

ADOPTED: 6 December 2017

doi: 10.2903/j.efsa.2018.5131

## Update of the list of QPS-recommended biological agents intentionally added to food or feed as notified to EFSA 7: suitability of taxonomic units notified to EFSA until September 2017

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### Abstract

The qualified presumption of safety (QPS) concept was developed to provide a harmonised generic pre-evaluation to support safety risk assessments of biological agents performed by EFSA's scientific Panels. The identity, body of knowledge, safety concerns and antimicrobial resistance of valid taxonomic units were assessed. Safety concerns identified for a taxonomic unit are, where possible and reasonable in number, considered to be 'qualifications' which should be assessed at the strain level by the EFSA's scientific Panels. No new information was found that would change the previously recommended QPS taxonomic units and their qualifications. The BIOHAZ Panel confirms that the QPS approach can be extended to a genetically modified production strain if the recipient strain qualifies for the QPS status, and if the genetic modification does not indicate a concern. Between April and September 2017, the QPS notification list was updated with 46 applications for market authorisation. From these, 14 biological agents already had QPS status and 16 were not included as they are filamentous fungi or enterococci. One notification of *Streptomyces* K-61 (notified as former *S. griseoviridis*) and four of *Escherichia coli* were not considered for the assessment as they belong to taxonomic units that were excluded from further evaluations within the current QPS mandate. Eight notifications of *Bacillus thuringiensis* and one of an oomycete are pending the reception of the complete application. Two taxonomic units were evaluated: *Kitasatospora paracochleata*, which had not been evaluated before, and *Komagataella phaffii*, previously notified as *Pichia pastoris* included due to a change in the taxonomic identity. *Kitasatospora paracochleata* cannot be granted QPS status due to lack of information on its biology and to its possible production of toxic secondary metabolites. The species *Komagataella phaffii* can be recommended for the QPS list when used for enzyme production.

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**Keywords:** safety, QPS, bacteria, yeast, *Kitasatospora paracochleata*, *Komagataella phaffii*

**Requestor:** EFSA

**Question number:** EFSA-Q-2016-00828

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**Acknowledgements:** The Panel wishes to thank EFSA staff members Jaime Aguilera, Margarita Aguilera-Gómez, Rosella Brozzi, Leng Heng and Frédérique Istace, for the support provided to this scientific output.

**Suggested citation:** EFSA BIOHAZ Panel (EFSA Panel on Biological Hazards), Ricci A, Allende A, Bolton D, Chemaly M, Davies R, Girones R, Koutsoumanis K, Lindqvist R, Nørrung B, Robertson L, Ru G, Fernández Escámez PS, Sanaa M, Simmons M, Skandamis P, Snary E, Speybroeck N, Ter Kuile B, Threlfall J, Wahlström H, Cocconcelli PS, Peixe L, Maradona MP, Querol A, Suarez JE, Sundh I, Vlak J, Barizzone F, Correia S and Herman L, 2018. Statement on the update of the list of QPS-recommended biological agents intentionally added to food or feed as notified to EFSA 7: suitability of taxonomic units notified to EFSA until September 2017. *EFSA Journal* 2018;16(1):5131, 43 pp. <https://doi.org/10.2903/j.efsa.2018.5131>

**ISSN:** 1831-4732

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## Summary

The European Food Safety Authority (EFSA) asked the Panel on Biological Hazards (BIOHAZ) to deliver a scientific Opinion on the maintenance of the list of qualified presumption of safety (QPS) biological agents intentionally added to food or feed. The request included three specific tasks as mentioned in the Terms of Reference (ToR).

The QPS process was developed to provide a harmonised generic pre-evaluation to support safety risk assessments of biological agents performed by EFSA's scientific Panels and Units. The taxonomic identity, body of knowledge, safety and antimicrobial resistance of biological agents are assessed. Safety concerns identified for a taxonomic unit (TU) are, where possible and reasonable in number, reflected as 'qualifications' which should be assessed at the strain level by the EFSA's scientific Panels. A generic qualification for all QPS bacterial TUs applies in relation to the absence of acquired genes conferring resistance to clinically-relevant antimicrobials and therefore this needs to be checked at strain level.

The evaluation is undertaken every 3 years in a scientific Opinion of the BIOHAZ Panel. Meanwhile, the list of microorganisms is maintained and re-evaluated approximately every 6 months in a Panel Statement. If new information is retrieved from extended literature searches that would change the QPS status of a microbial species or its qualifications, this is published in the Panel Statement. The Panel Statement also includes the evaluation of microbiological agents notified to EFSA within the 6-month period for an assessment for feed additives, food enzymes, food additives and flavourings, novel foods or plant protection products. The main results of the assessments completed from 2017 will be included in the scientific Opinion of the BIOHAZ Panel to be published by the end of the current mandate in December 2019. As a result of each Panel Statement, the '2016 updated list of QPS status recommended biological agents for safety risk assessments carried out by EFSA scientific Panels and Units' is updated with the inclusion of new recommendations for QPS status and appended to the Opinion adopted in December 2016 (Appendix E).

The *first ToR* requires ongoing updates of the list of biological agents notified to EFSA, in the context of a technical dossier, for intentional use in food and/or feed or as sources of food and feed additives, enzymes and plant protection products for safety assessment. The list was updated with the notifications received since the latest review in March 2017. The new notifications received between April and September 2017, were included in a table appended to the current Statement (Appendix F). Within this period, 46 notifications were received by EFSA, of which 16 were for feed additives, five for food enzymes, food additives and flavourings, and 25 for plant protection products.

The *second ToR* concerns the revision of the TUs previously recommended for the QPS list and their qualifications when new information has become available and to update the information provided in the Opinion adopted in December 2016. Although the main work for replying to this ToR will be published in an Opinion in December of 2019, according to a first extensive literature search (ELS) for articles published between June 2016 and June 2017, no new information that would affect those QPS TUs status and their qualifications was found.

The *third ToR* requires a (re)assessment of the suitability of TUs notified to EFSA not present in the current QPS list for their inclusion in the updated list. The current Statement focuses on the assessments of the TUs that were notified to EFSA between April 2017 and September 2017. Of the 46 notifications received, 14 biological agents already had the QPS status and did not require further evaluation in this Statement, 16 are filamentous fungi or enterococci which were excluded from the QPS exercise, one notification of *Streptomyces* K-61 (notified as former *S. griseoviridis*) and four of *Escherichia coli* were excluded from further QPS evaluations within the current QPS mandate, eight of *Bacillus thuringiensis* and one of an oomycete are pending the reception of the complete application. Two new TUs were considered for the QPS assessment within this Statement: *Kitasatospora paracochleata* which had not been evaluated before and *Komagataella phaffii*, which had been previously notified as *Pichia pastoris*, was now included due to that change in the taxonomic identity. In summary, five notifications related to four TUs dealing with food enzymes, food additives and flavourings, 16 notifications related to 10 TUs dealing with feed additives and 25 notifications related to 14 TUs dealing with plant protection products were received within the period between April and September of 2017.

*Kitasatospora paracochleata*, which has not been evaluated before, cannot be granted the QPS status due to lack of information on its biology and to its possible production of toxic secondary metabolites.

The species *Komagataella phaffii*, a sibling species of *K. pastoris*, can be recommended for the QPS list but only when the species is used for enzyme production.

Upon request of the FEEDAP Unit, the BIOHAZ Panel confirms that the QPS approach can be extended to a genetically modified production strain if the recipient strain qualifies for QPS status, and if the genetic modification does not indicate a concern.

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## 1. Introduction

A wide variety of microorganisms are intentionally added at different stages into the food chain, either directly or as a source of food and feed additives, enzymes or plant protection products. In the context of applications for market authorisation of these biological agents, the European Food Safety Authority (EFSA) is requested by the European Commission, National Competent Authorities or Applicants to assess their safety. The qualified presumption of safety (QPS) approach was developed by the EFSA Scientific Committee to provide a generic concept to prioritise and to harmonise risk assessment within EFSA of microorganisms intentionally introduced into the food chain, in support of the respective Scientific Panels and Units in the frame of market authorisations (EFSA, 2007). The list, first established in 2007, has been continuously revised and updated. The publication of the overall assessment of the taxonomic units (TUs) previously recommended for the QPS list is carried out every 3 years through a scientific Opinion by the Panel on Biological Hazards (BIOHAZ). The recommendations provided concerning that list of microorganisms are maintained and every 6 months re-evaluated based on extensive literature reviews and expert knowledge. Intermediate deliverables in the form of a Panel Statement are produced and published, should an assessment for a QPS classification of a microbiological agent notified to EFSA be requested by the Units dealing with feed additives, food enzymes, food additives and flavourings, novel foods, or plant protection products. Evaluations of these notifications will be compiled in single Panel Statements for periods of around 6 months. The main results of these assessments are included in the scientific Opinion to be published in December of 2019.

### 1.1. Background and Terms of Reference as provided by EFSA

#### 1.1.1. Background as provided by EFSA

A wide variety of microorganisms are intentionally added at different stages into the food and feed chain. In the context of applications for market authorisation of these biological agents used either directly or as sources of food and feed additives, food enzymes and plant protection products, EFSA is requested to assess their safety.

Several taxonomic units (usually species for bacteria and yeasts, families for viruses) have been included in the qualified presumption of safety (QPS) list either following notifications to EFSA or proposals made initially by stakeholders during a public consultation in 2005, even if they were not yet notified to EFSA (EFSA, 2005).<sup>1</sup> The EFSA Scientific Committee reviewed the range and numbers of microorganisms likely to be the subject of an EFSA Opinion and published in 2007 a list of microorganisms recommended for the QPS list.<sup>2</sup>

In 2007, the Scientific Committee recommended that a QPS approach should provide a generic concept to prioritise and to harmonise safety risk assessment of microorganisms intentionally introduced into the food chain, in support of the respective Scientific Panels and EFSA Units in the frame of the market authorisations. The same Committee recognised that there would have to be continuing provision for reviewing and modifying the QPS list and in line with this recommendation, the EFSA Scientific Panel on Biological Hazards (BIOHAZ) took the prime responsibility for this and started reviewing annually the existing QPS list. The first annual QPS update<sup>3</sup> was published in 2008 and EFSA's initial experience in applying the QPS approach was included. The potential application of the QPS approach to microbial plant protection products was discussed in the 2009 update.<sup>4</sup> Also in 2009, bacteriophages were assessed and were not considered appropriate for the QPS list. After consecutive years of reviewing the existing scientific information, the filamentous fungi (2008 to 2013 updates) and enterococci (2010 to 2013 updates) were not recommended for the QPS list. The 2013 update<sup>5</sup> of the recommended QPS list included 53 species of Gram-positive non-spore-forming bacteria, 13 Gram-positive spore forming

<sup>1</sup> Opinion of the Scientific Committee on a request from EFSA related to a generic approach to the safety assessment by EFSA of microorganisms used in food/feed and the production of food/feed additives. The EFSA Journal 2005, 226, 1–12.

