SUMMER SCHOOL 2019
RISK-BENEFIT IN FOOD SAFETY AND NUTRITION

Case study: Risk-benefit of food and feed additives

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Risk Benefit Analyis
RA or RM?

Risk: The probability of an adverse effect in an organism, system, or (sub)population in reaction to exposure to an agent

Benefit: The probability of a positive health effect and/or the probability of a reduction of an adverse health effect in an organism, system, or (sub)population, in reaction to exposure to an agent.

Risk Assessment	Benefit Assessment
Hazard identification	Positive health effect/reduced adverse effect identification
Hazard characterisation (dose response assessment)	Positive health effect/reduced adverse effect characterisation (dose response assessment)
Exposure assessment	Exposure assessment
Risk characterisation	Benefit characterisation

When Risk Benefit is appropriate?

- Where a single compound or food constituent has both positive and negative health effects.
- Where similar levels of dietary exposures can be associated with both risk and benefit
- Where chemicals are used to reduce microbial contamination

THE INTENTIONAL USE OF MICROORGANISMS IN THE FOOD CHAIN

USE	Authorisation	R/B
Food starter cultures	Not required	n.a.
Human probiotics	Health Claims	B
Animal probiotics	Feed Additives	RB
Feed fermentation-silage	Feed Additives	RB
Enzyme production	Feed Additives / Food Additives	RB/R
Amino acid production	Feed Additives / Food Additives	RB/R
Vitamin production	Feed Additives / Food Additives	RB/R
Biopesticide	Plant Protection Products	RB
Novel Food	Novel Food	R
Genetically Modified Microorg.	Feed Additives - Food Additives- GMO	RB

Microbiological Risk Assessment in practice:

Regulated Products

Risk Benefit Analyis – Two examples

Microbial Feed Additives

Qualified Presemption of Safety

Feed Additived: Risk Benefit Analyis?

Where an agent has both positive and negative health effects on:

- Consumers
- Users
- Animals
- Environment

Feed additive applications: overview and procedure

EFSA evaluates the safety and/or efficacy of additives, products or substances used in animal feed before they can be authorised for use in the EU. The European Commission decides whether or not to authorise the feed additive application following EFSA's evaluation.

