



Commentary

The potential impact of the *Lactobacillus* name change: The results of an expert meeting organised by the Lactic Acid Bacteria Industrial Platform (LABIP)



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ABSTRACT

Background: Taxonomy and **nomenclature** are important aspects of biological science, as they allow unambiguous communication about all living species. In contrast to higher life forms, microbes have no comparable sexual reproduction, upon which bacterial speciation can be based. Therefore, alternative criteria have to be used, which differ depending on the group of microorganisms. In the past, phenotypic criteria such as fermentation patterns, enzymatic profiles and DNA-DNA hybridisation were cornerstone techniques for speciation. But today, the wider availability of **high-throughput sequencing technology** and the relatively small genome size of bacteria have allowed phenotypic testing to be replaced by genome sequencing as the main source of taxonomic information.

Scope and approach: Not unexpectedly, the results of phylogenetic analyses based on these new data do not always match results from phenotypic approaches. Based on a recent analysis of the **genome sequences** of 222 species of the genus *Lactobacillus* and related taxa, it is expected that the genus *Lactobacillus* will be split in a considerable number of new genera.

Key findings and conclusions: In October 2018 LABIP organised an expert workshop to discuss the economic, scientific and **regulatory** consequences of this taxonomic change. This report represents a summary of the considerations and outcomes of this workshop, supplemented with some later reflections and recent literature.

1. Background

Members of the genus *Lactobacillus* are widely used in industrial fermentations. Fermentation has the potential to improve the taste, nutritional value and texture of foods and adds to food safety and shelf life by acidification and through the production of antibacterial compounds. Some species of the genus *Lactobacillus* have a long history of safe and legal use in foods. Other species within the genus do not benefit from this status and consequently proper nomenclature and taxonomy is a prerequisite for safety assessment.

Recently Salvetti et al. (2018) investigated the relatedness of 269 species belonging primarily to the Families Lactobacillaceae (genera *Lactobacillus* and *Pediococcus*) and Leuconostocaceae (*Convivina*, *Frustrabacillus*, *Leuconostoc*, *Oenococcus* and *Weissella*) as well as reference strains of the genera *Atopobium*, *Carnobacterium*, *Kandleria* and

Olsenella. Whole genome sequence analysis showed that many of these genera are phylogenetically interwoven and that the genus *Lactobacillus* in particular is very heterogeneous. Based on several parameters, including Average Amino acid Identity (AAI) and Percentage Of Conserved Proteins (POCP), the genus has a spread that largely exceeds the normal spread of a genus. These findings confirmed the results obtained by Sun et al. (2015), who showed that the Average Nucleotide Identity (ANI, pairwise comparison of homologous sequences) for species of the genus *Lactobacillus* was as low as values typically seen at the taxonomic level of an order. The authors therefore concluded that a formal split of the genus was unavoidable and 10 potential groups of microorganisms were proposed that could become the basis for a reclassification of the genus. In another study covering almost all the available *Lactobacillus* genome sequences, Parks et al. (2018) discriminated 16 groups within the genus. Based on 16S rRNA sequence similarity only, Salvetti et al.

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Table 1

List of 'invalid' species names, as these species were later shown to be homologous to species that had already been described and validated earlier.

Invalid species names	Synonymous with existing species	Reference
' <i>Lactobacillus arizonensis</i>	<i>Lactobacillus plantarum</i>	Kostinek et al. (2005)
' <i>Lactobacillus bavaricus</i>	<i>Lactobacillus sakei</i> subsp. <i>sakei</i>	Kagermeier-Callaway and Lauer (1995)
' <i>Lactobacillus bobalius</i>	<i>Lactobacillus paralimentarius</i>	Pang et al. (2012); but questioned by Yang et al. (2017)
' <i>Lactobacillus brevis</i>	<i>Lactobacillus parabrevis</i>	Vancanneyt et al. (2006)
' <i>Lactobacillus bulgaricus</i>	<i>Lactobacillus delbrueckii</i> subsp. <i>bulgaricus</i>	Weiss et al. (1983a)
' <i>Lactobacillus carnis</i>	' <i>Lactobacillus piscicola</i> ' (see Table 2)	Mora, Scarpellini, Franzetti, Colombo, and Galli (2003)
' <i>Lactobacillus casei</i> subsp. <i>alactosus</i>	<i>Lactobacillus paracasei</i> subsp. <i>paracasei</i>	Collins, Phillips, and Zanoni (1989)
' <i>Lactobacillus casei</i> subsp. <i>pseudoplanarum</i>	<i>Lactobacillus paracasei</i> subsp. <i>pseudoplanarum</i>	Collins et al. (1989)
' <i>Lactobacillus casei</i> subsp. <i>rhamnosus</i>	<i>Lactobacillus rhamnosus</i>	Collins et al. (1989)
' <i>Lactobacillus casei</i> subsp. <i>tolerans</i>	<i>Lactobacillus paracasei</i> subsp. <i>tolerans</i>	Collins et al. (1989)
' <i>Lactobacillus cellobiosus</i>	<i>Lactobacillus fermentum</i>	Dellaglio, Torriani, and Felis (2004)
' <i>Lactobacillus curvatus</i> subsp. <i>melibiosus</i>	<i>Lactobacillus sakei</i> subsp. <i>carnosus</i>	Koort, Vandamme, Schillinger, & Holzapfel, 2004
' <i>Lactobacillus cypricasei</i>	<i>Lactobacillus acidipiscis</i>	Naser, Vancanneyt, Hoste, Snauwaert, and Swings (2006)
' <i>Lactobacillus durianis</i>	<i>Lactobacillus vaccinostercus</i>	Dellaglio et al. (2006)
' <i>Lactobacillus ferintoshensis</i>	<i>Lactobacillus parabuchneri</i>	Vancanneyt et al. (2005)
' <i>Lactobacillus heterohiochii</i>	<i>Lactobacillus fructivorans</i>	Weiss et al. (1983b)
' <i>Lactobacillus kefirgranum</i>	<i>Lactobacillus kefiranoferiensis</i> subsp. <i>kefirgranum</i>	Vancanneyt et al. (2004)
' <i>Lactobacillus kimchii</i>	<i>Lactobacillus paralimentarius</i>	Pang et al. (2012); but questioned by Yang et al. (2017)
' <i>Lactobacillus lactis</i>	<i>Lactobacillus delbrueckii</i> subsp. <i>lactis</i>	Weiss et al. (1983a)
' <i>Lactobacillus leichmannii</i>	<i>Lactobacillus delbrueckii</i> subsp. <i>lactis</i>	Weiss et al. (1983a)
' <i>Lactobacillus sobrius</i>	<i>Lactobacillus amylovorus</i>	Jakava-Viljanen, Murros, Palva, and Björkroth (2008)
' <i>Lactobacillus suntoryeus</i>	<i>Lactobacillus helveticus</i>	Naser et al. (2006)
' <i>Lactobacillus thermotolerans</i>	<i>Lactobacillus ingluviei</i>	Felis et al. (2006)
' <i>Lactobacillus trichodes</i>	<i>Lactobacillus fructivorans</i>	Weiss et al. (1983b)
' <i>Lactobacillus yamanashiensis</i>	<i>Lactobacillus mali</i>	Kaneuchi, Seki, and Komagata (1988)

