



Criteria for the assessment of biocides in decreasing foodborne pathogens in food of animal origin

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Outline of the presentation

Foodborne infections within the EU

Legal background

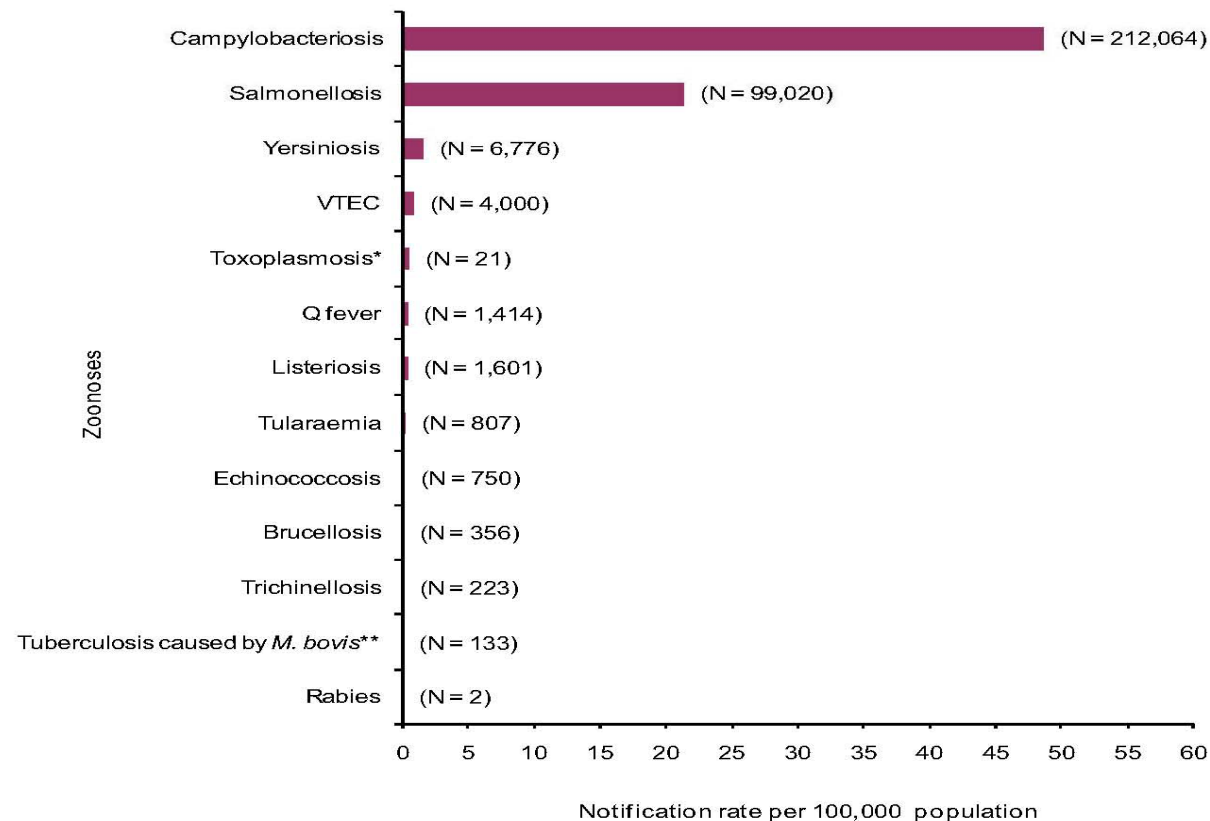
Guidelines for assessment of the efficacy of
Biocides as decontaminating agents

Examples of assessments (Lactic acid, Listex)



