Comments Received During Public Consultation of EFSA Draft Scientific Opinion on *"The use and mode of action of bacteriophages in food production"*

(Related to Question EFSA-Q-2008-400)

Issued on 22 April 2009

Contents

This compilation contains the comments received via the electronic form after the public consultation which closed on 6 March 2009. The comments received have been pasted literally without any editing to the text. Comments submitted formally on behalf of an organization appear with the name of the organization. A report on the outcome of the public consultation is published on the EFSA website: http://www.efsa.europa.eu/EFSA/efsa_locale-1178620753812_1211902525399.htm.

Organisations that submitted comments to the consultation (in alphabetical order)

Anova Food B.V.	NLD	**Bunderband der Deutschen Fischindustrie und des Fischgrosshandels e.V.**	DEU
CIAA (Confederation of the Food and Drink Industries of the EU)	BEL	**CLITRAVI (European Association for the Meat Processing Industry)**	BEL
EBI Food Safety	NLD	**FEEDAP Panel**	EFSA EU
FNLI (Federatie Nederlandse Levensmiddelenindustrie)	NLD	**Groupe3A**	FRA
HOC AS	NOR	**Leatherhead Food Int.**	GBR
Loch Fyne Oysters Ltd.	GBR	**Ministry of Health**	CYP
Reflektor AS	NOR	**University of Nottingham**	GBR
Westcountry smokehouses Ltd.	GBR		

Comments received (by chronological order of receipt)

Contributor	Section	Comment
Reflektor AS **NOR**	**General comments**	This comment points to several sections and therefore will be given as "general comments". Salmon has been selected as an example and basis for the comment. One major implication of the present Draft Opinion Paper will be the establishment of a correct terminology for the application of phage treatment to control Listeria in food products. This context justifies a brief comment as to the perception of the terms "additive" and "decontaminant" in a general context. Such considerations should clearly be given considerable weight – to the extent that the everyday comprehension does not conflict with the technical definitions of those terms. An additive would be expected to be present in the product at a detectable concentration, significantly different from a "natural" or "pure" product. Application of a decontaminant would be expected to remove contaminants resulting in a product significantly lower in that contaminant. Clearly such terms should not be imposed on substances or processes in a manner that requires the average customer to invest significant amounts of time in studying the underlying technology or science. While maintaining a technically precise and scientifically correct terminology, any doubt as to terminology should encourage a use of terms that fit with stringent, lay language practice. Are phages used in processing an additive to the salmon fillet? A piece of salmon produced by the aid of phage treatment was never altered, chemically nor biologically, relative to its original state, at any rate not more than by any process of washing with potable water. Labelling this product in a manner where phages are indicated as additives would therefore lead the consumer to regard the product as "processed" or "not pure", whereas this product contains nothing further than what is conferred from its natural history, where both bacteria and phages are integral parts. The line of reasoning backing e.g. the requirement for allergens in a food product to be declared regardless of concentration, seems not to be applicable to the present case, as neither physical amounts nor the chemical structures present are discernable from a product where phages have not been applied. Otherwise, this would have been a very important point. Clearly decontamination is a misleading term when applied to phage treatment of salmon. According to the documentation provided in the Draft Opinion Paper, the result of phage treatment is a product with a dramatically decreased risk of human