(2012) and Pot et al. (2014), earlier described the presence of at least 14 stable phylogenetic groups within the genus.

This aberrant taxonomic situation was discussed by the Taxonomic Subcommittee on *Bifidobacterium*, *Lactobacillus* and Related Genera at a meeting in Berlin, September 3rd, 2018. The conclusion of this discussion was that the Subcommittee would support a formal split of the genus and a working group of subcommittee members and external experts was created to collect all available genotypic and phenotypic information that would allow definition of a stable and reliable structure for the genus *Lactobacillus* and its closely related taxa.

While this is an ongoing academic process, it was clear that this renaming would have considerable economic and legal consequences, which may heavily impact the industry that is using these organisms in the production of fermented foods, food supplements and feed additives. The Lactic Acid Bacteria Industrial Platform (LABIP) therefore decided to organise an expert workshop (32 participants) to (i) explain the process of reclassification, (ii) make an inventory of the possible consequences and (iii) discuss possible solutions.

LABIP was established in 1995 with the purpose of securing a link between academic research and industry. Today the association accommodates 23 companies with an interest in the industrial use of lactic acid bacteria (LAB) in foods or food supplements. The topics of earlier workshops included amongst others, Food Safety (Adams & Marteau, 1995), Probiotics (Guarner & Schaafsma, 1998) and the Nago protocol (Johansen, 2017). As full partner in the SSA GutImpact project, LABIP has organised 3 technical expert workshops and 3 consumer related workshops, which included consumer representatives (Lahteenmaki & Ledebøer, 2006; Ledebøer et al., 2007; Ledebøer & Lahteenmaki, 2007).

2. Introduction to prokaryotic nomenclature

As mentioned above, a stable set of names (nomenclature) is needed to allow clear communication on microorganisms. While taxonomy is a matter of experience and agreement among scientists, nomenclature of prokaryotes, earlier called 'the handmaid of taxonomy' (Sneath, 2015, pp. 83–88), is regulated by the Nomenclatural Code (Lapage, 1992) revised after being presented and discussed at the Fourteenth International Congress of Bacteriology and Applied Microbiology (BAM) in

Montréal in 2014 (Parker, Tindall, & Garrity, 2019). The most recent version is available from Oren (2019).

The first 'Bacteriological Code', was developed in 1930, during the First International Congress on Taxonomy in Paris. An international Committee crafted a number of unanimously approved resolutions. The work was continued by the Nomenclature Committee on behalf of the International Society for Microbiology International Committee. After several intermediate documents had been proposed and discussed the first formal English text was officially published in March 1948 in the Journal of Bacteriology (Buchanan, St.John-Brooks, & Breed, 1948).

This code has further evolved and is now under the auspices of the 'International Committee on the Systematics of Prokaryotes' (ICSP), which includes the Archaea in their scope. The need to improve the quality of bacterial nomenclature, with fewer duplicate names and including the description of type species and type strains, resulted in publication on January 1st, 1980 of the 'Approved List of Bacterial Names', a list of bacterial names with standing in microbiology, published in the 'International Journal of Systematic Bacteriology' (IJSB). The list, consisting of 124 names of taxa above the rank of genus, encompasses 2212 genera, species and subspecies names. Till today, new names are added to this list only after valid publication in IJSB, known since 2000 as the 'International Journal of Systematic and Evolutionary Microbiology' (-IJSEM; consulted last on March 29th, 2019). Valid publication means that the species description is published as a formal article in IJSEM or appeared on the so-called 'Validation Lists' in IJSEM. In order to be on this list, authors must ask ICSP for formal validation of the taxa described in other peer reviewed scientific journals.