Reported notification rates of zoonoses in confirmed human cases in the EU 2010

Reported notification rates of zoonoses in confirmed human cases in the EU, 2010



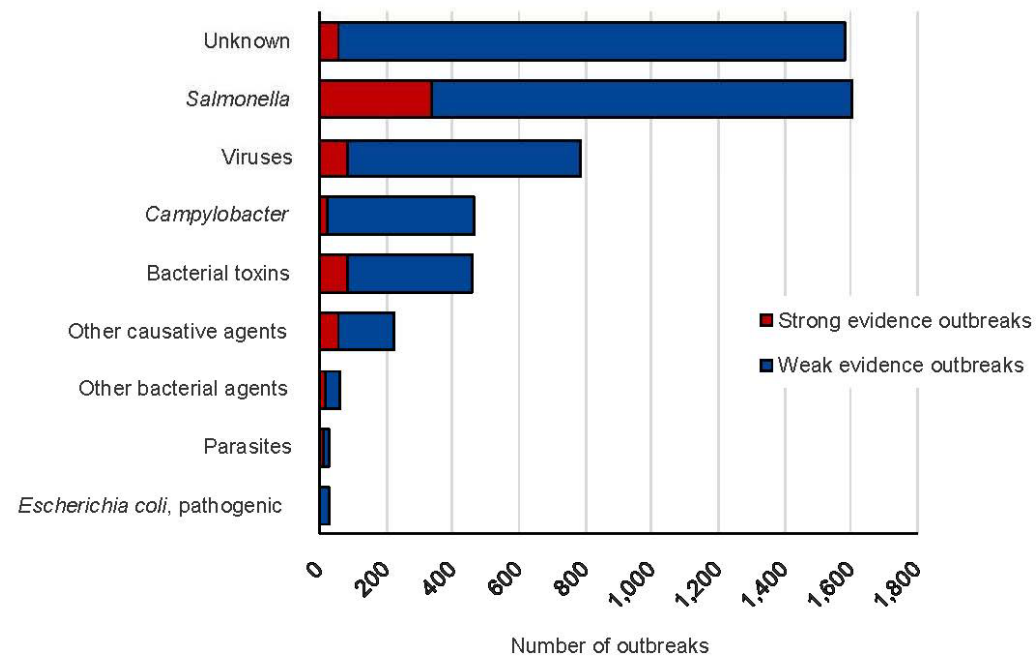
Note: Total number of confirmed cases is indicated in parenthesis at the end of each bar.

* Data for congenital toxoplasmosis.

** Data from 2009.



Distribution of food-borne outbreaks (weak and strong evidence - excluding strong evidence waterborne outbreaks) per causative agent in the EU, 2010



Note: Food-borne viruses include calicivirus, flavivirus, rotavirus, hepatitis A virus and other unspecified food-borne viruses. Bacterial toxins include toxins produced by *Bacillus*, *Clostridium* and *Staphylococcus*. Other causative agents include mushroom toxins, marine biotoxins, histamine, mycotoxins, wax esters and other unspecified agents. Parasites include primarily *Trichinella*, but also *Anisakis*, *Giardia* and *Cryptosporidium*. Other bacterial agents include *Brucella*, *Listeria*, *Shigella* and *Yersinia*.



Estimated fatality rates in humans at EU level, 2009, EUSR

Based on the reported fatality rates and the total numbers of reported confirmed cases, it was estimated that in 2009 there were in EU approximately:

- 270 human deaths due to listeriosis;
- 90 deaths due to salmonellosis; and
- 40 deaths due to campylobacteriosis.

Data provided by ECDC



Legal background

- Art 3(2) of Regulation (EC) No 853/2004: legal basis to approve/authorise the use of substances other than potable water to remove surface contamination from products of animal origin
- Before risk management decision, a risk analysis should be carried out taking into account the results of a risk assessment



To bear in mind:

Biocides or other decontaminating agents are considered as an **additional** measure

Not a substitution for good hygienic slaughtering practices and operating procedures

Integration into good hygiene practices and HACCP based systems.