<sup>2</sup> Introduction of a Qualified Presumption of Safety (QPS) approach for assessment of selected microorganisms referred to EFSA - Opinion of the Scientific Committee. The EFSA Journal 2007, 293, 1–85.

<sup>3</sup> Scientific Opinion of the Panel on Biological Hazards on a request from EFSA on the maintenance of the list of QPS microorganisms intentionally added to food or feed. The EFSA Journal 2008, 923, 1–48.

<sup>4</sup> Scientific Opinion of the Panel on Biological Hazards (BIOHAZ) on the maintenance of the list of QPS microorganisms intentionally added to food or feed (2009 update). EFSA Journal 2009; 7(12):1431, 92 pp. <https://doi.org/10.2903/j.efsa.2009.1431>

<sup>5</sup> EFSA BIOHAZ Panel (EFSA Panel on Biological Hazards), 2013. Scientific Opinion on the maintenance of the list of QPS biological agents intentionally added to food and feed (2013 update). EFSA Journal 2013;11(11):3449, 107 pp. <https://doi.org/10.2903/j.efsa.2013.3449>

bacteria (*Bacillus* species), one Gram-negative bacterium (*Gluconobacter oxydans*), 13 yeast species, and three virus families.

In 2014 the BIOHAZ Panel, in consultation with the Scientific Committee, decided to change the revision procedure: the overall assessment of the taxonomic units previously recommended for the QPS list (EFSA BIOHAZ Panel, 2013)<sup>5</sup> was no longer carried out annually but over the last 3-year period and it was adopted by the BIOHAZ Panel as a Scientific Opinion in December of 2016 (EFSA BIOHAZ Panel, 2017). The QPS list of microorganisms has been maintained and frequently checked, based on the evaluation of extensive literature searches. In the meantime and every 6 months, a Panel Statement, compiling the assessments for a QPS status of the microbiological agents notified to EFSA requested by the Feed Unit, the Food Ingredients and Packaging (FIP) Unit, the Nutrition Unit or by the Pesticides Unit, has been produced and published. In the follow up of the 2013 update,<sup>5</sup> the Scientific Committee agreed to exclude some biological groups (filamentous fungi, bacteriophages and enterococci) notified to EFSA from the QPS assessment because it was considered unlikely that any taxonomical units within these groups would be granted QPS status in the foreseeable future. Thus, the assessment of members of these biological groups needs to be done at a strain level, on a case- by-case basis, by the relevant EFSA Unit.

The QPS provides a generic safety pre-assessment approach for use within EFSA that covers risks for human, animals and the environment. In the QPS concept a safety assessment of a defined taxonomic unit is considered independently of any particular specific notification in the course of an authorisation process. The QPS concept does not address hazards linked to the formulation or other processing of the products containing the microbial agents and added into the food or feed chain. Although general human safety is part of the evaluation, specific issues connected to type and level of exposure of users handling the product (e.g. dermal, inhalation, ingestion) are not addressed. Genetically modified microorganisms are similarly not taken into account. Assessment of potential allergenicity to microbial residual components is beyond the QPS remit; if there is however, science-based evidence for some microbial species it is reported. These aspects are assessed, where applicable, separately by the EFSA Panel responsible for assessing the notification. Antimicrobial resistance was introduced as a possible safety concern for the assessment of the inclusion of bacterial species in the QPS list published in 2008 QPS Opinion (EFSA, 2008).<sup>3</sup> In the 2009 QPS Opinion (EFSA BIOHAZ Panel, 2009)<sup>4</sup> a qualification regarding the absence of antimycotic resistance for yeasts was introduced.

### 1.1.2. Terms of Reference as provided by EFSA

ToR 1: Keep updated the list of biological agents being notified in the context of a technical dossier to EFSA Units such as Feed, Pesticides, Food Ingredients and Packaging (FIP) and Nutrition, for intentional use directly or as sources of food and feed additives, food enzymes and plant protection products for safety assessment.

ToR 2: Review taxonomic units previously recommended for the QPS list and their qualifications when new information has become available. The latter is based on an review of the updated literature aiming at verifying if any new safety concern has arisen that could require the removal of the taxonomic unit from the list, and to verify if the qualifications still efficiently exclude safety concerns.

ToR 3: (Re) assess the suitability of new taxonomic units notified to EFSA for their inclusion in the QPS list. These microbiological agents are notified to EFSA and requested by the Feed Unit, the FIP Unit, the Nutrition Unit or by the Pesticides Unit.

## 2. Data and methodologies

### 2.1. Data

Only valid TUs covered by the relevant international committees on the nomenclature for microorganisms are considered for the QPS assessment.

In reply to ToR 3 ((re)assessment of the suitability of TUs notified to EFSA not present in the current QPS list for their inclusion in the updated list), for the TUs associated with the notifications compiled within the time period covered by this Statement (from April to September 2017), the literature review considered the identification, the body of knowledge, the potential safety concerns and the antimicrobial resistance. Relevant databases such as PubMed, Web of Science, Cases Database, CAB Abstracts or Food Science Technology Abstracts (FSTA) and Scopus were searched. More details on the search strategy, search keys and approach are described in Appendix A.

In reply to ToR 2, concerning the revision of the TUs previously recommended for the QPS list and their qualifications, an extensive literature search (ELS) was run as described in Appendices B and C.

## 2.2. Methodologies

### 2.2.1. Evaluation of a QPS recommendation for Taxonomic Units notified to EFSA

In response to ToR 1, the EFSA Units were asked to update the list of biological agents being notified to EFSA. Forty-six (46) notifications were received between April and September 2017, of which 16 were for a feed additive, five for food enzymes, and 25 for plant protection products (Table 1).

In response to ToR 3, out of the 46 notifications, 14 were related to TUs which already had QPS status and did not require further evaluation as did the TUs related to 30 out of the other 32 notifications:

- Fifteen notifications related to filamentous fungi and one to *Enterococcus faecium* which were excluded from QPS activities in the follow up of a recommendation of the QPS 2013 update (EFSA BIOHAZ Panel, 2013, 2014),
- Four notifications related to *E. coli* and one to *Streptomyces* spp. which were recently excluded from the current mandate by the BIOHAZ Panel,
- Eight notifications related to *Bacillus thuringiensis* and one to an oomycete that were kept on standby until receipt of a full dossier.

The TUs corresponding to the remaining two notifications were evaluated for possible QPS recommendation:

- *Kitasatospora paracochleata* was evaluated for the first time,
- *Komagataella phaffii*, which has been previously notified in February of 2017 as *Pichia pastoris* (see EFSA Panel Statement published in July 2017) was now included for the QPS assessment due to a change in the taxonomic identity.

The notifications received by EFSA, per risk assessment area, by biological group from April until September 2017 is presented in Table 1.

**Table 1:** Notifications received by EFSA, per risk assessment area and by biological group, from April until September 2017

Risk assessment area	Not evaluated in this Statement		Evaluated in this Statement	Total
	Already QPS	Excluded for QPS <sup>(a)</sup>		
<b>Biological group</b>				
<b>Feed additives</b>	<b>8</b>	<b>7</b>	<b>1</b>	<b>16</b>
Bacteria	7	5	0	12
Filamentous fungi	0	2	0	2
Yeasts	1	0	1 <sup>(b)</sup>	2
<b>Novel foods</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>0</b>
<b>Plant protection products</b>	<b>2</b>	<b>23</b>	<b>0</b>	<b>25</b>
Bacteria	1	9 <sup>(c)</sup>	0	10
Filamentous fungi	0	13	0	13
Oomycetes	0	1 <sup>(d)</sup>	0	1
Viruses	1	0	0	1
<b>Food enzymes, food additives and flavourings</b>	<b>4</b>	<b>0</b>	<b>1</b>	<b>5</b>
Bacteria	4	0	1	5
<b>Total</b>	<b>14</b>	<b>30</b>	<b>2</b>	<b>46</b>

(a): The number includes filamentous fungi or enterococci excluded from QPS evaluation in the 2013 QPS Opinion and also other bacterial species already excluded in the previous Panel Statement (*E. coli*, *Streptomyces*).

(b): Notification corresponding to *Komagataella phaffii* previously notified as *Pichia pastoris*.

(c): Eight of these notifications correspond to strains of *Bacillus thuringiensis* which were also kept on standby as agreed with Pesticides Unit until receipt of the full dossier (including the literature review).

(d): Notification kept on standby as agreed with Pesticides Unit until receipt of the full dossier (including the literature review).



On request of the EFSA Scientific Panel on Additives and Products or Substances used in Animal Feed (FEEDAP Panel) the suitability of the QPS approach for the assessment of GMM production strains and products was evaluated (see Section 3.2.3).

### 2.2.2. Monitoring of new safety concerns related to the QPS list

The aim of the ELS carried out to reply to ToR2 (review of the recommendations for the QPS list and specific qualifications), was to identify any publicly available studies reporting on safety concerns for humans, animals or the environment caused by QPS organisms since the previous QPS review (i.e. publications from 6 June of 2016 until the end of June 2017). For a detailed protocol of the process and search strategies, please refer to Annexes B and C.

After removal of duplicates 7,003 records were submitted to *Title screening* step which led to the exclusion of 6,303 of these. 700 records were found eligible for *Title and abstract screening* step which led to the exclusion of 497 of these. 203 articles finally reached the *Article appraisal step* (full text) and 83 were considered as relevant for the QPS Statement.

The flow of records from their identification by the different search strategies (as reported in Appendix C) till to their consideration as QPS potentially relevant papers is shown in Table 2:

**Table 2:** Flow of records by search strategy

Species	No papers (Title screening)	No papers (Title/abstract screening)	No papers (Article appraisal)	No papers Relevant for QPS
Alphaflexiviridae	57	5	0	No paper reached full text
<i>Bacillus</i> spp.	1,325	54	16	2
Baculoviridae	136	10	0	No paper reached full text
<i>Bifidobacterium</i> spp. <i>Carnobacterium divergens</i>	347	167	17	13
<i>Corynebacterium glutamicum</i>	73	8	1	1
<i>Gluconobacter oxydans</i> <i>Xanthomonas campestris</i>	394	2	0	No paper reached full text
<i>Lactobacillus</i> spp.	874	154	32	13
<i>Lactococcus lactis</i>	316	9	5	3
<i>Leuconostoc</i> spp. <i>Microbacterium imperiale</i>	151	18	6	5
<i>Oenococcus oeni</i> <i>Pasteuria nishizawae</i>	78	9	0	No paper reached full text
<i>Pediococcus</i> spp.	245	10	1	1
<i>Propionibacterium</i> spp.	64	1	1	1
<i>Streptococcus thermophilus</i>	110	13	3	2
Yeasts	2,833	240	121	42
<b>Total</b>	<b>7,003</b>	<b>700</b>	<b>203</b>	<b>83</b>
Excluded	6,303	497	120	

## 3. Assessment

### 3.1. Taxonomic Units evaluated during the previous QPS mandate and re-evaluated in the current Statement

None.

