Taxonomy and nomenclature of bacteria with clinical and scientific importance: current concepts for pharmacists and pharmaceutical scientists

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Abstract
Taxonomy is the science of the classification of various living organisms consisting of three independent, but interrelated disciplines, namely classification, nomenclature and identification. With the advent of molecular biological methods and sequencing, a revolution is currently occurring with regards to the reporting of novel taxa and changes in the taxonomy of already described bacterial species. The applications of taxonomic changes can be broad ranging: they may impact the clinical care of patients, through variations in choosing the appropriate antimicrobial susceptibility testing standards or data interpretation, or even their clinical relevance and epidemiology. The aim of this paper was to aid healthcare professionals and pharmaceutical scientists to navigate through the 'maze' of bacterial taxonomy, and to aid in finding authentic information regarding the description of taxonomic changes and to present some examples of changes in bacterial taxonomy which have proven to be clinically significant.

Keywords: *bacteria, taxonomy, nomenclature, identification, molecular, microbiology, educational*

1. Introduction to (bacterial) taxonomy

Taxonomy (from the greek words *taxis*=arrangement or order, and *nemein*=to distribute or govern) is the science of the classification of various living organisms [1,2]. In case of bacteria, taxonomy consists of three independent, but interrelated disciplines, namely *classification*, *nomenclature* and *identification* (sometimes referred to as the 'trinity' of taxonomy) [2]. The most basic taxonomic group (i.e. unit) in bacterial taxonomy is the species, while groups of species are collected into genera (genus), which are then collected into families (*Familia*), families into orders (*Ordo*), orders into classes (*Classis*), classes into phyla (*Phylum*) and phyla into a domain (or *Kingdom*, the highest level), however, there are subgroups to these main classifications (see *Table I* and *II* for examples). Groups of bacteria at each rank or level have names with endings or suffixes characteristic to that rank or level (*Table I*) [1-3].

Nevertheless, taxonomic units under species may still be relevant (especially in the case of medically-relevant bacteria), because members among specific species can be distinguished on the basis of certain biological or genetic characteristics: these members may be classified in a sub-group of members, called *subspecies* [1-3]. An example for this is the differentiation of *Campylobacter* species*: C. fetus subsp. veneralis* is a causative agent of sexually transmitted diseases and miscarriage among cattle, while *C. fetus subsp. fetus* may cause intrauterine infection in humans [4]. Antigenic characteristics may be another possible way to distinguish subgroups under the threshold of species, called

Table I *Example of taxonomic classification for a common Gram-positive, Gram-negative and an atypical pathogen*

	Staphylococcus aureus	***Pseudomonas aeruginosa***	***Mycoplasma pneumoniae***
Kingdom	Bacteria	Bacteria	Bacteria
Phylum	Firmicutes	Proteobacteria	Tenericutes
Class	Bacilli	Gammaproteobacteria	Mollicutes
Order	*Bacillales*	*Pseudomonadales*	*Mycoplasmatales*
Family	*Staphylococcaceae*	*Pseudomonadaceae*	*Mycoplasmataceae*
Genus	*Staphylococcus*	*Pseudomonas*	*Mycoplasma*
Species	*S. aureus*	*P. aeruginosa*	*M. pneumoniae*

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serogroups or *serovariants* [5]. In case of gut bacteria or *Enterobacteriaceae* (especially important for *Salmonella* species and *Escherichia coli*), hundreds of different serovariants may be differentiated, based on the cell wall (O; somatic antigen, based on oligosaccharides), capsule (K, from the German *Kapsel* or *Bacterienkapsel*) and flagellar (H; from the German *Hauch* meaning "breath" or "mist") antigens [6,7]. In fact, this is the basis of the Kauffman–White classification, which was frequently used for routine clinical microbiology and public health purposes for serotyping [8]. Similarly, bacteria may be further characterized based on their disease-causing capacity (pathogenicity) into *pathotypes*, e.g., extraintestinal-pathogenic *E. coli* (ExPEC), enteropathogenic *E. coli* (EPEC), enterotoxin-producing *E. coli* (ETEC), enteroinvasive *E. coli* (EIEC), enteroaggregative *E. coli* (EAEC), diffusely adherent *E. coli* (DAEC) and so on [9,10].