What EFSA evaluates:

- the toxicological safety
- the efficacy of microbial reduction
- the potential emergency of reduced susceptibility to biocides and/or resistance to therapeutic antimicrobials
- the environmental risk



Guidelines - definition

The use of a decontaminating agent will be regarded efficacious when:

- a reduction of the prevalence and/or numbers of pathogenic target microorganisms is statistically significant when compared to a non-treated control group
- The achieved reduction in contamination should be expected to provide benefits to public health.



Guidelines - definition

The benefits to public health will be evaluated by EFSA

Satisfactory level will be a risk management decision.



Guidelines for efficacy assessment

Information required to assess the efficacy of a formulated product

The proposal should be a coherent presentation of the arguments for use of the formulated product, supported by studies of the efficacy of pathogen reduction and of the potential development of acquired reduced susceptibility to the formulated product itself, performed according to the guidelines below and presented in a structured way.



Information required to assess the efficacy of a formulated product

- All studies should be made with the formulated product for which authorisation is sought
- The processing conditions used to evaluate the efficacy must be comparable with those for which the formulated product is intended.
- The study must include a comparison of the prevalence and/or numbers of the pathogenic microorganisms on the food of animal origin to which the formulated product will be applied and on the untreated control food.



Information required to assess the efficacy of a formulated product

- The study design should be as close as possible to the real conditions under which the formulated product is intended to be applied.
- The study design must be justified in relation to the specific claim(s) made for the formulated product and must include a consideration of sound statistical methodology.



Information required to assess the efficacy of a formulated product

- Firstly tests must be made with inoculated target pathogenic microorganisms, taking into account strain diversity.
- In addition the efficacy of the formulated product must be validated by testing on naturally contaminated foods of animal origin.



Information required to assess the efficacy of a formulated product

- Available scientific information on acquired reduced susceptibility to the formulated product should be provided.
- The determination of the efficacy of a formulated product must involve the use of an appropriate neutralization method or the removal of the formulated product



Evaluation of efficacy: body of evidence

Study type	Natural contamination	Spiking studies
Industrial	HIGH	Not applicable
Pilot-scale	HIGH/MEDIUM	MEDIUM
Laboratory	MEDIUM	LOW



Recent assessments of EFSA on decontamination treatments

Lactic acid for the removal of microbial surface contamination of beef carcasses, cuts and trimmings

Cecure® for the removal of microbial surface contamination of raw poultry products

Listex™ P100 for the removal of *Listeria monocytogenes* surface contamination of raw fish



LACTIC ACID DECONTAMINATION OF BEEF CARCASSES, CUTS AND TRIMMINGS



Mandate lactic acid in beef

- EC received an application dossier from USDA for approval of lactic acid for uses to reduce microbial contamination of beef hides, carcasses, cuts and trimmings and requested EFSA to deliver a Scientific Opinion (BIOHAZ and CEF)
- Approval was sought for treatments
 - ✓ Beef hides, carcasses, cuts and/or trimmings
 - ✓ Spray washing or misting
 - ✓ Lactic acid (LA) concentrations: 2% - 5%
 - ✓ Temperatures: < 55°C



Human toxicological safety

- Consumer exposure assessment
 - ✓ the treatments (with/without rinsing off) are expected to leave small amounts of residual LA on meat surface
- Toxicological data
 - ✓ LA is permitted food additive (E270)[†]
 - ✓ ADI «not specified» or «not limited»
 - ✓ endogenous substance

CONCLUSION: treatments will be of no safety concern, provided the substance used complies with EU specifications for food additives (Reg (EC) No 1333/2008) and with the purity criteria (Dir 2008/84/EC)



Efficacy LA: assessment included

- **Lactic acid (LA):**
 - concentrations: 2% - 5%
 - temperatures: < 55°C
- **Product groups:**
 - carcass pre-chill/post-chill, meat cuts, trimmings, hides
- **Method:**
 - spray washing or misting
 - without rinsing and with rinsing after treatment
 - controls: before/after treatment; treated/non-treated samples; water control (< 72°C)
- **Bacterial groups**

