmonized surveillance of viral outbreaks and virus occurrence in food commodities is helpful in source attribution studies. For that purpose, guidance documents for investigating foodborne virus-related outbreaks could be useful. Countries may also provide information via the "rapid alert system for food and feed" (RASFF notifications).

In the past, it was challenging to find the biological agent responsible for some foodborne outbreaks, especially where foodborne or waterborne viruses were involved. Some viruses are difficult to culture, such as the highly infective norovirus and HAV. But systematic incorporation of molecular typing into foodborne outbreak investigations allows better identification of food-related incidents in which viruses are involved. Five to ten years ago, a major factor limiting the uptake of virus testing into regulatory food controls worldwide was the absence of any standardized and validated methods (EFSA, 2011).

Although new viral test methods based on polymerase chain reaction (PCR) have been developed, exact data on the correlation between the number of virus genome copies detected by quantitative PCR and the real number of infectious virus particles are still lacking. These difficulties to discriminate between infectious and noninfectious virus particles make that quantitative PCR only can be used to provide an indirect measure of risk. In the absence of a specific quantitative risk assessment, it is evident that control options to reduce the risk are more difficult to implement. Before viral standards can be implemented into legislation, more data on the level of viral RNA in food, representing baseline and outbreak situations, must thus be collected to establish guidelines (EFSA, 2011; EFSA, 2012; Lowther et al., 2012; Nørrung, 2013). To

establish criteria for pathogenic viruses in live bivalve molluscs, reproducible and sensitive analytical methods are needed (EFSA, 2011). As an example, a European Union coordinated monitoring program on the prevalence of norovirus in raw oysters was completed in 2018, after which an EFSA working group performed an analysis of this 2-year European baseline survey. This has resulted in some recommendations, such as the need for ongoing monitoring of HuNoV in bivalve molluscs both in production areas and dispatch centers. The survey has also proven that defining a legislative threshold for HuNov in bivalve molluscs is difficult from the perspective of the analytical capability (EFSA, 2019).

In the Codex Alimentarius, risk is defined as the probability of an adverse effect on an organism, system, or (sub)population caused under specified circumstances by exposure to an agent. It is obvious that the probability of becoming infected increases with the amount of foodborne virus particles being ingested, but for HuNov (recently made replicable via the Human Intestinal Enteroid cultivation system) and HAV (a cell-culture adapted strain is available), the exact threshold infectivity limit is still unknown. Determining the minimum dose of virus particles that can initiate infection (minimum infective dose, MID) and the factors influencing this dose are important for the development of risk assessment models in the field of food production. The characteristics of the virus (virulence of the viral strain), time from initial release from an infected host, environmental conditions (temperature, humidity, food matrix, type of fomite, etc.), and a number of host factors (age, health status, and immune system capacity of a new infected host) may influence the degree of infectivity. The number of viruses required to infect 50% of the exposed population (Human ID_{50}; HID_{50}) is often used as an indicator for the MID of human viruses. This HID_{50} is derived from dose–response data usually obtained after experimental administration of attenuated virus strains to young, healthy volunteers. The HID_{50} value is always greater than the MID required to cause infection, which means that the actual number of virus particles involved in infection often remains unknown. Therefore, the biological feasibility of a nonthreshold infection mechanism has become widely accepted. This states that even a single virus may be capable of causing infection (single-hit model), which has steadily gained support especially in relation to viruses (Yezli & Otter, 2011; EFSA, 2011; EFSA, 2012; Lammerding, 2013; Nørrung, 2013). From volunteer studies with Norovirus GI.1, Teunis et al. (2008) determined the HID_{50} and estimated the probability of infection after exposure to a single Norovirus GI.1 particle. They found an HID_{50} of 18 virus particles and a probability of infection of 0.5 after exposure to a single Norovirus GI.1 particle.

Before analytical control measures could be implemented in EU legislation, the inclusion of a standardized and validated reference method for the detection of viruses in foods is needed. For that purpose, a qualitative and quantitative standard on detection methods for viruses in foods has been developed in the European Committee on Standardization, more specifically in the technical working group CEN/TC275/WG6/TAG4. Protocols for viral genome extraction and detection have been developed, and the validity of these protocols in a variety of food commodities (oysters, mussels, soft-fruits, and green onion), bottled water, and smooth surfaces has been studied (Lowther et al., 2019). But to facilitate the use of the harmonized and standardized CEN method for detection and quantification within a legislative context, there is always a need for more information about the practical application (e.g., sampling plans and result interpretation) of these methods (Schultz & Myrmel, 2013). In 2020, as a successor of CEN/TC275 "Food analysis" WG6, the recently established CEN/TC 463 "Microbiology of the food chain" will continue developing standards on horizontal microbiological methods for food, feed, or ingredients that can be a source of microbial contamination of food products. Most of its deliverables are developed in cooperation with ISO/TC 34/SC 9 "Food Products-Microbiology" under the CEN/ISO Vienna Agreement (Gulacsi, 2019).

The EU legislative process may take standards from the CAC to develop them for the EU market. Regulation (EC) No 178/2002 of the European Parliament and of the Council of 28 January 2002 laying down the general principles and requirements of food law recognizes the importance of international standards. In article 5 of this Regulation (EC) No 178/2002 is written: "Where international standards exist or their completion is imminent, they shall be taken into consideration in the development or adaptation of food law" (EU, 2002). As a result, guidelines released by the Codex Alimentarius can be used in the implementation of food law. An example of such a Codex Alimentarius guideline is CAC/GL 79–2012, which has as title: "Guidelines on the application of general principles of food hygiene to the control of viruses in food." The European Union has actively participated in the development of this guideline, and has regularly given comments on draft versions of this guideline during Sessions of the Codex Committee on Food Hygiene (CCFH). Furthermore, the general rules of hygiene laid down in Regulation EC No 852/2004 (good agriculture practice, good manufacturing practices, HACCP, use of clean and potable water) must be used in the control of virus contamination in food, as well as on food contact surfaces. Commission Regulation (EC) 2073/2005 lays down microbiological criteria for foods, but no specific criteria are set for viruses. To establish criteria for pathogenic viruses in live bivalve molluscs,

reproducible and sensitive analytical methods are needed (EFSA, 2011).

Risk management legislation for sanitary production of bivalve shellfish world-wide depends on the assessment of the impact of fecal pollution, with fecal coliforms or *E. coli* as indicator organisms. Because bivalve molluscs present different risks for norovirus connected with fecal pollution, Regulation (EC) No 854/2004 requires bivalve molluscs to be monitored and classified according to their *E. coli* content. *E. coli* is thus used as an indicator organism in the control of norovirus contamination in bivalve molluscs. Compliance with Regulation (EC) No 854/2004 requires <230 *E. coli* per 100 g of shellfish flesh (EU, 2004). However, even though the criteria of Regulation (EC) No 854/2004 are met, outbreaks of HuNoV after the consumption of bivalve shellfish still occur. The detection of norovirus and HAV is thus a more effective approach. Control of norovirus contamination in bivalve molluscs focuses on the careful selection of areas where they are grown and harvested. Bivalve molluscs production areas received protection through the Shellfish Waters Directive 2006/113/EC, which was repealed in 2013 by Framework Water Directive 2000/60/EC. Further contamination control measures are either depuration (self-purification in tanks of clean seawater), relaying (self-purification in the natural environment), or commercial heat treatment (cooking) by an approved method. Monitoring of norovirus by PCR has proven to be effective in the assessment of virus risk, and the implementation of permitted effective risk management controls in HACCP plans (EFSA, 2011).

The use of biocidal products, including those with (potential) virucidal activity, to inactivate foodborne and waterborne viruses on surfaces is also subject of European regulation. In the EU, Regulation (EU) No 528/2012 of the European Parliament and of the Council of 22 May 2012 on the use of biocidal products, also known as BPR, came into force on September 1, 2013 with the purpose of regulating all biocidal products (products designed to kill, repel, or inhibit undesirable organisms by any means other than merely physical or mechanical action) and the active ingredients used to give such products their biocidal efficacy. This Regulation on Biocidal products (EU) No. 528/2012 repealed and replaced the Biocidal Products Directive 98/8/EC. The regulation of biocidal products in the EU ensures that all biocides are risk assessed for toxicity to humans and the environment before they are permitted to be placed on the market, and that they are sufficiently active against the harmful organisms they are designed to target. This is done via processes of approval for biocidal active substances (the active ingredients) and via authorization of biocidal products (substances, formulations, or articles that contain the active substances and are intended to be used as biocides).

