La grande Bouffe - The great guzzle

Bacteriophages in the production of foodstuffs: a legal introduction

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"Your enemy's foe is your friend." If this slightly Machiavellian proverb were to be true, bacteriophages would have to be considered among the best friends of manufacturers and consumers of foodstuffs. These little viruses attack and kill certain harmful bacteria that disturb the production process of foodstuffs and that endanger the consumer health. Whether such a heartfelt friendship also exists in the area of food law, will be the topic of this article. The authors present the phages' functions and possible fields of application and put their use during the production of foodstuffs into a legal framework. The authors come to the conclusion that, according to German and European food law provisions, in most cases bacteriophages can be used without authorisation – provided that their use complies with the general requirements of food safety.

A. Introduction

When foodstuffs are contaminated with pathogenic, i.e. potentially disease causing, bacteria, neither consumer nor manufacturer nor distributor will be pleased: especially consumers with a weak immune system are exposed to serious or even fatal health risks[1]. The affected companies face high legal and financial risks in case of a contamination of their products; they are threatened by distribution bans, product recalls, destruction of goods and further sanctions.

Each year numerous cases of illnesses caused by microbiologically contaminated foodstuffs become known in Germany alone[2]. Luckily, in most cases these illnesses, which are usually caused by bacteria like listeria and salmonella, don't cause permanent harm or death. However, a number of reports about fatal infections can also be found[3]. In any case, the illnesses that are caused in this way, e.g. listeriose[4], go along with unpleasant diarrhoea, stomachache or headache[5]. Bacterial contaminations therefore are a serious issue when

1 Cf. *Kreft*, BIOspektrum 2001, 343.
2 Cf. *Hartung*, Journal für Verbraucherschutz und Lebensmittelsicherheit, vol. 1 Supplement 2 Dezember 2006, 196 ff. with the data of the zoonosis survey 2005 in foodstuffs.
3 A list can be found for example in *Werlein/Hildebrandt*, Hygiene-Report 2006, 18.
4 For the term cf. *Römpp*, Lexikon Lebensmittelchemie, 2. ed. 2006, 677.
5 With the most important symptoms of several pathogenic bacteria: *Ternes/Täufel/Tunger/Zobel*, Lebensmittel-Lexikon, 4. ed. 2005, 162.

producing and distributing foodstuffs; to reduce them, quite substantial resources are invested into research and development[6].

Microbiological contamination in the form of pathogenic bacteria like salmonella and listeria either originates from the process of slaughter of an animal or the extraction process, e.g. through contact with the animal's intestinal bacteria – in this case, contamination can be found everywhere in the foodstuff – or the contamination occurs on the surface area that has been subjected to contact with workspace, tools, hands or even only ambient air[7]. Usually, contamination shall be prevented by means of suitable hygienic ways of production, transport and storage[8].

Paradoxically, statistical records indicate an increase of microbiological contaminations with several types of harmful bacteria in foodstuffs in Germany despite ameliorated means of production, transport and storage[9]. This disconcerting discovery might by due to an ever-increasing customers' demand of perishable foodstuffs and the fact that each stage of production that is necessary in the industrialised processing of foodstuffs increases the risk of (cross) contamination.

Now what is it that can be done to minimise the danger of microbiological contamination of foodstuffs? Aiming to maintain a high standard of hygiene at all levels of production is an obvious remedy especially as a lack of hygiene can easily be identified as the main reason for unwanted bacterial infestation[10]. However, even strict standards of hygiene cannot exclude all possible sources of contamination. This is why research has recently been intensified to find methods to specifically target pathogenic bacteria; in the meantime several different solutions have been found that can be of use in practice and that in parts are already used[11]. Among those solutions bacteriophages play an important role[12]. These microorganisms and their field of application shall be briefly described in the following (B. and

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[6] An instructive overview on current scientific endeavours is provided by a summary protocol of an expert advisory board meeting in the BfR on 3.7.2006, published online on the BfR's website (www.bfr.de) under the title „Entwicklung von Handlungsoptionen zur Reduzierung von Campylobacter spp. im Geflügelbereich“. Cf. also *Werlein/Hildebrandt*, Hygiene-Report 2006, 20 for new methods in the fight against listeria monocytogenes.

[7] For sources of contamination with listeria cf. *Werlein/Hildebrandt*, Hygiene-Report 2006, 18 f.

[8] Cf. *Krämer* in: Frede (ed.), Taschenbuch für Lebensmittelchemiker, 2006, 453 f. and *Werlein/Hildebrandt*, Hygiene-Report 2006, 20.

[9] Comparative values in *Hartung*, Journal für Verbraucherschutz und Lebensmittelsicherheit, vol. 1 Supplement 2 December 2006, 196 ff. According to that, campylobacter have replaced salmonella as the most important source of infections. For the increasing number of cases of listeriose cf. *Werlein/Hildebrandt*, Hygiene-Report 2006, 19.

[10] Cf. summary protocol of an expert advisory board meeting in the BfR on 3.7.2006, published online on the BfR's website (www.bfr.de) under the title „Entwicklung von Handlungsoptionen zur Reduzierung von Campylobacter spp. im Geflügelbereich“, 1.

[11] Q.v. summary protocol loc. cit.; *Loessner*, BIOspektrum 2000, 454 and *Werlein/Hildebrandt*, Hygiene-Report 2006, 20.

[12] Cf. *Bradbury*, The Lancet 2004, 624; *Loessner*, BIOspektrum 2000, 454.

C.). Subsequently, the use of phages in the production of foodstuffs will be put into a legal context by means of the relevant legal provisions (D. and E.).

B. What are Bacteriophages?

Bacteriophages – or phages, from the Greek "*Φαγειν*" (phagein = to eat) – are viruses[13] that exist ubiquitously in our environment[14]. Viruses are defined as mobile genetic elements consisting of nucleic acids that can move outside of cells thanks to their protective protein coating[15]. Viruses possess no own metabolism, for their reproduction they need host cells whose biosynthetic activity they can use for their reproduction[16]. In order to achieve that, the viruses' genes encode proteins and thus influence the host cell's metabolic mechanism in a way that causes the host cell itself to die off[17].

The bacteriophages' characteristic – also visible in their name – lies in the fact that they attack specific bacteria: some phages attack a single bacterial genus, more often a specific species or a species' strain, whereas other bacteria are left unharmed[18]. By this means, phages can be specifically used on one or several kinds of unwanted bacteria without harming other – desirable – bacteria.

The underlying mechanism can be simplified as follows[19]: Bacterial strains have very diverse surface structures. Only when the phages' protein coating possesses a structure that allows the recognition of host cells and additionally has the enzymatic ability to perforate the bacterial cell surface, only then can the phages transfect the host cell with their genome, transform the genome into proteins and finally allow these proteins to reprogram the host cell's metabolism in favour of the phages. One kind of bacteriophages can only attack specific bacteria whose barriers it can override.

