

**17 March 2016**  
**[07–16]**

## Approval Report – Application A1111

### Bacteriophage S16 & FO1a as a Processing Aid

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Food Standards Australia New Zealand (FSANZ) has assessed an application made by Microos B.V. to approve a preparation of two bacteriophages (S16 and FO1a), *Salmonex*<sup>TM</sup>, (hereafter referred to as *Salmonella* phage) as a processing aid to reduce *Salmonella* spp. contamination in specific foods.

On 25 September 2015, FSANZ sought submissions on a draft variation and published an associated report. FSANZ received six submissions.

FSANZ approved the draft variation on 3 March 2016. The Australia and New Zealand Ministerial Forum on Food Regulation (Forum) was notified of FSANZ's decision on 16 March 2016.

This Report is provided pursuant to paragraph 33(1)(b) of the *Food Standards Australia New Zealand Act 1991* (the FSANZ Act).

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### Supporting document

The following document which informed the assessment of this Application is available on the FSANZ website at

<http://www.foodstandards.gov.au/code/applications/Pages/A1111BacteriophageS16-F01asPA.aspx>

SD1 Risk Assessment (At Approval)

## Executive summary

FSANZ received an application (A1111) from Microcos B.V. on 13 March 2015, seeking to permit a *Salmonella* phage preparation (S16 and FO1a), Salmonalex™ (subsequently called *Salmonella* phage in this report), for use as a processing aid to reduce *Salmonella* spp. during post-slaughter processing of fresh meat and poultry products.

*Salmonella* is one of the most commonly reported causes of foodborne illness, with raw fresh meat and poultry often implicated as a source of infection. Fresh raw meat and poultry can be contaminated with *Salmonella* which can cause illness if meat is consumed under-cooked or if cross contamination occurs during handling and preparation.

Use of *Salmonella* phage has been proposed as an additional control measure available to processors to reduce the concentration of pathogenic *Salmonella* spp. on raw meat and raw poultry meat.

Bacteriophages are viruses that infect and break down bacterial cells. They are specific to the strains of bacteria they infect and are not pathogenic to plants, animals or humans. Bacteriophages cannot actively locate bacterial cells; they are non-motile and rely on passive diffusion to locate and attach to receptor sites on target bacterial cells. Their use is not meant as a replacement for good hygienic practices nor as an alternative to approved and effective cleaning and sanitising agents generally used in the food industry.

The Applicant has provided evidence that the *Salmonella* phage is highly specific to *Salmonella* species and is for use during post-slaughter processing of raw meat and raw poultry meat. Challenge studies provided in the Application have demonstrated that an average reduction of 1.56 log can be achieved following surface treatment on these foods. *Salmonella* phage should be viewed as an additional tool for control of *Salmonella* in food, supplementing Good Manufacturing Practices (GMP), Hazard Analysis Critical Control Points (HACCP) and other measures aimed at reducing *Salmonella* contamination, and should not be seen as a replacement of good hygiene. These approaches in combination will reduce the community's exposure to *Salmonella* from raw meat and raw poultry meat resulting in less foodborne illness attributed to these sources.

No permissions currently exist for the *Salmonella* phage in the table to section S18—9 in Schedule 18. Permission does exist for another phage preparation, *Listeria* phage P100, which is specific for *Listeria monocytogenes* and is permitted for use as a listericidal treatment on approved food for use of phage under conditions of GMP.

FSANZ's risk assessment concluded that the *Salmonella* phage is completely characterised and its use, as proposed by the Applicant, was technologically justified and safe. Challenge studies were assessed to determine the efficacy and duration of technical function of Salmonalex™ on the surface of raw meat and raw poultry portions. Safety was assessed by considering the potential toxicity and allergenicity of the phage preparation when produced and used according to GMP. It was further concluded that the *Salmonella* phage is likely to maintain its efficacy (not develop reduced sensitivity to *Salmonella* spp.) provided appropriate GMP and good handling practices are maintained during processing.

FSANZ has approved a draft variation to permit use of *Salmonella* phage in the table to section S18—9. The approved draft variation differs from the variation circulated with the Call for Submissions. The drafting was amended to clarify use of the *Salmonella* phage only on the surfaces of raw meat and raw poultry meat during processing.

Permitted processing aids also require an appropriate specification for identity and purity. No specification monographs for the *Salmonella* phage exist within the references in sections S3—2 and S3—3 of Schedule 3. The draft variation also therefore includes specifications in Schedule 3 of the Code.

A soy peptone product is used during the manufacture of the *Salmonella* phage. Food manufacturers who use the *Salmonella* phage as a processing aid need to be aware of their responsibilities under subsection 1.2.3—4 should any residual soy product be present in the final food.

# 1 Introduction

## 1.1 The Applicant

The Applicant is Microcos B.V., a company specialising in supply of antibacterial products for human health and food safety.

## 1.2 The Application

FSANZ received an application (A1111) from Microcos B.V. on 13 March 2015, seeking to permit a *Salmonella* phage preparation (S16 and FO1a), tradename Salmonex<sup>TM</sup>, (subsequently called *Salmonella* phage in this report) for use as a processing aid aimed at reducing *Salmonella* spp. during post-slaughter processing of fresh raw meat and fresh raw poultry meat.

*Salmonella* is one of the most commonly reported causes of foodborne illness, with fresh raw meat and poultry often implicated as a source of infection. Fresh raw meat and poultry can be contaminated with *Salmonella* which can cause illness if meat is consumed under-cooked or if cross contamination occurs during handling and preparation.

Meat is susceptible to *Salmonella* contamination during processing, with poultry meat more susceptible than other meat. Poultry processing is a highly automated industry in which many points exist for cross-contamination when *Salmonella*-positive birds enter the processing plant. To address the multiple points where birds may be contaminated, several antimicrobial controls are applied at various steps during processing. This multi-hurdle approach usually results in multiple antimicrobial interventions being used. Generally, sites where antimicrobials are applied include online reprocessing or inside/outside bird wash stages, the poultry chiller and post-chill applications where carcasses are disassembled.