Several international standard test methods (CEN, OECD, ISO, etc.) currently exist for disinfectant products. In Europe, the use of CEN test methods is highly recommended, where these are available and relevant. Within the European Committee for Standardization (CEN), a Technical Committee (TC 216) was established to produce harmonized European methods for testing the activity of disinfectants (including the virucidal activity) used in medical, veterinary, food, industrial, domestic, and institutional areas. European standard EN 14885 gives information on the application and interpretation of CEN methods for the testing of chemical disinfectants within product types 1, 2, 3, and 4 of the Regulation on Biocidal products (EU) No. 528/2012. Product type 4 (PT 4) contains biocidal products to be used in the food and feed area, and a distinction is made between disinfectants for hard surfaces, inner surfaces in human drinking water systems, disinfection by soaking, and disinfection in dish washing machines and crate washers.

Hard surfaces may be tables, the outside of machinery, equipment, floors, walls, and so on in the food industry, kitchens, and so on onto which biocidal products are often wiped, sprayed, foamed, applied by high pressure, and so on. After a certain time, the biocidal products may be washed or wiped off. Inner surfaces of pipes, tanks, fillers, mixers, and other machines coming in contact with food and feed (including liquids) are disinfected by circulating the biocide (cleaning-in-place [CIP]) or by filling without circulation (not using CIP). Equipment, crates, boxes, and so on can be disinfected by soaking or in industrial washing machines.

The CEN methods for efficacy testing of disinfectants use a tiered approach, and in accordance with EN 14885, the following tiers can be distinguished (European Chemical Agency–ECHA, 2017):

- Phase 1–quantitative suspension tests to demonstrate that a chemical has virucidal activity without regard to specific conditions of intended use.
- Phase 2, step 1–quantitative suspension tests to prove that a product has virucidal activity, simulating practical conditions appropriate to its intended use (temperature, soiling, different surfaces, contact time, etc.). Reference methods are described in EN 13610 and EN14476.
- Phase 2, step 2–quantitative laboratory tests, often using carriers or living tissues with dried-on microorganisms, to establish that the product has virucidal activity, simulating practical conditions appropriate to its intended use (temperature, soiling, different surfaces, contact time, etc.). Reference method is EN 16777. In the absence of a CEN method, the "OECD guidance for the testing of chemicals" or "DVG Guidelines" can be used.

- Phase 3–field tests under practical conditions are more optional. Note that no validated test methods are available yet.

Besides other test microorganisms, EN 12353 provides information on how to preserve viruses used and defined in European Standards for the determination of virucidal (incl. bacteriophages) activity of chemical antiseptics and disinfectants classified by CEN/TC 216. With respect to viruses, the following surrogates can be used: adenovirus, type-5, strain Adenoid 75, ATCC VR-5, MNV, strain S99 Berlin, and murine parvovirus, strain Crawford, ATCC VR-1346 (for T ≥ 40°C).

Several methods for testing the efficacy of hard surface disinfectants are available. Tests with mechanical action might be adopted from the medical area (if appropriate), as published in EN 14476. In the case, a product is applied by airborne diffusion of an aerosol, a smoke, a vapor, or a gas with the intention to disinfect the surfaces of equipment, walls, floors, ceilings, and so on, the French method NF T72-281 can be used. The testing of disinfectant wipes is also described in detail to prove that what is written on the label is correct.

Biocides for use on inner surfaces by filling without circulation must undergo a phase 2, test 1 and phase 2, test 2. For inner surface disinfection using CIP, an overview is given in EN 14885, and phase 2, step 1 and phase 2, step 2 should be used. When disinfection of inner surfaces is done with a vaporized biocide, a simulated-use test or a filled test has to be provided. Besides viruses, phages are useful as test organisms especially in the dairy industry. When CIP disinfection is done at high temperatures (40–80°C), murine parvovirus shall be used as a test organism. For surfaces in cold machinery, testing should be done at low temperature conditions, such as 4 and 10°C.

Biocides used for disinfection by soaking require the execution of a phase 2, test 1 and phase 2, test 2. With respect to phase 2, test 1 and phase 2, test 2, EN 14885 provides the necessary guidance. In the absence of a CEN method, the "OECD guidance for the testing of chemicals" or "DVG Guidelines" can be used. For high temperature soaking (>60°C), murine parvovirus shall be used as a test organism.

For all surfaces, tests must be performed under the same conditions (temperature, contact time, clean, or dirty) as described on the label. A product will be considered sufficiently effective if it meets the criteria for the tests, which means a 4-$\log_{10}$ reduction.

In 2020, the CEN/TC 216 work group "Chemical disinfectants and antiseptics" will continue working on the revision of EN 14885 "Chemical disinfectants and antiseptics–Application of European standards for chemical disinfectants and antiseptics." TC 216 will also continue its reflection on the replacement of poliovirus across all its standards. The virus is used as a model for testing the efficacy of some biocidal products (Gulacsi, 2019).

5.3.2 | Legislation, guidelines, and surveillance in the United Kingdom

Since 1973, the United Kingdom has been part of the European Union. Many EU directives, regulations, and decisions regarding food product quality and safety were implemented into UK law by EU legislation, and will remain applicable until the UK government decides to withdraw, replace, or amend this legislation, taking into account its future relationship with the EU. It can be expected that UK trade policy will probably maintain the present EU-based food quality and safety legislation in UK law for a very long time to facilitate export of food products from the United Kingdom toward the European continent. Like on the European continent, general hygiene requirements written down in UK food legislation are not specific for viruses. Also, in the United Kingdom, the Codex Alimentarius guideline CAC/GL 79–2012 is used as guidance to control viruses in food production and handling, with focus on the implementation of proper food hygiene measures. PCR-based detection methods are also perceived as the proper tools to evaluate whether viral contamination occurs in the food supply chains, and to consider, evaluate, and validate foodborne virus control options (e.g., HACCP plans) (EFSA, 2011).

After the Brexit, the British Standards Institution (BSI) retained its full membership in the European Standards Organizations CEN and CENELEC. This means that the United Kingdom remains in the position to influence the process of development and maintenance of CEN and CENELEC standards (BSI, 2018). In reverse, standards developed by CEN and CENELEC will remain in force as long as they meet the autonomous regulatory policy of the United Kingdom. The current EN and ISO methods for qualitative and quantitative detection of viruses will remain applicable in the United Kingdom. The ISO/TS 15216-1:2013 standard for the quantitative and qualitative detection of norovirus and HAV in food, produced by the CEN/TC275/WG6/TAG4 working group, is such an example (ISO, 2019). But in the post-EU era, the BSI also wants to deliver UK-specific standards to support compliance with UK legal requirements (BSI, 2020).

Supported by the Centre for Environment, Fisheries & Aquaculture Science, the Culture Collections of Public Health England provide reference strains of norovirus (genogroups I and II) and HAV. These reference viruses

developed in parallel with the ISO/CEN–ISO/TS standard 15216:2013 can be used for quantitative molecular assays, such as real-time RT-PCR.

5.4 | Australia and New Zealand

Pattis et al. (2019) did a 10-year investigation on HuNov-induced gastroenteritis outbreaks in New Zealand over the period 2008–2017. During that period, 207 on a total of 2137 outbreaks of HuNov-induced gastroenteritis were associated with a suspected or known foodborne source. 9.5% of total number of HuNoV gastroenteritis outbreaks were thus indicated as foodborne. However, expert consultation estimated that–in reality–40% of all HuNoV infections could be due to foodborne transmission. Person-to-person transmission is the main cause of nonfoodborne HuNoV-induced gastroenteritis outbreaks in New Zealand. Over the period 2010–2020, 1585 outbreaks of HuNoV-induced gastroenteritis were registered in Australia (Bruggink et al., 2020). According to Kirk et al. (2014), in Australia, in 2010, 18% of the HuNov-induced gastroenteritis cases were foodborne in nature.