ICSP today supervises several subcommittees, including the 'Subcommittee on the taxonomy of *Bifidobacterium*, *Lactobacillus* and related organisms'. The Subcommittees are responsible for the maintenance of the Nomenclatural Code (Parker et al., 2016) in their respective range of taxa. The 'International Code of Nomenclature of Prokaryotes' (ICNP) defines the rules for the naming of bacterial taxa according to their taxonomic ranking. While covering many possible situations and exceptions, its principles are relatively simple and comprise a limited number of rules (Tindall et al., 2006). While it is not the intention of this report to review these rules, some aspects are important in order to better understand the reasons for name changes in the genus *Lactobacillus* (Table 1) and are presented in the

supplementary material of this article.

It is important to note that, in agreement with general principles in prokaryotic taxonomy, the goal is a monophyletic taxonomy, meaning that a phylogenetic analysis should demonstrate that all descendants of any given taxon (in this case a genus) are grouped together and are not mixed with members of other taxa. Also, in favour of clarity, taxa should be kept reasonably compact, comparable to analogous genera, and distinctive in terms of phenotypic and genotypic criteria. In the case of the genus *Lactobacillus*, the genetic distinctiveness has clearly been shown, but the differential phenotypic description of the different genotypic groups might be an issue, as species have been added to the genus based on a number of common phenotypic characteristics. One of the most important tasks of the above-mentioned working group therefore is to try and find discriminative sets of parameters that might, besides genome sequence parameters, allow reliable description of the new genera. The use of polyphasic datasets, including multiple types of genome sequence analyses, should guarantee a stable and clear separation of the genus. The working group has to collect all possible information on all species of the genus *Lactobacillus* and by exploring and comparing different bioinformatic approaches, derive the best possible reclassification for the genus. For some already recognised larger subgroups, as mentioned above, different phylogenetic approaches, including genome sequence-based and 16S rRNA based trees, have already confirmed their taxonomic status, but for other, smaller clusters or individual species, the new phylogenetic position is still uncertain and needs further dedicated work.

2.1. Why the genus has to be split

For the 237 *Lactobacillus* species (208, excluding synonyms and subspecies) the Total Nucleotide Identity (TNI) was found to be between the values expected between order and family and the ANI values between Order and Class (Salveti et al., 2018; Sun et al., 2015). Results also revealed that representatives of other genera, such as *Pediococcus*, and members of the family Leuconostocaceae (*Convivina*, *Fructobacillus*, *Leuconostoc*, *Oenococcus* and *Weissella*) are intermixed with species of the genus *Lactobacillus*, which of course is an infringement of the monophyletic requirement. The genus continues to grow, with new isolates being added at an ever increasing speed (Fig. 1a and b). This is unacceptable from a scientific point of view and the *status quo* was not considered an option.

2.2. The scientific rationale for the split

In the past, lactobacilli were grouped mainly based on phenotypic characteristics such as growth temperature or the fermentation of hexoses (homo/heterofermentative potential). The introduction of 16S rRNA gene sequence analysis allowed the development of a more exhaustive taxonomy for the genus, but unfortunately revealed little correlation between the traditional, phenotype-based classification and the phylogenetic relatedness. In addition, the massive description of novel *Lactobacillus* species led to the recognition of a growing number of variable phylogenetic subgroups (Felis & Dellaglio, 2007; Pot et al., 2014; Salvetti et al., 2012; Vandamme et al., 1996).

The decision to use whole genome sequences to further study the issue was based on earlier work performed on other genera (Coenye, Gevers, Van de Peer, Vandamme, & Swings, 2005; Gevers et al., 2005; Konstantinidis & Tiedje, 2005a,b; Rosselló-Mora, 2005; Wu et al., 2009; Sangal et al., 2016; Chun et al., 2018; Parks et al., 2018) with the use of a variety of new tools (Garrity, 2016; Hugenholtz, Sharshewski, & Parks, 2016; Qin et al., 2014; Segata et al., 2013; Yoon et al., 2017).

The first comparative genomics on LAB was performed by Makarova et al., 2006, which included 12 LAB genomes (encompassing genera *Lactobacillus*, *Oenococcus*, *Leuconostoc*, *Pediococcus*, *Streptococcus* and *Lactococcus*). The phylogenomic tree based on 54 ribosomal proteins showed that *Lactobacillus* species were intermixed with leuconostocs

and pediococci. This topology was later observed also by Zhang et al., (2011), who performed a phylogenetic analysis based on 232 genes derived from 28 LAB genomes, and Salvetti, Fondi, Fani, Torriani, and Felis (2013), who analysed 27 LAB genomes using different datasets (mainly ribosomal proteins and carbohydrate metabolism genes). Two consistent groups were obtained: the Enterococcaceae and Streptococcaceae families on the one hand, and the families Lactobacillaceae and Leuconostocaceae on the other hand. The latter contained two clades, one encompassed the *Lactobacillus acidophilus* complex (including *Lactobacillus delbrueckii*), *Lactobacillus sakei* and *Lactobacillus casei*. The second clade contained the *Lactobacillus salivarius* subgroup, *Lactobacillus plantarum*, *Lactobacillus reuteri*, *Lactobacillus brevis*, and the genera *Pediococcus*, *Oenococcus* and *Leuconostoc*, indicating the polyphyletic nature of the genus.