Phages are viruses that infect and break down bacterial cells. They are specific to the strains of bacteria they infect and are not pathogenic to plants, animals or humans and have therefore been considered safe for use in environmental, veterinary, agricultural, clinical and food-related applications. They are naturally abundant in saltwater, freshwater, soil, plants and animals (including people) and have been shown to be unavoidably present in foods.

Bacteriophages cannot actively locate bacterial cells; they are non-motile and rely on passive diffusion to locate and attach to receptor sites on target bacterial cells. They are not meant as a replacement of good hygienic practices nor as an alternative to approved and effective cleaning and sanitising agents generally used in the food industry.

The Applicant stated the *Salmonella* phage was highly specific to *Salmonella* species and would be used during post-slaughter processing of raw meat. Further, the use of the *Salmonella* phage should be viewed as an additional tool for control of *Salmonella* in food, GMP, HACCP and other measures aimed at reducing *Salmonella* contamination, and should not be seen as a replacement for good hygiene.

## 1.3 The current Standard

Paragraph 1.1.1—10(4)(c) in the *Australia New Zealand Food Standards Code* (the Code), provides that a food for sale must not have, as an ingredient or a component, a substance that is used as a processing aid, unless expressly permitted.

Section 1.1.2—13 defines the expression 'used as a processing aid'. Section 1.3.3—11 and the table to section S18—9 in Schedule 18 permit the use of processing aids that perform various technological functions in food.

No permissions currently exist for the *Salmonella* phage in the table to section S18—9.

Permission does exist for another phage preparation, *Listeria* phage P100, which is specific for *L. monocytogenes* and is permitted for use as a listericidal treatment on approved food for use of phage under conditions of GMP, in accordance with section S18—9.

In accordance with section 1.1.1—15, all permitted processing aids must comply with relevant specifications which are set out in Schedule 3. No specifications for the *Salmonella* phage are listed in specifications under section S3—2 (Substances with specifications in primary sources) or section S3—3 (Substances with specifications in secondary sources). Therefore, specifications for the *Salmonella* phage are proposed to be included in Schedule 3.

### 1.3.1 International Standards

Codex Alimentarius does not list standards for either processing aids or bacteriophages. Individual countries regulate the use of processing aids and bacteriophages differently. A number of permissions for bacteriophages used as processing aids in foods are provided in international regulations.

The European Food Safety Authority (EFSA) issued a scientific opinion in 2009 on the general use of bacteriophages in food products and concluded that each phage/food application should be considered on a case-by-case basis, taking into consideration the biology and safety aspects of each bacteriophage and the food matrix to which it is applied (EFSA 2009). In 2012, EFSA released an opinion on the safety and efficacy of using Listex P100™ to treat raw fish.

A number of Generally Recognized as Safe (GRAS) notifications have been made to the United States Food and Drug Administration (USFDA) for various *Salmonella* and *Listeria* bacteriophage preparations for use in foods.

#### 1.3.1.1 *Salmonella* bacteriophages

In December 2013, GRAS Notice No. GRN468, submitted by the Applicant (Microcos B.V.) to the USFDA, received a 'no questions' notification for the use of bacteriophage preparation S16 and FO1a (Salmonex™), as an antimicrobial to control *Salmonella* in meat and poultry, at up to 10<sup>8</sup> plaque forming units per gram (pfu/g) of food. This is the same phage preparation and intended use as proposed in this Application.

Intralytix Inc., a competitor to Microcos B.V., also received a 'no questions' notification from the USFDA in February 2013 to GRAS Notice, No. GRN435 for use of a preparation containing six bacterial monophages specific to *Salmonella* (tradename SalmoFresh™) for use as an antimicrobial in certain poultry products, fish, shellfish, and fresh and processed fruits and vegetables at levels up to 10<sup>7</sup> pfu/g.

### **1.3.1.2 *Listeria bacteriophages***

In 2014, the USFDA issued a 'no questions' notification to GRAS Notice No. GRN528 submitted by Intralytix Inc. The submission was for use of a preparation containing six bacterial monophages (LIST-36, IMSP-25, IMTA-34, IMT-57, IMTA-94 and IMTA-148) specific to *L. monocytogenes* (tradename ListShield™), for use as an antimicrobial to control *L. monocytogenes* in fish and shellfish, fresh and processed fruits, fresh and processed vegetables, and dairy products applied to food surfaces at levels up to  $1 \times 10^6$  pfu/g.

In 2012, FSANZ approved an application (Application A1045) submitted by the Applicant to this Application (Microcos B.V.), to permit the use of *Listeria* phage P100 (tradename Listex P100™) as a processing aid on approved foods for use of phage under conditions of GMP.

The product Listex P100™ is also approved for use in a number of other countries:

- The Dutch Ministry of Public Health permitted use of Listex P100™ as a processing aid for use on all foods in The Netherlands in July 2009.
- Listex P100™ is self-assessed GRAS in the USA in cheese (GRAS Notice No. GRN198 in 2006), and was extended to all food products susceptible to contamination with *L. monocytogenes* in 2007 (GRAS Notice GRN218), with labelling provisions. In 2011, USDA permitted its use as a processing aid on RTE meat and poultry products without labelling requirements.
- Health Canada issued a '*letter of no objection*' for use of Listex P100™ for use as a processing aid in several foods in 2010.

## **1.4 Reasons for accepting Application**

The Application was accepted for assessment because:

- it complied with the procedural requirements under subsection 22(2) of the FSANZ Act
- it related to a matter that might be developed as a food regulatory measure.

## **1.5 Procedure for assessment**

The Application was assessed under the General Procedure.