## 3.2. Taxonomic Units to be evaluated for the first time

### 3.2.1. *Kitasatospora paracochleata*

#### 3.2.1.1. Identity

The genus *Kitasatospora*, included in the Order Actinomycetales, comprises 23 species and resembles *Streptomyces* morphologically and physiologically. These present clear differences in their cell-wall compositions and 16S rRNA sequences that justify their separation into two genera (Omura et al., 1982; Zhang et al., 1997). *K. paracochleata* is a rather understudied species of the genus, and only two reports were highlighted in PubMed when only the name of the species was used as a keyword. One described the utility of an oligonucleotide microarray for identification of the genus members (Günther et al., 2006), while the other contained a description of *K. viridis* (Liu et al., 2005). Moreover, the whole genome sequence of *K. paracochleata* is as yet not available in the public domain.

#### 3.2.1.2. Body of knowledge

As indicated above, knowledge on *K. paracochleata* is scarce. On the other hand, collectively the members of the genus are responsible for production of more than 50 new biologically active compounds and multiple operons for secondary metabolite biosynthesis are present in the genomes of 15 sequenced strains of other species of the genus (Takahashi, 2017).

#### 3.2.1.3. Safety concerns

There is no information available on *K. paracochleata* pathogenicity.

#### 3.2.1.4. Antimicrobial resistance aspects

No information is available.

#### 3.2.1.5. Conclusions on a recommendation for the QPS list

*Kitasatospora paracochleata* cannot be granted the QPS status due to lack of information on its biology and to its possible production of toxic secondary metabolites. Based on the knowledge on the possible production of secondary metabolites of other species of the genus, the whole genus was considered ineligible for QPS.

### 3.2.2. *Komagataella phaffii*

#### 3.2.2.1. Identity

The anamorph of *Komagataella phaffii* is not described. *K. phaffii* is closely related to *Komagataella pastoris*, a species with a QPS status and from which it was separated (Kurtzman, 2005). The three species of the genus *Komagataella*, *K. pastoris*, *K. phaffii* and *K. pseudopastoris*, show no differences in standard fermentation and growth tests. Consequently, it is recommended that the species be separated based on differences in D1/D2 26S rRNA gene sequences or on differences in restriction patterns of SSU rRNA (Kurtzman et al., 2011).

#### 3.2.2.2. Body of knowledge

In total, 24 studies were identified (see Appendix A) and screened, dealing with the properties of the species as a protein expression and model organism.

*K. phaffii* is a sibling species of *K. pastoris* (Naumov et al., 2013). In the literature, it has been described to be used for the same purpose as *K. pastoris* that is for the production of heterologous proteins (Chessa et al., 2017).

There is very little information about the ecology of *K. phaffii*, but at least some strains have a similar ecology to *K. pastoris*, since both species have been isolated from sap fluxes in trees (Kurtzman et al., 2011).

#### 3.2.2.3. Safety concerns

There is no information available about any potential safety concerns regarding *K. phaffii*. However, reports on the safety of *K. pastoris* as production organism also have relevance for *K. phaffii* because this was changed as the basis of taxonomic position to the species *K. phaffii*.

#### 3.2.2.4. Resistance to antimycotics

No information is available about antimycotic resistance of *K. phaffii*.

#### 3.2.2.5. Conclusions on a recommendation for the QPS list

The species *Komagataella phaffii*, a sibling species of *K. pastoris*, can be recommended for the QPS list only when the species is used for enzyme production.

#### 3.2.3. Use of QPS approach in the assessment of genetically modified microorganisms when used as production strains

The BIOHAZ Panel evaluated the use of the QPS approach in the assessment of genetically modified microorganisms (GMM). In the case of GMMs being used as production organisms for which the recipient strain qualifies for the QPS status, and for which the genetic modification does not give rise to safety concerns, the QPS approach can be extended to the genetically modified production strain.

### 3.3. Monitoring of new safety concerns related to the QPS list

The summaries of the evaluation of the possible safety concerns for humans, animals or the environment caused by QPS organisms described and published since the previous ELS (i.e. between June 2016 and June 2017, as described in Appendices B and C) and the references selected as potentially relevant for the QPS exercise (Appendix D) for each of the TUs or groups of TUs that are part of the QPS list are presented below:

#### 3.3.1. Gram-positive non-sporulating bacteria

##### 3.3.1.1. *Bifidobacterium* spp.

Twelve papers were selected for *Bifidobacterium* for deep analysis with regard to safety concerns. The small number of cases reported was mostly presenting severe underlying conditions (cancer, preterm infants with health problems, alcoholic cirrhosis, etc.) (Esaïassen et al., 2016, 2017; Wilson and Ong, 2017) predisposing them to infections by some *Bifidobacterium* spp. (*B. longum*, *B. breve*, etc.).

These safety concerns, already described in the previous scientific Opinion (EFSA BIOHAZ Panel, 2017), are linked to predisposing factors and do not change the consideration for the QPS status of *Bifidobacterium*.

##### 3.3.1.2. *Carnobacterium divergens*

No safety concerns identified in the only article considered relevant for QPS exercise.

##### 3.3.1.3. *Corynebacterium glutamicum*

No safety concerns identified in the only article considered relevant for QPS exercise.

##### 3.3.1.4. *Lactobacillus* spp.

Thirty-six species of *Lactobacillus* are included in the QPS list. Thirteen papers have been selected to check possible safety concerns. Different *Lactobacillus* species were concerned (*L. salivarius*, *L. coryniformis*, *L. paracasei*, *L. acidophilus*, *L. delbrueckii*, *L. gasseri*, *L. animalis*, *L. rhamnosus*, *L. casei*). Invariably, all the patients suffered from predisposing health conditions.

For the cases where severe infections have been developed following probiotic consumption, the patients were suffering from predisposing conditions (cardiac insufficiencies, organ transplants, AIDS, injuries following a road accident, preterm infants). In three out of four cases (Haghighat and Crum-Cianflone, 2016; Vanichanan et al., 2016; Noreña et al., 2017), relationships between strains from probiotic preparations and clinical cases were not evident because of methodological shortcomings. In one case (Passera et al., 2016), the link was confirmed since strains from clinical cases and probiotic preparations were indistinguishable according to a genome sequencing methodology.

The safety concerns described are all considered linked to severe underlying health conditions and therefore do not change the consideration of *Lactobacillus* spp. for the QPS status.

##### 3.3.1.5. *Lactococcus lactis*

Out of the three papers selected on *Lactococcus lactis*, two dealt with infections of human patients that suffered predisposing conditions that might facilitate an infection even by innocuous

microorganisms. Furthermore, the identification procedures were not indicated at all (Fragkiadakis et al., 2017) or were negative for all samples but a single polymerase chain reaction (PCR) determination (Mansour et al., 2016). The paper on cow mastitis (Rodrigues et al., 2016) added to the increasing evidence that *L. lactis* may be considered as a sporadic agent for this problem.

Overall, the evidence provided does not suggest the need for a change in the QPS consideration of *Lactococcus lactis*.

#### **3.3.1.6. *Leuconostoc* spp.**

The three papers selected on *Leuconostoc mesenteroides* dealt with nosocomial infections of patients that suffered predisposing conditions. Franco-Cendejas et al. (2017) refer to a case of acute infection of a knee prosthesis associated with *L. mesenteroides* three years after surgery. The isolated strain was identified using both phenotypic tests and molecular analyses. The authors proposed that a patient's previous upper's respiratory tract infection, which caused hyperpermeability and the subsequent bacterial entrance into the bloodstream, may be the origin of the *L. mesenteroides* infection.

Two papers on *Leuconostoc pseudomesenteroides* were selected and studied: a case of *L. pseudomesenteroides* catheter-related sepsis in which the patient was successfully treated with antibiotic lock therapy (Ho et al., 2016) and a paper on bacteremia due to *L. pseudomesenteroides* in a patient with acute lymphoblastic leukaemia (Ino et al., 2016) without any indication of the identification procedures.

Overall, the evidence found does not require a change on the QPS consideration of *Leuconostoc* species.

#### **3.3.1.7. *Microbacterium imperiale***

No paper reached the final selection phase, so no new safety concern was found.

#### **3.3.1.8. *Oenococcus oeni***

No paper reached the final selection phase, so no new safety concern was found.

#### **3.3.1.9. *Pasteuria nishizawae***

No paper reached the final selection phase, so no new safety concern was found.

#### **3.3.1.10. *Pediococci***

One article (Han et al., 2016) describes an urinary tract infection caused by *Pediococcus pentosaceus*. There were methodological shortcomings in the identification of the microorganism and therefore it should not be considered further.

There is no requirement to change the QPS recommendation of the *P. pentosaceus* species as no additional safety concerns have been identified during the ELS revision.

#### **3.3.1.11. *Propionibacterium***

One article (Giok, 2016) about *Propionibacterium freudenreichii* describes resistance to several antimicrobials. It does not refer to a food-borne disease and there are methodological questions in the identification of the microorganism as no molecular identification was used, therefore it should not be considered further.

There is no requirement to change the QPS recommendation of the *Propionibacterium* species as no safety concerns have been identified during the ELS revision.

#### **3.3.1.12. *Streptococcus thermophilus***

None of the two retrieved papers reports safety concerns related to *S. thermophilus*; consequently, there is no requirement to change the QPS recommendation for this species.

### **3.3.2. Gram-positive spore-forming bacteria**

#### **3.3.2.1. *Bacillus***

Two papers were selected for *Bacillus* spp. for in-depth analysis. They were not considered relevant for further QPS assessment because of methodological shortcomings in the method used to identify *Bacillus* isolates to the species level: (i) a case of a 5-year old immunocompetent patient with a deep skin abscess due to *B. licheniformis* and related to a retained plant thorn (Yuste et al., 2016) and (ii) cases due to infection with *B. flexus* hospitalised in a burns unit (Uçar et al., 2016). Moreover, these

descriptions of opportunistic infections were linked to specific situational factors and do not suggest a risk for consumers or animals via exposure through the food and feed chain.

Therefore, there is no requirement to change the *Bacillus* species QPS list.

### 3.3.3. Gram-negative bacteria

#### 3.3.3.1. *Gluconobacter oxydans*

No paper reached the final selection phase so no new safety concern was found.