Zheng, Ruan, Sun and Gänzle (2015) published a phylogenetic perspective based on the concatenated protein sequences of 172 single-copy core genes of 174 *Lactobacillus* and *Pediococcus* type strains, focusing on ecology and biochemistry properties. A clear separation of homofermenters and heterofermenters within these genera was shown and the presence of 24 subgroups (including *Pediococcus*) was revealed.

Sun et al. (2015) sequenced 213 genomes from 174 type strains belonging to 9 genera and also included available genomes from *Oenococcus* and *Leuconostoc* in their analysis (11 genera and 185 species). Results revealed not only that the *Lactobacillus* ancestor was facultatively heterofermentative but also showed that the pairwise ANI values for the genus *Lactobacillus* differed substantially from the values traditionally found for a genus or even for a family, overlapping with values generally seen at the level of an order or even class. TNI values confirmed that the genomic diversity of the genus *Lactobacillus* is at the order and family level.

More recently, Salvetti et al., (2018) investigated the relatedness of 269 species belonging primarily to the families Lactobacillaceae and Leuconostocaceae through phylogenetic analyses (by the use of 16S rRNA genes, 29 ribosomal proteins and 12 housekeeping genes) and the assessment of the AAI and the POCV values. Both distance-based and sequence-based metrics showed that the *Lactobacillus* genus was paraphyletic and revealed the presence of 10 methodologically consistent subclades, whose suitability to be nuclei of novel genera was substantiated through the detection of putative clade-specific genes and other conventional taxonomic data. Their phylogenomic tree showed the association of obligately heterofermentative lactobacilli with members of the Leuconostocaceae, well-separated from the homofermentative and facultatively heterofermentative *Lactobacillus* species. This separation is consistent with the phylogenetic trees calculated based on ribosomal proteins, housekeeping and core genes and is congruent with carbohydrate fermentation profiles.

In the same period, Parks et al. (2018) proposed a standardized bacterial taxonomy based on a phylogenetic analysis of 120 proteins, performed from 94,759 prokaryotic genomes, with the purpose to normalize ranks based on relative evolutionary divergence. This taxonomic analysis, publicly available at the Genome Taxonomy Database website (<http://gtdb.ecogenomic.org>), suggested 16 separate lineages within the genus *Lactobacillus*, based on 205 genomes and also confirmed that leuconostocs and pediococci intermingle with lactobacilli, indicating that the family Leuconostocaceae might need to be absorbed by the family Lactobacillaceae.

More recently, Wittouck and co-workers (2019) presented their analysis of the *Lactobacillus* Genus Complex (LGC) based on 2459 publicly available genomes (96.1% of all genomes). They selected 'decent-quality' genomes (minimum completeness of 90% and maximum redundancy of 10%) and used a 94% Core Nucleotide Identity (CNI) threshold to show 239 discontinuous and exclusive clusters, representing *de novo* species. The analysis thereof allowed the merging of ten sets of published species and one species that can be split off. At least eight clusters could become new species. The data set also allowed classification of 98 previously unclassified genomes and re-identified 74