## **1.6 Decision**

The approved draft variation to the Code, as varied after consideration of submissions, and related explanatory statement are at Attachments A and B respectively. The variations are intended to take effect on gazettal. An explanatory statement is required to accompany an instrument if it is lodged on the Federal Register of Legislation.

The draft variation on which submissions were sought is at Attachment C.

# **2 Summary of the findings**

## **2.1 Summary of issues raised in submissions**

A number of issues were raised in submissions. Table 1 outlines the issues raised and FSANZ's response.

Overall, six submissions were received: four from jurisdictions, one industry association and a professional food technology association. Two supported the application with no concerns raised; three generally supported the application but raised a number of concerns, while one did not provide a position. These are discussed below and in Table 1.

### 2.1.1 Response to submissions

A number of submitters raised the issue of whether the *Salmonella* phage has an on-going technological function in various raw meat products, such as mince, and therefore whether it should be classified as a food additive. Several studies were also cited indicating reductions of *Salmonella* on various foodstuffs over several days following treatment with various phages. The concerns related to on-going functionality, and therefore whether *Salmonella* phage is more accurately classified as a food additive, centre on three main themes:

- presence of infective phage on foods
- mode of action
- on-going functionality.

As described in SD1, detailed descriptions of the mode of action, use and safety considerations for use of bacteriophages in foods were undertaken during consideration of the *Listeria* phage P100 application, A1045 – Bacteriophage Preparation P100 as a Processing Aid (FSANZ 2012)<sup>1</sup>. Many of the concerns raised in submissions reflect those that arose during assessment of Application A1045. Hence, where relevant, readers will also be directed to sections of the A1045 documents as appropriate, to address concerns raised.

#### 2.1.1.1 On-going technological function

A submitter cited *Salmonella* phage studies by Bigwood et al (2008) on raw beef cuts and Sharma et al. (2015) on turkey cutlets which showed reductions of *Salmonella* following phage application for up to 8 and 7 days, respectively. The submitter argued that these reductions demonstrated that the phage retains its infectivity and therefore technological function for periods beyond the initial treatment.

Evidence presented in the Application demonstrated no on-going technological function when the phage is used as intended (refer section 6 of SD1). FSANZ noted in SD1:

*Since Salmonella doesn't grow at 4°C, the statistical analysis of the challenge studies for the Salmonella phage is different to that undertaken for the previously assessed bacteriophage, Listeria phage P100.*

and continued:

*It may be hypothesised that for Salmonella on solid foods treated with the Salmonella phage and stored at 4°C, the regression lines fitted to the control and treatment concentration data would be parallel but with slopes equal to zero (i.e. horizontal lines) as no growth would occur. A difficulty in analysing data for Salmonella below the minimum growth temperature is the possibility of non-thermal inactivation due to cold temperatures which are unrelated to the presence of the Salmonella phage.*

Both Bigwood et al (2008) and Sharma et al (2015) performed the phage challenge experiments at temperatures below the minimum growth temperature for *Salmonella*, 5°C and 4°C, respectively. As a result, some inactivation may be expected to occur irrespective of the presence of phage on the meat surface.

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<sup>1</sup> <http://www.foodstandards.gov.au/code/applications/Pages/applicationa1045bact4797.aspx>

Interpretation of the Bigwood et al (2008) study is difficult due to the inconsistency between the short (up to 24 hours) and long (up to 8 days) incubation studies. Greater inactivation was observed for the short time experiments. The authors noted that the concentration of *Salmonella* cells declined slowly with storage time in both treated and untreated samples, since growth is not possible for *Salmonella* at 5°C.

Sharma et al (2015) reported *Salmonella* concentrations on turkey cutlets on day 0<sup>+</sup> (after an unspecified contact time) and days 1 and 7 following treatment with phage cocktail of six *Salmonella* monophages (Intralytix SalmoFresh™) and then stored at 4°C. Statistically significant differences were found between the control (untreated) and the phage treated samples on each of the three sampling days demonstrating a technological function of the phage cocktail. Although not specifically tested, there was only a small, but likely not statistically significant, change in concentration between day 0<sup>+</sup> and 1 for the phage treated samples. Further declines were observed for both the untreated (0.5 log) and treated (1.2 log) groups between day 1 and 7 of the study. That no difference in *Salmonella* concentration was observed in the phage treated samples between day 0<sup>+</sup> and 1 supports the conclusion that phage activity is of limited duration. That both experimental groups show declines in concentration between day 1 and 7, can be explained by non-thermal inactivation. These results therefore do not support the argument for on-going technological function of the phage cocktail on turkey cutlets.

### **2.1.1.2 Presence of infective phage**

Bacteriophages can persist on treated foods for up to 1-2 weeks. As discussed in section 2.1.2 of SD2 to Application A1045<sup>2</sup>, the presence of infectious phage in food does not mean it should be classified as a food additive. There is an important distinction between being able to isolate so called 'infective' phages from treated food surfaces, even after several days' storage, and these phages having functionality to seek, locate and destroy bacteria.

The definition of processing aid in Standard 1.3.3 does not require that the processing aid be absent from the food. Furthermore, presence on or in the food for sale does not automatically mean that a bacteriophage preparation would be considered a food additive. Presence is therefore not a criterion used to make a distinction between phage preparations as processing aids or food additives.

### **2.1.1.3 Mode of action**

For phage treatment to be effective it must satisfy requirements relating to distribution and diffusion, and be at a high enough concentration. Phages are non-mobile and, without diffusion, are unable to reach and attach to target cells. Guenther (2012) showed re-growth of *Salmonella* following initial phage treatment, despite infectious phage still being present in the samples. This effect can be explained by the immobilisation of the virus particles on the food surfaces – generally within 12–24h. The mode of action for effective use of phage is discussed in further detail in Section 1.2 of SD1 to Application A1045<sup>3</sup>.

Some submitters argued there is potential for on-going technological function of phage following initial treatment on raw meat surfaces when brought into contact with more *Salmonella*, such as through the action of mincing or other physical mixing or handling.