EFSA evaluates the safety and/or efficacy of additives

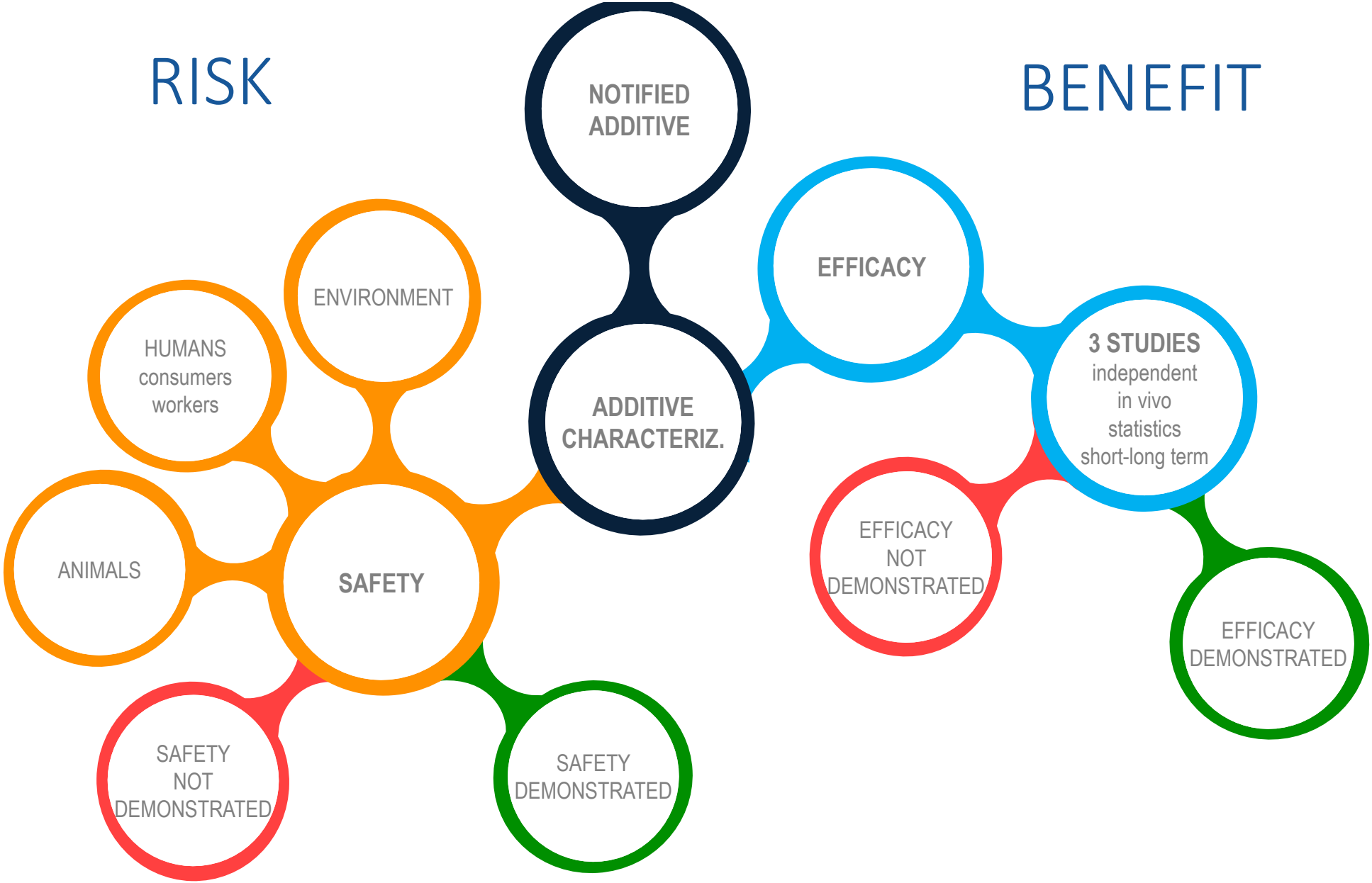
Feed Additives

substances, micro-organisms or preparations, other than feed material and premixtures, which are intentionally added to feed or water to:

- favourably affect the characteristics of feed,
- favourably affect the characteristics of animal products,
- favourably affect the colour of ornamental fish and birds,
- satisfy the nutritional needs of animals,
- favourably affect the environmental consequences of animal production,
- favourably affect animal production, performance or welfare, particularly by affecting the gastro-intestinal flora or digestibility of feedingstuffs,
- have a coccidiostatic or histomonostatic effect.

RISK


NOTIFIED ADDITIVE
ADDITIVE CHARACTERIZ.
ENVIRONMENT
HUMANS consumers workers
ANIMALS
SAFETY
SAFETY NOT DEMONSTRATED
SAFETY DEMONSTRATED


RISK
BENEFIT
NOTIFIED ADDITIVE
ADDITIVE CHARACTERIZ.
ENVIRONMENT
HUMANS consumers workers
ANIMALS
SAFETY
SAFETY NOT DEMONSTRATED
SAFETY DEMONSTRATED
EFFICACY
3 STUDIES independent in vivo statistics short-long term
EFFICACY NOT DEMONSTRATED
EFFICACY DEMONSTRATED

Feed Additives

- Guidance on the identity, characterisation and conditions of use of feed additives
- Guidance on the characterisation of microorganisms used as feed additives or as production organisms
- Guidance on the assessment of the safety of feed additives for the target species
  - Trial Protocol Data Sheet – Terrestrial Animals
  - Trial Protocol Data Sheet – Aquatic Animals
  - Feed Additives maximum safe Concentration in feed for Target Species calculator (FACTS) calculator
- Guidance on the assessment of the safety of feed additives for the consumer
  - Feed Additive Consumer Exposure (FACE) calculator
- Guidance on the assessment of the efficacy of feed additives
  - Trial Protocol Data Sheet – Terrestrial Animals
  - Trial Protocol Data Sheet – Aquatic Animals
- Guidance on user safety
- Guidance for assessing the safety of feed additives for the environment (applicable until 31 August 2019)
- Guidance on the assessment of the safety of feed additives for the environment (implementation date 1 September 2019)