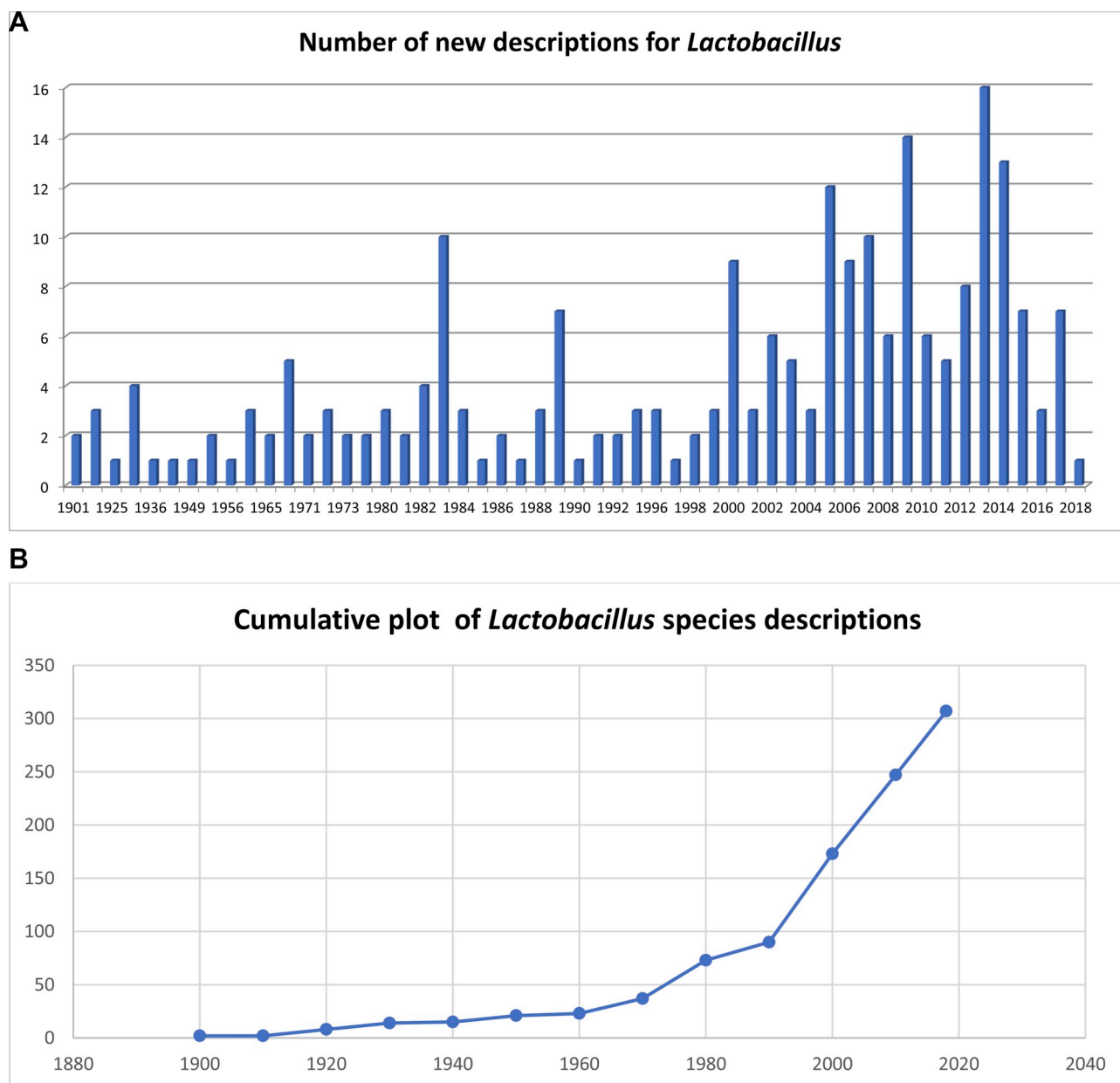


Fig. 1. Historical evolution of the species number in the genus *Lactobacillus*.

1a: number of newly described *Lactobacillus* species per year.

1b: number of newly described *Lactobacillus* species per decade.

wrongly classified genomes, albeit the latter was done based on 16S rDNA sequences.

This whole historical discussion leads us to the following question: How many species and genera can we actually find in the genus *Lactobacillus*?

2.3. The current dilemma: how many genera?

Distance based metrics, as used by Salvetti et al. (2018) are useful because they can be applied in a pragmatic and naïve manner. The TNI and ANI operational values available in the literature that should be used as cut-offs, however, are controversial and cannot be applied to all the species of the current genus *Lactobacillus*. At the amino acid level the result is somewhat better but still not adequate. CNI values have been used most recently and may need some further evaluation, especially when used to delineate genera rather than species. For the value of the POCP as a measure to define genera, the discussion is ongoing.

The bottom line is that depending on the methodology and cut-offs used, the resultant number of 'stable' groups in the genus *Lactobacillus* varies. The best path forward is to evaluate all these parameters, compare them and propose solutions which, based on multiple trees, represent the common clusters or groups. Other considerations, however, may need to be taken into account. In any case the methodological rationale will be mainly based on whole genome sequences in the first place, as most species of the genus show high phenotypic similarity, the reason for them to have been included in the genus. In the evaluation of genome similarity the most common criteria, such as TNI and ANI or AAI of core genome genes will be used, in accordance with the generally used standards for genus delineation.

One major concern of the LABIP workshop participants was related to the stability of the revised taxonomy. It would be unacceptable if in the next 25 years or so further taxonomic changes would be proposed for this genus. Therefore, it is important that the new scheme, in line with the rules above, is stable and able to cope with future expected

descriptions of new species in this genus and family. Fig. 1a and b shows the increase of the number of species in the ‘traditional’ genus *Lactobacillus* and this number is expected to rise as new DNA-based research is used to investigate complex microbiota in food, feed, environment, man or animal (Wittouck et al., 2019).

There was a consensus that the most stable structure, with the least chance of future subdivision, might be a structure with a higher number of genera, allowing to more flexibly accommodate future species. Besides being more stable, it would also allow to maybe describe subgroups of lactobacilli focusing on specific characteristics common to the members of these smaller taxa. These characteristics could e.g. be applications in food or feed, geography, physiological properties, even health effects, or may refer to characteristics which are not linked to humans or animals. This stable, detailed structure resembles the benefits of the taxonomic situation in the family Enterobacteriaceae, in which a detailed taxonomy and nomenclature was created. This was the historical result of the clinical importance of these organisms and has the advantage of being able to communicate efficiently about pathogenic performance, expected health consequences, clinical outcomes or treatment options. It is generally accepted that a genus in the family Enterobacteriaceae has the span of a species in most other Families (Public Health England, 2015). While this is considered a ‘medical’ advantage, the detailed taxonomy makes identification sometimes more difficult and more specialized (Adeolu, Alnajjar, Naushad, & Gupta, 2016). Clearly, at the level of the genus *Lactobacillus*, we currently do not have this type of detailed phenotypic support, but a finer subdivision of the genus *Lactobacillus* based on genome sequences, may represent important opportunities to improve, for example, communication, assist in improved regulation and support scientific investigation of molecular mechanisms of probiotic action.

In order to assist in this decision, the expert working group may consider ecological or health related factors, as well as metabolic or mechanistic properties to define and describe the new genera. If these data are not available, they may possibly be derived from genome sequences (Wittouck et al., 2019). In this context, the use of molecular characteristics such as Conserved Signature Insertions/deletions (CSIs) found in widely distributed proteins present in related groups of organisms (Gupta, 2014, 2016; Gupta, Nanda, & Khadka, 2017; Naushad, Lee, & Gupta, 2014), may provide reliable evidence of phylogenetic relationship, independent of traditional phylogenetic trees. Species with identical CSIs are related to each other since they share a common ancestor (synapomorphic characteristic) and could therefore contribute to a more reliable and more practical delineation and description of the new genera.