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<sup>2</sup> [http://www.foodstandards.gov.au/code/applications/documents/A1045\\_SD2.pdf](http://www.foodstandards.gov.au/code/applications/documents/A1045_SD2.pdf)

<sup>3</sup> [http://www.foodstandards.gov.au/code/applications/documents/A1045\\_SD1.pdf](http://www.foodstandards.gov.au/code/applications/documents/A1045_SD1.pdf)



Mincing raw meat post surface application of phage may allow remnant *Salmonella* into contact with infective, but immobilised phage. However, to see any effective reduction in the low levels of contamination typically seen in raw meat requires a high density of phage particles (ie  $10^8$  pfu/cm<sup>2</sup> or pfu/ml) and a contact time longer than 2 minutes (Abedon 2009). Mincing raw meat following treatment of the raw meat with phage dramatically increases the surface area of the food, thereby reducing the concentration of phage available. This effect was demonstrated by Sharma et al. (2015) where surface treatment of turkey breast with phage prior to grinding was not shown to be effective in reducing *Salmonella*.

**Table 1: Summary of issues**

Issue	Submitter	FSANZ response (including any amendments to drafting)
<p><b>Allergen labelling requirements</b></p> <p><b>Suggests manufacturer should clarify whether and to what extent any soy peptone may be carried over into final product</b></p>	<p>Food Technology Association of Australia</p>	<p>As discussed in section 2.2.2 of the assessment summary, a soy peptone buffer is used as a medium during the production of the <i>Salmonella</i> phage. It is the responsibility of a food manufacturer using the processing aid to be aware of their responsibilities under section 1.2.3—4 for labelling the final food.</p>
<p><b>Host range</b></p> <p><b>Suggests it would be useful to have more information about the effectiveness of the phage against the large number of <i>Salmonella</i> strains and serotypes, and addressing any potential risks of phage-resistance.</b></p>	<p>NSW Food Authority</p>	<p>FSANZ discussed the host range of the <i>Salmonella</i> phage in Section 2.2.1 of SD1. The <i>Salmonella</i> phage product (Salmonexlex™) comprises two phages – S16 and FO1a.</p> <p>S16 recognises outer membrane protein C (OmpC) which is present on all <i>Salmonella</i> strains, regardless of serovar. FO1a recognizes a part of the LPS molecule that is not variable. All <i>Salmonella</i> strains feature an Rs chemotype and have an N-acetylglucosamine residue in the outer core. This is the receptor for FO1a. FO1a infects even the second species in the genus <i>Salmonella</i> i.e. <i>S. bongori</i>.</p> <p>These two mechanisms ensure the <i>Salmonella</i> phage is effective against a broad host range.</p> <p>The issue of the potential for phage-resistance was discussed in section 2.2.2 of SD1. FSANZ is of the view that given the nature of application (high dosage of bacteriophage to low numbers of target bacteria), the breadth of the host range, and use of Good Hygienic Practices (GHP) in the production facility, the potential for reduced efficacy of the <i>Salmonella</i> phage due to the presence of phage-resistant <i>Salmonella</i> is minimal. This view is consistent with that of other international regulators regarding the application of bacteriophages in food manufacture.</p>

Issue	Submitter	FSANZ response (including any amendments to drafting)
<p><b>Clarification of intended use</b>  <b>Concerns regarding permitting use ‘in’ raw meat.</b>  <b>Suggests current drafting would not exclude the use of it in products such as mince, minced products (eg chicken nuggets), sausages, rissoles, manufactured meats, fermented comminuted meat products, pate, meat spreads, reformed meat products.</b>  <b>These products have not been assessed and may have on-going technological function.</b></p> <p><b>Notes the Code includes poultry meat in the definition of meat in Standard 2.2.1, but Schedule 22 makes a distinction between mammalian meat and poultry meat.</b>  <b>Suggests this may cause confusion.</b></p>	<p>Queensland Health,  NZ Ministry for  Primary Industries</p>	<p>The proposed drafting presented in the assessment summary gave permission for use of the <i>Salmonella</i> phage on or in raw meat during processing. The issue of application to meat products that are then mixed or minced does not change the assessment of technological function. As discussed in Section 2.1.1.3 above, no effective reduction was seen in minced meat when <i>Salmonella</i> phage was applied to the surface prior to mincing. FSANZ agrees that allowing use of the <i>Salmonella</i> phage ‘in’ raw meat may allow its use in products where there is no demonstrated efficacious use and has amended the drafting accordingly.</p> <p>Presence of <i>Salmonella</i> phage on or in food does not define it as a food additive or processing aid, rather, whether it has an on-going technological function. If the <i>Salmonella</i> phage has an on-going technological function, it ceases to be a processing aid as defined in subclause 1(1) of Standard 1.3.3, and operates instead as a food additive. <i>Salmonella</i> phage is not permitted for use as a food additive.</p> <p>FSANZ acknowledges the current drafting may cause unintended confusion and has amended the drafting to clarify use of the <i>Salmonella</i> phage on the surface of both raw meat and raw poultry meat.</p>
<p><b>Interference with <i>Salmonella</i> detection</b>  <b>Suggests the presence of phage in the food during sampling for routine testing of <i>Salmonella</i> could result in false negatives.</b></p>	<p>NZ Ministry for Primary  Industries</p>	<p>This issue was also addressed in section 2.5 of SD2 for A1045. FSANZ concluded that the treatment of foods with phage is unlikely to result in false negative results when an enrichment step is included. The same argument applies to <i>Salmonella</i> phage.</p>