However, a lot has changed since the first description of taxonomy (Augustin Pyramus de Candolle, 1813), when the available methods for the characterization of bacterial, plant or animal species were very limited [11]. Nowadays, with the advent of molecular biological methods and sequencing, a revolution is currently occurring with regards to the reporting of novel taxa [12]. The description of new bacterial species was further facilitated by the newfound interest in the characterization of the human microbiome [13]. One of the most important milestones was the launch of the Human Microbiome Project (HMB; the first phase of which was launched in 2007), with the aim of characterize the human gut microbial flora in healthy (physiological) and disease states; the long-term aim of this project was to find causation between human pathologies (e.g., autoimmune disorders, obesity, diabetes, neuropsychiatric disorders, diseases affecting the cardiovascular system) and qualitative/quantitative changes in the microbiome [14-16]. Microbial culturomics (a technique allowing for the culturing of previously *unculturable* bacterial species by reproducing their natural habitats using complex methods, with the aid of matrix-assisted laser desorption-ionization time-of-flight mass spectrometry [MALDI-TOF MS] and whole-genome sequencing [WGS]) has also resulted in the description of a staggering number of novel taxa [17-19]. Sequencing technologies also had a significant role in the description of the prokaryotic genetic diversity.

Table II *Characteristics of the current bacterial classification and the number validly published names for each classification level [22]*

Taxonomical level		n
Kingdom	*Regnum*	1
Subkingdom	*Subregnum*	2
Infrakingdom	*Infraregnum*	2
Superdivision/Superphyla	*Superdivisio*	1
Subdivision/Subphyla	*Subdivisio*	9
Superclass	*Superclassis*	2
Class	*Classis*	106
Subclass	*Subclassis*	8
Order	*Ordo*	188
Suborder	*Subordo*	19
Family	*Familia*	399
Subfamily	*Subfamilia*	0
Tribe	*Tribus*	24
Subtribe	*Subtribus*	0
Genus	*Genus*	2854
Species	*Species*	15626
Subspecies	*Subspecies*	586

Between 1990 and 2000, there was on average 200 novel bacterial species described per year [20]. Owing to these recent developments, the number of validly published genera and species has increased by approximately 50% since 2004, reducing the percentage of known prokaryotes that have been implicated in animal or human clinical conditions from ~15% to ~10% [21]. Based on the records of the bacterio.net database, there are currently 19,717 *validly* published bacterial names and 383 so-called *candidate* names published (as of 20th of October, 2019) [22]. However, the database of EZBioCloud.net (a freely-accesible database on prokaryotic diversity) contains 81,189 taxa (out of which, 24.89% has been *validly* published and 0.51% are *candidate* names), 64,416 16S rRNA sequences (a highly conserved, evolutionally-constant region) and 146,704 qualified genomes (as of 9th of August, 2019) [23]. Nonetheless, there are reports estimating that the currently known/described microbiological diversity only represents around 1-5% of the global prokaryotic diversity [20-21].

Bacterial systematics is a field, which is frequently used synonymously with taxonomy, however, the scope of systematics is much broader, including data on bacterial morphology, physiology, molecular biology and biochemistry, metabolic products, pathogenic potential, ecological niches and epidemiology to characterize, arrange and

classify bacteria [24]. Systematics became more relevant after the widespread adoption of molecular biological methods, ever higher resolution characterization of bacterial species [25] (*Figure 1*).

Due to the rapid developments in bacterial taxonomy, both consisting of the description of novel taxa and reclassification of existing bacterial genera to other taxonomical units (e.g., the history of *S. maltophilia*: it first described as *Bacterium booker* (1943), later on, it was redesignated as *Pseudomonas maltophilia* (1958) and *Xanthomonas maltophilia* (1981); finally, in 1993, the genus *Stenotrophomonas* was proposed), it is very difficult, if not impossible for researchers, officials, public health microbiologists and healthcare professionals to keep in mind all the accepted or proposed changes [26,27]. However, the importance of correct taxonomy in scientific communication and the diagnostics and therapy of bacterial infections cannot be underestimated [3]. Even if they are not aware of all the changes and the newly introduced species, relevant persons should be able to quickly find them in medical literature, scientific publications or other sources (Web pages or blogs kept up by taxonomists).