#### 3.3.3.2. *Xanthomonas campestris*

No paper reached the final selection phase so no new safety concern was found.

### 3.3.4. Yeasts

No information came up in the ELS that would change the current QPS status of any of the yeast species. Several of the yeasts with QPS status seldomly, but regularly, occur in fungal infections in immunocompromised or post-operational patients and in nosocomial infections. Collectively, for the QPS yeasts, the ELS identified 42 potentially relevant studies, of which 15 referred to *Candida kefir* (teleomorph = *Kluyveromyces marxianus*), 9 to *Saccharomyces cerevisiae* and 9 to *Candida famata* (teleomorph = *Debaryomyces hansenii*). Occasional reports were found for *Candida pelliculosa* (teleomorph = *Wickerhamomyces anomalus*), *Candida utilis* (teleomorph = *Lindnera jadinii*) and *Saccharomyces boulardii*. For the other yeast species with QPS status, no relevant studies were identified through the ELS.

### 3.3.5. Viruses used for plant protection

#### 3.3.5.1. Alphaflexiviridae

No paper reached the final selection phase so no new safety concern was found.

#### 3.3.5.2. Baculoviridae

No paper reached the final selection phase so no new safety concern was found.

## 4. Conclusions

ToR 1: *Keep updated the list of biological agents being notified, in the context of a technical dossier to EFSA Units (such as Feed, Food Ingredients and Packaging (FIP), Nutrition Unit and Pesticides Unit), for intentional use in feed and/or food or as sources of food and feed additives, enzymes and plant protection products for safety assessment:*

- Between the end of April 2017 and September 2017, the list was updated with 46 notifications, of which 16 related to feed additives, five to food enzymes, food additives and flavourings, and 25 to plant protection products.

ToR 2: *Review taxonomic units previously recommended for the QPS list and their qualifications when new information has become available:*

- In relation to the results of the monitoring of possible new safety concerns related to the QPS list, nothing was found that could justify a change in the QPS list or the respective qualifications.

ToR 3: *(Re)assess the suitability of taxonomic units notified to EFSA not present in the current QPS list for their inclusion in that list:*

- The TUs corresponding to 14 out of the 46 notifications received already had a QPS status.
- The TUs corresponding to 30 out of 32 notifications without a QPS status were: 15 filamentous fungi, one *Enterococcus faecium*, one *Streptomyces* species and four *E. coli*. They were not further assessed as they belong to taxonomic entities which have been excluded from QPS activities. Eight notifications related to *Bacillus thuringiensis* and one to an oomycete were also not evaluated but kept in standby until the reception of a full dossier.
- Two TUs corresponding to 2 notifications out of those 32 were evaluated for potential QPS recommendation: *Komagataella phaffii* (previously notified as *Pichia pastoris* is now included due to a change in the taxonomic classification) and *Kitasatospora paracochleata*.

- In the case of GMMs being used as production organisms for which the recipient strain qualifies for QPS status, and for which the genetic modification does not give rise to safety concerns, the QPS approach can be extended to the genetically modified production strain.

## 5. Recommendations

- *Kitasatospora paracochleata*, which has never been evaluated before, cannot be granted the QPS status due to lack of information on its biology and to its possible production of toxic secondary metabolites, which may place the whole genus in a position similar to that of *Streptomyces*, i.e. ineligibility for QPS.
- *Komagataella phaffii*, a sibling species of *K. pastoris*, can be recommended for the QPS list only when the species is used for enzyme production.

This new QPS recommendation will be included as an addition to the list of QPS status recommended biological agents (EFSA BIOHAZ Panel, 2016), published both as an update to the Scientific Opinion (EFSA BIOHAZ Panel, 2016) and as supporting information available on the Knowledge Junction at <https://doi.org/10.5281/zenodo.1146566>.

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## Glossary and Abbreviations

Antimicrobial compounds	antibiotics, bacteriocins and/or small peptides
AMR	antimicrobial resistance
BIOHAZ	EFSA Panel on Biological Hazards
ELS	extensive literature search
FEEDAP	EFSA Panel on Additives and Products or Substances used in Animal Feed
FIP	EFSA Food ingredients and packaging Unit
FSTA	Food Science Technology Abstracts
GMM	genetically modified microorganisms
QPS	Qualified Presumption of Safety
ToR	Term of Reference
TU	taxonomic unit



## **Appendix A – Search strategy followed for the (re)assessment of the suitability of TUs notified to EFSA not present in the current QPS list for their inclusion in the updated list (reply to ToR 3)**

### *Komagataella phaffii*

A literature search was performed in PubMed for the body of knowledge using the search terms “*Komagataella phaffii*”, considering all years available: 11 hits were identified and screened. Another search was done in “Web of Science”. In total, 24 studies were identified and screened.

### *Kitasatospora paracochleata*

A literature search was performed in PubMed, using the search terms “*Kitasatospora paracochleata*” for 2017: two hits were identified and screened.

## Appendix B – Protocol for Extensive literature search (ELS), relevance screening, and article evaluation for the maintenance and update of list of QPS-recommended biological agents (reply to ToR 2)

The following protocol for extensive literature search (ELS) will be used in the context of the EFSA self-task mandate on the list of QPS-recommended biological agents intentionally added to the food or feed (EFSA-Q-2016-00684).

### B.1. Description of the process

An ELS of studies related to safety concerns for humans, animals, plants and/or the environment of microorganisms recommended for the Qualified Presumption of Safety (QPS) 2019 list will be performed.

The process will be performed according to the following main steps:

- ELS for potentially relevant citations;
- Relevance screening to select the citations identified by the literature search, based on titles and abstract and then full-text;
- Evaluation of articles according to pre-specified categories of possible safety concerns;
- Discussion between experts to come to collective expert evaluation of the outcome, reflected in the QPS Opinion and Panel Statements.

Considering the purpose of the QPS approach, a broad search will be performed.

The review questions will be broken down into key elements using the PECO conceptual model:

- Population of interest (P)
- Exposure of interest (E)
- Comparator (C)
- Outcomes of interest (O)

#### B.1.1. Objective

The aim is to identify any publicly available studies reporting on safety concerns for humans, animals or the environment caused by microorganisms on the QPS recommended list (see Appendix E).

#### B.1.2. Target population

The populations of interest are humans, animals, plants and the environment.

#### B.1.3. Exposure

Citations must report on at least one species included in one of the five groups of named species specified in the EFSA QPS recommended list of the QPS 2016 update (see Table A.1 in Appendix A to (EFSA BIOHAZ Panel, 2017)):

- a) Gram-positive non-spore-forming bacteria;
- b) Gram-positive spore-forming bacteria;
- c) Gram-negative bacteria;
- d) Viruses used for plant protection;
- e) Yeasts

In more detail:

- a) Gram-positive non-spore forming bacteria:

*Bifidobacterium adolescentis*, *Bifidobacterium animalis*, *Bifidobacterium bifidum*, *Bifidobacterium breve*, *Bifidobacterium longum*, *Carnobacterium divergens*, *Corynebacterium glutamicum*, *Lactobacillus acidophilus*, *Lactobacillus amylolyticus*, *Lactobacillus animalis*, *Lactobacillus amylovorus*, *Lactobacillus alimentarius*, *Lactobacillus aviaries*, *Lactobacillus brevis*, *Lactobacillus buchneri*, *Lactobacillus casei*, *Lactobacillus cellobiosus*, *Lactobacillus collinoides*, *Lactobacillus coryniformis*, *Lactobacillus crispatus*, *Lactobacillus curvatus*, *Lactobacillus delbrueckii*, *Lactobacillus diolivorans*, *Lactobacillus farciminis*, *Lactobacillus*

*fermentum, Lactobacillus gallinarum, Lactobacillus gasseri, Lactobacillus helveticus, Lactobacillus hilgardii, Lactobacillus johnsonii, Lactobacillus kefiranofaciens, Lactobacillus kefir, Lactobacillus mucosae, Lactobacillus panis, Lactobacillus paracasei, Lactobacillus paraplantarum, Lactobacillus pentosus, Lactobacillus plantarum, Lactobacillus pontis, Lactobacillus reuteri, Lactobacillus rhamnosus, Lactobacillus sakei, Lactobacillus salivarius, Lactobacillus sanfranciscensis, Lactococcus lactis, Leuconostoc citreum, Leuconostoc lactis, Leuconostoc mesenteroides, Leuconostoc pseudomesenteroides, Microbacterium imperiale, Oenococcus oeni, Pasteuria nishizawae, Pediococcus acidilactici, Pediococcus dextrinicus, Pediococcus parvulus, Pediococcus pentosaceus, Propionibacterium freudenreichii, Propionibacterium acidopropionici, Streptococcus thermophilus;*

b) Gram-positive spore-forming bacteria:

*Bacillus amyloliquefaciens, Bacillus atropheus, Bacillus clausii, Bacillus coagulans, Bacillus flexus, Bacillus fusiformis, Bacillus lentus, Bacillus licheniformis, Bacillus megaterium, Bacillus mojavensis, Bacillus pumilus, Bacillus smithii, Bacillus subtilis, Bacillus vallismortis, Geobacillus stearothermophilus;*

c) Gram-negative bacteria:

*Gluconobacter oxydans; Xanthomonas campestris;*

d) Viruses used for plant protection: Plant viruses (Family):

Alphaflexiviridae, Potyviridae Insect viruses (Family): Baculoviridae;

e) Yeasts:

*Candida cylindracea, Debaryomyces hansenii, Hanseniaspora uvarum, Kluyveromyces lactis, Kluyveromyces marxianus, Komagataella pastoris, Lindnera jadinii, Ogataea angusta, Saccharomyces bayanus, Saccharomyces cerevisiae, Saccharomyces pastorianus, Schizosaccharomyces pombe, Wickerhamomyces anomalus, Xanthophyllomyces dendrorhous.*

For the yeast species, as previously, the name of the teleomorphic form is used in the list of QPS species, when available. Important synonyms and older names were also included in the searches. For instance, names of the anamorphic growth forms were included, when such a form is known:

- *Debaryomyces hansenii*: anamorph *Candida famata*;
- *Hanseniaspora uvarum*: anamorph *Kloeckera apiculata*;
- *Kluyveromyces lactis*: anamorph *Candida spherica*;
- *Kluyveromyces marxianus*: anamorph *Candida kefir*;
- *Komagataella pastoris*: synonym *Pichia pastoris*;
- *Lindnera jadinii*: synonyms *Pichia jadinii, Hansenula jadinii, Torulopsis utilis*, anamorph *Candida utilis*;
- *Ogataea angusta*: synonym *Pichia angusta*;
- *Saccharomyces cerevisiae*: synonym *Saccharomyces boulardii*;
- *Saccharomyces pastorianus*: synonym *Saccharomyces carlsbergensis*;
- *Wickerhamomyces anomalus*: synonyms *Hansenula anomala, Pichia anomala, Saccharomyces anomalus*, anamorph *Candida pelliculosa*;
- *Xanthophyllomyces dendrorhous*: anamorph *Phaffia rhodozyma*.