In a space where different phages and bacteria interact, the phages keep on moving until they find corresponding bacteria on whose surface they can "dock" on. There, they proliferate, kill the bacteria they have used as host cells and through this release the evolving viruses. This process of killing the host cell to release the viral offspring is also called "to

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[13] For this term cf. *Römpp*, Lexikon Lebensmittelchemie, 2. ed. 2006, 873 f.
[14] *Brüssow*, Journal of Bacteriology 2004, 3678.
[15] Cf. *Römpp*, Chemie Lexikon, 9. ed. 1992, vol. T-Z, 4928 for the term „Viren".
[16] *Römpp*, Chemie Lexikon, 9. ed. 1992, vol. T-Z, 4928 for the term „Viren".
[17] *Römpp*, Chemie Lexikon, 9. ed. 1992, vol. T-Z, 4928 f. for the term „Viren".
[18] Graphically *Loessner*, BIOspektrum 2000, 452.
[19] With an scientific description also on the following: *Römpp*, Chemie Lexikon, 9. ed. 1991, vol. M-Pk, 3331 f. for the term „Phagen".

lyse" or "lysis"[20]. Afterwards, the game begins anew: the augmented number of phages whir through the space until further suitable bacteria are found – if no more such bacteria are available, the bacteriophages gradually become inactive[21].

The astonishing biological effect of systematic infection with bacteria has been known for long times[22]. As early as in 1917 the Canadian scientist Félix Hubert d'Hérelle described bacterial phages as creatures that adapt to different bacteria that they use as host cells. He especially observed the infestation of the bacterium Escherichia coli through the corresponding phages[23]. His research concentrated on the medical use of bacteriophages to specifically kill harmful bacteria in the human body[24]. However, the concurrent breakthrough in the knowledge of the effects and ways of use of antibiotics caused the research on bacteriophages to be forgotten, as antibiotics seemed to be more promising for the practical possibilities of therapy[25]. Even though an institute in the Georgian Republic, that was founded by Félix Hubert d'Hérelle, has continuously done research on phages[26], these have only recently come back into the focus of science. A reason for this is the growing number of resistances against antibiotics that make a medical use of bacteriophages seem like an interesting alternative[27]. Research has also been intensified in food technology[28], there are already solutions that are in practical use; in the USA the FDA has only last year approved a spray with bacteriophages to be applied on the surface of certain foods[29].

C. Possible use of bacteriophages in the production of foodstuff

Due to the above-described working mechanisms bacteriophages in the production of foodstuffs can be used pointedly against unwanted bacteria[30]. Despite the high number of different pathogenic strains of bacteria some main trouble makers can be distinguished when looking at the described illnesses that can be ascribed to the consumption of contaminated

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[20] This expression originates from the term „lysis", with which the dissolution of cell membranes is described, cf. *Römpp*, Lexikon Biotechnologie 1992, 475 on the term „Lyse".

[21] *Noble, R. T.*, and *J. A. Fuhrman*, Virus Decay and Its Causes in Coastal Waters, Appl Environ Microbiol 63:77-83 (1997); *Hurst, C. J.*, *C. P. Gerba*, *I. Cech*, Effects of environmental variables and soil characteristics on virus survival in soil., Appl Environ Microbiol 40:1067-79(1980).

[22] Cf. *Loessner*, BIOspektrum 2000, 452.

[23] D'Hérelle's fundamental work was published in German some years later: "Der Bakteriophage und seine Bedeutung für die Immunität", Braunschweig 1922.

[24] Cf. *Loessner*, BIOspektrum 2000, 452.

[25] *Loessner*, BIOspektrum 2000, 452.

[26] In DIE ZEIT of 4.9.2003 No. 37, p. 38, a reportage by *Thomas Häusler* has been published on this topic which is worth reading.

[27] *Loessner*, BIOspektrum 2000, 452.

[28] Generally *Werlein/Hildebrandt*, Hygiene-Report 2006, 20.

[29] Federal Register 2006, 71:47729-47732.

[30] Cf. e.g. *Peek/Reddy*, Gastroenterology 2006, 131: 1370.

or otherwise negatively influenced foodstuffs: among those are campylobacter, salmonella and listeria, especially listeria monocytogenes[31]. The categories of foodstuffs that are affected most are especially fish, meat, poultry, products with raw eggs and raw milk, there especially cheese with raw milk[32].

When bacteriophages that specifically attack salmonella or listeria are integrated into the production process of foodstuffs, a dangerous contamination with the bacteria can be avoided or at least lessened[33] due to the described biological mechanism. For this the respective phages have to be applied in the form of special cultures either on the surface or inside of the foodstuffs, the latter for example through integration into the process of maturation of cheese. Technically this can happen through the isolated addition of phages, or the phages are carried through non-pathogenic i.e. harmless bacteria and thus integrated into the production process of foodstuffs. Bacteriophages that are pointedly used against harmful listeria monocytogenes can, for example be combined with the similar but harmless listeria innocua and in this way be brought into the foodstuffs. In the respective space of interaction, e.g. in cheese, the phages coincide with the existing pathogenic bacteria, they reprogram the metabolism of these unwanted bacteria, reproduce and lyse the bacteria, killing the harmful contamination in the process of their reproduction[34].

This process happens within a very short period of time after the application of bacteriophages onto or in the respective foodstuffs[35]. When the phages don't find any new host cells, they become inactive and are eliminated[36]. Contaminations can therefore only be fought in a tight temporal connection with the application of phages. The conservation of foodstuffs for long periods of time of production, transport and storage is not possible through the singular application of phage cultures in the process of production. For the food technology it is furthermore relevant what happens with any possible still existing remainders of bacteriophages when the consumer eats the treated foodstuffs. Only a few phages survive the passage through the stomach and the remaining ones are excreted. In fact, human excrements contain a high number of phages. If phages still manage to get into a person's bloodstream, i.e. through an injection, the phages will be fought and destroyed by the human

[31] Cf. *Hartung*, Journal für Verbraucherschutz und Lebensmittelsicherheit, vol. 1 Supplement 2 Dezember 2006, 196 ff.
[32] Cf. *Krämer* in: Frede (ed.), Taschenbuch für Lebensmittelchemiker, 2006, 441 f.
[33] *Peek/Reddy*, Gastroenterology 2006, 131: 1370 on the FDA-approved spray in the USA.
[34] Q.v. above B.
[35] *Loessner*, BIOspektrum 2000, 453.
[36] *Loessner*, BIOspektrum 2000, 452. *Noble, R. T., J. A. Fuhrman*, Appl Environ Microbiol 63:77-83 (1997); *Hurst, C. J., C. P. Gerba, I. Cech*, Appl Environ Microbiol 40:1067-79 (1980).

body's defence cells as an intruding foreign object[37]. Furthermore, according to science, the phages themselves do not have an own pathogenic impact in the human body[38]. Actually, due do the ubiquitous existence in the environment they are already to be found in large numbers and have not yet attracted attention as being harmful for health[39]. Accordingly, the FDA in the USA has - after an adequate check - given permission for a spray containing bacteriophages[40], another phage culture also received the so-called GRAS-status, it is "generally recognized as safe"[41].