As an answer to these HuNov-induced outbreaks of gastroenteritis, the Food Standards Australia New Zealand (FSANZ) authority recommended the implementation of the CAC guidelines for good hygienic practices (GHPs) throughout the food chain. In order to mitigate the risk of norovirus in seafoods, FSANZ (2017a) advises to follow the principles described in CAC/GL 79–2012 document "Guidelines on the application of general principles of food hygiene to the control of viruses in food" (CAC, 2012), which means: controlling viral contamination of cultivation grounds, as well as the harvesting, postharvesting, handling, production, storage, and distribution process. Additionally, heating food into the core up to 90°C for 90 s is recommended to inactivate norovirus (FSANZ, 2017a).

In Australia, widespread foodborne hepatitis A outbreaks have occurred in 1997 (associated with locally produced oysters), 2009 (associated with imported semidried tomatoes), 2015, 2017, and 2018 (associated with imported frozen berries) (Franklin et al., 2019). Pattis, Cressey, Lopez, Roos, Horn, and Soboleva (2019) did a 10-year investigation on HAV outbreaks in New Zealand over the period 2008–2017. During that period, 5 in 19 outbreaks of HAV were associated with a suspected or known foodborne source. An outbreak is classed as foodborne if food was recorded as one of the likely modes of transmission. The remaining 14 outbreaks could not be traced back to any food source, but were attributed to other risk factors (e.g., contact with an infected person, occupational exposure to human sewage, etc.).

The majority of foodborne HAV outbreaks in Australia and New Zealand are caused by consuming frozen fruit (Franklin et al., 2019), fresh fruit (FSANZ, 2019), oyster, mussel (NSWG, 2019), shellfish (FSANZ, 2017b), ready-to-eat food (FSANZ, 2019), frozen pomegranate, semidried tomato, lettuce, and shallot (NSWG, 2019). FSANZ (2015) recommended the use of adequate thermal processing conditions (time/temperature) for HAV inactivation in various foods. The heat resistance of HAV varies considerably with the characteristics of the food. As an example, pH and sugar content in berries impact the heat resistance of HAV. In general, to inactivate hepatitis A virus, FSANZ and the Ministry for Primary Industries (MPI) recommended to heat food at a core temperature of 85°C during 1 min. To minimize infection by hepatitis A virus via fruits and vegetables, Australian governments required the implementation of the "Code of hygienic practice for fresh fruits and vegetables" (CAC, 2017) recommending GAPs and GHPs throughout the food chain (FSANZ, 2019). The New South Wales Government (NSWG) published a guideline to prevent HAV infections caused by food handlers, through adequate handwashing, safe sewage disposal, hygienic food handling across the food chain, and vaccination of selected cohorts (NSWG, 2019).

Although SARS-CoV-2 is a respiratory virus, on imported frozen chicken from Brazil and on packaging of seafood imported from Ecuador into China, traces of SARS-CoV-2 have been detected (FSANZ, 2020). But according to Australian Government–Department of Health (2020), there is no evidence of any risk of infection with SARS-CoV-2 after swallowing contaminated food or drinks. Furthermore, FSANZ (2020) excludes the risk of being infected with SARS-CoV-2 via food packaging. Currently, the New Zealand Food Safety authority (MPI, 2020) does not advise any form of disinfection of food packaging. Where there are concerns about SARS-CoV-2, the Health Department of Australia recommends to sanitize food and nonfood contact surfaces by using household disinfectants (FSANZ, 2020).

5.5 | Asia

In 2010, the WHO reported 31 food safety incidents responsible for 420–960 million cases of foodborne illness and more than 400,000 deaths. The highest burden of foodborne disease per population was recorded in low-income regions, for example, Africa followed by the South-East Asian subregions SEAR B and SEAR D and the Eastern Mediterranean subregion EMR D (WHO, 2015). According to the microbiological risk assessment performed by FAO/WHO experts (FAO/WHO, 2008), viruses in food, in particular HuNoV and HAV, were major causes of

foodborne illness in Asia. Additionally, HEV, type-1, and type-4 have been endemic in Asia (Todd & Grieg, 2015).

Asian countries adhere to internationally accepted criteria for food safety, quality, and fair trade (CAC, 2018) by following the Food Code publications of the CAC. All member states in SEAR also have started to harmonize their national food safety regulations in agreement with the Food Code texts (WHO, 2018). Currently, the CAC encourages Asian countries to implement guidelines, such as documents CXC 1–1969, CXC 58–2005, CXG 20–1995, CXG 26–1997, CXG 38–2001, CXG 47–2003, and CXG 89–2016. Furthermore, some Asian countries have started to update their national guidelines for controlling and preventing foodborne viral disease based on guideline CAC/GL 79–2012 (CAC, 2012). As an example, the Food Safety and Standards Authority of India (FSSAI, 2020) has published guidance to control food safety over the whole food supply chain, from food handling to consumption. It focusses on personal hygiene, sanitation of food establishments, Standards Operating Procedures for food businesses, and guidance for community kitchens (FSSAI, 2020).

5.5.1 | China

SARS-CoV (2003 corona virus, sometimes indicated by SARS-CoV-1) and SARS-CoV-2 have proven that interspecies transmission of viruses may occur, with animals infecting humans (Li et al., 2005; Chan et al., 2020). Therefore, it is vital to implement suitable preventive measures, eliminating or reducing transmission of emerging viruses (Yuan et al., 2020). Although there is no proof of peroral intake of SARS-CoV-1 and SARS-CoV-2 through food, certain provinces and cities in China recently banned the consumption of meat of wildlife, dogs, and cats.

China spent a lot of efforts in the development of food regulations (Tan et al., 2015), and currently, the Chinese food safety authority and food industry are tackling food safety issues, such as chemical and microbial contamination of foods. Liu et al. (2019) concluded that food safety management systems are not working efficiently in China, as human-related factors are responsible for more than 66% of all food safety incidents (Hong & Wu, 2017). Lack of food risk awareness, low social responsibility, inferior processing technology, and pursuit of economic profits also contribute to the high number of food safety incidents in China (Guo et al., 2019). Food regulation in China needs further improvement so that food safety management systems become as efficient as in the EU, United States, and Japan.

5.6 | Africa

In the African region, poverty is considered as the underlying cause of the consumption of unsafe foodstuffs responsible for food poisoning. Food safety problems are due to unsanitary living conditions in rapidly growing urban centers, lack of access to clean water, unhygienic distribution and storage of foods, low education levels among food handlers and consumers, and the consumption of bushmeat (Malangu, 2016).

To achieve better health among the population, the national food safety agency of each African country must set up and implement a policy focusing on the quality and safety of food and other regulated products, manufactured, imported, distributed, advertised, sold, used, and consumed in their country (Mensah et al., 2012). The food safety strategies should involve several levels of intervention targeting different settings, high-risk groups, as well as professional food handlers, including street food vendors. To support the development and implementation of food safety policies, the WHO regional office for Africa, the Africa Center for Disease Control formed by the African Union must intensify its collaboration with the regional food safety centers in Africa.

The national food safety agency of each of the 54 countries in the continent will be required to increase efforts in limiting foodborne viral infections. The risk assessment techniques and appropriate control measures as suggested in guideline CAC/GL 79–2012 of the CAC may allow them to reduce the presence of foodborne viruses in the food chain (CAC, 1995). Intervention strategies especially should be focused on certain high priority commodities likely contaminated by specific viruses. The virus–commodity combinations need to be reviewed for each specific region using the specified criteria, and they need revision when new data become available (FAO/WHO, 2008). Conducting meta-analysis in an effort to systematically understand virus persistence and inactivation in different food commodities is recommended. Virus- and commodity-specific guidance may assist risk managers in better addressing the issue of foodborne virus contamination and in taking the measures needed in the event of outbreaks (FAO/WHO, 2008). Furthermore, new and existing pre and postharvest processing technologies should be assessed for their virucidal potential in high-risk food products.

To adequately control foodborne viral infections in Africa, the following elements need to be addressed (FAO/WHO, 2008):

- Consumers must be informed about the risks presented by foodborne viruses, especially in the consumption of wildlife (bushmeat).
- Among food handlers, awareness that they may transfer foodborne viruses onto food when infected, especially via the fecal–oral route, must be increased.
- HACCP plans focused on reducing viral contamination of food must be available in all food premises.
- Food handlers must be trained, especially with regard to hygiene and cleaning/disinfection practices.
- Presence of a food quality and food safety management system in the food premises.
- Inspection of facilities where food is produced, distributed, marketed, and consumed is required to verify compliance with food safety regulations, by implementing food safety measures as described in international and national food safety guides.
- Infrastructure and methods for detection of foodborne viruses must be in place.
- Laboratory-based surveillance of large common-source foodborne viral disease outbreaks at an early stage is recommended.