GUIDANCE

EFSA Journal

ADOPTED: 17 April 2018

doi: 10.2903/j.efsa.2018.5274

Guidance on the assessment of the efficacy of feed additives

EFSA Panel on Additives and Products or Substances used in Animal Feed (FEEDAP), Guido Rychen, Gabriele Aquilina, Giovanna Azimonti, Vasileios Bampidis, Maria de Lourdes Bastos, Georges Bories, Andrew Chesson, Pier Sandro Cocconcelli, Gerhard Flachowsky, Jürgen Gropp, Boris Kolar, Maryline Kouba, Marta López-Alonso, Secundino López Puente, Alberto Mantovani, Baltasar Mayo, Fernando Ramos, Maria Saarela, Roberto Edoardo Villa, Robert John Wallace, Pieter Wester, Montserrat Anguita, Jaume Galobart, Matteo Lorenzo Innocenti and Laura Martino

Additives affecting:

- animal production or performance
- the environmental consequences of animal production
- the characteristics of food of animal origin
- animal welfare
- coccidiosis

SCIENTIFIC OPINION

EFSA Journal

ADOPTED: 2 October 2018

doi: 10.2903/j.efsa.2018.5456

Safety and efficacy of Hostazym® X (endo-1,4-beta-xylanase) as a feed additive for sows in order to have benefit in piglets

SAFETY

- Microbial strain *T. reseii*
- Genetic Modification
- Toxicology
- Tolerance (overdose animal study)

SCIENTIFIC OPINION

EFSA Journal

ADOPTED: 23 January 2019

doi: 10.2903/j.efsa.2019.5610

Safety and efficacy of Beltherm MP/ML (endo-1,4-beta-xylanase) as a feed additive for piglets, pigs for fattening and other porcine species

BENEFIT

- Welfare (morbidity mortality)
- Performances
  - body weight gain
  - feed conversion rate

SCIENTIFIC OPINION

EFSA Journal

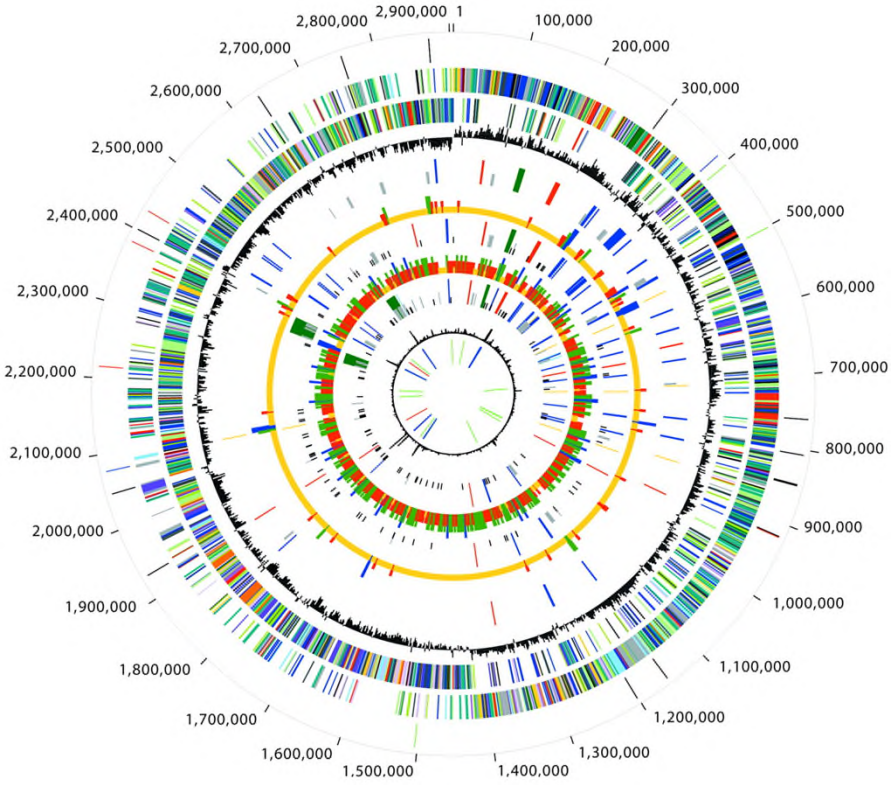
ADOPTED: 21 February 2018

doi: 10.2903/j.efsa.2018.5206

Guidance on the characterisation of microorganisms used as feed additives or as production organisms