After the findings on the ways of work of bacterial phages that have only been presented here in a general conspectus; their use in the production of foodstuff seems like an attractive, modern method to fight unwanted, pathogenic bacteria[42]. The practical embedding into the different production processes is advancing[43]. The above-mentioned example from the USA shows that surface sprays with phages are already on the market. The purposeful addition of phages to starter cultures, as they are known from cheese and meat production, has become reality, and a study proves the potential usefulness of such phages[44]. From a legal point of view, the question arises how the use of bacteriophages can be put into the context of food law.

D. Legal problem

When putting the application of bacteriophages into a legal context there are essentially two questions. Firstly, it is of special importance that the requirements of food safety are met. Especially the manufacturer of foodstuffs would want to know whether the use of phages in the production of his goods is legally possible at all, whether it can happen without prior authorisation and which labelling requirements have to be met.

Due to the complex scientific findings in connection with phages the legal context given here can naturally only serve as an overview. A lot depends, like it usually does with food technologies, on the scientific evaluation of food safety. However, the above described

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[37] *Loessner*, BIOspektrum 2000, 452; *Merril et al*., Long-circulating bacteriophage as antibacterial agents, Proceedings of the National Academy of Science/USA/93, 3188–3193 (1992).
[38] *Loessner*, BIOspektrum 2000, 45; *Bruttin, A./Brussow, H.,* Human volunteers receiving Escherichia coli phage T4 orally: a safety test of phage therapy, Antimicrob Agents Chemother, 2005 Jul, 49 (7):2874-8.
[39] *Loessner*, BIOspektrum 2000, 452.
[40] Federal Register 2006, 71:47729-47732.
[41] http://www.cfsan.fda.gov/~rdb/opa-g198.html.
[42] Cf. also *Werlein/Hildebrandt*, Hygiene-Report 2006, 20.
[43] With a practical example *Peek/Reddy*, Gastroenterology 2006, 131: 1370 on the FDA-approved spray in the USA.
[44] This reports *Loessner*, BIOspektrum 2000, 452.

effects and fields of use for phage cultures allow a categorisation with the help of existing food law principles.

It almost seems like a reflex, that new food technologies today become subject to the regulatory demands of the state or the EU. An example for this is the *"Regulation (EC) No 258/97 of the European Parliament and of the Council of 27 January 1997 concerning novel foods and novel food ingredients"*, the so-called Novel Food Regulation[45]. However, the – at least for now – basic principle that prevails in food law is a different one. Foodstuffs and their ingredients can generally be marketed without prior authorisation when their safety is guaranteed[46]. This principle has been penetrated for some time, e.g. through the authorisation requirements for technological food additives and more and more other foodstuffs, e.g. decontaminants in food hygiene, in addition to the regulatory requirements for the already mentioned "Novel Foods"[47].

Bacteriophages which are used specifically to kill unwanted bacteria in the foodstuff production are somewhere in this area of conflict between freedom of marketing and authorisation requirements: On the one hand phages surely are no usual and long known foodstuff ingredients whose application without prior authorisation is out of doubt. On the other hand bacteriophages are part of the scientific and legal category of microorganisms[48]. They find themselves in the company of substances that have long been used in the production of several foodstuffs like cheese and meat without prior authorisation, and for which an exemption from the forbiddance of additives in Art 6 (2) I of the German Act on Food and Feedstuffs (LFGB) has expressively been created[49].

The concrete legal appraisal of the application of bacteriophages in foodstuff production has to be measured against the central command of food law, which is the principle of food safety that is laid down in Art 14 of *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, establishing the European Food Safety Authority and laying down procedures in matters of food safety*. The further legal appraisal of phages depends on the classification of the viruses into the different categories of food law. This classification begins with the question whether phages, from a hygiene law perspective, represent decontaminants in the sense of Regulation (EC) No 853/2004. Following that It shall be discussed whether

[45] Further particulars of this *Schroeter*, ZLR 1997, 373; *Groß*, ZLR 2003, 543.
[46] This follows from recital 30 of Reg. (EC) No. 178/2002; cf. also *Zipfel/Rathke*, Lebensmittelrecht, C 102, § 6 LFGB marginal number 9.
[47] Further particulars of the creeping transition into the direction of a principle of prohibition *Schroeter* ZLR 2005, 191, 197 ff.
[48] Cf. *Römpp*, Chemie Lexikon, 9. ed. 1991, vol. M-Pk, 2781 for the term „Mikroorganismen".
[49] *Zipfel/Rathke*, Lebensmittelrecht, C 102, § 6 LFGB marginal number 1.

bacteriophages are to be classified as food additives or as processing aids. This problem leads to the question, whether phages fall into the exception area from the authorisation requirements for additives, which exist for microorganisms in German food law. Lastly, after an intermediary result, there remains the question if and maybe how bacteriophages have to be labelled on the final product.

E. Legal classification

1. Basic requirements of food safety

Food safety represents the most important precondition for lawfully marketing foodstuffs and their ingredients[50]. This principle which is central for the whole area of food law is described in Art 14 Regulation (EC) No 178/2002 for the entire European community. It has to be observed by every responsible food operator during each step of the production, transport and distribution of foodstuffs[51]. Therefore, if foodstuffs are treated with bacteriophages, the foodstuffs will have to be safe when they are used by the consumer, independent from the actual application of phages.

Art 14 (2) Regulation (EC) No 178/2002 defines that foodstuffs are considered "unsafe" when they are "injurious to health" or when they are "unfit for human consumption". Pursuant to Art 14 (5) Regulation (EC) No 178/2002, "*in determining whether any food is unfit for human consumption regard shall be had to whether the food is unacceptable for human consumption according to its intended use, for reasons of contamination, whether by extraneous matter or otherwise, or through putrefaction, deterioration or decay*"[52]. At first sight one might consider that the treatment of a foodstuff with phages – that belong to the category of viruses[53] – is a contamination of the foodstuff. However, Art 14 (2) lit. b Regulation (EC) No 178/2002 means the unintended contamination with harmful materials[54]. The phages are used specifically to fight unwanted contamination of foodstuffs with bacteria such as listeria and salmonella[55]. This is why their use can only fall under the first alternative of Art 14 (2).

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[50] Cf. also *Zipfel/Rathke*, Lebensmittelrecht, C 102, § 6 LFGB marginal number 31.

[51] *Gorny*, Grundlagen des Europäischen Lebensmittelrechts, marginal number 289. However, Art 14 of Reg. (EC) No. 178/2002 does not comprise – according to its wording – the manufacturing of unsafe foodstuffs, but only the marketing of such products. This seeming loophole is covered in German law through sec. 5 para. 1 LFGB, according to which the manufacturing of unsafe products is also forbidden. The principle of food safety thus applies for the entire production and marketing chain.

[52] Meyer/Streinz-*Meyer*, Kommentar LFGB u. Basis-VO, Art. 14 Basis-VO, marginal number 31.

[53] Q.v. above B.

[54] Cf. Meyer/Streinz-*Meyer*, Kommentar LFGB u. Basis-VO, Art. 14 Basis-VO, marginal number 32.

[55] Q.v. above B.