2.4. The naming of the future genera

In the light of the description of new genera, LABIP workshop participants suggested keeping the initial “L” for the names of the new genera in order to minimize confusion. In this way, commercially important species such as *Lactobacillus casei*, *Lactobacillus plantarum* and *Lactobacillus reuteri*, which will be no longer lactobacilli and will be included in novel genera, will still be abbreviated as *L. casei*, *L. plantarum* and *L. reuteri*. There is already such an example in the literature regarding the former human pathogen ‘*Clostridium*’ *difficile*, recently reclassified as *Clostridioides difficile* maintaining the common abbreviation *C. difficile*, preventing confusion (Lawson, Citron, Tyrrell, & Finegold, 2016).

2.5. Genera and species: the future for taxonomic descriptions

While official ‘minimal standards’ are available for the description of new taxa of LAB (Mattarelli et al., 2014), these indications are focused on the species level and cannot be considered really ‘minimal’, making the description quite cumbersome. Therefore, it would be useful to suggest a revision (simplification) of these standards. At the

same time, the Taxonomic Subcommittee should think about the requirement for culturing of the bacteria, given the fact that with increased use of sequencing technology, the discovery of new species that cannot currently be cultured, will only increase. Maybe Mol% G + C content, ANI, TNI, CNI, CSI or POCV values, digital (or wet lab measured) DNA:DNA homology values or combinations thereof, using whole genome sequence based phylogenomics should nowadays be used, while the importance of cell wall structure, chemotaxonomic or other phenotypic markers may need to be reduced in future requirements for the description of new taxa.

Examples were discussed during the workshop for genera other than *Lactobacillus*. Next-generation sequencing (NGS) combined with new bioinformatics approaches for phylogeny, based on whole genome sequences, have been used successfully for strain discrimination and for phylogenetic characterization of novel species, even of species in complex communities such as the gut (Ramamany et al., 2014; Vernikou et al., 2015). Extensive attempts have recently been made to survey bifidobacterial populations in mammals, resulting in the identification of several putative novel bifidobacterial species. Ventura and co-workers described a methodology based on whole-genome comparisons, similar to that used for the reclassification of members of the Gram-positive genus *Bacillus* (Dunlap, 2015), with the ambition to unambiguously redefine the taxonomy of members of the genus *Bifidobacterium* (Milani et al., 2014; Lugli et al., 2018 a,b).

The recent introduction of a Digital Protologue Database (DPD) by the journals ‘Systematic and Applied Microbiology’ and ‘Antonie van Leeuwenhoek’ (Rosselló-Mora, Trujillo, & Sutcliffe, 2017) may also be a next step in the modernisation of taxonomic publications. In the DPD, the protologues given in the taxonomic manuscripts (i.e. the formal descriptions) would be extracted from a Digital Protologue (DP) compulsorily filled by the authors. Their accumulated contributions are creating a public and interactive database (<http://imedea.uib-csic.es/dprotologue/>, now with > 700 species), which generates a unique Taxonumber. The initiative, already supported by a number of journals, also encompasses the descriptions of taxa in papers as a protologue table rather than difficult to read text, traditionally presented at the end of the manuscript. Practical details can be found on e.g. the SAM website (last consulted March 19th, 2019). The link also contains 13 other standard requirements for the submission of taxonomic manuscripts. The use of this procedure is thought to largely limit future duplicate or wrong descriptions as seen in the past (Tables 1 and 2; Wittouck et al., 2019). Unfortunately, however, this useful initiative has not been adopted by the IJSEM. This is unfortunate, as this journal is instrumental in valid taxonomic descriptions. In the frame of the current renaming of the genus *Lactobacillus*, the availability of a formal public website, listing all official names and their taxonomic history, might avoid confusion for governmental, legal, medical and scientific stakeholders.

2.6. The legal and other consequences

Commercially important *Lactobacillus* species, including species and strains with well-known fermentation capacity or proven probiotic activity, will be found in most of the newly defined genera. The LABIP workshop participants were concerned about the scale of the renaming. While frequent name changes have occurred in the past for species of the genus *Lactobacillus* (Tables 1 and 2), it is likely that close to 200 species will change genus name in a single operation. This is an unprecedented scale of change for the LAB, with the potential to confuse the various stakeholders.

The renaming of the majority of the lactobacilli will impact the consumer, the scientific and medical or veterinary communities, regulators, governments, lawyers and companies. Consumers may wonder why an ingredient list no longer contains the name of a familiar microbe and therefore have doubts about the content of the product (feed, food or food supplement). Scientific literature surveys will need to

Table 2
List of *Lactobacillus* species that have already been transferred to other genera.