EFSA Panel on Additives and Products or Substances used in Animal Feed (FEEDAP), Guido Rychen, Gabriele Aquilina, Giovanna Azimonti, Vasileios Bampidis, Maria de Lourdes Bastos, Georges Bories, Andrew Chesson, Pier Sandro Cocconcelli, Gerhard Flachowsky, Jürgen Gropp, Boris Kolar, Maryline Kouba, Marta López-Alonso, Secundino López Puente, Alberto Mantovani, Baltasar Mayo, Fernando Ramos, Maria Saarela, Roberto Edoardo Villa, Robert John Wallace, Pieter Wester, Boet Glandorf, Lieve Herman, Sirpa Kärenlampi, Jaime Aguilera, Montserrat Anguita, Rosella Brozzi and Jaume Galobart

Draft Endorsed by the FEEDAP Panel*	18 May 2017
Submitted for public consultation	15 June 2017
End of public consultation	15 September 2017
Adopted by the FEEDAP Panel	21 February 2018
Implementation date	1 September 2018



Whole Genome Sequence for Risk Assessment of microorganisms: the EFSA Guidance

efsa
European Food Safety Authority

WGS

	Feed additives containing viable microorganisms		
	Bacteria	Yeasts	Fungi
Identification	✓	✓	✓
Antimicrobial susceptibility	✓		
Antimicrobial production	✓	✓	✓
Toxigenicity and pathogenicity	✓	✓	✓
Genetic modification	GMM-only	GMM-only	GMM-only

Risk Assessment	Benefit Assessment
Hazard identification ✓☐	Positive health effect/reduced adverse effect identification ✓☐
Hazard characterisation (dose response assessment) ✓☐	Positive health effect/reduced adverse effect characterisation (dose response assessment) ✓☐
Exposure assessment ✓☐	Exposure assessment ✓☐
Risk characterisation ✓☐	Benefit characterisation ✓☐

SCIENTIFIC OPINION

EFSA Journal

ADOPTED: 30 November 2016

doi: 10.2903/j.efsa.2017.4664

Scientific Opinion on the update of the list of QPS-recommended biological agents intentionally added to food or feed as notified to EFSA*