6 | REVIEW OF DRY AND WET CLEANING METHODS

6.1 | Dry cleaning

In dry food production facilities for powdery products, nuts and seeds, mixed products, such as soups, sauces, seasonings, desserts, and instant meals processes, proceed nearly exclusively dry without the use of liquids or water. In dry food processing environments, deposits may form with time compromising the quality and safety of the food produced. Also, food dust particles can act as rafts of virus particles in air. Asadi et al. (2020) demonstrated that dust allowed influenza A virus to become airborne infecting virus-naïve guinea pigs, while Khare and Marr (2015)–using an atmospheric transport model–predicted the concentrations of resuspended influenza virus as a function of the carrier particle size, height of the room, and relative humidity of air. As a result of this study, it can be expected that also food dust may spread foodborne viruses to other surfaces, food products, or be inhaled by food workers. Regular cleaning of dry food processing equipment as well as other dry food material handling areas is thus of utmost importance.

Wet cleaning must be avoided because water can compromise the quality of the product (lump formation, non-homogeneous mixing, or changes in product consistency) or create conditions stimulating the growth of pathogens and spoilage microorganisms. In dry food handling areas, dry cleaning is often the only method to reduce the build-up of objectionable matter, as well as residues of aged or modified products. The common rule is: "where dry particulate food products are handled, preference must be given to dry cleaning" (Moerman & Mager, 2016).

"Dry cleaning" refers to cleaning surfaces without any involvement of aqueous detergent solutions. It is a purely mechanical process relying on the soil being physically removed by means of scrapers, brushes, or vacuum systems in various combinations. Cleaning with disposable impregnated wet wipes also falls under the umbrella of dry cleaning, but its use is rather limited to lightly soiled conditions. In this case, "wet" refers to the use of alcohol-based solutions. However, dry cleaning methods cannot remove all traces of product (including allergens) or destroy microorganisms, including viruses. Sweeping with disposable high-alcohol wipes is the only dry cleaning method that can reduce the number of infectious virus particles on surfaces (Moerman & Mager, 2016).

Disposable single-use wipes contain alcohol usually saturated at an amount of 70–80% v/v. With respect to the requirements for the production of Halal and Kosher food, isopropyl alcohol is the commonly used alcohol. Due to the fast evaporation, the surface is left dry after wiping with high-alcohol wipes, making undesirable wipe-dry operations unnecessary. Wipes with lower concentrations of alcohol (they contain more water) are less effective against microorganisms including viruses, and it takes longer for alcohol residues to evaporate from the cleaned surfaces. As the alcohol residues stay longer on the cleaned surface, this may be an issue for some religious groups who are concerned that the alcohol residues may contaminate the food products. The water remaining on the surface may also cause microbial growth if not thoroughly dried, although viruses cannot multiply outside host cells. Low-alcohol wipes are usually impregnated with biocides, such as quaternary ammonium compounds (150–400 ppm). The wipes must be stored in a storage container or pack to avoid excessive evaporation of the fluid content before use (Moerman & Mager, 2016; Nikoleiski et al., 2021).

As surface soiling can reduce the efficacy of alcohol impregnated wipes, it first must be removed. A first wipe taken from its storage container or pack is used to remove loosely adhered soils from the surfaces, after which a second one is used to disinfect the surface. After one application, careful disposal of the used wipes is needed, especially because Asadi et al. (2020) have proven that crumpling, rubbing, and folding of dried wipes containing virus particles (influenza virus) could release the virions into the air, carried on airborne particulates in the respirable range. Disposing of the wipes safely may also assist to avoid cross-contamination between surfaces.

Although wiping is a fast and effective method of cleaning, it is laborious, subject to operative variability (it relies on the staff spraying and wiping all surfaces including hard-to-reach areas), and only useful to clean small product contact areas. Wipes or pieces of wipe may not be left behind in or on the process equipment as they may become a foreign body contaminant. Substances added in the wipes also may cause skin and eye-irritations, requiring operators to wear safety glasses and gloves (Moerman & Mager, 2016). But, the cleaning-up of dust also requires operators to wear a face mask to decrease the chance of inhaling virus-laden dust (Winter et al., 2009). As an example, many hantavirus infections in humans are attributed to the inhalation of dust particles contaminated with virus containing rodent excreta, and stirring up of settled virus-laden dust during cleaning practices is often responsible for it (Watson et al., 2014; Avšič-Županc et al., 2019). Williamson (1999) has provided guidelines on cleaning up virus-laden dust, with a warning that vacuuming or sweeping dry surfaces may generate potentially infectious particulate material.

6.2 | Wet cleaning

"Wet" cleaning involves the use of water, and according to Sinner's circle requires the use of liquid detergent chemicals in combination with mechanical action and higher temperatures over a sufficient contact time to achieve a visually clean surface.

6.2.1 | "Open plant cleaning" versus "cleaning-in-place"

"Open plant cleaning" is the general method to clean and disinfect open processing lines, where food is exposed to the processing environment. In "open plant cleaning," disassembly of the equipment can be required and equipment components (hoses, fittings, nozzles, trays, knives, clamps, gaskets, and even conveyor belts) are taken to a designated cleaning station (often tank) for cleaning and disinfection, also called "Cleaning-out-of-place" (COP). As the safety of the operator during "open plant cleaning" comes first, there are limitations with regard to the temperature and detergent concentration of the cleaning solution. The same applies for the disinfectant solution. Moreover, if the pressure applied is too high during "open plant cleaning," a mist of small water droplets containing food residues, food spoilage microorganisms, and food pathogens (including foodborne viruses) may form. Apart from endangering the health of the cleaning operators, the aerosols laden with microorganisms (including viruses) may drift down and settle on surfaces recontaminating the cleaned equipment. Recontamination may also occur during the cleaning of factory floors, when a cleaning solution laden with dirt is splashed on the process line. Open process lines can be disinfected chemically, by means of heat or UV-C irradiation (Moerman et al., 2014).

"Cleaning of closed process equipment" can be done without disassembly of the equipment, with fluids at sufficient detergent strength and a suitable temperature being circulated through piping and closed process systems for a set period of time. The mechanical action provided by the cleaning solution is only sufficient if the velocity of the cleaning fluid through all piping of the process line is at least 1.5 m/s. CIP of closed process lines allows for more aggressive cleaning regimes at higher detergent concentrations and temperatures. Also, more aggressive disinfectants at higher strength and temperature can be used during closed circuit disinfection. But closed process. equipment can also be disinfected by means of heat applied by hot water, steam, or hot air (Moerman et al., 2014).

6.2.2 | "Wet cleaning" parameters

During cleaning, the temperature, detergent, or disinfectant concentration, as well as the contact time needed to remove food residues or inactivate microbial contaminants, must be carefully controlled. For reasons of operator safety, the temperature of the alkaline and acid cleaning solutions during open plant cleaning cannot be higher than 60°C. Higher temperatures and detergent concentrations can be used during the CIP of closed process equipment. After the 2–10 min prerinse applied to remove 95% of the gross and loosely adherent soil, a 1–3% caustic detergent solution at 70–90°C is circulated through the process system during 5–30 min in order to remove the organic soil (food residues). Up to 5% may be needed to clean heavily soiled equipment. Following an intermediate rinse, a 0.5–2% acid cleaning solution at a temperature of 50–70°C is circulated through the process system during 3–20 min to remove the mineral deposits. After rinsing away all the residues, the cleaning process can be followed by a wet disinfection and final rinse step, performed at a temperature of 20–30°C during, respectively, 3–15 min and 4–10 min (Moerman et al., 2014; Nikoleiski et al., 2021).