Issue	Submitter	FSANZ response (including any amendments to drafting)
<p><b>More suitably classified as a food additive</b></p> <p><b>See above regarding 'on-going technological function' concerns</b></p>	<p>NZ Ministry for Primary Industries, NSW Food Authority, Queensland Health</p>	<p>Food additives perform an on-going technological function in the final food (such as a preservative), while processing aids perform their technological function during manufacture or processing of the food but have no on-going function in the final food.</p> <p>The consideration of technological function is summarised in section 2.1 of SD1, and in more detail in SD1 for the Approval Report for the assessment of A1045. The assessment of the function of the phage for this Application confirms the earlier conclusion that <i>Salmonella</i> phage performs as a processing aid and not as a food additive as its function is ineffective soon after application to the food (see section 6.2 of SD1).</p>
<p><b>The need for the Applicant to contact the biosecurity authority of Australia and Environmental Protection Authority of New Zealand</b></p>	<p>NZ Ministry for Primary Industries</p>	<p>The same concern was raised during the assessment of A1045. As the Applicant is the same for both applications, and was advised of this requirement previously, it is reasonable to assume the Applicant is aware of their responsibilities prior to importing any product.</p>

## 2.2 Risk assessment

FSANZ conducted a risk assessment on the use of the *Salmonella* phage which considered the technological suitability, the potential hazards and any public health and safety issues arising from use of the *Salmonella* phage to treat food. A brief overview of the assessment is provided below – refer to SD1 for full details.

The stated purpose for the *Salmonella* phage is as a processing aid to reduce *Salmonella* during post-slaughter processing of raw fresh meat and poultry. FSANZ investigated how the *Salmonella* phage performs its technological function when used as proposed by the Applicant. In assessing the technological function, both efficacy (ability to reduce numbers of *Salmonella* on application) and on-going technological function (ability to *continuously* reduce bacterial numbers) were considered. On-going technological function was qualitatively assessed from the changes in *Salmonella* concentration throughout the challenge studies provided by the Applicant. Efficacy was determined by statistical analysis of *Salmonella* concentrations between untreated and treated samples at different times.

Overall, the *Salmonella* phage was found to be efficacious and does not have an on-going technological function on raw fresh meat and poultry products. How the *Salmonella* phage is applied to the surface (spraying vs dipping), the concentration of the phage and the contact time prior to further processing (eg mincing), are all factors which would need consideration before use. The *Salmonella* phage is highly specific to *Salmonella* species and is intended for use during post-slaughter processing of fresh meat. Use of the *Salmonella* phage should be viewed as an additional tool for control of *Salmonella* in food, supplementing GMP, HACCP and other measures aimed at the reducing *Salmonella* contamination, and should not be seen as a replacement of good hygiene. The *Salmonella* phage is likely to maintain its efficacy (ie remain effective at reducing *Salmonella* spp.) provided appropriate GMP and good handling practices are maintained during processing.

The *Salmonella* phage is unlikely to pose any health risk due to toxicity or allergenicity when used as intended to treat the surface of fresh raw meat and poultry. Further, the proposed use of the *Salmonella* phage as a processing aid to reduce the populations of *Salmonella* during post-slaughter processing of raw fresh meat and poultry, is technologically justified in the form and prescribed amounts, and demonstrated to be effective. The *Salmonella* phage is completely characterised and there is no on-going technological function performed when used as intended.

## 2.3 Risk management

The conclusions of the risk assessment were that the use of the *Salmonella* phage was safe for use and technologically justified for the intended purpose. FSANZ has considered the risk management matters relevant to the Application.

### 2.3.1 Specification for *Salmonella* phage preparation (S16 and FO1a)

There are no specifications for *Salmonella* phage in any of the primary or secondary references for specifications or in Schedule 3 – Identity and Purity. A proposed specification has been prepared and is included in the approved draft variations at Attachment A.

Consistent with specifications written for *Listeria* phage P100, specifications for lead and arsenic are addressed by the requirements of section S3—4. The Applicant has demonstrated that the *Salmonella* phage is manufactured according to GMP.

The Application provided product specifications including microbial limits for the *Salmonella* phage. The Applicant also provided results confirming production of the preparation to meet these microbial limits. FSANZ assessed the specifications and results and concluded that there is no need to include microbial limits as part of the proposed *Salmonella* phage specification. There are no concerns that the Applicant cannot produce the *Salmonella* phage without microbial contamination.

### **2.3.2 Labelling considerations**

Soy peptone is used as a medium in the production of the *Salmonella* phage. A soy peptone-salt buffer is used to elute the bound phages from the chromatography column. Soybean products are identified as substances requiring declaration due to section 1.2.3—4 of the Code if present in a food for sale. Food manufacturers who use the *Salmonella* phage as a processing aid need to be aware of their responsibilities under section 1.2.3—4.

## **2.4 Risk communication**

Consultation is a key part of FSANZ's standards development process. FSANZ acknowledges the time taken by individuals and organisations to make submissions on this Application. Every submission on an application or proposal was considered by the FSANZ Board. All comments are valued and contribute to the rigour of our assessment.

FSANZ developed and applied a basic communication strategy to this Application. The call for submissions was notified via the Food Standards Notification Circular, media release, FSANZ's social media tools and Food Standards News.

The process by which FSANZ considers standard development matters is open, accountable, consultative and transparent. Public submissions were called to obtain the views of interested parties on issues raised by the Application and the impacts of regulatory options.

The FSANZ Board considered the draft variation taking into account public comments received from the call for submissions.

The FSANZ Board's decision has been notified to the Australia and New Zealand Ministerial Forum on Food Regulation<sup>4</sup> (the Forum). If the decision is not subject to a request for a review, the Applicant and stakeholders including the public will be notified of the gazettal of the variation to the Code in the national press and on the FSANZ website.

## **2.5 FSANZ Act assessment requirements**

### **2.5.1 Section 29**

#### **2.5.1.1 Cost benefit analysis**

FSANZ was required to consider the impact of various regulatory and non-regulatory options on all sectors of the community, especially relevant stakeholders who may be affected by this Application. The benefits and costs associated with the proposed amendments to the revised Code have been considered using regulatory impact principles. The level of analysis was commensurate with the nature of the Application and significance of the impacts.