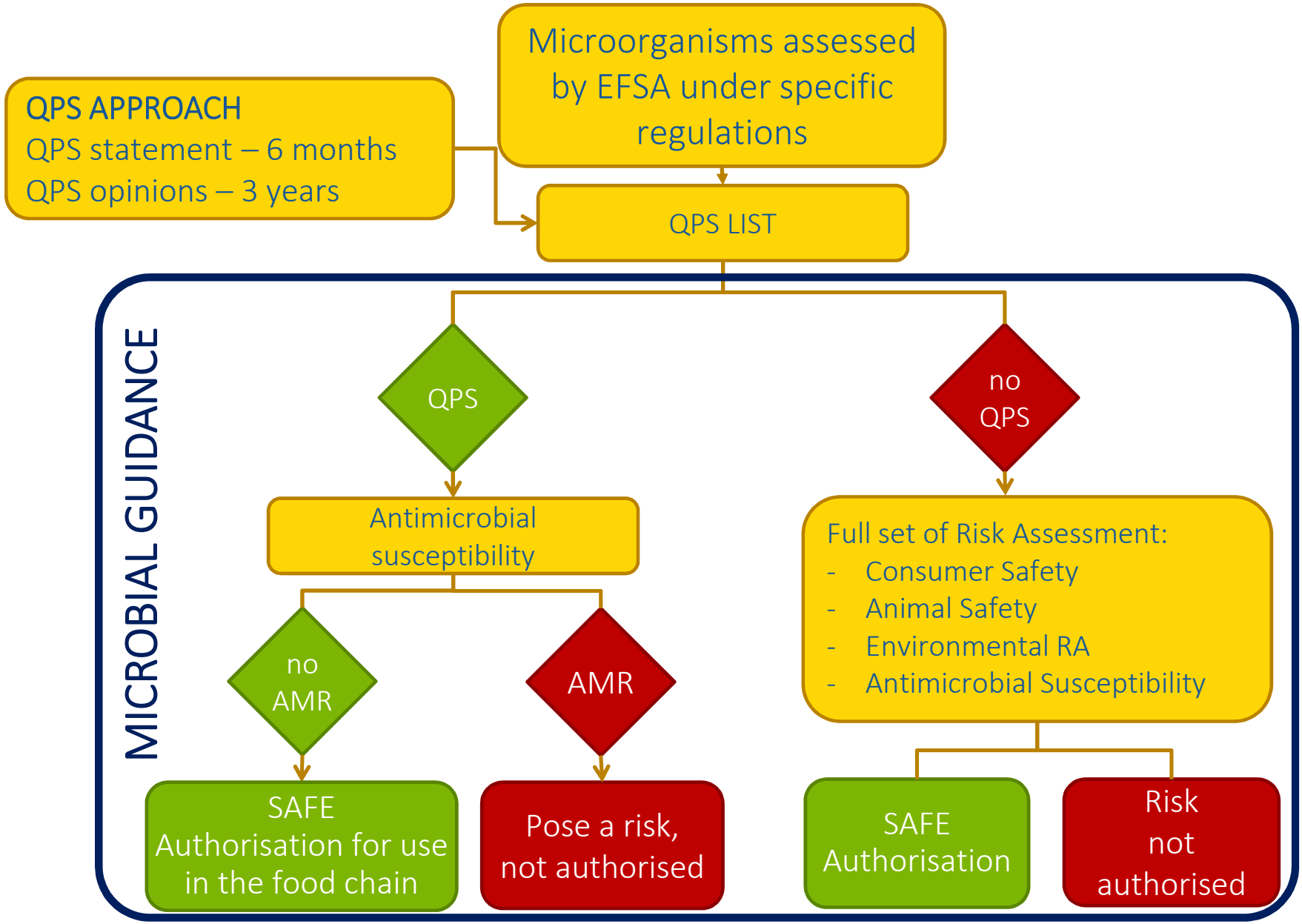
EFSA Panel on Biological Hazards (BIOHAZ),
Antonia Ricci, Ana Allende, Declan Bolton, Marianne Chemaly, Robert Davies, Rosina Girones, Lieve Herman, Konstantinos Koutsoumanis, Roland Lindqvist, Birgit Nørrung, Lucy Robertson, Giuseppe Ru, Moez Sanaa, Marion Simmons, Panagiotis Skandamis, Emma Snary, Niko Speybroeck, Benno Ter Kuile, John Threlfall, Helene Wahlström, Pier Sandro Cocconcelli, Günter Klein (deceased), Miguel Prieto Maradona, Amparo Querol, Luisa Peixe, Juan Evaristo Suarez, Ingvar Sundh, Just M. Vlak, Margarita Aguilera-Gómez, Fulvio Barizzone, Rosella Brozzi, Sandra Correia, Leng Heng, Frédérique Istace, Christopher Lythgo and Pablo Salvador Fernández Escámez

QPS pillars:

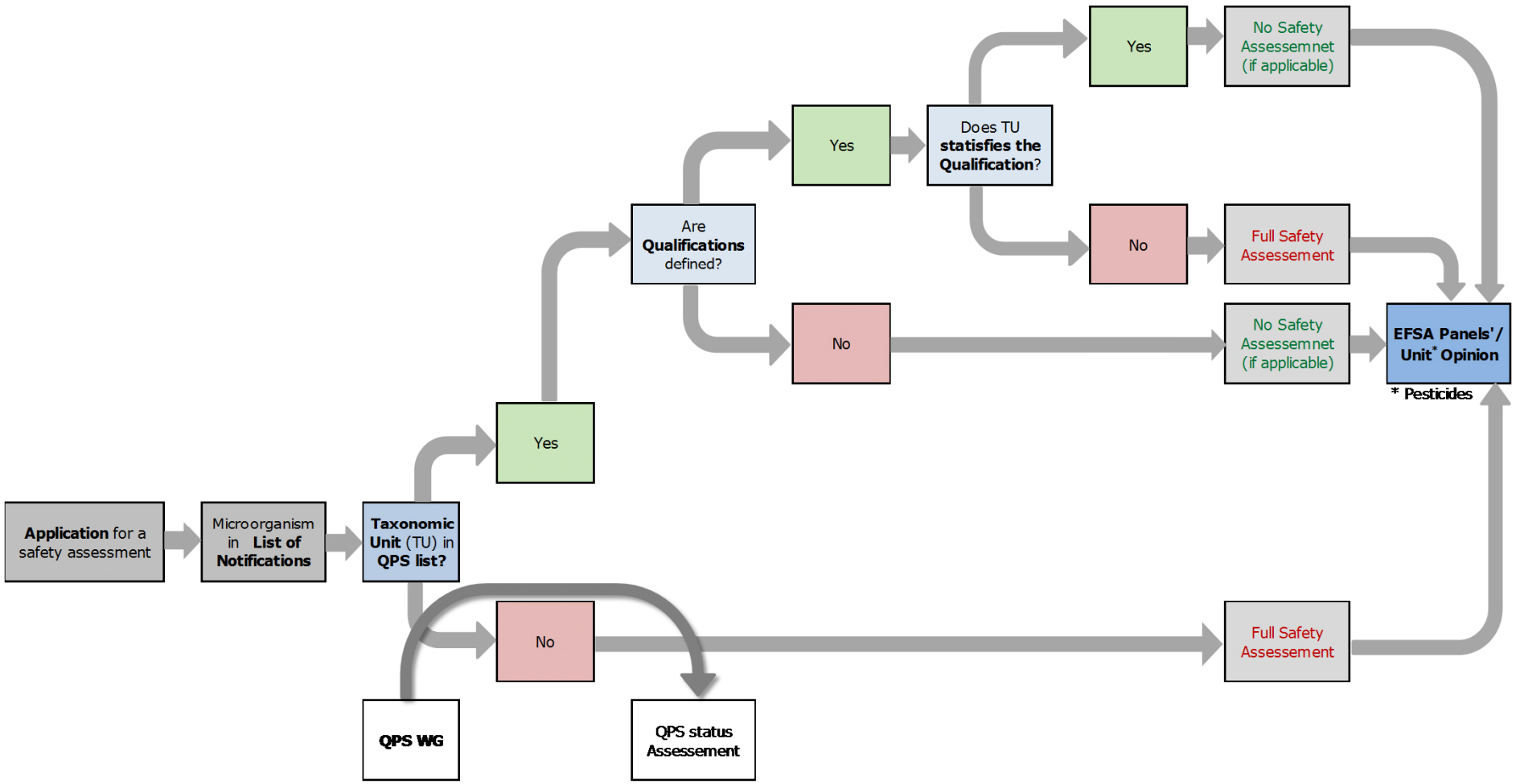
- **Taxonomy** – definition of the taxonomic unit (species/genus) for which QPS status is sought
- **Body of knowledge** – whether there is sufficient knowledge concerning the group of microorganisms to reach a decision on their safety
- Pathogenicity
  - known pathogens in the taxonomic unit
  - Knowledge about virulence determinants or toxigenic potential
  - Possibility to exclude pathogenic strains
- End use
  - live, dead, or products thereof

The QPS status of the more commonly notified microorganisms will be determined in advance and independently of applications of Notifiers.