6.2.3 | Virucidal effects of cleaning chemicals

Alkaline solutions
A fraction of the virus population can be destroyed due to the high pH and the hydrolyzing and peptizing power of the alkaline (usually NaOH) affecting, respectively, lipids

and proteins. Enveloped viruses can be rendered noninfectious by the disrupting effect of both NaOH and surfactants on their lipid envelope, while the peptizing effect of alkaline on the viral capsid proteins may inactivate a fraction of the nonenveloped viruses (Moerman et al., 2014). When exposed to alkaline conditions, Ausar et al. (2006) observed significant capsid disruption in empty, noninfectious virus-like particles of norovirus, which are morphologically similar to infective HuNoV particles still containing their RNA genome. Due to the presence of ionizable surface-exposed capsid amino acid residues (amino acid residues on the surfaces of individual capsid proteins), pH-dependent variations in the charge of the capsid protein (VP1) molecules constituting the continuous protein shell (viral capsid) are possible. They were considered to be responsible for the pH-dependent changes in the morphology and assembly/disassembly of the viral capsid of noroviruses. Although viral capsids have some elastic behavior, capsid disintegration may take place if large highly inhomogeneous deformations in the viral capsid (overstretch) occur due to the repulsion between the identical charges (negative charges at high pH) (da Silva et al., 2011; Roshal et al., 2019).

At neutral and high pH, most viral particles have a net negative charge because they have an isoelectric point below 7. Above a pH of 7, the negatively charged virus particles are adsorbed significantly less on a stainless-steel surface because of electrostatic repulsion, given that both virion and substrate surface have negative charges at these pH levels. Increasing repulsion results in decreased attachment and increased detachment rates. As a consequence, during the alkaline cleaning step, the less attached virions are more easily removed (Joonaki et al., 2020).

Mertens and Velev (2015) have studied the aggregation of norovirus virus-like particles as a function of the pH. Studies have shown that virus aggregates help sustain infectivity by shielding viruses at the inside of aggregates from virucidal treatments. Norovirus virus-like particles were well dispersed at low and high pH due to the repulsion between, respectively, the positively and negatively charged virions. Where the net capsid charge was lowest in magnitude around the isoelectric point of the capsid proteins (pH $\sim$ 4.5), also the electrostatic repulsion between the norovirus virus-like particles was at its lowest. As a consequence, their aggregation by van der Waals and hydrophobic forces is highest at pH around the isoelectric point of the capsid proteins (pH $\sim$ 4.5), and lowest during alkaline and acid cleaning conditions (Gutierrez et al., 2010; Mertens & Velev, 2015).

Borovec et al. (1998) found that NaOH alone is usually not sufficient to inactivate all types of viruses (especially nonenveloped viruses) or it takes long contact times to do so. After 10 min, a 0.1 M NaOH solution delivered a 2.5-$\log_{10}$ reduction in HAV, and only after 175 min, a 5.5-$\log_{10}$ reduction was achieved. With a 0.5 and 1 M NaOH solution, a 4-$\log_{10}$ HAV reduction was obtained after 10 min exposure, and an up to 5.5-$\log_{10}$ viral reduction was obtained after 30 min. At 22°C, Roberts and Lloyd (2007) found a >6.5-$\log_{10}$ reduction in enveloped herpes simplex, type-1 virus and a 4.9-$\log_{10}$ reduction in nonenveloped poliovirus, type-1 after 1–2 min exposure at 0.5 M NaOH. Nowak et al. (2011) demonstrated the successful virolysis of human GII.4 norovirus (nonenveloped) when exposed to 0.1 M and higher concentrations of NaOH at 50°C. They suggested that the primary effect of alkali was on the viral capsid resulting in exposure of the viral RNA. RNA degradation then could take place due to alkali destabilization of the phosphodiester backbone in this viral RNA. Using nanoindentation, in which pressure by extremely small mechanical tips is applied to the virus capsid and the amount of compression is measured, Cuellar et al. (2010) found that norovirus virus-like particles were much less rigid at pH 10.0 than at neutral and lower pH (e.g., pH 2.0).

But the chemical activity as well as the disinfecting capacity of NaOH can be enhanced by increasing the temperature of the cleaning solution. Higher temperatures facilitate the denaturation of viral capsid proteins and any enzymes present in the virion. This denaturation of the viral capsid surface proteins may prohibit the binding to receptors on the surface of host cells. But also, the temperature of the cleaning solutions alone was not always sufficient to inactivate all viruses. So, both heat and sodium hydroxide are needed, acting synergistically to affect a virtually instantaneous and complete inactivation of virus particles. As an example, to kill hepatitis A virus, both heat and NaOH alone only delivered a 0.9-$\log_{10}$ viral reduction, but together, they provided a >5.7-$\log_{10}$ viral reduction (Borovec et al., 1998; Ausar et al., 2006). Borovec et al. (1998) hypothesized that heating mediates a relaxing of the viral capsid allowing penetration of NaOH. It is evident that the higher temperatures and NaOH-concentrations during CIP allow for higher viral killing rates.

Surfactants

Surface active agents (surfactants) have a hydrophilic polar head group and a lipophilic hydrocarbon chain (hydrophobic tail), which makes them amphiphilic in nature. Surfactants are categorized into anionic, cationic, nonionic, and zwitterionic surfactants. They are one of the most important essential molecules in detergents because of their many functions: wetting, soil penetration, soil suspension, dispersion, and emulsification. Furthermore, they facilitate the rinsing of the equipment surface by reducing the surface tension. Nonionic surfactants are the most frequently used in detergent formulations due to the fact that the cationic surfactants rather have low detergency and

anionic surfactants are highly foaming (Moerman et al., 2014).

Surfactants have demonstrated to be fairly weak disinfectants, with the exception of quaternary ammonium compounds. However, surfactants still can make an essential contribution in the control of the transmission of lipid enveloped viruses. They can strip these viruses off their lipid envelope, preventing them from fusing with and entering in the host cell. Surfactants have thus the capacity to render enveloped viruses noninfectious.

Cationic surfactants have a positive charge on their hydrophilic end, being a quaternary ammonium function (QACs or Quats). They inactivate enveloped viruses by solvating and disrupting the lipid envelope, although inactivation of some nonenveloped viruses is also demonstrated. Due to their efficacy, they will be treated in the wet disinfection part of this review paper.

Anionic surfactants have a negative charge on their hydrophilic end, allowing the surfactant molecule to lift and suspend soils in micelles. Derivatives of sulfates, sulfonates, and gluconates are the most common anionic surfactants. Apart from solubilizing and disrupting the lipid envelope of enveloped viruses, they also have the ability to denature and unfold both monomeric and subunit proteins in the viral capsid structure of nonenveloped viruses (destructive loss of the quaternary and tertiary structure of capsid proteins) (Knight, 1975; Rapp, 2017; Lin et al., 2020).

Knight (1975) found that the anionic surfactant sodium dodecyl sulfate (SDS) could destroy aggregates of complex and simple viruses. He also noted that SDS can dissociate the proteins of nonenveloped virions into their constituent polypeptide chains. As an example, Howett et al. (1999) demonstrated the inactivation of nonenveloped rabbit, bovine, and human papillomaviruses after brief treatment with dilute solutions of SDS. In the study of Mertens and Velev (2015), it was shown that any concentration of SDS higher than the critical micelle concentration (CMC) induced capsid disassembly in norovirus virus-like particles. CMC is defined as the concentration of surfactants above which micelles spontaneously form. During surfactant micellization, a strong anionic surfactant like SDS is efficient in disrupting interactions between viral capsid proteins and solubilizing individual proteins or dimers. The final result is disassembly of the viral capsid structure. The norovirus virus-like particles even can become entrapped in these micelles, because the hydrophobic tail of SDS can adsorb to hydrophobic regions on the capsid surface. Sodium lauryl sulfate (SLS) is another strong anionic surfactant that targets the capsid proteins to unfold and extract them. In the study of Piret et al. (2002), SLS was found to be a potent inhibitor of several nonenveloped viruses, such as papillomaviruses, reovirus, rotavirus, and poliovirus.

When a detergent solution with an anionic surfactant is applied to a soiled surface, thorough rinsing prior to the application of a quaternary ammonium-based disinfectant is required. In solution, the positively charged quaternary ammonium compounds combine readily with the negatively charged anionic surfactant residues, rendering the quaternary ammonium disinfectant totally inactivated. Apart from a lack of germicidal activity, the resulting anionic-quat residues contain nutrients favoring the growth of spoilage microorganisms and bacterial food pathogens (Bari & Kawamoto, 2014).