Old name	Synonymous with	Renamed to	Synonymous with (Final name)	Reference
' <i>Lactobacillus</i> ' <i>carnis</i>	' <i>Lactobacillus piscicola</i> '	' <i>Carnobacterium piscicola</i> '	<i>Carnobacterium maltaromaticum</i>	Mora et al. (2003)
' <i>Lactobacillus</i> ' <i>catenaformis</i>			<i>Eggerthia catenaformis</i>	Salveti et al. (2011)
' <i>Lactobacillus</i> ' <i>confusus</i>			<i>Weissella confusa</i>	Collins, Samelis, Metaxopoulos, and Wallbanks (1993)
' <i>Lactobacillus</i> ' <i>divergens</i>			<i>Carnobacterium divergens</i>	Collins, Farrow, Phillips, Feresu, and Jones (1987)
' <i>Lactobacillus</i> ' <i>fructosus</i>		' <i>Leuconostoc</i> ' <i>fructosum</i>	<i>Fructobacillus fructosus</i>	Endo and Okada (2008)
' <i>Lactobacillus</i> ' <i>halotolerans</i>			<i>Weissella halotolerans</i>	Collins et al. (1993)
' <i>Lactobacillus</i> ' <i>kandleri</i>			<i>Weissella kandleri</i>	Collins et al. (1993)
' <i>Lactobacillus</i> ' <i>maltaromaticum</i>			<i>Carnobacterium maltaromaticum</i>	Mora et al. (2003)
' <i>Lactobacillus</i> ' <i>minor</i>			<i>Weissella minor</i>	Collins et al. (1993)
' <i>Lactobacillus</i> ' <i>minutus</i>			<i>Atopobium minutum</i>	Collins and Wallbanks (1992)
' <i>Lactobacillus</i> ' <i>piscicola</i>		' <i>Carnobacterium piscicola</i> '	<i>Carnobacterium maltaromaticum</i>	Mora et al. (2003)
' <i>Lactobacillus</i> ' <i>rimae</i>			<i>Atopobium rimae</i>	Collins and Wallbanks (1992)
' <i>Lactobacillus</i> ' <i>uli</i>			<i>Olsenella uli</i>	Dewhirst et al. (2001)
' <i>Lactobacillus</i> ' <i>viridescens</i>			<i>Weissella viridescens</i>	Collins et al. (1993)
' <i>Lactobacillus</i> ' <i>vitulinus</i>			<i>Kandleria vitulina</i>	Salveti et al. (2011)
' <i>Lactobacillus</i> ' <i>xylosum</i>			<i>Lactococcus lactis</i> subsp. <i>lactis</i>	Schleifer et al. (1985)

account for historical and new genus names. Residual use of the historical names is likely to occur in books. Lawyers or scientists involved in the validation of patent applications or trademarks may be confronted with the same issue for many years to come. Patent officers will not find prior art for the new bacterial genera and the risk exists that in this way existing patents may be undermined. This risk is real, as according to Espacenet there are more than 10.000 patents with the term '*Lactobacillus*' in the title or the abstract. In the medical and veterinary field, specific taxonomic names are familiar, referring to either innocence or danger. New names will surely require further information to be collected. Regulators and governments will need to compare laboratory reports with biosafety and biosecurity lists (Laulund, Wind, Derkx, & Zuliani, 2017), important for considerations on quarantine or certification, to decide on Nagoya protocol requirements, or in the food and feed arena, to verify with QPS-, GRAS-, GMO-, additive-, IDF inventory- or national positive lists, the latter existing in Canada, China, Brazil, Malaysia, and Thailand. In the EU Register of Feed Additives (Anonymous) more than 90% of the listed products with lactobacilli will be concerned by the name change.

In transportation, International Airline Transportation Authorities and truck companies may face issues during border controls, as import/export of specific products may lead to unexpected delays, because responsible officers may not be aware of the official name changes of organisms that are normally 'approved for import/export'. For companies, taxonomic names are not only important for their research and manufacturing, but also for master regulatory dossiers, product authorizations, marketing materials, ingredient lists, safety dossiers, product websites, patent monitoring, export certificates, and other documentation.

While all these issues seem quite alarming, the general impression, based on experiences in the past, was that the impact of the name change could be manageable with time and dedicated resources but will have a significant cost for companies. As an example, the legal consequences of the name changes were explored in a presentation of a member of the European Scientific Panel on BIOHAZ and member of the EFSA Working Group on QPS (28 of 36 QPS species of the genus *Lactobacillus* might be renamed, 12 species have strains with GRAS notifications). It was clear that the normal approval procedure, as explained in Herman et al. (2019), can be used for the approval of the new names, even if the taxonomic changes concern name changes at the genus level (and not on the species level as usually dealt with).

In the USA, the FDA discriminates common or market names from scientific names. While they generally regard common names as appropriate market names, provided they are not misleading or confusing (Principle 2), they generally use the valid scientific names in accordance with the scientific literature. The new official genus names will be introduced through submission of specific dossiers to the FDA,

and since companies may make individual decisions regarding the use of the new names, an abrupt disruption in the use of the old names is very unlikely.

More specific changes in labelling of probiotics may be needed as labelling with current nomenclature for genus and species is stipulated in several published guidelines (FAO/WHO Working group, 2002; CRN and IPA guidelines, 2017).

2.7. What can be done?

A call was launched for a comprehensive and easy-to-use document or website where the official name changes are listed and updated when necessary. The site should explain in a comprehensible way why the name was changed and give a clear representation of the 'BEFORE' versus 'NEW' names, noting the date that the change was officially introduced. This document or site should be available before the publication of the new names, so that it can be activated simultaneously with the official publication of the new names in the IJSEM. The provider of the system should have a high credibility, preferably an academic or governmental institution. While similar websites already exist (for example, <https://www.itis.gov/>; <http://www.bacterio.net/>), some require substantial background knowledge to be used efficiently and may also not provide the right explanation and context for the name changes in, for example, the food, veterinary or medical sector.