<i>Salmonella</i>	}	Pathogenic groups
STEC/VTEC		
<i>Enterobacteriaceae</i>	}	Indicator bacteria



Efficacy: papers

52 papers submitted by the applicant

27 excluded

- outside scope of approval
- evaluated only aerobic plate count



25 remaining

Range of experimental designs (products, settings, application, LA concentration, controls, microorganisms)

These parameters impacted on the efficacy both within and between studies (wide range of efficacies)

Evaluation did not attempt to differentiate effects due to different factors

=> the total volume of data is regarded **sufficient**

Efficacy: body of evidence

Study type	Natural contamination	Inoculated studies
Industrial	HIGH	Not applicable
Pilot-scale ¹	HIGH/MEDIUM	MEDIUM
Laboratory	MEDIUM	LOW

- **HIGH:**

- ✓ industrial scale studies
- ✓ pilot scale studies (representative of industrial scale with naturally contaminated products)

- **MEDIUM:**

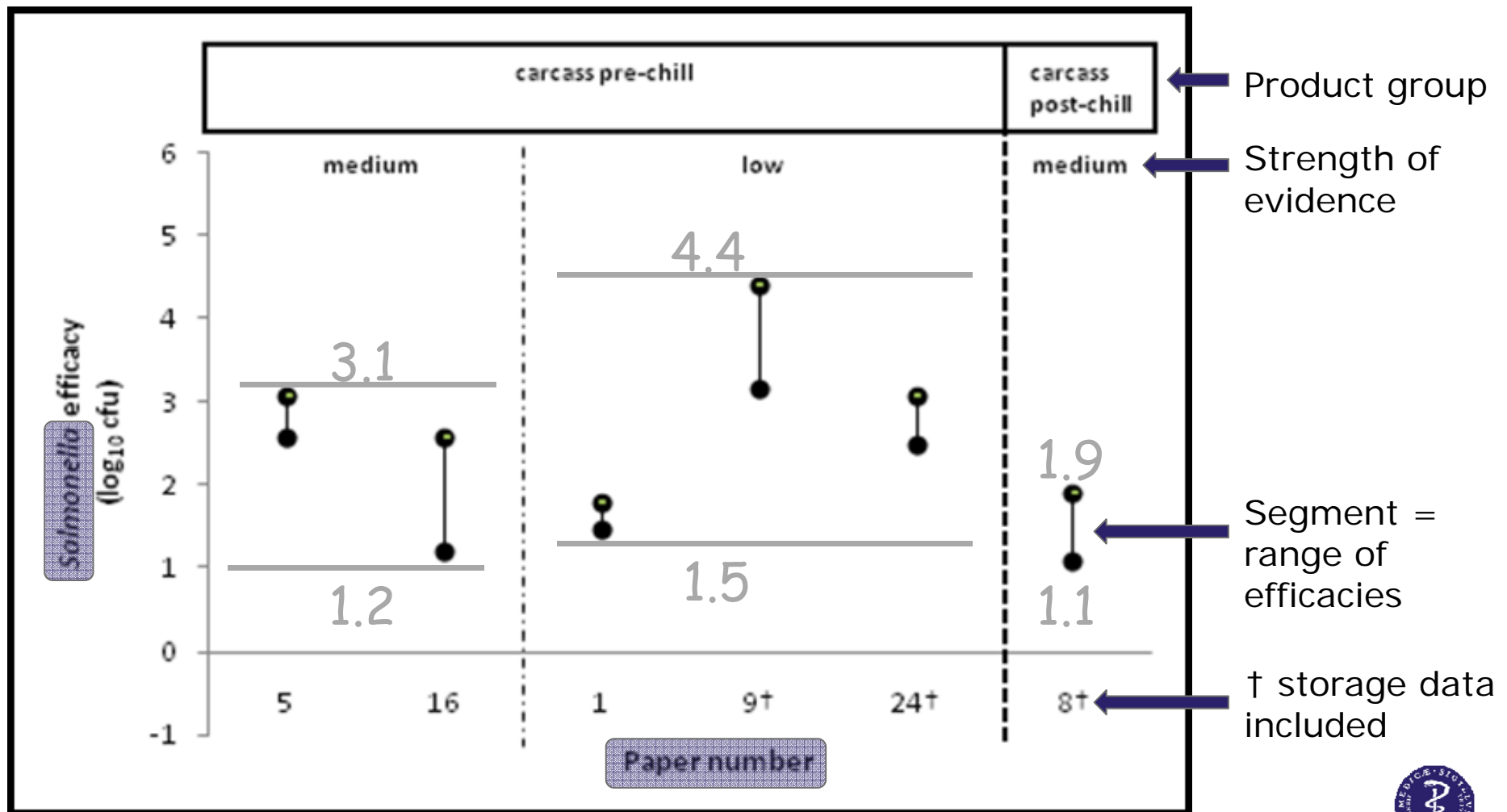
- ✓ pilot scale studies with naturally contaminated products and with inoculated pathogens
- ✓ laboratory scale studies with naturally contaminated products