Nonionic detergents consist of hydrophobic and hydrophilic moieties linked together by ether, ester, amide, or ether–ester bonds. Typical nonionic surfactants are (1) alkylphenyl ethers of poly(ethylene glycol), (2) alkylethers of poly(ethylene glycol), poly(propylene glycol), or glycerol, (3) derivatives of ethanolamine, or (4) hydrophilic sugars functionalized with hydrophobic tails. Their polar head groups are not electrically charged. In general, the solubility of nonionic surfactants is not as good as the solubility of ionic surfactants, but they do not change the pH of the solution.

Nonionic surfactants only weakly interact with proteins due to the lack of the contribution of electrostatic forces. They rather bind to proteins through hydrophobic interactions and hydrogen bonds, which do not strongly influence the structure of proteins. They cannot denature viral proteins because they do not break protein/protein interactions. Mertens and Velev (2015) have proven that the nonionic surfactant Tween 20 (polysorbate 20) could not disassemble norovirus virus-like particles and may even stabilize them in a well-dispersed, single-virus form. Nonionic surfactants, however, have the capacity to dissolve lipid structures, for example, bilayer membranes and virus envelopes (Chattopadhyay et al., 2002; Jelińska et al., 2017; Rapp, 2017).

Asculai et al. (1978) have found that nonionic surfactants with an ether or amide bond between the hydrophilic and hydrophobic moieties of the molecule were more active in reducing the infectivity of herpes simplex virus, type-1 and herpes simplex virus, type-2 than nonionic surfactants having an ester or ether–ester linkage. At 37°C, a nearly 5-$\log_{10}$ reduction was obtained when the herpes simplex viruses were exposed to a 1% concentration of the nonionic surfactants having an ether and amide linkage, while only a 0.5-$\log_{10}$ reduction was obtained if the same herpes simplex viruses were exposed to a 1% concentration of the nonionic surfactants having an ester and ether–ester linkage. To find the specific target of these nonionic surfactants, the same viruses were treated with a 5% concentration of nonoxynol-9 (nonylphenoxy-polyethoxy ethanol) during 10 s (exposure at 37°C). Electron microscopy revealed that not only the envelope was destroyed, but the nucleocapsid was also

prone to degradation. Triton X-100, which has a polar oligo (ethylene glycol) tail bound to an alkylphenol that acts as the hydrophobic head, achieves greater than 4-$\log_{10}$ inactivation of several enveloped viruses under a diverse set of experimental conditions, but it is not eco-friendly.

Amphoteric surfactants have a positive and negative charge on their hydrophilic end. As both charges cancel each other out, the overall net charge is zero, referred to as zwitterionic. The pH of any given solution will determine how the amphoteric surfactants react. In acidic solutions, the amphoteric surfactants become positively charged and behave similarly to cationic surfactants. In alkaline solutions, they develop a negative charge, similar to anionic surfactants. Zwitterionic surfactants are generally mild surface-active agents, and as such do not denature proteins.

Crawford et al. (1984) observed that Empigen BB®, a zwitterionic alkylbetaine surfactant based on a predominantly C12-C14 alcohol, could inactivate influenza A and B virus strains. Under an electron microscope, disruption of the influenza A virions was observed after being treated with 0.5% of the same zwitterionic alkylbetaine surfactant (exposure time 18 h). As a result of this disruption, individual spikes and lipid fragments bearing spikes were visible. Selective solubilization of surface proteins, which typically occurs when influenza viruses are treated with cationic and nonionic surfactants, is not suggested as a mode of action.

Conley et al. (2017) have identified several zwitterionic surfactants (sulfobetaines, as well as lauryldimethylamine N-oxide) that succeeded to solubilize lipophilic envelope proteins without denaturing them. As a consequence of this solubilization activity, disruption of the virus envelope may occur. After 5 min exposure to these zwitterionic surfactants, the titer of xenotropic murine leukemia retrovirus (X-MuLV) was reduced to below detectable levels (low-volume sampling) and an overall >4-$\log_{10}$ virus reduction was achieved after 120 min of incubation (large-volume sampling).

Sequestrants

Stochiometric sequestrants (EDTA and NTA) improve the removal of inorganic soil (mineral deposits) and prevent the formation of water scale on equipment surfaces during the cleaning process, while threshold sequestrants active in substoichiometric concentrations prohibit precipitation of the surplus water hardness in the rinsing water during the rinse cycles (Moerman et al., 2014). By removing mineral deposits, previously protected viruses become better exposed to the virucidal effect of other chemical substances. Sequestrants may also reduce the attachment of viruses on surfaces. With increasing concentration of divalent and/or monovalent cations (Na$^+$, Ca^{2+}, and Mg^{2+}) at high pH, the repulsion between negatively charged virus particles and negatively charged surfaces (e.g., stainless steel) decreases, due to the fact that the repulsive charges of both the virus and surface are screened by the counterions. In high ionic strength conditions, larger quantities of viruses are adsorbed on the surface (e.g., stainless steel) (Gerba, 1984; da Silva et, al., 2011; Joonaki et al., 2020).

In alkaline conditions, cations also enhance virus adsorption to soil due to the formation of salt bridges between the negatively charged viruses and soil particles. As viruses appear to survive better in the adsorbed state, this indirectly increases survival of virions. Certain cations have also a thermal stabilizing effect on viruses, hence, increasing virus survival (Medema et al., 2003). Furthermore, Gutierrez et al. (2010) demonstrated Mg^{2+} and Ca^{2+} mediated aggregation of rotavirus particles, making them less prone to virucidal treatments.

Acid solutions

After the alkaline cleaning and subsequent intermediate rinsing step, acid detergent formulations are used to remove mineral deposits. Nishide et al. (2011) demonstrated that acids are effective against enveloped viruses, but in most cases not effective against nonenveloped viruses. In their study, they found acid induced inactivation of the enveloped herpes simplex viruses, type-1 and type-2, as well as influenza virus A. However, also for enveloped viruses, differences were seen in their sensitivity to acid. Influenza virus A was more sensitive to acid than the herpex simplex viruses. According to Conley et al. (2017), the virucidal effect of acid on enveloped viruses is due to the damage that low pH causes to envelope proteins. Nonenveloped poliovirus, type-1 showed no apparent inactivation due to its resistance to acidic conditions. Duizer et al. (2004) have shown that noroviruses (nonenveloped) are able to persist pH 2.7 for more than 3 h at room temperature. However, nonenveloped rhinoviruses are sensitive to acids. As a reminder, the acid cleaning step in the usual CIP-cycle proceeds at a temperature of 50–70°C with a maximum cleaning time of 20–30 min or even much shorter.

Antivirucidal potential of enzymatic cleaners

Treatment of enveloped viruses with proteases may render them noninfectious due to the fact that removal of their glycoprotein spikes makes them unable to attach to host cells (Knight, 1975). Amtmann et al. (2020) studied the inactivation of koi herpesvirus and viral hemorrhagic septicemia virus in suspension by means of a proteolytic enzyme produced with the help of Bacillus amyloliquefaciens. A 3-$\log_{10}$ reduction in the titer of these two viruses was achieved with this protease. According to

the authors, the glycoprotein spikes located in the viral envelopes might be destroyed due to the proteolytic activity of the protease. Wild and Brown (1967) mention the inactivation of nonenveloped foot-and-mouth disease virus by means of the well-known small intestine protease trypsin. However, nonenveloped viruses tend to be quite resistant to inactivation by proteases (trypsin, chymotrypsin, pepsin, papain, bromelain, pronase, etc.), unless the coat protein is denatured by some other means (Knight, 1975). Even more, treatment with trypsin just may increase the infectivity of some viruses. After treatment with trypsin, an increase in the infectivity of rotavirus and influenza A virus was seen by, respectively, Clark et al. (1981) and Klenk et al. (1975).

Phospholipases often inactivate enveloped viruses by attacking the phospholipid components of the envelope and presumably disorganizing the structure required for attachment and penetration (Knight, 1975). Lipases secreted by Chromobacterium bacterium have demonstrated to possess virucidal activity against several enveloped viruses, such as dengue, zika, human immunodeficiency, herpes simplex virus, and SARS-CoV-2, but not against influenza A virus. They could degrade the viral lipid envelope (Yu et al., 2020).

Amos (1953) mentioned the virucidal effect of acid and alkaline phosphatase on herpex simplex virus. A 3-$\log_{10}$ reduction was seen after 4–6 h exposure to the enzyme at 37°C. It was speculated that some molecule essential to infectivity is rendered inactive due to the removal of a phosphate group.