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		exposure to Listeria. However the treatment is not of a nature as to accomplish a complete eradication of Listeria. The net effect of phage treatment therefore seems to be maintaining a homeostatic state, where Listeria is kept under control until freezing or consumption. The conclusion of this comment is that phages used to aid the processing of salmon can not be labelled as "additive" or "decontaminant". Rather it may be assumed that the simple insight also is correct, namely that phages used to aid the processing of salmon should be regarded, and termed, a "processing aid"
Loch Fyne Oysters Ltd / Salmon Smokers & Processors Group **GBR**	**Conclusions**	It is unclear in the conclusions section of the report whether based on the references in the background section into which category the product falls into. The conclusion should have made clear whether this is treated as a processing aid so that some indication of the timescale and activities required to gain approval could be realised. While I realise that the duration of activity and whether the phage is still active/surviving at the end of the production period is still to be concluded, some conlcusion would be expected.
Anova Food B.V. **NLD**	**General Comments**	Phages should be acknowledged as an processing aid in food industrie.
	Recommendations	Research on possibility of using bacteriophage as a processing aid in different foods and specially farmed seafood should be encouraged. On the part of seafood production Listeria is very frequently found and because smoking / chilling/ freezing is not sufficient. Bacteriaphages can be a big help in pushing back food contamination in this part of the industrie.

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HØC AS **NOR**	**General Comments**	Reaction to Summary line 25 The introduction of the draft describes the use of phages on a variety of foodstuffs but does not mention the use or possibility of use on fish. This is surprising to us, since Listeria frequently colonizes fish farmed in fresh water environments. Farmed salmon skin and gills especially are colonized by Listeria. Since the process of smoking does not kill all the bacteria present, phages would be highly suitable to remove these bacteria before they enter the processing facility. Since rinsing with water does not remove the bacteria either, currently no method exists for avoiding dissemination of Listeria throughout the processing facility via cross-contamination from colonized fish. Hygiene methods cannot prevent or control this dissemination throughout plant and manufacture of the final product which complies with microbial standards in regard to Listeria is almost impossible. Phages seem to us the ideal vehicle for tackling this problem which has enormous economic consequences and is potentially dangerous to public health. Unlike classical decontaminant which may be used to hide all kinds of sloppy manufacturing practices, highly specific phages would allow tackling of a specific problem that at the moment cannot be avoided nor controlled by any measure since the fish are colonized by Listeria in their natural environment thus inevitably entering processing facilities. Research as that by S. Guenther et al. shows that these phages work for a short period only and therefore we believe phages should not be considered an additive. Since raw product cannot be purchased without presence, and no hygiene measure can prevent this, the specific removal of this pathogen should not be considered decontamination.

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Groupe3A **FRA**	**General Comments**	background as provided by the EC + 3.2.1 examples of use in dairy products Arguments from the cheese industry Listeria poses a major concern for the cheese processing industry. Listeria is a ubiquitous bacterium that can be commonly found in the food processing environment, irrespective of sound hygiene regimens. Several types of cheese are more at risk of being contaminated during processing because of the particular traditional handling procedures employed during the long ripening periods. Raw milk cheeses constitute a separate issue because of the possibility of the raw ingredient being contaminated. But other susceptible soft cheeses such as red smear cheeses, washed cheeses and mould ripened cheeses undergo processing that carries high and mostly unavoidable risks of introducing Listeria onto the cheeses. The issue comes from the fact that a single Listeria bacterium which can be transferred to the cheese after forming, is able to grow into a colony which can cross-contaminate entire batches through processes such as smearing, washing, brushing and piercing of the cheeses. Regardless of the origin of the primary contamination it is the processing and handling steps which become the vectors for contaminating other cheeses. An effective anti-Listeria bacteriophage preparation is ideally suited to prevent contamination of entire batches of cheeses by ensuring that the smear or wash water, brines and manual handling do not become vectors for cross-contamination. It is these processing steps which can be used to prevent contamination and to our mind it seems clear that Listex, like other microbial cultures is a processing aid. Because of the long ripening periods involved, contaminated batches of cheeses mostly contain high numbers of Listeria by the time the cheeses would be ready to be released. Bacteriophages cannot reduce these high numbers of Listeria below levels of detection. Therefore we fail to understand why bacteriophages such as Listex would be considered a decontaminant nor how it could be considered an additive, i.e. since it would be employed to treat ingredients/processing steps to protect against contamination of the cheese, whilst the phages are rapidly inactivated after application and have no remaining protective effect on the food product, as research has shown.