- **LOW:**

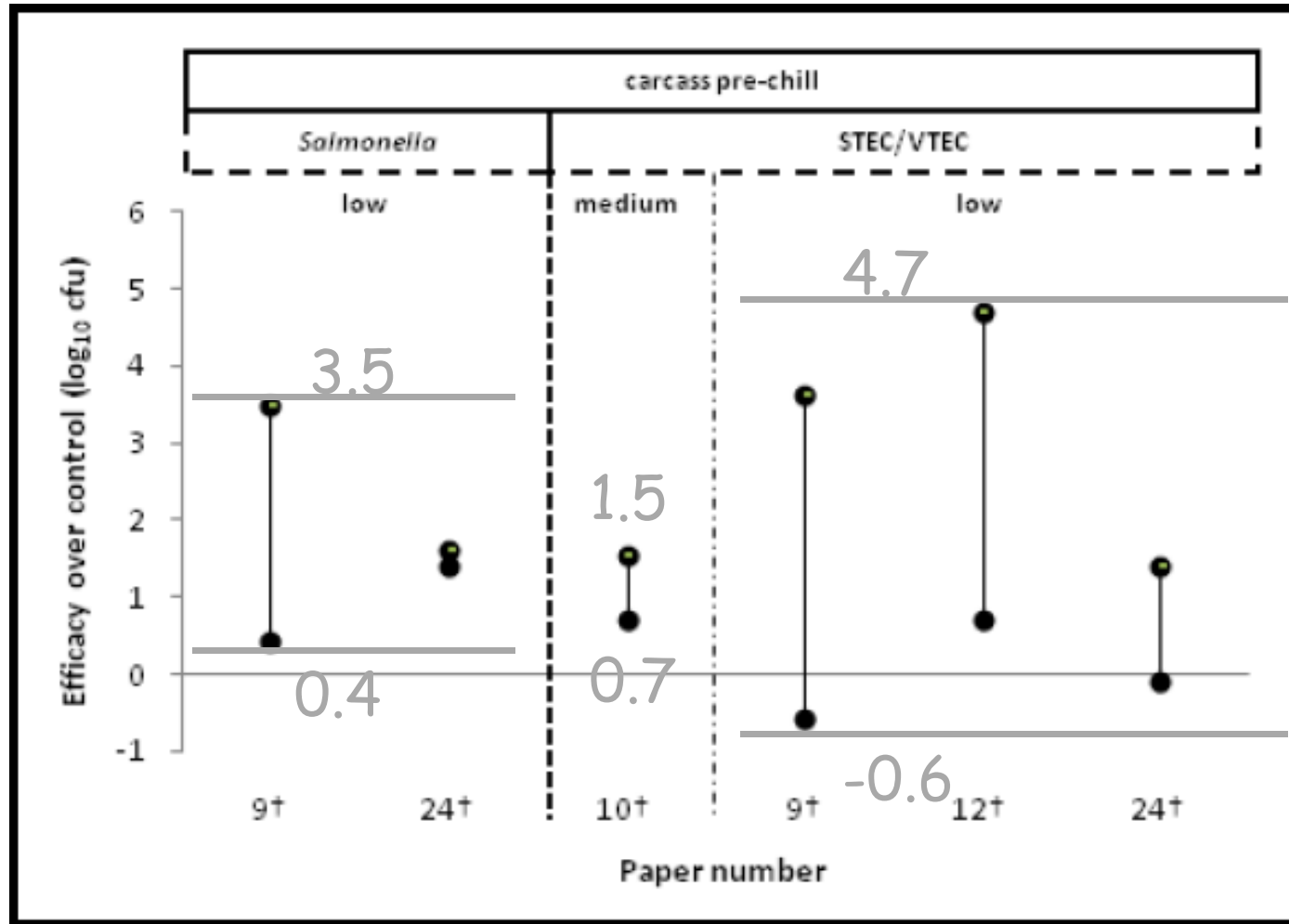
- ✓ laboratory scale studies with inoculated pathogens