Pursuant to Art 14 (2) lit. a Regulation (EC) No 178/2002, foodstuffs are considered not safe when they are injurious to health, with regard to "*not only to the probable immediate and/or short-term and/or long-term effects of that food on the health of a person consuming it, but also on subsequent generations*", as well as to any "*probable cumulative toxic effects*" and "*any particular health sensitivities of a specific category of consumers where the food is intended for that category of consumers*" (cf. Art 14 (4)). A person that is legally responsible according to food law also has to assure himself that the respective products – including all ingredients in the specific matrix of the foodstuff – have no disadvantageous effects for the health of the consumer. According to Art 14 (7) of the regulation, this can be achieved by taking regress to the specific food law provisions for foodstuffs and their ingredients and by showing that these requirements are met in the specific case: "*Food that complies with specific Community provisions governing food safety shall be deemed to be safe insofar as the aspects covered by the specific Community provisions are concerned*." As there are no special provisions in respect to bacteriophages for the time being, a self-contained proof for the harmlessness for human health in the sense of Art 14 (2) and (4) Regulation (EC) No 178/2002 has to be brought forward by means of a scientific approach.

An adequate scientific proof of food safety can, for example, be achieved through studies, but also in any other scientific way[56]. It does not have to originate from a European source or even have been appraised by the EFSA. Art 14 (2) Regulation (EC) No 178/2002 does not contain any further requirements in this respect; therefore it is sufficient to put forward any scientific proof for the safety, whose validity has to be revised by the authorities and courts, maybe with the help of an expert, in case of a controversy.

In this context, it is important to remember, that Art 14 (2) Regulation (EC) No 178/2002 itself and in combination with the whole Regulation is rested upon the principle of individual responsibility[57]. Therefore on one hand, it is the duty of the person that has the food law responsibility to assure himself of the safety of his products (not only pro-forma) and to be able to document it when necessary, on the other hand, the competent authorities and courts have to have well-founded doubts about the safety that has been documented by the foodstuff producing company to be able to intervene against the marketing of the foodstuff[58]. When the proof of the safety of a foodstuff is scientifically well founded, the counter-evidence also has to be on a scientific basis in order to justify governmental interference with the private freedom of marketing. When an enterprise can document the safety of its products

[56] On the requirement of a scientific safeguarding cf. also *Zipfel/Rathke*, Lebensmittelrecht, C 101, Art. 14 Basis-VO marginal number 47 f.
[57] Cf. recital 30 and Art. 19 of Reg. No. 178/2002.
[58] Cf. OVG Nordrhein-Westfalen, ZLR 2006, 302, 327 – Lactobact Omni FOS II.

through the attestation of a well-known scientific institution or even through an official appraisal like the US-American GRAS-status, there have to be well-founded doubts about the scientific procedural methods to justify measures against the placing on the market of the foodstuff according to Art 14 Regulation (EC) No 178/2002[59].

Concerning the bacteriophages that are here of interest, the existing scientific findings indicate that consumption of phages together with the treated foodstuffs does not have disadvantageous effects on the health of the consumer. This is officially documented though the permission of a spray with phages in the US after a safety examination and the apportionment of the so-called GRAS-status in another case of a culture of bacteriophages that is to be used in foodstuffs[60]. When they are used only once in the process of production, in the final product at the time of consumption, the phages will only be found in an inactive state or in very small numbers. Without bacteria as host cells the viruses loose their livelihood, as they have no own metabolism. Another argument to back up the thesis that phages that have remained after the consumption of foodstuffs develop no disadvantageous effects for the health of the consumer is the fact that they are naturally existent in the human body. However, according to Art 14 (2) Regulation (EC) No 178/2002, it is the duty of the affected company to be able to document the safety of its product not only through the provided indications but also specifically product-related[61], maybe through a recourse to the supplier.

2. Are bacteriophages decontaminants in terms of the Regulation on food hygiene?

The legal assessment of substances that are used in the foodstuff production largely depends on the question into which of the existing food law categories the substances have to be classified. This is due to the fact that the classification into one of the food law categories can lead to authorization requirements – this becomes apparent when it comes to the question whether a substance is an additive that requires authorization or a (non) additive that is in principle free of authorization requirements. The above described effects[62]

[59] On this also *Zipfel/Rathke*, Lebensmittelrecht, C 101, Art. 14 Basis-VO marginal number 47.
[60] Q.v. above B.
[61] This follows in reverse from the ban to market unsafe foodstuffs. The manufacturer has to assure himself that his product is safe before marketing it. In case of a legal challenge, he has to be able to document that he was right to assume the safety of the product – if necessary, through relevant scientific proof. On the other hand, it's the authority's job to prove a lack of sufficient food safety in case they want to intervene against the marketing of a product.
[62] Q.v. above B. and C.

of phages when fighting harmful bacteria may evoke the thought of hygiene law regulations. Against this background it will firstly be examined whether bacteriophages have to be considered "decontaminants"[63] pursuant to *Regulation (EC) No 853/2004 of the European Parliament and of the Council of 29 April 2004 laying down specific hygiene rules for food of animal origin.*

According to Art 3 (2) 1st sentence Regulation (EC) No 853/2004, *"food business operators shall not use any substance other than potable water or - when Regulation (EC) No 852/2004 or this Regulation permits its use, clean water - to remove surface contamination from products of animal origin, unless use of the substance has been approved in accordance with the procedure referred to in Article 12 (2)."* The regulation therefore explicitly allows only potable water for surface cleaning and, under certain conditions, clean water without drinking quality. However, in the authorization procedure of Art 12 of the Regulation, other products can as well be allowed. In this procedure, the European commission is supported by the Standing Committee on the Food Chain and Animal Health pursuant to Art 12 (1) Regulation (EC) No 853/2004. This means that a scientific assessment of the quality of the substance and the ways of use of the substance takes place[64] before it can be used as a decontaminant in the sense of Art 3 (2) Regulation (EC) No 853/2004. So far, such an authorization does not exist for bacteriophages, so that the first question that has to be answered is whether bacteriophages in their described specific ways of use against pathogenic bacteria actually underlie the authorization requirements pursuant to Art 3 (2) in combination with Art 12 (1) Regulation (EC) No 853/2004.

Based on the wording of the Regulation, substances for decontamination firstly have to have the aim to remove surface contamination from products of animal origin. As phages, according to the above said, actually primarily are applied in foodstuffs with animal origin – pathogenic bacteria like salmonella and listeria will mainly be found in the product groups of raw milk products, meat and poultry – the essential criteria of above mentioned definition are "surface contamination" and "remove". When bacteriophages are used in foodstuffs which are not of animal origin, a classification as a decontaminant is ruled out from the beginning.

As a surface contamination according to the original meaning of the word one would have to consider staining of the surface area i.e. through dust and blood and the like. Those contaminations can usually be easily removed through water – like Art 3 (2) Regulation (EC)

[63] This term is not mentioned in Regulation (EC) No 853/2004, but follows from the objective that is put down in Art. 3 (2) of the directive, i.e. to remove contamination.

[64] For the function of the Committee cf. *Hagenmeyer/Teufer* in: Dauses (ed.) EU-Wirtschaftsrecht, Kapitel C IV. „EG-Lebensmittelrecht", marginal number 292 (published soon).