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Individual staff member from University of Nottingham **GBR**	**General Comments**	As a general comment the decision whether to use bacteriophage or not for the purpose of food safety should not be taken on the basis of whether the phage can be considered as processing aids or additives simply to make them fit within existing legislation. It is not that the argument for such could not be made but that the decision is being reduced to a semantic argument rather than a consideration of the benefits to the consumer. I note, however, that the position on safety is to be considered separately, which is appropriate. The conclusion of the report is that the panel cannot discern whether "bacteriophages are able or unable to protect against recontamination of food with bacterial pathogens". In reality the survival of phage will depend upon several factors that are specific to the product on to which they are applied, the storage of the product and the nature of the bacteriophages. However, the recovery of infectious bacteriophages is not sufficient to conclude they will continue to confer protection against recontamination of any food to which they are applied. The application of bacteriophages in this context requires that high titers of phage are applied such that they exceed the inundation threshold (lysis from without) ie such that they act as specific bacteriocidal agent rather than relying on completing the bacteriophage life cycle to lyse the target pathogen (active therapy) (see Cairns et al 2009 PLoS Pathogens 5, e1000253 for the theoretical background). This has two key advantages: 1. the target pathogenic bacteria do not have to be metabolically active to be susceptible 2. the populations of the target pathogen can be low and will still be effected by the application. Once the bacteriophages have been deployed their effective numbers will decline through adsorption in excess and subsequent lysis of any target pathogens and non-specific binding to the food matrix. The residuals may be infectious to target bacteria but could not be considered as protective against recontamination. In this context the application of phage to food surfaces are processing aid.

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EBI Food Safety **NLD**	**Conclusions**	(lines 789-791) In response to the deliberations on the fact that a short period of activity on foodstuffs would have to be established for phages other than P100 (Listex), EBI Food Safety would like to include the following: All (relevant) phages are proteinaceous consisting of genetic information encapsulated in a protein hull. Furthermore all phage structural proteins have similar physiochemical properties, such a low isoelectric point (pI). It therefore stands to reason that interactions between all phages and food matrices will be similar and while exact speeds may vary, immobilisation will occur with all phages. Unpublished data by ETH (personal communication ETH) shows the window of activity of Salmonella phage FO1 in RTE food applications to be similarly short as that of Listeria phage P100. The two phages (and hosts) are in no way related but display highly similar behaviour during application. Conclusion on the inability of phage to protect against recontamination on the basis of published data (Summary (lines 37+) and Conclusion (lines 794+) Although no data on deliberate recontamination have been published to date, the data presented in the study by Guenther et al. (2009) is highly indicative of what would happen in such experiments. In the published experiments that failed to result in complete eradication of the artificially introduced target bacteria, surviving bacteria started to multiply. In most of these cases the bacterial numbers soon exceeded the number of bacteria initially introduced. By definition these new bacteria must have expanded into areas previously not colonized. These bacteria are not affected in a significant, measurable way by the immobilized and therefore functionally inactivated phages in or on the food. The suggestion that phages protect against recontamination could in fact be misleading to the public, suggesting that a phage-treated food product remains protected against a dangerous pathogen, which is clearly not the case). Therefore we propose an adjustment of the text to reflect this crucial observation, namely that, based on the state of the art, phages can not be expected to protect against recontamination. References: Guenther et al. (2009). "Virulent bacteriophage for efficient biocontrol of Listeria monocytogenes in ready-to-eat foods." Appl Environ Microbiol 75(1): 93-100.