Efficacy of LA on carcasses: *Salmonella*



Efficacy of LA over control on carcasses:
Salmonella and STEC/VTEC



Efficacy: conclusions

- Overall, reductions $> 1 \log_{10}$ unit and in many cases were much higher, reaching

Carcasses

- ✓ $5.2 \log_{10}$ units for carcasses pre-chill
- ✓ $5.8 \log_{10}$ units for carcasses post-chill
- ✓ $4.7 \log_{10}$ units for carcasses pre-chill or post-chill over a control treatment.

Meat cuts

/ trimmings

- ✓ $4.2 \log_{10}$ units for meat cuts and trimmings
- ✓ $2.3 \log_{10}$ units for meat cuts and trimmings over a control treatment

Efficacy: conclusions

- **Naturally occurring *Enterobacteriaceae* counts**

⇒ reduced to variable degree, but usually reductions were significantly higher compared to untreated or water treated controls (**HIGH**).

- ***Salmonella* and/or STEC/VTEC prevalence**

⇒ reduced to variable degrees depending on study design and contamination level, but reductions were generally significantly higher compared to controls (**HIGH/MEDIUM**)

- **Inoculated pathogens (*Salmonella* and/or STEC/VTEC) counts**

⇒ reduced to variable degree. Usually reductions higher on carcasses compared to meat cuts and trimmings (**MEDIUM**).



Antimicrobial resistance - LA

CONCLUSIONS:

- Development of enzymatic resistance to therapeutic antimicrobials as a result of exposure to LA is unlikely.
- Considering the extensive natural presence of LA in fermented food, the possibility of mutational change resulting in developing of resistance to therapeutic antimicrobials is unlikely to be significant issue.
- Some evidence suggests that repeated exposure to LA can select for reduced susceptibility to the substance. Under GHP, this possibility is not considered a significant issue.



Environmental risk - LA

- Concentration of LA just before entering the wastewater treatment system estimated as 10 mg/L => contribution to pH decrease negligible
- LA is fully biodegradable

CONCLUSION: The concentration of LA just before entering the wastewater treatment system can be considered as negligible and an environmental risk assessment was therefore considered not necessary.

Recommendations - LA

- According to HACCP principles, during use, food business operators verify LA concentration, temperature of application and other factors affecting its efficacy as a decontaminating agent.
- Because of the variability between various studies, food business operators validate the antimicrobial efficacy under their specific processing conditions.