#### B.1.4. Comparator

It is expected that the prevalent study designs will be case reports or case series and studies based on surveys or isolate collections. The remaining study designs may include: studies using laboratory isolates; randomised controlled trials, field trials, or experimental designs in the laboratory; experimental designs in live animals with a deliberate disease challenge; observational study designs; animal or insect models; investigations to identify or to understand the causes of safety concerns (e.g. identification, characterisation of toxic factors, virulence mechanisms); studies to demonstrate beneficial effects but with reporting of unwanted side-effects.

Since it is expected that in the majority of the study designs relevant for the review question, the comparator will not be available, the latter will not be included as a key element in the search strategy.

### B.1.5. Outcomes of interest

The outcomes of interest to this ELS are:

Question 1:

- potential harms
- safety issues
- virulence or infectivity
- intoxication

Question 2:

- (acquired/intrinsic) antimicrobial resistance (AMR) covering phenotypic and genotypic aspects

The QPS concept does not address hazards linked to the formulation or processing of the products based on biological agents added into the food or feed chain. Neither the safety of users handling the product nor the genetic modifications are taken into account.

### B.1.6. Identification of the review questions

The following research questions will be addressed:

- Is there evidence of any safety concerns, including virulence features and toxin production, for humans, animals, plants and/or the environment associated with microbial species currently recommended for the QPS list since the previous QPS review (i.e. published since June 2016 till June 2019)?
- Is there evidence related to the presence or absence of antimicrobial resistance or antimicrobial resistance genes for the same microbial species published during the same time period?

## B.2. Eligibility criteria for study selection

The selection of studies relevant to question 1 and 2 will be performed applying the eligibility criteria described in Table B.1 below.

**Table B.1:** Eligibility criteria for questions 1 and 2

	Criteria
Study design	No specific type of study design will be used to include/exclude relevant studies, although it is expected that the prevalent study designs will be case reports or case series and studies based on surveys or isolate collections
Study characteristics	No exclusion will be based on study characteristics
Population	Humans, animals, plants, environment
Exposure	Studies must report on at least one TU as identified in Section B.1.3
Outcome of interest	Outcomes as listed in Section B.1.5
Language	English
Time	June 2016 until end June 2019
Publication type	Primary research studies and secondary studies reporting previously unpublished primary studies

## B.3. Literature searches

Searches will be conducted in a range of relevant information sources to identify any evidence of safety concerns and AMR regarding the target microbial species.

Considering the results of the previous QPS exercise, to handle the high number of studies identified in each group, 20 search strategies were prepared: three for yeasts, one for insect viruses, one for plant viruses, 13 for Gram-positive bacteria and two for Gram-negative bacteria according to named species specified by EFSA in the QPS recommended list of the QPS 2016 update (see Table A.1 in Appendix A to (EFSA BIOHAZ Panel, 2017)).

The 20 subgroups of target microbial species will be searched separately.

Each search strategy will comprise two elements: the search terms (Section B.3.1) and the information sources (Section B.3.2) to be searched.

### B.3.1. Search terms

The search strategies used to identify studies are given in Appendix C.

Each strategy will comprise two key elements:

- Target microbial species as described in Section B.1.3 ('Exposure')
- Safety issues as described in Section B.1.5 ('Outcomes').

In order to maximise the sensitivity of the search for the species for which the number of overall publications in the relevant time period is expected to be low, the search strategy will not include outcome-related terms.

The population of interest (humans, animals, plants or the environment) will not be included as a key element in the search strategies, as it is often not explicitly described within a title or abstract. It would also have been difficult to describe adequately such a broad population using title/abstract words and/or subject headings. Population information will be captured at the time of evaluating the articles (see Section B.1 above).

Search terms for safety issues were identified in close collaboration with the information specialist; example of such terms, are the following: 'toxin\*', 'disease\*', 'infection\*', 'clinical\*', 'virulen\*', 'antimicrobial resistan\*', 'endocarditis'.

The 20 subgroups of target microbial species will be entered on separate search lines. The search line for each group will be combined with the safety terms individually.

The searches will not be limited by language or study design.

The review period will be from June 2016 to June 2019.

### B.3.2. Information sources searched

The same information sources used for the previous QPS exercise (EFSA BIOHAZ Panel, 2017) will be searched for studies reporting safety concerns regarding the target microbial species (see Table B.2 below).

**Table B.2:** Information sources to be searched to identify relevant studies

Information source	Interface
Web of Science Core Collection	Web of Science, Thomson Reuters 2017
CAB Abstracts	Web of Science, Thomson Reuters 2017
BIOSIS Citation Index	Web of Science, Thomson Reuters 2017
MEDLINE	Web of Science, Thomson Reuters 2017
Food Science Technology Abstracts (FSTA)	Web of Science, Thomson Reuters 2017

Search results will be downloaded from the information sources and imported into EndNote® X8 bibliographic management software. For each of the 20 species groups, within-group removal of duplicate entries will be done in EndNote® X8. Following uploading of the species groups into the DistillerSR<sup>6</sup> online software, removal of duplicates will again be undertaken, using the Duplicate Detection feature.

### B.4. Study selection and article evaluation

To identify potentially relevant studies to be included in the review the studies will be selected by a three-step procedure using the DistillerSR online software.

The results of the different phases of the study selection process will be reported in a flowchart as recommended in the PRISMA statement on preferred reporting items for systematic reviews and meta-analyses (Moher et al., 2009).

<sup>6</sup> DistillerSR, Evidence Partners, Ottawa, Canada. <https://www.evidencepartners.com/products/distillersr-systematic-review-software/>

### B.4.1. Screening for potential relevance at title level

Articles will initially be screened at title level in parallel by two reviewers by experts and, if needed, EFSA staff.

If the information in the title is not relevant for the research objectives the article will not proceed to the next step (Section B.4.2).

Articles that will be excluded during screening at this step will be stored in Distiller SR.

In case of doubts or divergences between the reviewers, the paper will proceed to step 2.

### B.4.2. Screening for potential relevance at title and abstract level

The articles passing the first step will undergo a screening at abstract level in parallel by two experts.

If the information in title and abstract is not relevant for the research objectives the article will not proceed to the next step (Section B.4.3).

Articles that will be excluded during screening at this step will be stored in Distiller SR.

In case of doubts or divergences between the reviewers, the paper will proceed to step 2.

### B.4.3. Article evaluation

The aim of this step will be to confirm that the article is relevant for the QPS project and, in case it is, to evaluate it. It will be carried out at full text level.

The articles passing the second step will undergo a validation procedure carried out by two Experts. One reviewer will initially be tasked with the evaluation of a paper. The evaluation will be then forwarded to another reviewer for the validation the appraisal received.

In case of disagreement with the initial appraisal, the second reviewer will write down his comments. The reviewers will initially try to solve the disagreement. In case this will not be possible the conflicting information will be presented for Collective expert evaluation of the ELS outcome (see Section B.5).

If the information contained in the article is not relevant for the research objectives, the article will not be evaluated. Articles that will not be considered relevant will be stored in Distiller SR.

#### B.4.3.1. Questions for study selection and article evaluation

STEP 1 (Screening for potential relevance):

*Question 1:* Is the full text available, in English and relevant for the QPS project?

- Yes: Include and continue to Article evaluation form
- Full text not available: Exclude
- Full text not in English: Exclude
- Full text in English but not relevant: Exclude

STEP 2 (Article evaluation):

*Question 2: Identification of the microorganisms*

- The article will be characterised in terms of the microorganisms involved

Single choice question: the Experts will identify the microorganism/s described in the article. In case more than one microorganism is described in the paper the form will be repeated for each microorganism.

*Question 3: Please report any safety concern with an impact on human health*

- Free text

*Question 4: Please report any safety concern with an impact on animal health*

- Free text

*Question 5: Please report any safety concern with an impact on the environment*

- Free text

*Question 6: Please report any safety concern related to AMR*

- Free text

*Question 7: Other safety concerns (please specify)*

- Free text

## **B.5. Collective expert evaluation of the ELS outcome and presentation in the QPS opinion**

The overall results of the searches and evaluations of individual articles will be presented in tabular format for each group/sub-group and species. These results will be further evaluated collectively by the working group and the outcome will be reflected in the QPS opinion to be adopted in December of 2019.

## **B.6. Update of the process**

The literature search, study selection and collective expert evaluation will be repeated every 6 months.

## **References**

- EFSA BIOHAZ Panel (EFSA Panel on Biological Hazards), 2017. Scientific Opinion on the update of the list of QPS-recommended biological agents intentionally added to food or feed as notified to EFSA. EFSA Journal 2017;15(3):4664, 177 pp. <https://doi.org/10.2903/j.efsa.2017.4664>
- Moher et al., 2009. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS Med, 6, e1000097.

## Appendix C – Search strategies for the maintenance and update of list of QPS-recommended biological agents (reply to ToR 2)

### Gram-Positive Non-Spore-forming Bacteria

#### *Bifidobacterium* spp.

<b>String for species</b>	
"Bifidobacterium adolescentis" OR "Bifidobacterium animalis" OR "Bifidobacterium bifidum" OR "Bifidobacterium breve" OR "Bifidobacterium longum" OR "B adolescentis" OR "B animalis" OR "B bifidum" OR "B breve" OR "B longum"	
<b>OUTCOME</b>	<b>String</b>
1) Antimicrobial/Antibiotic/Antimycotic	"antimicrobial resistan*" OR "antibiotic resistan*" OR "antimicrobial susceptibil*"
2) Infection/Bacteremia/Fungemia/Sepsis	infection* OR abscess* OR sepsis* or septic* OR bacteremia OR bacteraemia OR toxin*
3) Type of disease	endocarditis OR abscess OR meningitis
4) Mortality/Morbidity	clinical* OR death* OR morbidit* OR mortalit* OR disease* OR illness*
5) Disease Risk	opportunistic OR virulen*

#### *Carnobacterium divergens*

<b>String for species</b>	
"Carnobacterium divergens" OR "C divergens"	
<b>OUTCOME</b>	<b>String</b>
6) Antimicrobial/Antibiotic/Antimycotic	<i>Not applied</i>
7) Infection/Bacteremia/Fungemia/Sepsis	<i>Not applied</i>
8) Type of disease	<i>Not applied</i>
9) Mortality/Morbidity	<i>Not applied</i>
10) Disease Risk	<i>Not applied</i>