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	Summary	Conclusion on the inability of phage to protect against recontamination on the basis of published data (Summary (lines 37+) and Conclusion (lines 794+) Although no data on deliberate recontamination have been published to date, the data presented in the study by Guenther et al. (2009) is highly indicative of what would happen in such experiments. In the published experiments that failed to result in complete eradication of the artificially introduced target bacteria, surviving bacteria started to multiply. In most of these cases the bacterial numbers soon exceeded the number of bacteria initially introduced. By definition these new bacteria must have expanded into areas previously not colonized. These bacteria are not affected in a significant, measurable way by the immobilized and therefore functionally inactivated phages in or on the food. The suggestion that phages protect against recontamination could in fact be misleading to the public, suggesting that a phage-treated food product remains protected against a dangerous pathogen, which is clearly not the case). Therefore we propose an adjustment of the text to reflect this crucial observation, namely that, based on the state of the art, phages can not be expected to protect against recontamination. References: Guenther et al. (2009). "Virulent bacteriophage for efficient biocontrol of Listeria monocytogenes in ready-to-eat foods." Appl Environ Microbiol 75(1): 93-100.

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	General Comments	Avoidance of confusion between 'immobilised' and 'active' phages The draft document contains several phrases where terminology is essential for the reader to build understanding, and which in its current form can be confusing. It concerns all passages which deal with phages that have become immobilized on the food surface. These immobilised phages have no remaining function in the final food product as they are clearly not active on or in the food product. Theoretically one could remove these phages from a food product in a laboratory and find that some have retained their infectivity (as opposed to being structurally degraded). However, whilst this latter observation may be interesting scientifically, it is not relevant in the real life situation. In the draft document the terms "active" and "infective" or "viable" are now used interchangeably, depending on the quoted literature; this terminology should be unified. It is essential to differentiate between: 1) phages that have been immobilised on or in the food product and thus have no remaining function on or in the food product (yet can still be recovered from the material in a laboratory and may then still be infective/viable), and 2) phages that are actually still active on or in the food product (these phages have not (yet) been immobilised on the food matrix). We suggest the consistent use of the terms "immobilised phages" for the former group, leaving the term 'active phages' to be used only for phages that still show a measurable killing effect in situ on the treated food items. While it is true that the speed at which phages are inactivated by immobilisation may differ between phages, they are all proteinaceous and as such will adsorb to surfaces and therefore lose activity over time. Adsorption to surfaces has been shown to be a major cause for loss of phage activity in natural systems (Suttle and Chen, 1992). Reference: Suttle, C. A. and F. Chen (1992). "Mechanisms and Rates of Decay of Marine Viruses in Seawater." Appl Environ Microbiol 58(11): 3721-3729.

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	3.2. Use of bacteriophages in the biocontrol of microorganisms in food	Progeny phages irrelevant in eradication of bacteria on foodstuffs While phages "used in active treatment" (lines 454+) may be an option in control of unwanted zoonotic bacteria in the "in vivo" treatment of food animals and in similar applications, only "passive treatment" is a viable option in the treatment of food items, where bacterial host numbers are low and their growth slow. This is discussed in detail in a review by Hagens and Loessner (in press for 2009). Because initial host numbers are low, a sufficiently high number of phages need to be added to infect the majority of these cells. This critical phage concentration is identical whether the initial bacterial numbers are 10, 100 or 1000 cfu/cm2. Experiments with various phage/host/food systems show this critical number to be in the range of 1x107-3x108 phages per cm2. Therefore it is not the ratio of phages vs. bacteria which is essential for effective elimination of bacteria. With initial phage numbers being this high it is easy to see that progeny phage play no role in the eradication of the bacteria. With 100 infected target cells and a burst size of 50 the total number of progeny phage would be 5000. Compared to the 1x107-3x108 phages applied initially this is completely inconsequential and could not even be measured statistically. Therefore an infection of the target bacterium by a phage also does not need to be immediately productive. If the metabolic state of the bacterium does not allow phage proliferation at that moment in time, this does not mean that the target bacterium survives this infection – it will not. As soon as circumstances change the phage will lyse the host – or in other words: the bacterium will eventually die, but it cannot grow or multiply. Only in fluid systems with high host numbers (either initially high host numbers such as in the fermentation of yoghurt and similar products, or in broth systems which allow quick host proliferation and thus eventual high host numbers) could low numbers of phages outpace and eradicate their bacterial host (see also Bigwood et al. 2009; Cairns et al. 2009). References: Hagens, S. and M. J. Loessner (2009). " Bacteriophage for Biocontrol of Foodborne pathogens: Calculations and Considerations." Curr. Pharm. Biotechnol. (in press, available on request) Bigwood, T., J. A. Hudson, et al. (2009). "Influence of host and bacteriophage concentrations on the inactivation of food-borne pathogenic bacteria by two phages." FEMS Microbiol Lett 291(1): 59-64. Cairns, B. J., A. R. Timms, et al. (2009). "Quantitative models of in vitro bacteriophage-host dynamics and their application to phage therapy." PLoS Pathog 5(1): e1000253.