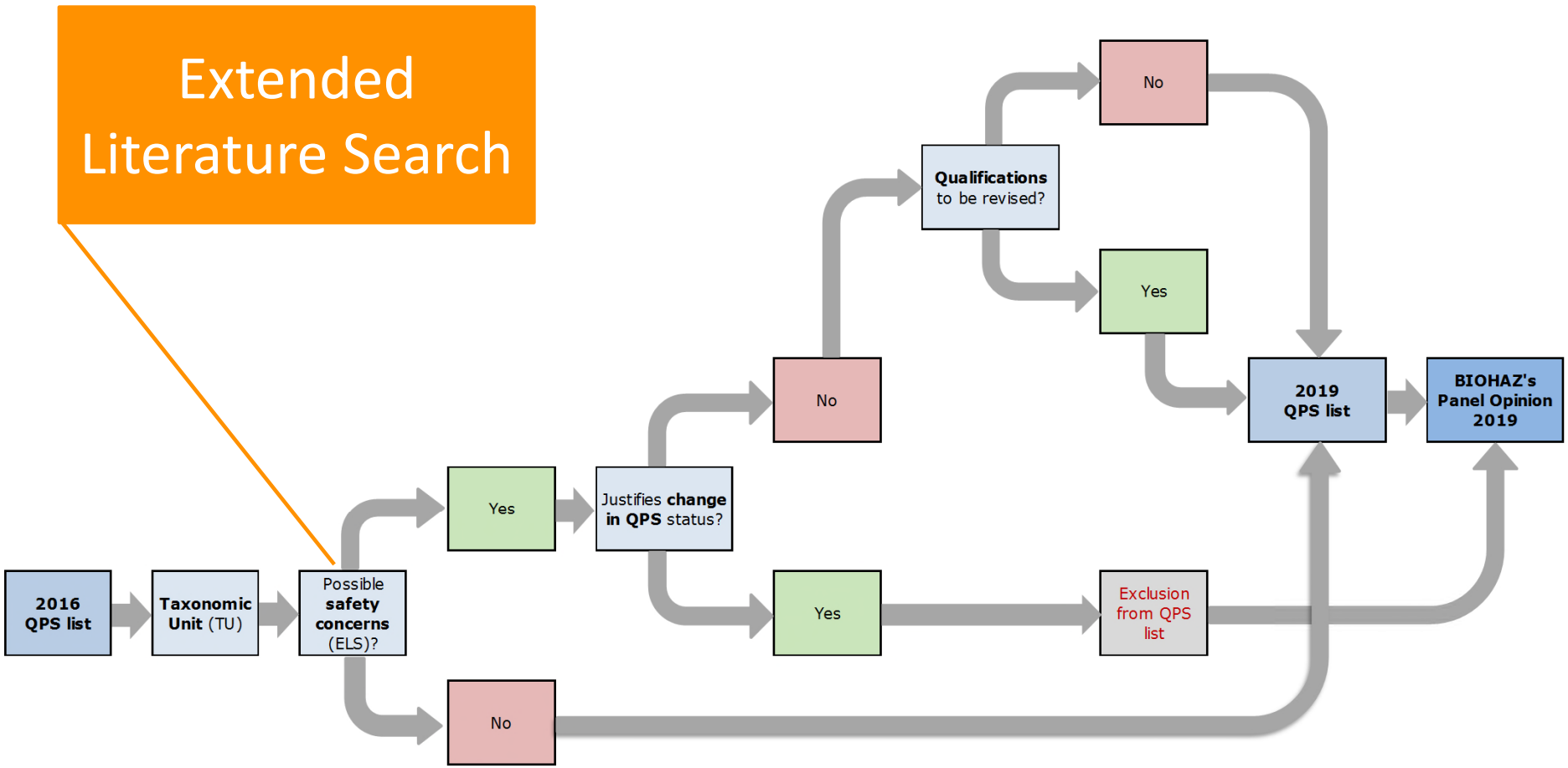
Products or processes involving organisms not considered suitable for QPS will not be excluded but will be subject to a full safety assessment.


QPS APPROACH
QPS statement – 6 months
QPS opinions – 3 years
Microorganisms assessed by EFSA under specific regulations
QPS LIST
MICROBIAL GUIDANCE
QPS
no QPS
Antimicrobial susceptibility
no AMR
AMR
Full set of Risk Assessment:
- Consumer Safety
- Animal Safety
- Environmental RA
- Antimicrobial Susceptibility
SAFE Authorisation for use in the food chain
Pose a risk, not authorised
SAFE Authorisation
Risk not authorised

QPS work-flow



QPS work-flow



QPS 2017 – *Lactobacillus rhamnosus*
Risk Benefit Analysis ?

Extended Literature Search

- eight reports on infection with L. rhamnosus were detected
- QPS conclusion

Conclusion regarding the maintenance of the QPS recommendation

There is no requirement to change the QPS recommendation of the previously recommended *Lactobacillus* species, as the infections reported to be due to members of the genus were extremely scarce and affected patients that already suffered from highly debilitating illnesses and/or were significantly immunodepressed. As already noted in the 2013 Opinion, *L. rhamnosus* produced most of the clinical cases reported, probably due to frequent inclusion of isolates of this species into human 'probiotic' preparations. Consumption of microorganisms by patients with immunosuppression and/or underlying disease may be considered as the origin of the infection. The use of microorganisms intended to be used as 'probiotic' for humans as a health claim does not fall under the remit of the QPS assessment.

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Exposure assessment ?	Exposure assessment ?
Risk characterisation ✓☐	Benefit characterisation ✓☐

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CONCLUSIONS