As viruses seem to react differently on an enzymatic treatment, it will be necessary to study the effect of enzymatic cleaners on foodborne viruses, species by species. Because the results were obtained from experiments with the enzymes directly added to a suspension of the specific virus under study, the question remains whether the virucidal effect of enzymatic cleaning solutions applied to equipment surfaces during open plant cleaning will be significant. Enzymatic cleaning solutions are usually more effective in CIP operations, or when equipment components are soaked in a tank, such as in automated COP. Furthermore, food residues may drastically reduce the virucidal effect of enzymes, although enzymatic removal of food residues and biofilms may expose previously protected viruses to the disinfectants. Temperature and pH considerations also put limits on the use of enzymatic cleaners. The temperature of an enzymatic CIP solution must be limited to 55°C. Due to the proteinaceous nature of enzymes, they may also become a nutrient source for bacteria to grow. Finally, there are also allergic reactions and cost price issues (Moerman et al., 2014).

6.2.4 | Effect of cleansers and soaps on SARS-CoV-2, foodborne viruses, and their surrogates

As infectious SARS-CoV-2 brings about safety issues, experimenting with the virus is difficult. Some viral surrogates were suggested as references to monitor the possible viability, infectivity, and behavior of SARS-CoV-2 when exposed to cleanser formulations and soaps. Since the Covid-19 pandemic, the effectivity of disinfectants against virus surrogates of SARS-CoV-2 has been largely studied. The virucidal effect of cleanser formulations and soaps, however, has received little attention. Table 1 overviews the results of a few studies dealing with the effect of several cleanser formulations and soaps on SARS-CoV-2 or its surrogates. As a comparison, the effect of similar cleanser formulations and soaps on some foodborne viruses or their surrogates is given in Table 2. All viruses mentioned in Table 1 have in common that they are all enveloped viruses, while those mentioned in Table 2 are all nonenveloped viruses. Longer exposure times resulted in higher $\log_{10}$ reductions for the viruses mentioned in both Tables 1 and 2. Cleanser formulations or soaps with microbicidal agents (including QAC and betaine derivatives) increase the antiviral effect on the viruses mentioned in both Tables 1 and 2.

6.3 | Cleaning as a first step in the removal of foodborne viruses from surfaces

Although wet cleaning is not intended to disinfect, it may have some inactivating effect on foodborne viruses due to the impact of some cleaning chemicals on their lipid envelope or protein capsid. But wet cleaning alone without disinfection is not sufficient for all virus particles to be removed, inactivated, or rendered noninfectious, especially because the disinfecting power of cleaning agents is rather weak or limited to certain viruses. Cleaning agents are not disinfectants, although enveloped viruses could be quite sensitive to alkaline and acid cleaning agents. Wet cleaning of food contact surfaces with cleaning agents within time periods commonly used in the food industry only achieves a 1–2-$\log_{10}$ reduction in viral particles. However, appropriate wet cleaning is of utmost importance to make the subsequent disinfection process adequate.

Takahashi et al. (2011) have proven that even small amounts of food residues left on cleaned surfaces could protect viruses against the virucidal activity of sodium hypochlorite. Many viruses can be stabilized and protected by dissolved, colloid, and solid organic matter. Vasickova

TABLE 1 Effect of cleanser formulations and soaps on SARS-CoV-2 and its surrogates

SARS-CoV-2 (surrogate)	Strain	Present in matrix	Interfering substance	Test method	Cleaning agent	Dose/ concentration	Cleaning temp. °C	Rinsing temp. °C	Exposure time (min)	Log_{10} reduction	Method of analysis	References
SARS-CoV-2	NA	TSB	NDA	SHS fabric	[a] Liquid hand soap	0.57 ± 0.03% w/w	RT	NDA	1	1.7	$TCID_{50}$	Cano-Vicent et al. (2021)
SARS-CoV-2	HKU-001a	MEM-FBS	NDA	Suspension	[b] Liquid hand soap	NDA	RT	NDA	1	≥2 ± 1.56	$TCID_{50}$	Chan et al. (2020)
									5	≥2.25		
					[c] Hand wash				1	≥0.83 ± 0.29		
									5	≥0.92 ± 0.38		
SARS-CoV-2	NA	MEM-FBS	5% FBS organic load	Suspension	[d] Liquid hand wash	0.025% w/w	37	NDA	1	≥3.1	$TCID_{50}$	Ijaz et al. (2020)
					[e] Bar soap	0.018% w/w	38		1	≥3		
					[f] Surface cleanser	0.077% w/w	21		5	≥4.1		
SARS-CoV-2	USA-WA1/2020	NDA	NDA	3D-printed materials	[g] QA impregnated wipes	NDA	NDA	NA	<0.15	>5.5	$TCID_{50}$	Welch et al. (2021)
HCoV	229E	FBS-DMEM	Organic load/5% BSA soil	Suspension	[h] Baby shampoo	1%	RT	NDA	0.5	1–3	$TCID_{50}$	Meyers et al. (2020)
									1	2–3		
									2	>3		
HCoV	229E	NDA	NDA	3D-printed materials	[g] QA impregnated wipes	NDA	NDA	NA	<0.1	>3.5	$TCID_{50}$	Welch et al. (2021)
MHV	A59	NDA	NDA	3D-printed materials	[g] QA impregnated wipes	NDA	NDA	NA	<0.1	>6	$TCID_{50}$	
Phi6	NDA	TSB	NDA	SHS fabric	[a] Liquid hand soap	0.57 ± 0.03% w/w	RT	NDA	1	2	Plaque assay	Cano-Vicent et al. (2021)

(Continues)

TABLE 1 (Continued)

SARS-CoV-2 (surrogate)	Strain	Present in matrix	Interfering substance	Test method	Cleaning agent	Dose/ concentration	Cleaning temp. °C	Rinsing temp. °C	Exposure time (min)	Log$_{10}$ reduction	Method of analysis	References
BCV	S378 Riems	Oatmeal slime	Oatmeal slime	Stainless steel					10	2	Propidium monoazide RT qPCR	Lucassen RT et al. (2021)
									30	2		
					[i]Commercial dishwash-ingtab	NDA	45	30	45	>3		
								50	45	>4.7		
								70	45	>5.3		
					[j]Reference detergent	NDA	45	50	45	~3		
					Reference detergent with bleach	NDA	45	50	45	~4.5		

Viral surrogates–BCV, bovine coronavirus; HCoV, human corona virus; MHV, mouse hepatitis virus; Phi6, bacteriophage Phi6.

Media–BSA, bovine serum albumin; DMEM, Dulbecco's Modified Eagle's Medium; FBS, fetal bovine serum; MEM, Minimal Essential Medium.

Abbreviations: NA, not applicable; NDA, no data available; RT, room temperature; SHS, solidified hand soap; 3D-printed materials, a biocompatible thermoplastic used in medical applications.

[a]Liquid hand soap, ingredients: water, sodium lauryl ether sulfate, sodium chloride, cocamidopropyl betaine, cocamide diethanolamine, disodium EDTA, propylene glycol, styrene/acrylates copolymer, lactic acid, parfum, benzyl alcohol, limonene, linalool, 1,2-dimethylol-5,6-dimethylhydantoin, imidazolidinyl urea, methylchloroisothia-zolinone, methylisothiazolinone, and sodium benzoate.

[b]Liquid hand soap, ingredients: biodegradable amphoteric surfactants and 1,2-dimethylol-5,6-dimethylhydantoin.

[c]Hand wash, ingredients: sodium lauryl ether sulfate and cocamidopropyl betaine.

[d]Liquid hand wash, ingredients: 0.1% w/w salicylic acid.

[e]Bar soap, ingredients: 0.11% w/w para-chloro-meta-xylenol (PCMX).

[f]Surface cleanser, ingredients: 0.096% w/w quaternary ammonium compound (alkyl [C12–C16] dimethyl benzyl ammonium chloride).

[g]Quaternary ammonium (QA) impregnated disposable wipes AF3, ingredients: 0.14% w/w n-alkyl [68% C12, 32% C14] dimethyl ethylbenzyl ammonium chloride; 0.14% w/w n-Alkyl [60% C14, 30% C12, 5% C18] dimethyl benzyl ammonium chloride.