EVALUATION OF THE SAFETY AND
EFFICACY OF LISTEX™ P100 FOR
THE REMOVAL OF *LISTERIA*
MONOCYTOGENES SURFACE
CONTAMINATION OF RAW FISH



Application dossier

- Listex™ P100
 - ✓ Water formulated product containing phage P100 at concentration of 2×10^{11} pfu/ml
 - ✓ Production is based on fermentation process using non-pathogenic *Listeria innocua* followed by several filtration steps
 - ✓ P100 recognizes all serovars within genus *Listeria*
- Approval was sought for treatments
 - ✓ Product: raw fish
 - ✓ Application: spraying or dipping
 - ✓ Dose: variable ($<10^9$ pfu/g product)
 - ✓ Removal step: not needed



Terms of Reference

EFSA is requested to evaluate the safety and efficacy of Listex™ P100 for uses to remove *Listeria monocytogenes* surface contamination of raw fish, considering:

- the toxicological safety of the substance;
- the efficacy, i.e. does the use of the substance significantly reduce the level of contamination of *Listeria monocytogenes*;
- the potential emergence of reduced susceptibility to biocides and/or resistance to therapeutic antimicrobials linked to the use of the substance;
- the risk related to the release of the processing plant effluents, linked to the use of the substance, into the environment.

BIOHAZ



Conclusions toxicological safety

The Listex™ P100 preparation should not present toxicological problems if used in fish decontamination because:

- The bacteriophage P100 used as active principle is not regarded as harmful to consumers.
- The Listex™ P100 fabrication parameters do not include any components or steps that might compromise safe use of the preparation.



Conclusions efficacy

- The two 'low strength of evidence' relevant studies do not allow definitive conclusions on the efficacy of the product in reducing *Lm* counts on raw fish.
- Listex™ P100 is listericidal (1.4-3.5 log₁₀ cfu/g) on the two inoculated raw fish types (catfish and salmon fillet) tested.
- Data were not adequate to draw firm conclusions on persistence or activity of P100 and fate of surviving *Lm* during storage of treated fish samples.



Conclusions efficacy

- Efficacy of Listex™ P100 treatment against levels of *Lm* usually expected to occur naturally on fish was not studied.
- No evidence was provided to demonstrate the impact of treating raw fish on *Lm* levels in the finished product.
- Overall, the evidence provided is not adequate to allow estimation of potential human listeriosis risk reduction by treating raw fish with Listex™ P100.



Recommendations

- Pilot and industrial scale studies should be considered to address parameters such as types and size of fish, stage of processing for application, strains, contamination levels.
- Verification is needed that treatment of raw fish with Listex™ P100 will have impact on *Lm* levels in final fish product.



More information:



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efsa European Food Safety Authority
Committed since 2002 to ensuring that Europe's food is safe

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Decontamination substance applications

In the European Union all substances other than potable water used for the removal of microbial surface contamination of foods of animal origin require prior authorisation. EFSA carries out the safety and efficacy evaluation of these 'decontamination substances'.

Frequently Asked Questions

1. I have submitted an application for the safety evaluation of a decontamination substance by EFSA. How can I check the status of my application?
2. I am not sure if a decontamination substance requires approval. Who should I contact?
3. Is there an official list of all authorised decontamination substances?
4. I am a new applicant. How do I prepare an application?
5. What happens to my application when EFSA has received it?
6. How long does EFSA's evaluation take?
7. Do I need to pay?
8. Does EFSA authorise decontamination substances for food of animal origin?
9. Short cuts for applicants

See also

- Food ingredients and packaging
- Animal health and welfare
- Biological hazards

EFSA guidance for submission of data:

<http://www.efsa.europa.eu/en/efsajournal/pub/1544.htm>

Lactic acid/beef: <http://www.efsa.europa.eu/en/efsajournal/doc/2317.pdf>

Cecure®/poultry: <http://www.efsa.europa.eu/en/efsajournal/doc/2612.pdf>

Listex™ P100/fish: <http://www.efsa.europa.eu/en/efsajournal/doc/2615.pdf>



Future perspectives

Next steps are decisions to be made by risk managers





Thank you very much for
your attention