There are various resources for pharmaceutical scientists and microbiologists to get informed regarding the recognition of novel bacterial species or describing proposed reclassification of an older species. The official publication prokaryotic taxonomy and source of data regarding these matters in the International Journal of Systematic and Evolutionary Microbiology (IJSEM); the main aim and role of this publication is to report the description of new taxa or the reclassification of existing species [28]. The rules associated with the proposal of new bacterial taxa were described in the *Bacteriological Code* (1990), which was updated though the publication of the Taxonomic Outline of the Bacteria and Archaea (TOBA; 2006) [29,30]. Additional amendments to these rules are generally published in IJSEM. The proposed new species and species names (*candidate*) are to be submitted to the Editorial Office of IJSEM for evaluation, with the suffix *nova* (genus *nova*, species *nova*). The new taxonomy and nomenclature can only be considered as official, if the Editorial Board of IJSEM and the International Committee on Systematics of Prokaryotes (ICSP) both approve the submission [21]. If approved, the proposed name receives the approved state (*valid name*), which is formalized by the certificate of approval awarded by the IJSEM and ICSP [21,28]. However, once these taxa are on the approved lists, they may still be subject to reclassification, based on the designation of synonyms or due to a transfer to another genus. The validation of a new taxa is finalized if designated type strains of the species are deposited into internationally-recognized culture collections (e.g., American Type Culture Collection [ATCC], Asian Bacterial Bank [ABB], Anaerobe Reference Laboratory, Helsinki Collection [AHN], Culture Collection of Switzerland [CCOS], Collection de l'Institut Pasteur [CIP], United Kingdom National Culture Collection [UKNCC]) at least in two separate countries [31].

The Antoine van Leeuwenhoek Journal of Microbiology has become the second main journal in this field in the recent years, reporting on >100 new candidate species per year, since 2014 [32]. In addition, several other journals with interests in microbiology/infectious diseases may be vehicles in reporting novel taxa, including but not limited to: Systematic and Applied Microbiology, Journal of Medical Microbiology, Current Microbiology, Clinical Microbiology and Infection, Diagnostic Microbiology and Infectious Disease, Anaerobe, Infection, Genetics and Evolution, Journal of Antimicrobial Chemotherapy, Emerging Microbes and Infections, New Microbes and New Infections, Microbiology and Immunology, Frontiers in Genetics, Frontiers in Microbiology, Archives of Microbiology, MicrobiologyOpen, Standards in Genomic Sci-