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Leatherhead Food International **GBR**	**Recommendations**	Lines 799-801:- If phages can prevent re-contamination of food products with pathogens, this suggests that there is a "residual activity". Therefore, would applications of phages be classified as a "food additive" rather than a "processing aid"?
	3.2.2.5. Examples of use in food processing environments	Recent information on Pseudomonas and Staphylococcus phages indicates that application of these to a biofilm (single or dual species) on stainless steel can reduce markedly the numbers of the host bacteria. In addition, adhesion of phages to the substrate minimizes the adhesion of the host cells and formation of a new biofilm (Sillankorva et6 al., J. Applied Microbiol. 105; 196-202; Sillankorva, S.M., PhD thesis 2009, University of Minho, Portugal "Use of bacteriophages to control biofilms".
	3.2.2.1. Examples of use in chicken products	Lines 559-562:- In the results of Atterbury et al. (2006) was the elimination of salmonellae on refrigerated chicken skin samples a real effect or an artifact of the enumeration process for salmonellae? i.e. were the phages active in lysing salmonellae in chill temperatures, or during the resuscitation/dilution/plating procedures.
	3.2.2. Examples of use in carcasses, meats and meat products	Lines 545-549:- I strongly support the requirement for efficacy to be determined on a case-by-case basis. Each meat and meat product and pathogen-phage couple, will behave differently due to mobility of the phages in surface application, solid vs. semi-solid products, the time of mixing /addition of the phage suspension, physico-chemical properties of the different products, etc.
	General Comments	In the current situation of increasing cases / outbreaks of food borne infections / intoxications, and the increasing occurrence of antibiotic-resistant pathogens in hospitals and foods, bacteriophages deserve serious and intensified studies on their efficacy for controlling these organisms. Even if phage-resistant mutants do arise, it is comparatively easy and rapid to isolate, characterise and produce further lytic phages for incorporation into a cocktail. Whilst treatment of live animals may not result in elimination of a particular pathogen, e.g. salmonellae, campylobacters in poultry, reductions in the pathogen load entering the processing facility, will assist other hygiene measures to reduce the overall pathogen load in the facility and on the final product.

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FNLI **NLD**	**General Comments**	The FNLI agrees with the assessment of EFSA that phages have the potential to prevent outbreak or even presence of certain bacteria, and is therefore considered an essential part of the total hygiene measures to avoid possible diseases by consumers. Phages are only part of those measures as the product shelf life is not extended as all other micro-organisms are not affected by phages. We consider the assessment clear on the following point: phages act immediately after application, before being inactivated through adsorption in the food matrix. Therefore it must be concluded that phages have no function in the final food product and should be classified as a processing aid. Phages are therefore not the same as decontaminants. The use of phages is safe and is to be seen as an essential part of a total package of measures to ensure the hygiene of the final product.
CLITRAVI **BEL**	**General Comments**	CLITRAVI, the European Association for the Meat Processing industry, supports the draft opinion developed by the working group and endorsed by the BIOHAZ Panel.