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<sup>4</sup> Convening as the Australia and New Zealand Food Regulation Ministerial Council

The Office of Best Practice Regulation, in a letter dated 24 November 2010 (reference 12065), provided a standing exemption from the need to assess if a Regulation Impact Statement is required for applications relating to processing aids as they are machinery in nature and their use is voluntary.

Notwithstanding this exemption, FSANZ undertook a limited impact analysis and concluded that the direct and indirect benefits that would arise from a food regulatory measure developed or varied as a result of the Application outweighed the costs to the community, Government or industry that would arise from the development or variation of the food regulatory measure. The risk assessment concludes there is no public health and safety risk from use of the *Salmonella* phage preparation. Use of the product provides the opportunity for reduced risk of illness from salmonellosis which benefits both consumers and government.

#### **2.5.1.2 Other measures**

There are no other measures (whether available to FSANZ or not) that would be more cost-effective than a food regulatory measure developed or varied as a result of the Application.

#### **2.5.1.3 Any relevant New Zealand standards**

Schedules 3 and 18 apply in New Zealand. There are no other relevant New Zealand Standards.

#### **2.5.1.4 Any other relevant matters**

Other relevant matters are explained below.

### **2.5.2 Subsection 18(1)**

FSANZ has also considered the three objectives in subsection 18(1) of the FSANZ Act during the assessment.

#### **2.5.2.1 Protection of public health and safety**

FSANZ has undertaken a safety assessment (SD1) and concluded that there are no public health and safety concerns related to use of *Salmonella* phage as a processing aid. Additionally, the use of *Salmonella* phage to treat raw meat and raw poultry meat will reduce the exposure of the community to *Salmonella* from these foods resulting in less illness. This will reduce the burden on Government to treat illnesses associated with salmonellosis.

#### **2.5.2.2 The provision of adequate information relating to food to enable consumers to make informed choices**

No issues have been identified for this Application relevant to this objective. The labelling requirements for this processing aid are discussed in Section 2.3.2 – Labelling considerations.

#### **2.5.2.3 The prevention of misleading or deceptive conduct**

No issues were identified for this Application relevant to this objective.

### **2.5.3 Subsection 18(2) considerations**

FSANZ has also had regard to:

- **the need for standards to be based on risk analysis using the best available scientific evidence**

FSANZ has used the best available scientific evidence to conduct the risk analysis which is provided in SD1. The Applicant submitted a dossier of evidence as part of their Application. Other technical information including scientific literature was also used in assessing the Application.

- **the promotion of consistency between domestic and international food standards**

Section 1.3.1 describes the current permissions for various bacteriophages in different countries. The attributes of using bacteriophages as a component of food safety management systems to control bacterial contamination on foods has been described.

- **the desirability of an efficient and internationally competitive food industry**

The food industry will make their own economic decisions, taking account of costs and benefits of using phage as part of their hurdle technology to control *Salmonella* to determine if it benefits their business.

- **the promotion of fair trading in food**

No issues were identified for this Application relevant to this consumer protection objective.

- **any written policy guidelines formulated by the Forum on Food Regulation**

The *Addition to Food of Substances other than Vitamins and Minerals*<sup>5</sup> includes specific order policy principles for substances added to achieve a solely technological function, such as processing aids. These specific order policy principles state that permission should be granted where:

- the purpose for adding the substance can be articulated clearly by the manufacturer as achieving a solely technological function (i.e. the 'stated purpose')
- the addition of the substance to food is safe for human consumption
- the amounts added are consistent with achieving the technological function
- the substance is added in a quantity and a form which is consistent with delivering the stated purpose
- no nutrition, health or related claims are to be made in regard to the substance.

FSANZ has determined that permitting the use of *Salmonella* phage as a processing aid is consistent with the specific order policy principles for 'Technological Function'.

### 3 References

Abedon ST (2009), *Kinetics of phage-mediated biocontrol of bacteria*, Foodborne Pathogens and Disease 6(7):807–815

Bigwood T, Hudson JA, Billington C, Carey-Smith GV, Heinemann JA (2008) Phage inactivation of foodborne pathogens on cooked and raw meat. Food Microbiology 25:400-406

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<sup>5</sup> <http://www.foodstandards.gov.au/code/fofr/fofrpolicy/pages/default.aspx>



EFSA (2009). "The use and mode of action of bacteriophages in food production", Scientific Opinion of the EFSA Panel on Biological Hazards (BIOHAZ) – EFSA Journal 2009:1076  
<http://www.efsa.europa.eu/en/efsajournal/pub/1076>

Guenther S, Herzig O, Fieseler L, Klumpp J, Loessner MJ (2012) Biocontrol of *Salmonella* Typhimurium in RTE foods with the virulent bacteriophage FO1-E2. International Journal of Food Microbiology 154:66-72

Sharma CS, Dhakal J, Nannapaneni R (2015) Efficacy of lytic bacteriophage preparation in reducing *Salmonella* in vitro, on turkey breast cutlets and on ground turkey. Journal of Food Protection 78(7):1357-1362

US FDA (2013) GRAS Notice No. GRN 468 Preparation containing the bacterial monophages, Fo1a and S16, specific to *Salmonella*. Submitted by Microcos B.V. to U.S. Food and Drug Administration (US FDA), on 30 April 2013. Releasable dossier and Agency Response Letter available at this link  
[http://www.accessdata.fda.gov/scripts/fdcc/?set=GRASNotices&id=468&sort=GRN\\_No&order=DESC&startrow=1&type=basic&search=468](http://www.accessdata.fda.gov/scripts/fdcc/?set=GRASNotices&id=468&sort=GRN_No&order=DESC&startrow=1&type=basic&search=468) Accessed on 7 September 2015