No 853/2004 provides for the normal cases. Whether the word "contamination" also includes contamination with pathogenic bacteria remains at least doubtful. The considerations upon which the regulation is based remain silent on that matter. Even though in the strict sense of the word, contaminations are also a kind of pollution, the fact that water is mentioned as the main means of decontamination indicates that the European legislator understands by a contamination in the sense of the regulation primarily the superficial soiling through substances like blood and dust that can easily be removed through water. Bacteria, however, can only very rarely be fought with water. The possibilities to receive an authorization via Art 12 of the Regulation correspond – according to this understanding of Art 3 (2) – to chemical or similar additives, which are added to the water that has been directly mentioned in the regulation to remove surface contaminations of blood and dust more effectively. This thesis is also reinforced by the word "removed". What is "removed" in the strict sense of the word is usually superficial dirt; bacteria however are "fought" or "killed".

Additionally, the phages do not always have to be applied on the surface of the foodstuff[65]. Bacteria will be found preferably, but not only, on the surface of contaminated foodstuffs[66]. Therefore it can also be sensible to let bacteriophages cultures work on the inside of foodstuffs, e.g. by adding a starter culture to the process of cheese production or directly to the milk or by injecting the phages deeper into meat and poultry. Art 3 (2) Regulation (EC) No 853/2004 obviously does not relate to such treatments of foodstuffs.

These considerations show that a classification of bacteriophages as decontaminants according to the regulation does not do justice to the way of functioning of those viruses. Bacteriophages aren't tools with a hygienic focus that work mechanically or chemically to clean the surface of foodstuffs but rather constitute biologically effective microorganisms that can more realistically be compared with the functioning of desirable bacteria in starter cultures of milk and meat products. The explicit permission of microorganisms – including viruses – in Art 6 (2) German Act on Food and Feedstuffs (LFGB) also backs up this thesis[67]. The legislator hasn't seen any further requirement for regulation, and for this reason has generally allowed their use in the production of foodstuffs..

This result is confirmed by the efforts of the EC-Commission to regulate chemical decontaminants. Since 2004, there exists a draft regulation that specifically deals with certain

[65] Cf. *Loessner*, BIOspektrum 2000, 453.
[66] Q.v. above B.
[67] Cf. *Zipfel/Rathke*, C 102, § 6 LFGB marginal number 29 and 31, in more detail q.v. below E. 5.

chemicals that are meant to remove pathogenic bacteria exclusively from poultry[68] ("*Draft Commission Regulation laying down specific conditions for the antimicrobial treatment of food of animal origin"*). These concrete regulations are embedded into a larger scale of regulatory endeavour, which is meant to cover all means of decontamination for surface contamination of foodstuffs with an animal origin[69]. However, the considerations on which the draft is based make it clear that the commission is concerned with the possible dangers of chemical changes in the affected foodstuffs[70]. To the present day, the object of the regulation is meant to be the use of artificially created decontaminants, that, chemically cause the removal of all surface bacteria with which they come into contact[71]. Those chemicals do not work specifically on one certain type of bacteria, but onto the bacterial fauna of the product as a whole[72]. This is to say that the commission wants to subject the effects of the destruction of the entire bacterial fauna to scientific control[73]. Bacteriophages, however, work biologically and not chemically[74], the viruses furthermore work targetedly by attacking only the pathogenic bacteria for which they are destined[75]. The remaining bacterial fauna remains intact[76]. One will come to the conclusion that the need for regulation of phages cannot be compared with the need of regulation concerning chemicals – consequently bacteriophages neither at present day nor in future can be classified as means of decontamination, not even on the background of the new Draft Regulation.

Nevertheless, the European Commission's regulatory plans and activities for chemical cleaning agents show an important aspect concerning Regulation (EC) No 853/2004. Evidently, the Commission itself assumes that substances that are specifically used against bacterial contamination do not underlie the special authorization procedure pursuant to Art 3 (2) and Art 12 of this Regulation. Otherwise, either this special admission procedure or the new provisions of the *Draft Commission Regulation laying down specific conditions for the antimicrobial treatment of food of animal origin* would be superfluous. Therefore, the Draft Regulation also suggest that the authorization requirements of Art 3 (2) Regulation (EC) No 853/2004 shall not comprise substances that work antibacterially and whose application on the surface of foodstuffs is not compulsory.

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[68] Draft Commission Regulation laying down specific conditions for the antimicrobial treatment of food of animal origin, SANCO/2111/2004 Rev. 1.
[69] Cf. recital 5 and. Art. 1 of the Draft Regulation, loc.cit..
[70] Cf. recital 8 of the Draft Regulation (loc.cit.) that speaks of „chemical changes".
[71] Annex 1 of the Regulation Draft (loc.cit.) contains four chemical substances that are supposed to be allowed. The Statement of the BfR on the Regulation Draft also relates only to chemical decontaminations, cf. BfR-Statement Nr. 016/2006 of 21.1.2006, available online on the BfR's website (www.bfr.de).
[72] BfR-Statement Nr. 016/2006 of 21.1.2006, p. 1 and 4, available online on the BfR's website (www.bfr.de).
[73] BfR-Statement Nr. 016/2006 of 21.1.2006, p. 1 f, available online on the BfR's website (www.bfr.de).
[74] Q.v. above B.
[75] *Loessner*, BIOspektrum 2000, 452.
[76] *Loessner*, loc.cit.

As a result, one can say that bacteriophages, which are used in the production of foodstuffs to targetedly fight pathogenic bacteria, are not subject to prior approval pursuant to Art 3 (2) Regulation (EC) No 853/2004.

3. Bacteriophages and the concept of food additives

The above-described ways in which bacteriophages are used in the production of foodstuffs are – in the broadest sense – technological ones. The question therefore arises whether these viruses or the inactive bacteria that are occupied with phages constitute an additive in the sense of the uniform European definition. Pursuant to the definition of the "*Council Directive 89/107/EEC on the approximation of the laws of the member states concerning food additives authorized for use in foodstuffs intended for human consumption"* an additive is

> "*any substance not normally consumed as a food in itself and not normally used as a characteristic ingredient of food whether or no it has nutritive value, the intentional addition of which to food for a technological purpose in the manufacture, processing, preparation, treatment, packaging, transport or storage of such food results, or may be reasonably expected to result, in it or its by-products becoming directly or indirectly a component of such foods*."

This definition has been incorporated in Art 2 (3) 1st sentence of the German Act on Food and Feedstuffs (LFGB) almost word by word[77]. The Proposal of the European Commission for a regulation on food additives does not change anything about this definition.

For the classification as an additive it is therefore of importance whether the phages themselves or their by-products or reaction products indirectly or directly become an ingredient of the foodstuff or at least could become such an ingredient. A technological function of the additive exists without doubt. However, a line has to be drawn between bacteriophages and processing aids[78]. This is also done in the applicable provisions. Pursuant to Art 1 (3) lit a, the Council Directive 89/107/EEC does not apply to processing aids, and processing aids are not considered as food additives pursuant to Art 2 (3) No 1

[77] COM (2006) 428 final – 2006/145 (COD); for further information on the draft cf. *Hagenmeyer*, EffL 2006, 295.
[78] According to *Zipfel/Rathke*, C 102, § 2 LFGB marginal number 22, 85 this means that processing aids are no additives in the sense of the European definition.