[h]Johnson's Baby Shampoo, ingredients: water, cocamidopropyl betaine, decyl glucoside, sodium cocoyl isothionate, lauryl glucoside, PEG-80, sorbitan laurate, glycerin, citric acid, sodium benzoate, PEG-150 distearate, sodium methyl cocoyl taurate, fragrance, polyquaternium-10, and disodium EDTA.

[i]Henkel's somat classic dishwasher tablet, ingredients: oxygen bleach (5–15%), about 5% nonionic surfactants, soda, perfumes, phosphonates, and enzymes.

[j]Reference detergent, ingredients: phosphate-free percarbonate-based detergent with active enzymes.

TABLE 2 Effect of cleanser formulations and soaps on some foodborne viruses or their surrogates

Foodborne virus	Strain	Present in matrix	Interfering substance	Test method	Cleaning agent	Dose/ concentration	Cleaning temp. °C	Rinsing temp. °C	Exposure time (min)	Log_{10} reduction	Method of analysis	References
Adenovirus	Type 5	NDA	NDA	3D-printed materials	[a]QA impregnated wipes	NDA	NDA	NA	<0.1	>4	$TCID_{50}$	Welch et al. (2021)
MNV	S99	Oatmeal slime	Oatmeal slime	Stainless steel	[b]Commercial dishwashingtab	NDA	45	30	45	3.2	Propidium monoazid qPCR	Lucassen, Weide, and Bockmühl (2021)
								50	45	4.8		
								70	45	5.4		
					[c]Reference detergent	NDA	45	50	45	4.5		
					Reference detergent with bleach	NDA	45	50	45	3		
Poliovirus	Type 1	MEM-FBS	NDA	Whole-hand washing	[d]handwashing Ligana® hand soap bar	5%	RT	RT	5	2-4	Plaque assay	Schürmann and Eggers (1985)
Poliovirus	NDA	Fecal suspension	Fecal substances	Whole-hand washing	[e]Aquaress® s	NDA	RT	RT	0.15	0.6	Plaque assay	Mbithi et al. (1993)
HAV	HM-175	Fecal suspension	Fecal substances	Whole-hand washing	[e]Aquaress® soap	NDA	RT	RT	0.15	1	Plaque assay	Mbithi et al. (1993)
Human rotavirus	Wa	MEM-FBS	Fecal substances	Whole-hand washing	[f]Ivory® liquid soap	1:10	40	NA	0.15	0.56	Plaque assay	Ansari et al. (1989)

(Continues)

TABLE 2 (Continued)

Foodborne virus	Strain	Present in matrix	Interfering substance	Test method	Cleaning agent	Dose/ concentration	Cleaning temp. °C	Rinsing temp. °C	Exposure time (min)	Log$_{10}$ reduction	Method of analysis	References
HuNoV	NDA	Fecal suspension	Fecal substances	Human finger pad	[g]Liquid soap with 0.5% triclosan	NDA	RT	RT	0.15	0.1	RT-qPCR	Liu et al. (2015)

Abbreviations: NA, not applicable; NDA, no data available; RT, room temperature.

[a]Quaternary ammonium (QA) impregnated disposable wipes AF3, ingredients: 0.14% w/w n-alkyl [68% C12, 32% C14] dimethyl ethylbenzyl ammonium chloride; 0.14% w/w n-Alkyl [60% C14, 30% C12, 5% C18] dimethyl benzyl ammonium chloride.

[b]Henkel's somat classic dishwasher tablet, ingredients: oxygen bleach (5–15%), about 5% nonionic surfactants, soda, perfumes, phosphonates, and enzymes.

[c]Reference detergent, ingredients: phosphate-free percarbonate-based detergent with active enzymes.

[d]Ligana® hand soap bar, ingredients: water, disodium lauryl sulfosuccinate, sodium cocosulfate, wheat, starch, cetearyl alcohol, parrafin, PEG-15, glyceryl isostearate, disodium cocoamphodicacetate, and parfum.

[e]Aquaress® soap, ingredients: water, glycerine, sodium lauryl ether sulfate, triethanolamine salt of lauryl sulfate, cocamide diethanolamine, sodium benzoate, 1,2-di-methylol-5,6-dimethylhydantoin, citric acid, parfum, tetrasodium EDTA, and plant extracts.

[f]Ivory® liquid soap, ingredients: water, sodium lauryl ether sulfate, sodium lauryl sulfate, sodium sulfate, cocamidopropyl betaine, citric acid, sodium chloride, fragrance, 1,2-dimethylol-5,6-dimethylhydantoin, and tetrasodium EDTA.

[g]Fisher Scientific International Liquid Soap, ingredients: sodium lauryl ether sulfate, cocamidopropyl betaine, solulan, propylene glycol, sodium chloride, dyes, and fragrances.

et al. (2010) have demonstrated that organic matter and food residues may increase the resistance of foodborne viruses against drying. Food residues also prohibit intimate contact between the virus and disinfectant, and even can neutralize the disinfectant.

The cleaning process must also remove biofilms, because they can also act as a reservoir of foodborne viruses responsible for numerous foodborne outbreaks (Lacroix-Gueu et al., 2005). Viral particles are able to penetrate inside the extracellular polymeric substances structure of mucoid biofilms. In the biofilm matrix, viruses may find protection against environmental stress, such as desiccation or the virucidal action of disinfectants (Vasickova et al., 2010). The level of viral protection may depend on parameters, such as the composition, thickness, or structure of the biofilm. As an example, Storey and Ashbolt (2003) and Quignon et al. (1997) reported the persistence of, respectively, enteric virions and poliovirus, type-1 in microbial biofilms. If biofilms are not removed after intensive cleaning, biofilm erosion or sloughing may release the protected and immobilized virus particles in the food product once production resumes. After desorption, most of these viral particles keep their infectious potential. Also, increasing amounts of microbes can protect viruses from desiccation and disinfection (Vasickova et al., 2010).

7 | CONCLUSION

Foodborne viral diseases emerge due to the globalization of the food production chain and retail, increased international travel, evolving consumer demands, changes in food processing (e.g., minimal food processing), consumption of undercooked meals, and the evolution in pathogenic strains. Foodborne viruses can be transmitted via food, such as fresh-cut and fresh produce, the food workers' hands, and food contact surfaces (e.g., tools, equipment, etc.), as well as bivalves. However, most documented foodborne viral outbreaks can be traced to food manually handled by an infected food handler, rather than to industrially processed foods.

Traditionally, food producers and food suppliers consider food spoilage microorganisms and foodborne/waterborne pathogens of prokaryotic (bacteria) and eukaryotic (yeast and molds) origin as the most troublesome with regard to food quality and safety, and therefore nearly all existing disinfection/decontamination technologies are quasi only focused on the inactivation of these microorganisms. Although foodborne or waterborne viral pathogens may cause gastroenteritis (e.g., HuNoV), or hepatitis (e.g., HAV) or other pathologies, they receive little attention in daily disinfection and decontamination practices. The COVID-19 pandemic may increase the

awareness of viral food pathogens and workplace security to reduce the risk of transmission of human viruses. According to the international legislations, established testing practices have proven that norovirus and hepatitis A virus are the major viruses of concern in foods. As for SARS-CoV-2, there is no scientific evidence that coronavirus can be transmitted directly via food or food packaging despite the recent claims of a possible route through frozen foods. However, in order to reduce the risk of SARS-CoV-2, foodborne and waterborne outbreaks of viral disease, the recommendations for the food sector are to follow best practices by implementing food hygiene, controlling viruses in foods and surfaces via available testing and disinfection methods, and by further developing and testing of novel physical and biological methods.

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Tatiana Koutchma: conceptualization-equal; investigation-equal; project administration-equal; writing-review & editing-equal. Hamid Ezzatpanah: conceptualization-equal; investigation-equal; project administration-equal; writing-original draft-equal; writing-review & editing-equal. F Lavafpour: writing-original draft-equal. Vicente Gómez-López: writing-original draft-equal; writing-review & editing-equal. Fran Moerman: conceptualization-equal; writing-original draft-equal; writing-review & editing-equal. Mohamadi Mohamadi: writing-original draft-equal. Dele Raheem: writing-original draft-equal.

CONFLICTS OF INTEREST

None to declare.

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