It was furthermore suggested that similar information should be made available at websites for and from governmental organisations including FDA, EFSA, CDC, ECDC, WHO, FAO, EMA, Public health agencies (last consulted March 19th, 2019) or research organisations such as NIH - NCBI, NHS. The issue should also be taken up by ongoing education and training programs of Public health agencies, as suggested by the Institute of Medicine (US) (2003) (or homologues in other parts of the world). Also, a smartphone application was suggested as a way to collect name changes in a timely fashion. Companies will need to plan and implement name changes on their commercial products, their websites, packaging materials and ingredient lists as well as their associated marketing material, product composition and import or export certificates. They will need to communicate transparently with all their stakeholders and end-users and be ready to answer their questions in a comprehensive way. The possibility, however, to be able to refer to an independent, preferably academic source to support their communication is considered key. Finally, it should be stressed that while the genus and species name of a specific strain can change, its official strain designation (strain number as known in one or more reference culture collections) will remain the same, as the renaming procedure will only change the genus name '*Lactobacillus*' and not the species epithet. '*Lactobacillus*' may be replaced by the genus name '*Examplebacillus*', but the species epithet and the strain indication will not change:

Lactobacillus casei strain XY123 in this example will be renamed to *Examplebacillus casei* strain XY123. Using the strain designation or strain number could therefore be an important way to also limit confusion.

2.8. What to expect in the future?

The recent finding of 25 new bifidobacterial species in non-human primates is a clear sign that the discovery of the bacterial diversity and therefore the extension and finetuning of the bacterial taxonomy and nomenclature is only at its beginning. It is to be expected that new species, new genera and even new families will be described in fields that are relevant for the food business or crucial in human and animal health or disease considerations. It is important that these new taxa are dealt with efficiently and unambiguously. Therefore, careful attention is necessary regarding the optimal criteria to use for the description of these new taxa, taking into considerations new sources of phylogenetic information and revisiting existing nomenclatural and taxonomic structures as needed. Taxonomy is a dynamic process, able to accommodate new scientific findings and insights. The anticipated renaming in the genus *Lactobacillus*, and likely also in *Bifidobacterium*, can be considered a logical scientific reflection of these new insights. The economic absorption and the integration in society of the results, however, are known to be slow processes. In July 2004, as an example, the two species *Bifidobacterium animalis* and *Bifidobacterium lactis* were merged and became officially *Bifidobacterium animalis* subsp. *animalis* and *Bifidobacterium animalis* subsp. *lactis* respectively (Masco, Ventura, Zink, Huys, & Swings, 2004). At present, 15 years after date, there are still many “*B. lactis*” products on the market. This could be due to the commercial interest of the name *B. lactis* as well as because producers are not yet aware of the name change. It can therefore be expected that during a considerable transition period the current *Lactobacillus* nomenclature will be used in parallel to the new one. Another example, on the genus level, is the renaming of ‘*Streptococcus lactis*’ to *Lactococcus lactis* in 1985 by Schleifer et al. (1985). While more than 30 years ago, there are still products in the market with the name *Streptococcus lactis*. While this is probably unavoidable, it is definitely not desirable, as it will lead to confusion. Therefore, the above mentioned measures are important and their availability needs to be spread widely.

3. Conclusion

Although lactobacilli are ubiquitous and appear in diverse niches, they have common phenotypic properties that were the basis of their taxonomic grouping. The use of modern sequencing technology recently revealed their extraordinary diversity, putting a shadow on their current classification.

Lactobacilli have significant scientific and economic value, but, as mentioned by a speaker, the history of the genus *Lactobacillus* has been ‘long, painful and torturous’, led by many different people, in different times, with different methodologies. Evolution is a keyword in this, both referring to the microbes themselves as well as to the methodologies used. Recent technological evolutions have enabled us to gather the complete genome sequence of any bacterium we find. In the past already the importance of the genotypic information for taxonomic work has been recognised, but the methods to study DNA were limited. Nowadays this hurdle has been largely overcome and consequences of this are major in terms of expected nomenclatural changes. The taxonomy and nomenclature of important genera such as *Bacillus* and *Clostridium* have already been revised. Next in line is *Lactobacillus*, most probably followed by the genus *Bifidobacterium*. While nomenclatural changes have been common in the past, the anticipated scale in a group of bacteria that have such an important economic impact raised some concerns. While these concerns may often be from a practical and financial point of view, there is a clear request for stability of the new classification scheme, urging the scientific community to make the new

nomenclature suitably robust to withstand future methodology changes in the field for at least the next 25 years. This is especially important to accommodate the slow pace of change evident in the regulatory compared to the scientific arenas.

The new entities should be defined by an as wide as possible bioinformatic approach, using all information available within the complete genome sequences, and possibly tracing uniform patterns of the presence/absence of specific (sets of) genes, linked to biological features relevant for their grouping and description. On the positive side, reclassification of the genus *Lactobacillus* into more uniform and stable taxa will (i) create opportunities for more accurate communication, and (ii) assist in defining more accurate molecular markers that will facilitate regulatory assessment of applications (Salveti & O’Toole, 2017). The upcoming renaming of the genus *Lactobacillus* should therefore not be regarded solely as a possible cause of confusion for stakeholders, but also as an opportunity to start a new nomenclatural situation, adapted to the new scientific reality and ready to cope with future evolutions in the field of microbiology. The translation of this scientific reality to legal, economic and societal structures may take some years but a lot can be done to smoothen that transition.

Conflicts of interest

BP is an employee of Yakult Europe BV.

Availability of data and materials

Not applicable.

Consent for publication

Publication of this Communication was approved by LABIP and agreed to by the workshop participants.

Ethics approval and consent to participate

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Appendix A. Supplementary data

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