German Act on Food and Feedstuffs (LFGB). Pursuant to Art 2 No 2a of the aforementioned Draft Regulation on additives, processing aids also are not considered as additives.

Due to this negative definition, it has to be determined in a first step whether bacteriophages are to be considered as processing aids in the described ways of use.

4. Bacteriophages as processing aids

According to the official annotations to Art 1 (3a) of Council Directive 89/107/EEC, a processing aid is defined as

> *"any substance not consumed as a food ingredient by itself, intentionally used in the processing of raw materials, foods or their ingredients, to fulfil a certain technological purpose during treatment or processing and which may result in the unintentional but technically unavoidable presence of residues of the substance or its derivatives in the final product, provided that these residues do not present any health risk and do not have any technological effect on the finished product."*

This definition has, similar in its wording and with identical content been incorporated in Art 2 (3) 3rd sentence No 1 LFGB. The definition of processing aids in Art 3 No 2 b of the Draft Regulation on food additives also takes up this definition contained in the directive.

The addition of isolated phages to foodstuffs as well as an addition via their non-pathogenic, i.e. already lysed host cells, which in turn can for example be part of starter cultures, happens for technological reasons, just as it is the case with additives. It is therefore of central importance whether the final product contains more than only

- unintended,
- technically unavoidable

residues of these substances or their derivates, and whether those residues

- are harmless for health and
- have no technological impact on the final product.

a) When only *residues* of a substance used in the production may be contained in the final product, this usually means that it is the added amount of substance in relation to the final product that has to be reduced to residues[79]. How this happens is irrelevant; therefore an

[79] Cf. *Zipfel/Rathke*, C 102, § 2 LFGB, marginal number 88; Meyer/Streinz-*Meyer*, LFGB, § 2, marginal number 84.

active elimination of the substance is not required. However, the sole deactivation of the substance is not always considered to be sufficient[80].

For bacteriophages, these requirements would be met, when after completion of the production process there are only a small number of phages left in the foodstuff in comparison to the originally used number of phages.

aa) In their original, active form, the phages are no longer contained in the final product (for this term, cf. below under bb)), however they might still be existent in an inactive, i.e. dead form. As long as the number of the inactive phages does not greatly differ from the original number of active phages, the question arises whether they can still be defined as residues in the sense of a processing aid.

According to the wording of the German implementation provision, only residues from decomposition products or reaction products may still be contained in the final product. The Council Directive 89/107/EEC on additives and the Draft Regulation speak of *"residues of the substance or its derivatives in the final product"*

The further requirements of the term "processing aid" suggest an equalisation of inactive substances with the active ones and therefore allow for a "numeric" interpretation of the term "residues". Those other requirements, e.g. the technical unavoidability, safety for health and a lack of technological functions in the final product would render the term "residues" useless, if those requirements were the only things that mattered. On the other hand, according to the intended purpose of the differentiation, the amount of residues cannot matter for the qualification of a substance. Processing aids are therefore not part of the definition of an additive, because they shall not be subject to an approval procedure. Such a procedure is considered to be necessary for additives as they are still effective in the final product and it therefore has to be determined whether they are safe for health. These two issues are entwined: every substance that is still active or at least could become active again might have an impact on the human metabolism and health so that a prior official examination of its addition to a foodstuff can be required. However, substances that for various reasons are no longer active in the final product and for which it can be assumed that they are no longer relevant under the aspect of safety, it is considered to be sufficient when the food operator itself is responsible to make sure that the use of these substances in the production of foodstuffs cannot lead to safety risks in the final product.

[80] Cf. *Zipfel/Rathke*, Meyer/Streinz-*Meyer* ibid.

Substances that are only of importance during the production process therefore have to be distinguished from substances pursuant to Art 5 (2) Nr. 2 German Labelling Ordinance (LMKV) or to Art 6 (4) lit.c ii) of *Directive 2000/13/EC of the European Parliament and of the Council of 20 March 2000 on the approximation of the laws of the Member States relating to the labelling, presentation and advertising of foodstuffs*, i.e. substances that are additives, but do no have to be specified on the label of the final product. These are substances in an ingredient that had a technological impact there, i.e. preserving agents to allow for a longer storage period of the ingredients. These are, in relation to the specific ingredient, considered as an additive and in principle also constitute an ingredient of the final product that would be subject to authorization requirements and provisions on labelling, but the aforementioned provisions exclude those ingredients from the labelling requirements as long as they are not allergenic.

bb) Taking into consideration the above described functioning of phages in the production of foodstuffs, and taking further into account the fact that these phages do not become inactive directly after their application in the manufacturing of foodstuffs, but instead depending on their surroundings become inactive only after a short delay, the question of when the production process is completed, is not only essential for the question whether the phages can be found only as a "residue", but also for the fulfilment of the further requirements that lie in the definition of a processing aid. The completion of the production process means the moment at which a final product comes into existence in the sense of the official annotations to Art 1 (3a) of the Council Directive 89/107/EEC on additives or in the sense of the corresponding definition in the Draft Regulation for additives.

The term "final product" is also mentioned in the definition of a "food additive" in Art 1 (2) 89/107/EEC, however it remains undefined in the directive as well as it remains undefined everywhere else, e.g. in the Regulation (EC) No 178/2002.

If one took into consideration only the strict sense of the word "final product", one might come to the conclusion that a "final product" would already exist at the moment at which the production process has been finished, i.e. when the producer of the foodstuff has ceased to influence the foodstuff in the sense of a treatment or anything similar. If that was the case, the latest possible moment for observation would be the one in which the foodstuff - in whose production bacteriophages had been used - is packaged.

However, this would not comply with the purposes of the provisions on processing aids on the one hand and additives on the other hand. According to the purposes of these provisions

one has to take into account the moment in which the foodstuff is brought to use, i.e. when it is eaten by the consumer or at which it can be eaten by the consumer, and it has to be determined, whether residues are still existent at that time, whether these are technically unavoidable, and safe for health etc.

This interpretation convenes even better with the wording of the German implementation of the directive on food additives in Art 2 (3) 3rd sentence No 1 Act on Food and Feedstuffs (LFGB). The German legislator has not chosen the word "Endprodukt" ("final product"), but rather the term "a foodstuff destined for consumers".

As a result one may say that inactive phages or bacteria constitute only residues in the sense of the definition of processing aids.

b) Further requirements, for example that the residues have to remain *unintendedly* in the final product, are *technically unavoidable* and have *no technological impact* on the product, are interdependent of each other. One cannot speak of an unwanted remainder of the residues when these have a technological impact on the final product[81]. The mere acquiescence of the existence in the final product does not change this, and it especially does not make them "intended" residues except for when the remaining of the residues is technically avoidable[82].

For several times it has been the topic of discussions which endeavours the manufacturer has to undertake to assure that the remaining of residues is considered as technically unavoidable. On the one hand, it is the best available technology that has to be considered, meaning that the residues cannot be entirely removed with all the methods available in technology to the present day. The possibilities, which the individual manufacturer has, are therefore not taken into account. On the other hand, the principle of proportionality that enjoys constitutional status, is respected as the costs for the removal have to be put into perspective with the manufacturing costs for the foodstuff, so that very expensive and time consuming measures are not demanded[83].