US FDA (2013) GRAS Notice No. GRN 435 Preparation consisting of six bacterial monophage specific to *Salmonella enterica* (monophage cocktail). Submitted by Intralytix, Inc. to U.S. Food and Drug Administration (US FDA), on 6 July, 2012. Releasable dossier and Agency Response Letter available at this link  
[http://www.accessdata.fda.gov/scripts/fdcc/?set=GRASNotices&id=435&sort=GRN\\_No&order=DESC&startrow=1&type=basic&search=435](http://www.accessdata.fda.gov/scripts/fdcc/?set=GRASNotices&id=435&sort=GRN_No&order=DESC&startrow=1&type=basic&search=435) Accessed on 7 September 2015

US FDA (2013) GRAS Notice No. GRN 528 Preparation containing six bacterial monophages (LIST-36, LMSP-25, LMTA-34, LMTA-57, LMTA-94 and LMTA-148) specific to *Listeria monocytogenes*. Submitted by Intralytix, Inc to U.S. Food and Drug Administration (US FDA), on 31 July 2014. Releasable dossier and Agency Response Letter available at this link  
[http://www.accessdata.fda.gov/scripts/fdcc/?set=GRASNotices&id=528&sort=GRN\\_No&order=DESC&startrow=1&type=basic&search=528](http://www.accessdata.fda.gov/scripts/fdcc/?set=GRASNotices&id=528&sort=GRN_No&order=DESC&startrow=1&type=basic&search=528) Accessed on 7 September 2015

US FDA (2013). GRAS Notice No. GRN 198 Bacteriophage P100 preparation from *Listeria innocua*. Submitted by EBI Food Safety B.V. to U.S. Food and Drug Administration (US FDA), on 20 April 2006. Releasable dossier and Agency Response Letter available at this link  
[http://www.accessdata.fda.gov/scripts/fdcc/?set=GRASNotices&id=198&sort=GRN\\_No&order=DESC&startrow=1&type=basic&search=198](http://www.accessdata.fda.gov/scripts/fdcc/?set=GRASNotices&id=198&sort=GRN_No&order=DESC&startrow=1&type=basic&search=198) Accessed on 7 September 2015

US FDA (2013) GRAS Notice No. GRN 218 Bacteriophage P100 preparation from *Listeria innocua*, Submitted by EBI Food Safety B.V. to U.S. Food and Drug Administration (US FDA), on 17 December 2006. Releasable dossier and Agency Response Letter available at this link  
[http://www.accessdata.fda.gov/scripts/fdcc/?set=GRASNotices&id=218&sort=GRN\\_No&order=DESC&startrow=1&type=basic&search=218](http://www.accessdata.fda.gov/scripts/fdcc/?set=GRASNotices&id=218&sort=GRN_No&order=DESC&startrow=1&type=basic&search=218) Accessed on 7 September 2015

## Attachments

- A. Approved draft variations to the *Australia New Zealand Food Standards Code*
- B. Explanatory Statement
- C. Draft variations to the *Australia New Zealand Food Standards Code* (call for submissions)

## Attachment A – Approved draft variations to the *Australia New Zealand Food Standards Code*



### Food Standards (Application A1111 – Bacteriophage S16 & FO1a as a Processing Aid) Variation

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The Board of Food Standards Australia New Zealand gives notice of the making of this variation under section 92 of the *Food Standards Australia New Zealand Act 1991*. The variation commences on the date specified in clause 3 of this variation.

Dated [To be completed by Standards Management Officer]

Standards Management Officer  
Delegate of the Board of Food Standards Australia New Zealand

**Note:**

This variation will be published in the Commonwealth of Australia Gazette No. FSC **XX on XX Month 20XX**. This means that this date is the gazettal date for the purposes of clause 3 of the variation.

## 1 Name

This instrument is the *Food Standards (Application A1111 – Bacteriophage S16 & FO1a as a Processing Aid) Variation*.

## 2 Variation to standards in the *Australia New Zealand Food Standards Code*

The Schedule varies a schedule in the *Australia New Zealand Food Standards Code*.

## 3 Commencement

This instrument commences on gazettal.

### Schedule

[1] **Schedule 3** is varied by

[1.1] inserting in the table to subsection S3—2(2) in alphabetical order

*Salmonella* phage preparation (S16 and FO1a)      section S3—33

[1.2] inserting after section S3—32

### **S3—33 Specifications for *Salmonella* phage preparation (S16 and FO1a)**

(1) In this section:

**a preparation** means a *Salmonella* phage preparation (S16 and FO1a).

***Salmonella* phage preparation (S16 and FO1a)** means a solution of a 1:1 blend of *Salmonella* phage S16 and *Salmonella* phage FO1a.

(2) *Salmonella* phage S16 in a preparation must comply with the specification in subsection (4).

(3) *Salmonella* phage FO1a in a preparation must comply with the specification in subsection (5).

(4) The biological classification for *Salmonella* phage S16 in a preparation is the following:

- (a) order—Caudavirales;
- (b) family—Myoviridae;
- (c) genus—T4-like;
- (d) species—*Salmonella* phage S16;
- (e) GenBank Accession Number—HQ331142

(5) The biological classification for *Salmonella* phage FO1a in a preparation is the following:

- (a) order—Caudavirales;
- (b) family—Myoviridae;
- (c) genus—FelixO1-like;
- (d) species—*Salmonella* phage FO1a;
- (e) GenBank Accession Number—JF461087.

[2] Schedule 18 is varied by inserting in the Table to section S18—9 in alphabetical order

<i>Salmonella</i> phage preparation (S16 and FO1a)	Reduce population of <i>Salmonella</i> species on the surface of raw meat and raw poultry meat during processing.	GMP
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## **Attachment B – Explanatory Statement**

### **1. Authority**

Section 13 of the *Food Standards Australia New Zealand Act 1991* (the FSANZ Act) provides that the functions of Food Standards Australia New Zealand (the Authority) include the development of standards and variations of standards for inclusion in the *Australia New Zealand Food Standards Code* (the Code).