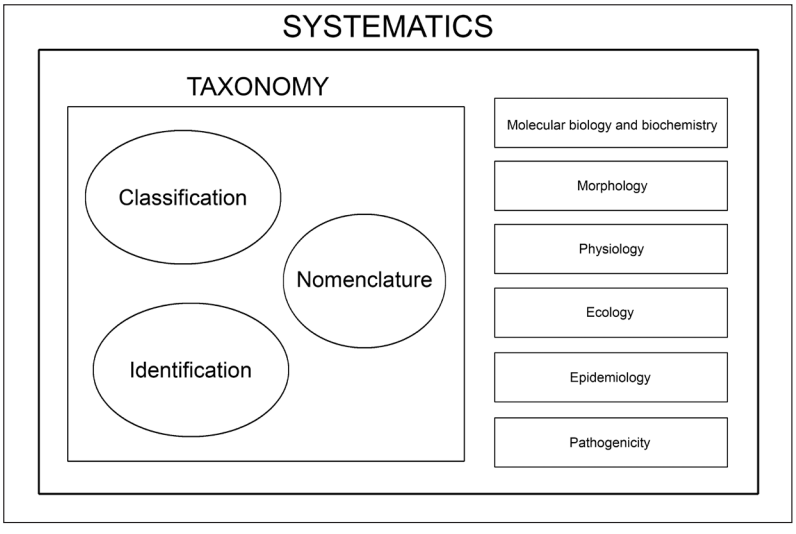

Figure 1 *Relationship of the field of taxonomy and bacterial systematics*

ences, Acta Pathologica Microbiologica et Immunologica Scandinavica (APMIS), Zentralblatt für Bakteriologie, Research in Microbiology [33]. Nevertheless, it is important to note that for the novel or revised taxa to be validly published (and the study was not submitted to IJSEM), the proposition must be included on an "approved" list in IJSEM. IJSEM publishes papers entitled "*List of new names and new combinations previously effectively, but not validly, published*" six-to-twelve times per year, which gives a good idea about the momentum of bacterial taxonomy [21,28,33]. The proposed taxa that have been previously described in other journals will be footnoted in IJSEM.

2. What is in a name: nomenclature in bacteriology

The discipline of *nomenclature* is mainly concerned with the assignment of names to taxonomic units or groups, on the basis of specific rules [34]. Before a name could be designated for any microorganism, one has to describe its biological characteristics (for its future identification), allowing for its classification in the subordinate system, as previously described [1-3]. The origins of nomenclature date back to 1753, when Carl Linnaeus published *Species Plantarum*, introducing the *binomial* nomenclature and the currently used classification hierarchy, based on greek-latin terms as the normal system of naming organisms [35]. Species Plantarum (later functioning as the International Code of Botanical Nomenclature [ICBN]) was first set of rules and recommendations of its kind. Because bacteria were once classified among plants, the nomenclature of these microorganisms was subject to the rules of the ICBN until the 1930s, when the bacteriological society has decided on the preparation of an independent code. The International Code of Bacteriological Nomenclature (or Bacteriological Code for short) was first approved in Copenhangen, 1947 [29,30]. The entire framework of naming bacteria is too complex to be described in its entirety, as the Bacteriological Code currently had more than 500 rules and regulations regarding name proposals for novel species names (which are periodically being updated; the updates are published in IJSEM) [36]. As the "intellectual capital" (i.e. available empirical and experimental data) available for the scientists submitting the candidate names for consideration constantly grows, so does the scientific accuracy of the bacterial names. The etymology (the study of the origin and history of words) of bacterial genus/species name is very diverse; here are several examples on the etymology of some bacterial genera:

- **Famous microbiologists (or scientists):** *Rothia* (Genevieve D. Roth), *Kingella* and *Elizabethkingia* (Elizabeth O. King), *Escherichia* (Theodor Escherich), *Pasterurella* (Louis Pasteur), *Gaffyka* (Georg Theodor A. Gaffky), *Burkholderia* (W.H. Burkholder), *Ehrlichia* (Paul Ehrlich), *Serratia* (Serafino Serrati, physicist)
- **Mythological names:** *Cronobacter* (Cronos, a titan), *Proteus* (Proteus, a prophetic sea-god), *Telluria* (Tellus, a Roman goddess personifying the Earth)
- **Morphological characteristics:** *Bacillus* (rod), *Streptococcus* (spheres with grape-like organization), *Helicobacter* (helical-shaped), *Campylobacter* (curved rod), *Clostridium* (greek word for *spindle*)
- **Biochemical characteristics:** *Achromobacter* (has no pigment), *Acinetobacter* (non-motile), *Chromobacterium* (produces pigment), *Anaerococcus* (strict anaerobe)
- **Geographical (e.g., site of first isolation):** *Budvicium* (Latin name of the city České Budějovice where the bacterium was first isolated), *Hafnia* (old name for Copenhagen), *Orientia* (the Orient, the area where the organisms are widely distributed), *Sinorhizobium* (which lives in a root in China)
- **Distribution:** *Aerococcus* (air), *Enterococcus* (gut), *Coprococcus* (feces), *Leptotrichia* (fine hair [of rabbits])
- **Disease-causing capability:** *S. pneumoniae* (pneumonia), *Vibrio cholerae* (cholera: watery diarrhoea), *N. meningitidis* (meningitis), *P. multocida* (lethal to many)
- **Institutions:** Centers for Disease Contol and Prevention (CDC): *Cedaceae*, Armed Forces Institute of Pathology (AFIP): *Apifia*