A removal of the inactive phages or the lysed bacteria is not possible in a physical way. One might only think of a chemical treatment, but this would be counterproductive for the foodstuff and its safety. Their presence in the final product would therefore be technically unavoidable.

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[81] Cf. *Zipfel/Rathke*, C 102 § 2 LFGB marginal number 90.
[82] Cf. *Zipfel/Rathke*, ibid.; Meyer/Streinz-*Meyer*, § 2 LFGB marginal number 84.
[83] Cf. *Zipfel/Rathke*, loc.cit. marginal number 91; cf. also *Bergmann*, ZLR 2003, 628, 634 ff. for the comparable problem concerning § 31 LMBG.

Moreover, as described above, a technological use in the final product, i.e. in the product that is to be eaten by the consumer, no longer exists. In particular the inactive bacteria and phages do not have the impact that a preservative might have nor do they have any other technological effects.

c) Furthermore the remaining residues have to "not present any health risk". The question of food safety in connection with the application of bacteriophages has already been discussed above in E 1. The wording "do not present any health risk" is not identical with the term "injurious to health" in Art 14 of Regulation (EC) No 178/2002. However, a difference in content is not visible. Therefore it is the general opinion that a processing aid can only then be a health risk when it is *unsafe* in the sense of Art 14 of Regulation (EC) No 178/2002. [84]

d) Under the premise that they are safe for human health, bacteriophages can therefore be considered as processing aids.

5. Bacteriophages as food additives without mandatory authorization?

The question arises whether above mentioned conclusion, i.e. that the use of bacteriophages is possible without prior authorization, would still be correct when those substances were not be considered as processing aids like in the aforementioned way of use. Then, they would rather be considered as additives due to their technological function.

The use of additives is generally only allowed when the additives are expressly authorized for the specific way of use. In German law, this follows from Art 6 (1) No.1a Act on Food and Feedstuffs (LFGB), which is in so far based on Art 2 (1) of Directive 89/107/EC, although in this Directive that reservation only applies to categories of additives which are listed in Annex 1 of the Directive[85].

a) According to German law (Art 6 (2) LFGB), the ban for additives that have not been authorized (which is laid down in Art 6 (1) No 1a LFGB), does not apply for enzymes and cultures of microorganisms. Among these microorganisms are bacteria, yeast and mould, but also viruses[86].

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[84] *Zipfel/Rathke*, loc.cit., marginal number 92; Meyer/Streinz-*Meyer*, LFGB ibid.
[85] *Zipfel/Rathke*, loc.cit., marginal number 19, notes correctly that the categories of additives not named in Annex 1 are also subject to the reserve as they fall into the realm of application of Directive 95/2/EC.
[86] Cf. *Zipfel/Rathke*, C 102, § 6 LFGB; marginal number 31.

This exception for microorganisms serving a technological purpose does not contradict the European provisions in Directive 89/107/EC, as the requirement of authorization only applies for the categories that are listed in Annex 1 of this Directive or which are now enumerated in other directives[87]. Due to their functioning microorganisms do not fall under one of the categories of additives mentioned in these directives, because they, if they are used for technological reasons at all, usually take effect during the production, e.g. like starter cultures, and therefore have no technological effect on the final product. The differentiation to processing aids is somewhat vague; a clear line can – if at all – be drawn through the legal concept of a “residue”.

The German Act on Food and Feedstuffs (LFGB) speaks of "cultures of microorganisms". This means "pure" cultures containing only a certain type of microorganisms specifically grown for its designated, mostly technological purpose[88]. This confinement to pure cultures of microorganisms also makes it clear that a mixture of different microorganisms shall not be privileged when it is meant to be used for technological purposes.

When used specifically to fight a certain type of unwanted bacteria, bacteriophages will be used as a pure culture. One would also use cultures of microorganisms when the bacteriophages are not applied in an isolated way but via inactive host cells or via other bacteria with another technological purpose.

Therefore the use of specific cultures of bacteriophages in the production of foodstuffs is – at least according to German law – exempt from authorization requirements.

b) However the question of the permissibility in the production of cheese needs some further consideration.

The German Cheese Ordinance (KäseVO), which is not yet part of the EU-wide harmonised law, controls - just like the EC-directive on fruit juice - those ingredients that are permissible in the production of cheese, independent from the question whether they are additives or not. Whereas Art 23 KäseVO recurs to the German Ordinance on Additives (ZusatzstoffzulassungsVO) for those additives that, according to Art 6 (1) German Food and Feedstuffs Act (LFGB), need permission, in addition Art 23 KäseVO allows smoke for external use and Art 3 (1) Nr. 1c allows bacteria, yeast and fungal cultures in the production

[87] Cf. *Zipfel/Rathke*, ibid.
[88] Cf. *Zipfel/Rathke*, ibid.

of cheese except for cheese made of whey. For cream cheese the admission of bacterial cultures is in so far restricted as they are not allowed to lead to a surface maturation.

A similar provision can be found in the French cheese ordinance[89]. The provision says

> *"Peuvent être utilises lors de la fabrication des denrées définies au présent décret un ou plusieurs des produits suivants:*
> *…*
> *e) Présure, cultures inoffensives de bactéries lactiques, de levure et de moisissures;*
> *…"*

Because not all cultures of microorganisms and in particular not those that consist only of viruses are admitted, an isolated addition of bacteriophages would be forbidden in the cheese production process in Germany. However, if bacteriophages are not applied isolatedly, but instead together with their inactivated host cells, e.g. safe listeria innocua bacteria, bacteria are added, that bring their phages along, which also could not be avoided when using lactobacilli.

Art 3(1) No 1c KäseVO remains silent as to whether the bacterial cultures that may be used in the production of cheese, have to be active or not. If one takes into consideration, what kinds of bacterial cultures the legislator had in mind when drafting the ordinance, e.g. classical starter cultures, which work as an acid trigger for the coagulation of cheese dairy milk, one would have to assume a technological function of the bacteria.

This technological effect of the bacteria however does not depend on whether they are active or not. Looking at the example of the application of listeria innocua which are inactivated ("lysed") through their own phages, these bacteria together with their phages have the technological function to inactivate or lyse the dangerous listeria monocytogenes bacteria.

No grounds can be found for a restrictive interpretation of the word "bacteria" in the German Cheese Ordinance, that excludes technical developments like the one described afore and therefore also the application of inactive bacteria. An example from today's practice in connection with starter cultures in the cheese production backs up this interpretation. There are several starter cultures for the fermentation of cheese, which contain phages that

[89] Décret n° 88-1206 du 30 décembre 1988 portant application de la loi du 1er août 1905 sur les fraudes et falsifications en matière de produits ou de services et de la loi du 2 juillet 1935 tendant à l'organisation et l'assainissement du marché du lait en ce qui concerne les fromages.

influence specific bacteria at a certain point of time during he process of fermentation[90]. The bacteria that are thus inactivated become an integrated enzymatic part of the organic structure of the cheese they are used for[91]. This example illustrates that a lysed bacterium can also have a technical function in the production of cheese.