#### *Corynebacterium glutamicum*

<b>String for species</b>	
"Corynebacterium glutamicum" OR "C glutamicum" OR "Brevibacterium lactofermentum" OR "B lactofermentum"	
<b>OUTCOME</b>	<b>String</b>
1) Antimicrobial/Antibiotic/Antimycotic	"antimicrobial resistan*" OR "antibiotic resistan*" OR "antimicrobial susceptibil*"
2) Infection/Bacteremia/Fungemia/Sepsis	infection* OR abscess* OR sepsis* or septic* OR bacteremia OR bacteraemia OR toxin* OR "pathogen*"
3) Type of disease	<i>Not applied</i>
4) Mortality/Morbidity	clinical* OR death* OR morbidit* OR mortalit* OR disease* OR illness*
5) Disease Risk	opportunistic OR virulen*



### **Lactobacillus spp.**

<b>String for species</b>	
"Lactobacillus acidophilus" OR "Lactobacillus amylolyticus" OR "Lactobacillus amylovorus" OR "Lactobacillus alimentarius" OR "Lactobacillus animalis" OR "Lactobacillus aviaries" OR "Lactobacillus brevis" OR "Lactobacillus buchneri" OR "Lactobacillus casei" OR "Lactobacillus zeae" OR "Lactobacillus cellobiosus" OR "Lactobacillus coryniformis" OR "Lactobacillus crispatus" OR "Lactobacillus curvatus" OR "Lactobacillus delbrueckii" OR "Lactobacillus diolivorans" OR "Lactobacillus farciminis" OR "Lactobacillus fermentum" OR "Lactobacillus gallinarum" OR "Lactobacillus gasseri" OR "Lactobacillus helveticus" OR "Lactobacillus hilgardii" OR "Lactobacillus johnsonii" OR "Lactobacillus kefirifaciens" OR "Lactobacillus kefiri" OR "Lactobacillus mucosae" OR "Lactobacillus panis" OR "Lactobacillus collinoides" OR "Lactobacillus paracasei" OR "Lactobacillus paraplantarum" OR "Lactobacillus pentosus" OR "Lactobacillus plantarum" OR "Lactobacillus pontis" OR "Lactobacillus reuteri" OR "Lactobacillus rhamnosus" OR "Lactobacillus sakei" OR "Lactobacillus salivarius" OR "Lactobacillus sanfranciscensis" OR "L acidophilus" OR "L amylolyticus" OR "L amylovorus" OR "L alimentarius" OR "L animalis" OR "L aviaries" OR "L brevis" OR "L buchneri" OR "L casei" OR "L zeae" OR "L cellobiosus" OR "L coryniformis" OR "L crispatus" OR "L curvatus" OR "L delbrueckii" OR "L diolivorans" OR "L farciminis" OR "L fermentum" OR "L gallinarum" OR "L gasseri" OR "L helveticus" OR "L hilgardii" OR "L johnsonii" OR "L kefirifaciens" OR "L kefiri" OR "L mucosae" OR "L panis" OR "L collinoides" OR "L paracasei" OR "L paraplantarum" OR "L pentosus" OR "L plantarum" OR "L pontis" OR "L reuteri" OR "L rhamnosus" OR "L sakei" OR "L salivarius" OR "L sanfranciscensis"	
<b>OUTCOME</b>	<b>String</b>
1) Antimicrobial/Antibiotic/Antimycotic	"antimicrobial resistan*" OR "antibiotic resistan*" OR "antimicrobial susceptibil*"
2) Infection/Bacteremia/Fungemia/Sepsis	infection* OR abscess* OR sepsis* or septic* OR bacteremia OR bacteraemia OR toxin*
3) Type of disease	endocarditis OR abscess OR meningitis
4) Mortality/Morbidity	<i>Not applied</i>
5) Disease Risk	opportunistic OR virulen*

### **Lactococcus lactis**

<b>String for species</b>	
"Lactococcus lactis" OR "L lactis"	
<b>OUTCOME</b>	<b>String</b>
1) Antimicrobial/Antibiotic/Antimycotic	"antimicrobial resistan*" OR "antibiotic resistan*" OR "antimicrobial susceptibil*"
2) Infection/Bacteremia/Fungemia/Sepsis	infection* OR abscess* OR sepsis* or septic* OR bacteremia OR bacteraemia OR toxin*
3) Type of disease	endocarditis OR abscess OR meningitis
4) Mortality/Morbidity	clinical* OR death* OR morbidit* OR mortalit* OR disease* OR illness*
5) Disease Risk	opportunistic OR virulen*

### ***Leuconostoc* spp.**

<b>String for species</b>	
"Leuconostoc mesenteroides" OR "Leuconostoc lactis" OR "Leuconostoc pseudomesenteroides" OR "Leuconostoc citreum" OR "L mesenteroides" OR "L lactis" OR "L pseudomesenteroides" OR "L citreum"	
<b>OUTCOME</b>	<b>String</b>
1) Antimicrobial/Antibiotic/Antimycotic	"antimicrobial resistan*" OR "antibiotic resistan*" OR "antimicrobial susceptibil*"
2) Infection/Bacteremia/Fungemia/Sepsis	infection* OR abscess* OR sepsis* or septic* OR bacteremia OR bacteraemia OR toxin*
3) Type of disease	<i>Not applied</i>
4) Mortality/Morbidity	clinical* OR death* OR morbidit* OR mortalit* OR disease* OR illness*
5) Disease Risk	opportunistic OR virulen*

### ***Microbacterium imperiale***

<b>String for species</b>	
"Microbacterium imperiale" OR "M imperiale"	
<b>OUTCOME</b>	<b>String</b>
6) Antimicrobial/Antibiotic/Antimycotic	<i>Not applied</i>
7) Infection/Bacteremia/Fungemia/Sepsis	<i>Not applied</i>
8) Type of disease	<i>Not applied</i>
9) Mortality/Morbidity	<i>Not applied</i>
10) Disease Risk	<i>Not applied</i>

### ***Oenococcus* spp.**

<b>String for species</b>	
"Oenococcus oeni" OR "O oeni"	
<b>OUTCOME</b>	<b>String</b>
1) Antimicrobial/Antibiotic/Antimycotic	<i>Not applied</i>
2) Infection/Bacteremia/Fungemia/Sepsis	<i>Not applied</i>
3) Type of disease	<i>Not applied</i>
4) Mortality/Morbidity	<i>Not applied</i>
5) Disease Risk	<i>Not applied</i>

### ***Pasteuria nishizawae***

<b>String for species</b>	
"Pasteuria nishizawae" OR "P nishizawae"	
<b>OUTCOME</b>	<b>String</b>
11) Antimicrobial/Antibiotic/Antimycotic	<i>Not applied</i>
12) Infection/Bacteremia/Fungemia/Sepsis	<i>Not applied</i>
13) Type of disease	<i>Not applied</i>
14) Mortality/Morbidity	<i>Not applied</i>
15) Disease Risk	<i>Not applied</i>

***Pediococcus* spp.**

<b>String for species</b>	
"Pediococcus pentosaceus" OR "Pediococcus dextrinicus" OR "Pediococcus acidilactici" OR "Pediococcus parvulus" OR "P pentosaceus" OR "P dextrinicus" OR "P acidilactici" OR "P parvulus"	
<b>OUTCOME</b>	<b>String</b>
1) Antimicrobial/Antibiotic/Antimycotic	<i>Not applied</i>
2) Infection/Bacteremia/Fungemia/Sepsis	<i>Not applied</i>
3) Type of disease	<i>Not applied</i>
4) Mortality/Morbidity	<i>Not applied</i>
5) Disease Risk	<i>Not applied</i>

***Propionibacterium* spp.**

<b>String for species</b>	<b>Number papers retrieved and notes</b>
"Propionibacterium acidipropionici" OR "Propionibacterium freudenreichii" OR "P acidipropionici" OR "P freudenreichii"	<b>176</b>
<b>OUTCOME</b>	<b>String</b>
1) Antimicrobial/Antibiotic/Antimycotic	<i>Not applied</i>
2) Infection/Bacteremia/Fungemia/Sepsis	<i>Not applied</i>
3) Type of disease	<i>Not applied</i>
4) Mortality/Morbidity	<i>Not applied</i>
5) Disease Risk	<i>Not applied</i>

***Streptococcus thermophilus***

<b>String for species</b>	
"Streptococcus thermophilus" OR "S thermophilus" "Streptococcus thermophilus" OR "S thermophilus"	
<b>OUTCOME</b>	<b>String</b>
1) Antimicrobial/Antibiotic/Antimycotic	"antimicrobial resistan*" OR "antibiotic resistan*" OR "antimicrobial susceptibil*"
2) Infection/Bacteremia/Fungemia/Sepsis	infection* OR abscess* OR sepsis* or septic* OR bacteremia OR bacteraemia OR toxin*
3) Type of disease	<i>Not applied</i>
4) Mortality/Morbidity	clinical* OR death* OR morbidit* OR mortalit* OR disease* OR illness*
5) Disease Risk	opportunistic OR virulen*

## Gram-Positive Spore-forming Bacteria

### *Bacillus* spp.

String for species	
"Bacillus amyloliquefaciens" OR "Bacillus coagulans" OR "Bacillus clausii" OR "Bacillus atrophaeus" OR "Bacillus flexus" OR "Bacillus fusiformis" OR "Lysinibacillus fusiformis" OR "Bacillus licheniformis" OR "Bacillus lentus" OR "Bacillus mojavensis" OR "Bacillus megaterium" OR "Bacillus vallismortis" OR "Bacillus smithii" OR "Bacillus subtilis" OR "Bacillus pumilus" OR "Geobacillus stearothermophilus" OR "B amyloliquefaciens" OR "B coagulans" OR "B clausii" OR "B atrophaeus" OR "B flexus" OR "B fusiformis" OR "L fusiformis" OR "B licheniformis" OR "B lentus" OR "B mojavensis" OR "B megaterium" OR "B vallismortis" OR "B smithii" OR "B subtilis" OR "B pumilus" OR "G stearothermophilus"	
OUTCOME	String
1) Antimicrobial/Antibiotic/Antimycotic	"antimicrobial resistan*" OR "antibiotic resistan*" OR "antimicrobial susceptibil*"
2) Infection/Bacteremia/Fungemia/Sepsis	infection* OR abscess* OR sepsis* or septic* OR bacteremia OR bacteraemia OR toxin*
3) Type of disease	endocarditis OR abscess OR meningitis
4) Mortality/Morbidity	<i>Not applied</i>
5) Disease Risk	opportunistic OR virulen*

## Gram-negative bacteria

### *Gluconobacter oxydans*

String for species	
"Gluconobacter oxydans" OR "G oxydans"	
OUTCOME	String
1) Antimicrobial/Antibiotic/Antimycotic	<i>Not applied</i>
2) Infection/Bacteremia/Fungemia/Sepsis	<i>Not applied</i>
3) Type of disease	<i>Not applied</i>
4) Mortality/Morbidity	<i>Not applied</i>
5) Disease Risk	<i>Not applied</i>