Changes at higher taxonomical levels (e.g., at orders and classes) are obviously much less likely to occur than in lower units, therefore one of the most common conventions on denominations is that the family name is based on the name of the most typical genus (i.e. a type species) in its domain [29-36]. A typical example is the *Legionellaceae* family, where the most characteristic genera is the one containing the *Legionella* species, namely *L. pneumophila*, the causative agent of Legionairre's disease. In contrast, for *Enterobacteriaceae*, *E. coli* is considered the type species, but the family

is not called *Escherichiaceae*; instead, due to the anatomical localization of most of these bacteria in the gut flora, they are classified in *Enterobacteriaceae*. Interestingly, the family *Enterobacteriaceae* contains a genus called *Enterobacter*, however, if one of the members of this genus would be the type species in the family, it would need to be called *Enterobacteraceae* [29-37]. The correct writing of bacterial taxonomical designations are also strictly defined by this convention, e.g. names of the species, genera and family are written in *italics*, however, at higher taxonomical designations, this is not done [29-36].

The use of abbreviations is also common in the literature and the routine clinical practice. Although there are official (defined in the Bacterial Code) three-letter abbreviations for a variety of bacterial genera (e.g., *Acp.* for *Acidophilum*, Rsc. for *Roseococcus*) to ease correspondences regarding anoxygenic phototrophic bacteria, other "real word" examples include mosaic terms derived from names of bacterial groups (e.g., GAS: Group A *Streptococcus*; ESKAPE: *Enterococcus faecium*, *S. aureus*, *Klebsiella* spp., *Acinetobacter baumannii*, *P. aeruginosa*, *Enterobacter* spp.), therapeutic recommendations (e.g., MRSA: methicillin-resistant *S. aureus*) or public health significance (e.g., MSTM: multidrug-resistant *Stenotrophomonas maltophilia*, MDRAB: multidrug-resistant *A. baumannii*) [27, 38-43]. It must be noted that in medicine (especially as far as the clinical microbiologist-physician relationship is concerned), the use of commonly known names is preferred, which are not subject to change (irrespective of taxonomic changes), so that the doctors reading the reports, e.g., of a susceptibility test can comprehend them [29-36].

3. Laboratory methods used in bacterial taxonomy and identification

The discipline of *classification* refers to the act of arranging bacteria into these group or taxa, based on their evolutionary relationships and similarity [44]. In the early days of bacterial taxonomy, the basis of classification was solely on the determination of microscopic morphology and phenotypic characteristics, which could be observed by a light microscope or by organoleptic analysis in liquid or solid media [11]. Later on, this was complemented by the detection of the presence or absence of various enzymes, such as coagulase (differentiates between coagulase positive *S. aureus* and coagulase-negative *Staphylococcus* species), catalase (among other things, it differentiates between *Staphylococcus* and *Streptococcus* species), oxidase (aids in the differentiation of non-fermenting Gram-negative bacteria, e.g., *Pseudomonas* and *Acinetobacter*), urease (among other things, it differentiates between *Ureaplasma* and *Mycoplasma* species) and the study of the use of different sugars (i.e. their oxidative or fermentative breakdown) [45]. For a very long period of time, these biochemical tests were the mainstay of *identification* in clinical bacteriology. Identification may be considered as *applied taxonomy*, during which microbiologists determine whether a particular isolate belongs to a recognized taxon (i.e., genus, species or subspecies) [1-3]. One of the main utilizers of bacterial identification in medicine is the field of clinical microbiology (where bacterial pathogens are identified from various clinical samples to establish the patient's illness and to guide targeted antimicrobial therapy) and public health (the follow-up of outbreaks caused by bacteria), however, companies involved in pharmaceutical research, biotechnology, forensics are all relevant stakeholders [21].