Consequentially this means that the application of bacteriophages via bacterial cultures which they have previously inactivated, is allowed in the production of cheese at least in Germany.

c) After having established that bacteriophages fall under the scope of the term "technological additive" two further differentiations can be made in respect to possible food law categories. The phages are neither new foodstuffs in the sense of the "Regulation (EC) No 258/97 of the European Parliament and of the Council of 27 January 1997 concerning novel foods and novel food ingredients", nor biocidal products in the sense of "Directive 98/8/EC of the European Parliament and of the Council of 16 February 1998 concerning the placing of biocidal products on the market".

aa) The scope of application of the Novel Food Regulation is limited by Art 2 (1) lit. a of the Regulation. Accordingly, food additives in the sense of Directive 89/107/EEC shall not be comprised by the Novel Food Regulation. According to the aforesaid, phages fall under the scope of the term "additive" and for this reason alone are excluded from the category "novel food". Furthermore, processing aids will also have to be taken out of the scope of the Novel Food Regulation as they are comparable with additives and are also defined in Directive 89/107/EEC.

bb) The Biocide Directive 98/8/EC likewise doesn't cover food additives according to its Art 1 (2) lit i. For the same reasons as in the Novel Food Regulation, bacteriophages therefore do not fall into the scope of application of the Biocide Directive.

6. Provisional results

As a provisional result it can be said that the use of bacteriophages in the production of foodstuffs does not require an explicit authorization.

[90] *El Soda et al,* Adjunct cultures; Recent Developments and Potential Significance to the Cheese Industry, 2000 J Dairy Science 83: 609-619.
[91] *El Soda et al*, ibid.

As far as phages are used on the surface of foodstuffs from animal origin, there are good reasons not to classify them as "decontaminants" in the sense of Regulation (EC) No. 853/2004.

Phages can be considered as processing aids when they do not have any technological effect in the final product. But even if bacteriophages weren't considered as processing aids, being cultures of microorganisms, in Germany they would be free from authorization requirements. When used in the production of cheese, however, this only applies as long as they are applied via bacteria serving as host cells.

Finally, phages do not fall under the scope of the Novel Food Regulation and the Biocide Directive due to their status as a processing aid and as an additive.

7. Labelling requirements for the use of bacteriophages

However this result does not answer the question whether and in which way bacteriophages or the host-cell-bacteria that have been applied together with the phages have to be labelled on the final product. As far they represent ingredients of the product, during whose production they were used, they have to be declared in the list of ingredients pursuant to Art 3 (1) No 4, 5 and 6 German Labelling Ordinance (LMKV).

According to the further definition of the term “ingredient” in Art 5 (1) LMKV, this comprises every substance including additives that is used in the production of the foodstuff, and remains changed or unchanged in the final product. This would – among additives – also comprise processing aids, as long as they are still found in the final product in residues or otherwise changed.

Art 5 (2) No 3 LMKV however explicitly excludes processing aids from the ingredient definition, as long as they are not made of any ingredients from Annex 3 No 1, i.e. allergenic substances.

Cultures of microorganisms that have been contained in one or several ingredients of a foodstuff are also excluded from the term “ingredient” pursuant to Art 5 (2) No 2 LMKV as far as they do not have any technological effect in the final product.

According to this provision, as well as the provision in Art 6 (4) c II of the *Directive 2000/13/EC of the European Parliament and of the Council of 20 March 2000 on the*

approximation of the laws of the Member States relating to the labelling, presentation and advertising of foodstuffs, on which it is based, it is decisive whether the addition of cultures of microorganisms happens directly or indirectly. In the first case the culture would be considered as an additive, regardless of whether it still has a technological effect on the final product or not. Whether this differentiation makes sense, has already been questioned[92]. However the European Court of Justice[93] has confirmed the interpretation of the mentioned provision of the Labelling Directive, saying that an additive that is applied during the production of an ingredient for technological reasons, e.g. to prevent its discolouring, no longer has a technological effect, if it does not have to be existent for the change of discolouring in the final product.

According to this, bacteriophages or the cultures of bacteria serving as host cells for the phages would not be considered ingredients of the final product, when they are only added to an ingredient and had no technological effect on the final product. This would be the case if they were added to the raw milk unfolding their effect there but no longer in the cheese itself as the final product. The reasons for which it can be followed that bacteriophages do not have a technological effect on the final product, like cheese, have already been shown above[94]. As they also do not have a preserving effect, they do not have to be present for reasons of shelf life so that in this example the exception from the definition of the term "ingredient" applies.

Particularly in this example, one might consider, that a labelling requirement for bacteriophages can already be ruled out due to Art 14 para 2 Nr. 3 KäseVO (German Cheese Ordinance). According to this provision, those milk ingredients, enzymes and cultures of microorganisms, which are necessary for the production of cheese, do not have to be labelled on the final product. This leads to a liberation from the labelling requirement for cultures of microorganisms, independent from the question of whether they are effective in the final product or not. As long as, just like it is the case with bacteria carrying phages, they are used for technological reasons, their necessity evolves from this purpose[95].

As a result, one can say that bacteriophages, being processing aids, do not have to be labelled on the packaging of the foodstuffs in whose production they are used. As far as they are considered as additives they would at least be exempt form labelling requirements in the ingredient list, when they are only applied to ingredients of the final product, as they do not

[92] Cf. *Zipfel/Rathke*, C 110 § 5 LMKV, marginal number 10 c ff.
[93] EuGH, ZLR 1995, 181.
[94] Q.v. above C.
[95] Likewise *Zipfel/Rathke*, C 277, § 14 KäseVO, marginal number 32.

have a technological effect in the final product itself. Among those ingredients to which bacteriophages can be added are also starter cultures.

F. Conclusions

The use of bacteriophages to targetedly destroy pathogenic bacteria during the process of food production has become a reality. Technologically speaking the basic work of putting the use of phages into practice has largely been done; from a legal point of view however, a classification still remains to be determined.

In this essay it has been tried to integrate the use of phages into one of the already existing categories in food law. It was shown that they can't be classified as decontaminants according to Regulation (EC) No 853/2004 on Food Hygiene, as they do not correspond to the substances for surface cleaning that are the subject of this Regulation. Taking the technological functioning of the phages as a basis, consequently a distinction between the categories of "processing aid" and "technological additive" has been made, which mainly depends on whether the final product shows only residues of the phages that have been used during the manufacturing production. Independently from this decision, it could also be put forward that phages being considered processing aids as well as being considered technological additives do not require prior authorization neither according to German nor European law. Their lawful use depends only on the question whether phages themselves are safe in the sense of Art 14 Regulation (EC) No 178/2002 and whether they do not interfere with the safety for the final product. General proof of food safety for the bacteriophages exists in scientific literature as well as in the form of an authorization and the granting of the GRAS-status through the American food authority FDA. Finally it has been found that the bacteriophages in use normally do not have to be labelled on the packaging of the final product independent from their legal classification as a processing aid or as an additive.

As a result bacteriophages can be used without prior authorization to specifically fight harmful bacteria in the food production process according to German and European law – as far as their safety according to the principles in Art. 14 Regulation (EC) No 178/2002 is guaranteed in respect to the concrete product they are applied in.