### *Xanthomonas campestris*

String for species	
"Xanthomonas campestris" OR "X campestris"	
OUTCOME	String
1) Antimicrobial/Antibiotic/Antimycotic	<i>Not applied</i>
2) Infection/Bacteremia/Fungemia/Sepsis	<i>Not applied</i>
3) Type of disease	<i>Not applied</i>
4) Mortality/Morbidity	<i>Not applied</i>
5) Disease Risk	<i>Not applied</i>

## Yeasts

### TUs without keywords for OUTCOME

String for species	
"Candida cylindracea" OR "Debaryomyces hansenii" OR "Candida famata" OR "Hanseniaspora uvarum" OR "Kloeckera apiculata" OR "Ogataea angusta" OR "Pichia angusta" OR "Saccharomyces bayanus" OR "Saccharomyces pastorianus" OR "Saccharomyces carlsbergensis" OR "Wickerhamomyces anomalus" OR "Hansenula anomala" OR "Pichia anomala" OR "Saccharomyces anomalus" OR "Candida pelliculosa" OR "Xanthophyllomyces dendrorhous" OR "Phaffia rhodozyma" OR "C cylindracea" OR "D hansenii" OR "C famata" OR "H uvarum" OR "K apiculata" OR "O angusta" OR "P angusta" OR "S bayanus" OR "S pastorianus" OR "S carlsbergensis" OR "W anomalus" OR "H anomala" OR "P anomala" OR "S anomalus" OR "C pelliculosa" OR "X dendrorhous" OR "P rhodozyma"	
OUTCOME	String
1) Antimicrobial/Antibiotic/Antimycotic	<i>Not applied</i>
2) Infection/Bacteremia/Fungemia/Sepsis	<i>Not applied</i>
3) Type of disease	<i>Not applied</i>
4) Mortality/Morbidity	<i>Not applied</i>
5) Disease Risk	<i>Not applied</i>

### TUs with keywords for OUTCOME except for type of disease and morbidity/mortality

String for species	
"Kluyveromyces lactis" OR "Candida spherica" OR "Kluyveromyces marxianus" OR "Candida kefir" OR "Komagataella pastoris" OR "Pichia pastoris" OR "Lindnera jadinii" OR "Pichia jadinii" OR "Hansenula jadinii" OR "Torulopsis utilis" OR "Candida utilis" OR "Schizosaccharomyces pombe" OR "K lactis" OR "C spherica" OR "K marxianus" OR "C kefir" OR "K pastoris" OR "P pastoris" OR "L jadinii" OR "P jadinii" OR "H jadinii" OR "T utilis" OR "C utilis" OR "S pombe"	
OUTCOME	String
1) Antimicrobial/Antibiotic/Antimycotic	"antimicrobial resistan*" OR "antimycotic resistan*" OR "antimicrobial susceptibil*"
2) Infection/Bacteremia/Fungemia/Sepsis	infection* OR abscess* OR sepsis* OR septic* OR fungemia OR fungaemia OR mycos*
3) Type of disease	<i>Not applied</i>
4) Mortality/Morbidity	<i>Not applied</i>
5) Disease Risk	opportunistic OR virulen*

**TUs with keywords for OUTCOME except for type of disease**

String for species	
"Saccharomyces cerevisiae" OR "Saccharomyces boulardii" OR "S cerevisiae" OR "S boulardii"	
OUTCOME	String
1) Antimicrobial/Antibiotic/Antimycotic	"antimicrobial resistan*" OR "antimycotic resistan*" OR "antimicrobial susceptibil*"
2) Infection/Bacteremia/Fungemia/Sepsis	infection* OR abscess* OR sepsis* or septic* OR fungemia OR fungaemia OR mycos*
3) Type of disease	<i>Not applied</i>
4) Mortality/Morbidity	clinical* OR death* OR morbidit* OR mortalit* OR disease* OR illness*
5) Disease Risk	opportunistic OR virulen*

**Viruses used for plant protection**

**Alphaflexiviridae**

String for species	
Alphaflexiviridae OR Potyviridae	
OUTCOME	String
1) Antimicrobial/Antibiotic/Antimycotic	Not applied
2) Infection/Bacteremia/Fungemia/Sepsis	necros*
3) Type of disease	Not applied
4) Mortality/Morbidity	mortalit* OR "safety concern*" OR "health hazard"
5) Disease Risk	virulen*

**Baculoviridae**

String for species	
"Nuclear polyhedrosis virus" OR granulovirus OR baculoviridae	
OUTCOME	String
1) Antimicrobial/Antibiotic/Antimycotic	<i>Not applied</i>
2) Infection/Bacteremia/Fungemia/Sepsis	<i>Not applied</i>
3) Type of disease	"nuclear polyhedrosis" OR granulosis
4) Mortality/Morbidity	mortalit* OR "safety concern*" OR "health hazard"
5) Disease Risk	<i>Not applied</i>

## Appendix D – References selected from the ELS exercise as relevant for the QPS for searches from June 2016 to June 2017 (reply to ToR 2)

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None

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None

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None

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None

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None

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None

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### **Other yeasts**

None

### **Viruses used for plant protection**

#### **Alphaflexiviridae**

None

#### **Baculoviridae**

None

## **Appendix E – The 2016 updated list of QPS status recommended biological agents in support of EFSA risk assessments**

The list of QPS status recommended biological agents (EFSA BIOHAZ Panel, 2016) is being maintained in accordance with the self-task mandate of the BIOHAZ Panel (2017-2019). Possible additions to this list are included around every 6 months, with the first Panel Statement adopted in June 2017 and the last Panel Statement planned for adoption in December 2019. These additions are published as updates to the Scientific Opinion (EFSA BIOHAZ Panel, 2016) available at <https://doi.org/10.2903/j.efsa.2017.4664> and, as of January 2018, also as supporting information linked to every Panel Statement available on the Knowledge Junction at <https://doi.org/10.5281/zenodo.1146566>.

**Appendix F – Microbial species as notified to EFSA, received between April and September 2017 (reply to ToR 1)**

EFSA risk assessment area	Microorganism species/strain	Intended use	EFSA Question number <sup>(a)</sup> and EFSA webpage link <sup>(b)</sup>	Additional information provided by the EFSA Scientific Unit	Previous QPS status? <sup>(c)</sup>	To be evaluated? yes or no <sup>(d)</sup>
<b>Bacteria</b>						
<b>Food additives, food enzymes, flavourings</b>	<i>Bacillus amyloliquefaciens</i> (strain MAS)	Production of food enzyme 4-beta-glucanotransferase	EFSA-Q-2017-00405	GMM strain	Yes	No
<b>Food additives, food enzymes, flavourings</b>	<i>Bacillus subtilis</i> (strain BABSC)	Production of food enzyme maltogenic amylase	EFSA-Q-2017-00546	GMM strain	Yes	No
<b>Food additives, food enzymes, flavourings</b>	<i>Bacillus subtilis</i> (strain BR151 (pUAQ2))	Production of food enzyme 1,4-beta-glucan	EFSA-Q-2017-00408	GMM strain	Yes	No
<b>Food additives, food enzymes, flavourings</b>	<i>Bacillus subtilis</i> (strain HPN 131)	Production of bacillolysin	EFSA-Q-2017-00543		Yes	No
<b>Food additives, food enzymes, flavourings</b>	<i>Kitasatospora paracochleata</i>	Production of phospholipase	EFSA-Q-2017-00544		No	Yes
<b>Feed additives</b>	<i>Bacillus licheniformis</i>	Zootechnical additive	EFSA-Q-2017-00524		Yes	No
<b>Feed additives</b>	<i>Corynebacterium glutamicum</i>	Production of arginine	EFSA-Q-2017-00483		Yes	No
<b>Feed additives</b>	<i>Corynebacterium glutamicum</i>	Production of arginine	EFSA-Q-2017-00484		Yes	No
<b>Feed additives</b>	<i>Corynebacterium glutamicum</i>	Production of lysine	EFSA-Q-2017-00501		Yes	No
<b>Feed additives</b>	<i>Enterococcus faecium</i>	Zootechnical additive	EFSA-Q-2017-00525		No	No
<b>Feed additives</b>	<i>Escherichia coli</i> K-12	Production of arginine	EFSA-Q-2017-00480		No	No
<b>Feed additives</b>	<i>Escherichia coli</i> K-12	Production of tryptophan	EFSA-Q-2017-00542		No	No
<b>Feed additives</b>	<i>Escherichia coli</i> K-12	Production of threonine	EFSA-Q-2017-00610		No	No
<b>Feed additives</b>	<i>Escherichia coli</i> K-12	Production of tryptophane	EFSA-Q-2017-00613		No	No
<b>Feed additives</b>	<i>Lactobacillus acidophilus</i>	Zootechnical additive	EFSA-Q-2017-00536		Yes	No
<b>Feed additives</b>	<i>Pediococcus pentosaceus</i>	Technological additive	EFSA-Q-2017-00449		Yes	No

EFSA risk assessment area	Microorganism species/strain	Intended use	EFSA Question number <sup>(a)</sup> and EFSA webpage link <sup>(b)</sup>	Additional information provided by the EFSA Scientific Unit	Previous QPS status? <sup>(c)</sup>	To be evaluated? yes or no <sup>(d)</sup>
<b>Feed additives</b>	<i>Propionibacterium freudenreichii</i> ssp. <i>shermanii</i>	Technological additive	EFSA-Q-2017-00613		Yes	No
<b>Plant protection products</b>	<i>Bacillus amyloliquefaciens</i> strain QST 713 (formerly <i>subtilis</i> )	Plant protection product	EFSA-Q-2016-00172	Request for an EFSA peer review (EFSA Conclusion) on the active substance <i>Bacillus amyloliquefaciens</i> strain QST 713 (formerly <i>subtilis</i> ) according to Article 13 of Regulation (EU) No 844/2012	Yes	No
<b>Plant protection products</b>	<i>Bacillus thuringiensis aizawai</i> strain ABTS-1857	Plant protection product	EFSA-Q-2016-00696	Request for an EFSA peer review (EFSA Conclusion) on the active substance <i>Bacillus thuringiensis Aizawai</i> strain ABTS-1857 according to Article 13 of Regulation (EU) No 844/2012 (AIR IV)	No	No
<b>Plant protection products</b>	<i>Bacillus thuringiensis</i> ssp. <i>kurstaki</i> (strain ABTS-351)	Plant protection product	EFSA-Q-2016-00697	Request for an EFSA peer review (EFSA Conclusion) on the active substance <i>Bacillus thuringiensis</i> ssp. <i>kurstaki</i> (strain ABTS-351) according to Article 13 of Regulation (EU) No 844/2012 (AIR IV)	No	No
<b>Plant protection products</b>	<i>Bacillus thuringiensis</i> subsp. <i>aizawai</i> GC-91	Plant protection product	EFSA-Q-2016-00698	Request for an EFSA peer review (EFSA Conclusion) on the active substance <i>Bacillus thuringiensis</i> subsp. <i>aizawai</i> GC-91 according to Article 13 of Regulation (EU) No 844/2012 (AIR IV)	No	No
<b>Plant protection products</b>	<i>Bacillus thuringiensis</i> subsp. <i>israelensis</i> strain AM65-52	Plant protection product	EFSA-Q-2016-00699	Request for an EFSA peer review (EFSA Conclusion) on the active substance <i>Bacillus thuringiensis</i> subsp. <i>israelensis</i> strain AM65-52 according to Article 13 of Regulation (EU) No 844/2012 (AIR IV)	No	No
<b>Plant protection products</b>	<i>Bacillus thuringiensis</i> subsp. <i>kurstaki</i> EG 2348	Plant protection product	EFSA-Q-2017-00131	Request for an EFSA peer review (EFSA Conclusion) on the active substance <i>Bacillus thuringiensis</i> subsp. <i>kurstaki</i> EG 2348 according to Article 13 of Regulation (EU) No 844/2012 (AIR IV)	No	No