Division 1 of Part 3 of the FSANZ Act specifies that the Authority may accept applications for the development or variation of food regulatory measures, including standards. This Division also stipulates the procedure for considering an application for the development or variation of food regulatory measures.

FSANZ accepted Application A1111 which seeks approval for a preparation of two bacteriophages (S16 and FO1a) (tradename Salmorex™) as a processing aid to reduce *Salmonella* contamination in specific foods. The Authority considered the Application in accordance with Division 1 of Part 3 and has proposed a draft variation.

Following consideration by the Australia and New Zealand Ministerial Forum on Food Regulation, section 92 of the FSANZ Act stipulates that the Authority must publish a notice about the standard or draft variation of a standard.

Section 94 of the FSANZ Act specifies that a standard, or a variation of a standard, in relation to which a notice is published under section 92 is a legislative instrument, but is not subject to parliamentary disallowance or sunseting under the *Legislation Act 2003*.

### **2. Purpose**

The Authority has proposed that *Salmonella* phage preparation (S16 and FO1a) be added to the list of approved processing aids with miscellaneous technological functions for use in specific foods. The table to section S18—9 in Schedule 18 lists permissions for these processing aids, as well as the foods and levels which are allowed. An entry for *Salmonella* phage preparation (S16 and FO1a) will be included for use on the surface of raw meat and raw poultry meat during processing at levels up to Good Manufacturing Practice (GMP). A specification stating what the preparation is composed of will also be included into Schedule 3.

### **3. Documents incorporated by reference**

The variations to food regulatory measures do not incorporate any documents by reference.

### **4. Consultation**

In accordance with the procedure in Division 1 of Part 3 of the FSANZ Act, the Authority's consideration of Application A1111 included one round of public consultation following an assessment and the preparation of a draft variation and associated report.

A Regulation Impact Statement was not required because the proposed variation to Schedule 18 and Schedule 3 are likely to have a minor impact on business and individuals.

### **5. Statement of compatibility with human rights**

This instrument is exempt from the requirements for a statement of compatibility with human rights as it is a non-disallowable instrument under section 94 of the FSANZ Act.

## 6. Variation

Item [1] varies Schedule 3.

Item [1.1] amends the table to subsection S3—2(2) by inserting a reference to *Salmonella* phage preparation (S16 and FO1a) and to new subsection S3—33. This in effect provides that the specification listed in new subsection S3—33 is the specification for *Salmonella* phage preparation (S16 and FO1a).

Item [1.2] new subsection S3—33 into Schedule 3. The new subsection provides a compositional specification for *Salmonella* phage preparation (S16 and FO1a) (S3—33) by reference to the biological classification of its component phages.

Item [2] varies Schedule 18 by amending the table to section S18—9 to include an entry for *Salmonella* phage preparation (S16 and FO1a) in the list of approved processing aids with miscellaneous technological functions. The new entry states that the phage preparation can be used for the technological purpose of reducing *Salmonella* species on the surface of raw meat and raw poultry meat during processing. The entry also states that the maximum permitted level is that which is consistent with GMP.

## **Attachment C – Draft variation to the revised *Australia New Zealand Food Standards Code* (to commence on 1 March 2016) (call for submissions)**



### **Food Standards (Application A1111 – Bacteriophage S16 & FO1a as a Processing Aid) Variation**

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The Board of Food Standards Australia New Zealand gives notice of the making of this variation under section 92 of the *Food Standards Australia New Zealand Act 1991*. The variation commences on the date specified in clause 3 of this variation.

Dated [To be completed by Standards Management Officer]

Standards Management Officer  
Delegate of the Board of Food Standards Australia New Zealand

**Note:**

This variation will be published in the Commonwealth of Australia Gazette No. FSC **XX on XX Month 20XX**. This means that this date is the gazettal date for the purposes of clause 3 of the variation.

## 1 Name

This instrument is the *Food Standards (Application A1111 – Bacteriophage S16 & FO1a as a Processing Aid) Variation*.

## 2 Variation to a Standard in the *Australia New Zealand Food Standards Code*

The Schedule varies a Standard in the *Australia New Zealand Food Standards Code*.

## 3 Commencement

This instrument commences on gazettal.

### Schedule

[1] **Schedule 3** is varied by

[1.1] inserting in the table to subsection S3—2(2) in alphabetical order

“

*Salmonella* phage preparation (S16 and FO1a)      section S3—33

”

[1.2] inserting after section S3—32

### “S3—33      **Specifications for *Salmonella* phage preparation (S16 and FO1a)**

(1) In this section:

**a preparation** means a *Salmonella* phage preparation (S16 and FO1a).

**Salmonella phage preparation (S16 and FO1a)** means a solution of a 1:1 blend of *Salmonella* phage S16 and *Salmonella* phage FO1a.

(2) *Salmonella* phage S16 in a preparation must comply with the specification in subsection (4).

(3) *Salmonella* phage FO1a in a preparation must comply with the specification in subsection (5).

(4) The biological classification for *Salmonella* phage S16 in a preparation is the following:

- (a) order—Caudavirales;
- (b) family—Myoviridae;
- (c) genus—T4-like;
- (d) species—*Salmonella* phage S16;
- (e) GenBank Accession Number—HQ331142

(5) The biological classification for *Salmonella* phage FO1a in a preparation is the following:

- (a) order—Caudavirales;
- (b) family—Myoviridae;
- (c) genus—FelixO1-like;
- (d) species—*Salmonella* phage FO1a;
- (e) GenBank Accession Number—JF461087.”

[2] **Schedule 18** is varied by inserting in the Table to section S18—9 in alphabetical order

“

<i>Salmonella</i> phage preparation (S16 and FO1a)	Reduce <i>Salmonella</i> species on or in raw meat during processing.	GMP
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”