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Westcountry Smokehouses Ltd **GBR**	**General Comments**	The introduction of the draft EFSA report describes the use of phages on a variety of foodstuffs but does not mention the use or possibility of use on fish. This is surprising to us, since Listeria frequently colonizes fish farmed in fresh water environments. Farmed salmon skin and gills especially are colonized by Listeria. Since the process of smoking does not kill all the bacteria present, phages would be highly suitable to remove these bacteria before they enter the processing facility. Since rinsing with water does not remove the bacteria either, currently no method exists for avoiding dissemination of Listeria throughout the processing facility via cross-contamination from colonized fish. Hygiene methods cannot prevent or control this dissemination throughout the plant. Therefore manufacture of a final product which complies with microbial standards in regard to Listeria, is almost impossible. Phages seem to us the ideal vehicle for tackling this problem which has enormous economic consequences and is potentially dangerous to public health. Unlike classical decontaminant which may be used to hide all kinds of sloppy manufacturing practices, highly specific phages would allow tackling of a specific problem that at the moment cannot be avoided nor controlled by any measure since the fish are colonized by Listeria in their natural environment thus inevitably entering processing facilities. Research as that by S. Guenther et al. shows that these phages work for a short period only and therefore we believe phages should not be considered an additive. Since raw product cannot be purchased without presence, and no hygiene measure can prevent this, the specific removal of this pathogen should not be considered decontamination.
Bundesverband der deutschen Fischindustrie und des Fischgrosshandels e.V. **DEU**	**3.2.2.4. Examples of use in seafood**	As we understand it, bacteriophages used specifically to combat listeria in the processing of fish act by attacking and breaking down listeria organisms in and on the fish, rendering them ultimately harmless. At the end of this process, they lose their effect, as documented in the publication by S. Guenther et al. They then no longer have any effect in the finished processed fish offered for sale. It makes no difference if the effectiveness of the treatment of fish products with bacteriphages is enhanced by raising the concentration (cf. lines 608ff). The effect of minimising listeria achieved by the use of bacteriophages in the processing of fish products is in fact the desired effect. The fewer listeria organisms there are in the finished product, the less they will be able to multiply. Our understanding of the action of the bacteriophages used against listeria is that they may be classed as processing aids.

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	3.1. Ecology of bacteriophages in food (natural abundance)	The scientific report from EFSA is mainly concerned with ways of decontaminating foodstuffs "contaminated" with unwanted bacteria. In this connection, the point is often made that such bacteria may be found on the surface of food and that bacteriophages can therefore only work effectively on the surface also (cf. e.g. line 44, 360). This conveys the impression that bacteria are a problem mainly because of a lack of hygiene in the production of foodstuffs. Based on the example of listeria, which may constitute a significant microbiological (and hence medical) problem in the processing of fish, especially smoked fish, we aim to show that this assumption is only part of the truth. In the case of fish for example, particularly farmed freshwater fish, colonisation with listeria in their natural environment is unavoidable, and certainly not the result of a lack of hygiene. The skin and especially the gills of salmon – not just the surface of the fish – are colonised in this way because river water, especially after rainfall, is washed into the fjords and estuaries in which the fish are farmed. This makes it impossible to prevent these germs from entering into fish processing plants. Nor can they be flushed out with water alone. Even the strictest hygiene rules cannot help because, as already stated, listeria infestation is not the result of a lack of hygiene. It is true that in a process like smoking, some of the bacteria may be removed from the fish, but by no means all. The natural and unavoidable colonisation of fish by listeria is seldom extensive in the sense that high germ counts are found. However, the frequency is high, which makes it almost impossible to monitor processing of the pathogen in the plant. As the fish are processed further, we must therefore assume that not only will the fish itself no longer meet food safety requirements, but that listeria may spread further within the plant via the tools etc. used in processing. Our understanding of the action of the bacteriophages used against listeria is that they may be classed as processing aids.
State General Laboratory, Ministry of Health **Cyprus**	**General Comments**	In general we agree with the approach of the Panel on Biological Hazards, concerning the use of bacteriophages in food production We do support the followings: 1. The authors statements that "it can not be concluded whether bacteriophages are able or unable to protect against recontamination of food with bacterial pathogens". 2. The recommendation of the Panel on Biological Hazards lines 43-45. 3. With the final conclusions and recommendations lines 760-804.