EFSA risk assessment area	Microorganism species/strain	Intended use	EFSA Question number <sup>(a)</sup> and EFSA webpage link <sup>(b)</sup>	Additional information provided by the EFSA Scientific Unit	Previous QPS status? <sup>(c)</sup>	To be evaluated? yes or no <sup>(d)</sup>
<b>Plant protection products</b>	<i>Bacillus thuringiensis</i> subsp. <i>kurstaki</i> SA-11	Plant protection product	EFSA-Q-2017-00132	Request for an EFSA peer review (EFSA Conclusion) on the active substance <i>Bacillus thuringiensis</i> subsp. <i>kurstaki</i> SA-11 according to Article 13 of Regulation (EU) No 844/2012 (AIR IV)	No	No
<b>Plant protection products</b>	<i>Bacillus thuringiensis</i> subsp. <i>kurstaki</i> SA-12	Plant protection product	EFSA-Q-2016-00700	Request for an EFSA peer review (EFSA Conclusion) on the active substance <i>Bacillus thuringiensis</i> subsp. <i>kurstaki</i> SA-12 according to Article 13 of Regulation (EU) No 844/2012 (AIR IV)	No	No
<b>Plant protection products</b>	<i>Bacillus thuringiensis</i> subsp. <i>kurstaki</i> strain PB 54	Plant protection product	EFSA-Q-2017-00133	Request for an EFSA peer review (EFSA Conclusion) on the active substance <i>Bacillus thuringiensis</i> subsp. <i>kurstaki</i> strain PB 54 according to Article 13 of Regulation (EU) No 844/2012 (AIR IV)	No	No
<b>Plant protection products</b>	<i>Streptomyces</i> K-61 (formerly <i>griseoviridis</i> )	Plant protection product	EFSA-Q-2017-00142	Request for an EFSA peer review (EFSA Conclusion) on the active substance streptomycetes K-61 (formerly <i>griseoviridis</i> ) according to Article 13 of Regulation (EU) No 844/2012 (AIR IV)	No	No
<b>Filamentous fungi</b>						
<b>Feed additives</b>	<i>Aspergillus oryzae</i>	Production of phytase	EFSA-Q-2017-00446			
<b>Feed additives</b>	<i>Trichoderma reesei</i>	Production of muramidase	EFSA-Q-2017-00632		No	No
<b>Plant protection products</b>	<i>Beauveria bassiana</i> ATCC-74040	Plant protection product	EFSA-Q-2017-00134	Request for an EFSA peer review (EFSA Conclusion) on the active substance <i>Beauveria bassiana</i> ATCC-74040 according to Article 13 of Regulation (EU) No 844/2012 (AIR IV)	No	No
<b>Plant protection products</b>	<i>Beauveria bassiana</i> GHA	Plant protection product	EFSA-Q-2017-00135	Request for an EFSA peer review (EFSA Conclusion) on the active substance <i>Beauveria bassiana</i> GHA according to Article 13 of Regulation (EU) No 844/2012 (AIR IV)	No	No



EFSA risk assessment area	Microorganism species/strain	Intended use	EFSA Question number <sup>(a)</sup> and EFSA webpage link <sup>(b)</sup>	Additional information provided by the EFSA Scientific Unit	Previous QPS status? <sup>(c)</sup>	To be evaluated? yes or no <sup>(d)</sup>
Plant protection products	<i>Lecanicillium muscarium</i> Ve6	Plant protection product	EFSA-Q-2017-00055	Request for an EFSA peer review (EFSA Conclusion) on the active substance <i>Lecanicillium muscarium</i> Ve6 according to Article 13 of Regulation (EU) No 844/2012 (AIR IV)	No	No
Plant protection products	<i>Paecilomyces lilacinus</i> (strain 251)	Plant protection product	EFSA-Q-2015-00520	Request for an EFSA peer review (EFSA Conclusion) on the active substance <i>Paecilomyces lilacinus</i> (strain 251) according to Article 13 of Regulation (EU) No 844/2012	No	No
Plant protection products	<i>Phlebiopsis gigantea</i> strain VRA 1835, VRA 1984 and PG 410.3	Plant protection product	EFSA-Q-2017-00140	Request for an EFSA peer review (EFSA Conclusion) on the active substance <i>Phlebiopsis gigantea</i> strain VRA 1835, VRA 1984 and PG 410.3 according to Article 13 of Regulation (EU) No 844/2012 (AIR IV)	No	No
Plant protection products	<i>Trichoderma asperellum</i> ICC012	Plant protection product	EFSA-Q-2017-00143	Request for an EFSA peer review (EFSA Conclusion) on the active substance <i>Trichoderma asperellum</i> ICC012 according to Article 13 of Regulation (EU) No 844/2012 (AIR IV)	No	No
Plant protection products	<i>Trichoderma asperellum</i> strain T25	Plant protection product	EFSA-Q-2017-00144	Request for an EFSA peer review (EFSA Conclusion) on the active substance <i>Trichoderma asperellum</i> strain T25 according to Article 13 of Regulation (EU) No 844/2012 (AIR IV)	No	No
Plant protection products	<i>Trichoderma asperellum</i> TV1	Plant protection product	EFSA-Q-2017-00145	Request for an EFSA peer review (EFSA Conclusion) on the active substance <i>Trichoderma asperellum</i> TV1 according to Article 13 of Regulation (EU) No 844/2012 (AIR IV)	No	No
Plant protection products	<i>Trichoderma atroviride</i> T11	Plant protection product	EFSA-Q-2017-00276	Request for an EFSA peer review (EFSA Conclusion) on the active substance <i>Trichoderma atroviride</i> T11 according to Article 13 of Regulation (EU) No 844/2012 (AIR IV)	No	No

EFSA risk assessment area	Microorganism species/strain	Intended use	EFSA Question number <sup>(a)</sup> and EFSA webpage link <sup>(b)</sup>	Additional information provided by the EFSA Scientific Unit	Previous QPS status? <sup>(c)</sup>	To be evaluated? yes or no <sup>(d)</sup>
<b>Plant protection products</b>	<i>Trichoderma gamsii</i> ICC080	Plant protection product	EFSA-Q-2017-00277	Request for an EFSA peer review (EFSA Conclusion) on the active substance <i>Trichoderma gamsii</i> ICC080 according to Article 13 of Regulation (EU) No 844/2012 (AIR IV)	No	No
<b>Plant protection products</b>	<i>Trichoderma harzianum</i> ITEM908	Plant protection product	EFSA-Q-2017-00278	Request for an EFSA peer review (EFSA Conclusion) on the active substance <i>Trichoderma harzianum</i> ITEM908 according to Article 13 of Regulation (EU) No 844/2012 (AIR IV)	No	No
<b>Plant protection products</b>	<i>Trichoderma harzianum</i> T-22	Plant protection product	EFSA-Q-2017-00279	Request for an EFSA peer review (EFSA Conclusion) on the active substance <i>Trichoderma harzianum</i> T-22 according to Article 13 of Regulation (EU) No 844/2012 (AIR IV)	No	No
<b>Plant protection products</b>	<i>Verticillium albo-atrum</i> WCS850	Plant protection product	EFSA-Q-2017-00296	Request for an EFSA peer review (EFSA Conclusion) on the active substance <i>Verticillium albo-atrum</i> WCS850 according to Article 13 of Regulation (EU) No 844/2012 (AIR IV)	No	No
<b>Oomycetes</b>						
<b>Plant protection products</b>	<i>Pythium oligandrum</i> M1	Plant protection product	EFSA-Q-2017-00141	Request for an EFSA peer review (EFSA Conclusion) on the active substance <i>Pythium oligandrum</i> M1 according to Article 13 of Regulation (EU) No 844/2012 (AIR IV)	No	No
<b>Yeasts</b>						
<b>Feed additives</b>	<i>Komagataella phaffii</i>	Production of fumonisin esterase	EFSA-Q-2017-00073 <sup>(e)</sup>	Previously identified as <i>Pichia pastoris</i>	No	Yes
<b>Feed additives</b>	<i>Pichia pastoris</i>	Production of 3-phytase	EFSA-Q-2017-00447		Yes	No

EFSA risk assessment area	Microorganism species/strain	Intended use	EFSA Question number <sup>(a)</sup> and EFSA webpage link <sup>(b)</sup>	Additional information provided by the EFSA Scientific Unit	Previous QPS status? <sup>(c)</sup>	To be evaluated? yes or no <sup>(d)</sup>
<b>Viruses</b>						
<b>Plant protection products</b>	<i>Cydia pomonella Granulovirus</i> (CpGV)	Plant protection product	EFSA-Q-2017-00304	Request for an EFSA peer review (EFSA Conclusion) on the active substance <i>Cydia pomonella Granulovirus</i> (CpGV) according to Article 13 of Regulation (EU) No 844/2012 (AIR IV)	Yes	No

(a): To find more details on specific applications please access the EFSA website - Register of Questions: <http://registerofquestions.efsa.europa.eu/roqFrontend/ListOfQuestionsNoLogin?0&panel=ALL>

(b): Where no link is given this means that the risk assessment has not yet been published.

(c): Not present in the QPS list as adopted in December of 2016 (Scientific Opinion on the update of the list of QPS-recommended biological agents intentionally added to food or feed as notified to EFSA).

(d): In the current Panel Statement.

(e): Already notified in the Panel Statement (EFSA BIOHAZ Panel, 2017).