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CIAA (Confederation of the Food and Drink Industries of the EU) **BEL**	**General Comments**	We would like to thank you for providing us with the opportunity to comment on the EFSA draft Opinion on the use and mode of action of bacteriophages in food production. The Confederation of the Food and Drink Industries of the EU (CIAA) strongly supports the need for bacteriophages as a crucial tool in the fight against dangerous foodborne bacteria. We note moreover that according to the definition provided in the new Additives Regulation EC/1333/2008, processing aids are "*substances not consumed as food itself but used intentionally in the processing of foods, which only remain as residues in the final food and do not have a technological effect in the final product.*" Therefore, we would strongly support the classification of bacteriophages as a **processing aid**, given that phages act immediately after application, before being inactivated through adsorption in the food matrix, and therefore have no function in the final food product. In addition, phages do not act as decontaminants, like chorine, and therefore cannot replace proper hygiene measures. Consequently, they should not be classified as such. The application of phages works only as a component of a hygiene regime. Finally, the use of phages does not allow the extension of the product shelf life as not all other microorganisms are affected.

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FEEDAP Panel **EFSA**	**General Comments**	We would like to thank the BIOHAZ Panel for the possibility to comment this very interesting document. As a result of the publication for consultation of the aforementioned draft opinion, the FEEDAP Panel has discussed it in the last plenary meeting held in Parma on March 3-5. Please find below the comments derived thereof: Although the Commission is not seeking advice regarding the safety of bacteriophages in food, the FEEDAP Panel retains that, in case of an agent sought for the control of pathogenic bacteria in the food chain, mode of action, efficacy and safety are closely connected. Any failure in efficacy may result in outgrowth of pathogenic bacteria in food, exposing the consumer to unsafe products. Moreover, bacteriophages as such may pose a risk for the consumers. Bacterial viruses are involved in the horizontal transfer of antibiotic resistances and of key virulence factors in several relevant food pathogens, such as *Clostridium botulinum*, Shiga toxin producing *Escherichia coli* and *Salmonella enterica*. Since bacteriophages are reproduced in strains belonging to pathogenic species, the risk of transducing genetic determinants from production strains to wider bacterial communities in food or in the gastrointestinal tract should be discussed. Phage-mediated genetic exchange of virulence determinants has been actually reported between different bacterial species and genera, making an additional risk associated to the spread of virulence determinants in bacterial communities more than just a theoretical possibility. For example, in an experiment modelling phage therapy for bovine mastitis, the transfer of a staphylococcal pathogenicity island, containing superantigen genes, from *Staphylococcus aureus* to *Listeria monocytogenes* in raw milk was observed. **Conclusion to the Terms of reference 2** Although the presence of bacterial defence mechanisms against bacteriophages has been recognized in the text, no specific comment has been made on this issue in the conclusions of ToR(ii). The use of bacteriophages may lead to the emergence of BIMs (bacteriophages insensitive mutants) or select strains harbouring specific resistance mechanisms, such as restriction and modification and abortive infection systems. Several studies and the analysis of bacterial genomes, including those of food pathogenic bacteria, have revealed that bacteriophages resistance mechanisms are widely diffused in Prokaria. Therefore the emergence of phage resistant strains could be foreseen. This may interfere with the continual functioning of bacteriophages in the food for the control of pathogenic bacteria. As a last comment, the assessment of bacteriophages in feed falls under the remit of the FEEDAP Panel and therefore a common approach would be advisable and desirable.