In the last several decades, pronounced changes were brought about in bacterial taxonomy, due to the introduction of nucleic acid-based and molecular techniques, thus making phenotypic methods less and less relevant [46]. These methods have demonstrated that genotypic/phylogenetic relatedness does not necessary correlate well with phenotypic attributes, such as a Gram-staining pattern, microscopic morphology, oxygen-tolerance or fastidious growth characteristics [47]. These molecular methods include comparison of DNA-denaturation or melting temperatures (T_m), characterization of GC (guanine and cytosine) ratios of bacterial DNA, DNA-DNA and DNA-RNA hybridization, pulse-field gel electrophoresis (PFGE), multi-locus sequence typing (MLST), average nucleotide identity (ANI), MALDI-TOF MS, 16S rRNA gene and whole genome sequencing (WGS) and next-generation sequencing (NGS) [48-50]. The use of these methods in increasingly prevalent not only in classification, but also in identification thus, revolutionizing the field of microbiology in the process [48-50]. The prevalence of their use is mainly determined by their accuracy, robustness and their price. Based on the abovementioned methods, two bacteria are considered to be the same species, if their nucleotide sequences are at least 70% identical, and the difference between their T_m values is less, than 5% [47]. The analysis

of the GC ratio (G+C content) in genomic DNA is also a suitable taxonomic method: the GC ratio is the most variable in prokaryotic genomes (20-80%); however, in strains of a specific species, the GC content is shown to be constant. It is basically defined as percentage of the G and C amino nucleotides in the bacterial genome, which was frequently used for the division of various bacterial genera (e.g., staphylococci and micrococci highly resemble each other, based on phenotypic and biochemical characteristics, however, the difference in their GC ratios has been shown to be pronounced [~30-40% vs. ~65-75%]) [51]. DNA–DNA hybridization was considered the gold standard for decades: genomic hybridization allows for the measurement of the degree of similarity between two genomes; this technique is very useful in the differentiation of closely-related bacterial species [52,53]. In contrast, DNA-RNA hybridization is useful in the genetic analysis of two phylogenetically distant bacteria: this is possible, because ribosomal RNA (rRNA) is transfer RNA (tRNA) only represent a minor portion of bacterial genes, which evolves in a slower pace (i.e. they are more conserved), compared to other genes coding for proteins [52,53]. Currently, various nucleic acid sequencing methods (of which, WGS and NGS are one of the most modern) represent the top-tier methods for bacterial classification and the comparison of genomic structures [48-50]. Nucleic acid (DNA and RNA) sequencing is another molecular characteristic that helps directly compare the genomic structures. The sequencing of 5S rRNA (from the 50S prokaryotic ribosomal subunit), 16S rRNA and 16S rDNA (from the 30S prokaryotic ribosomal subunit) has received the most substantial attention [47-50]. In fact, current recommendations state that for the submission of a novel species, the performance of MLST or sequencing (to characterize genomic relatedness) and the submission of a preferably full-length 16S rRNA gene sequence are recommended [47].

Nevertheless, it is now well-known that the phenotypic as well as the genotypic characteristics of bacteria may be subject to change due to exogenous genetic material (i.e. conjugation, transformation and transduction), which entails the transfer of plasmid DNA from one species/genus/family of bacteria to another. In reality, these properties may also be useful to characterize relations between different bacterial taxa [47-50]. *E. coli* species conjugate well with *Salmonella* and *Shigella* species (which are more closely related taxonomically), but not with members of the genera *Proteus, Providencia* or *Enterobacter*. Similar results were found in transformation studies on *Rhizobium*, *Micrococcus*, *Bacillus* and *Haemophilus* species, showing that transformation events more frequently occur with different species of the same genera (smaller genomic variation), compared to species of different genera (larger genomic variation) [47-50].

Table III *Examples of bacterial species undergone taxonomic revisions in the last 20-year period*

Previous taxonomic designation	Current taxonomic designation
Actinobaculum schaali	*Actinotignum schaali*
Actinobacillus actinomycetemcomitans	*Aggregatibacter actinomycetemcomitans*
Bacteroides forsythus	*Tannerella forsythia*
Bacteroides gracilis	*Campylobacter gracilis*
Bacteroides melaninogenicus	*Prevotella melaninogenica*
Bacteroides pneumosintes	*Dialister pneumosintes*
Borellia burgdorferi	*Borelliella burgdorferi*
Clostridium difficile	*Clostridioides difficile*
Enterobacter shakazakii	*Cronobacter shakazakii*
Enterobacter aerogenes	*Klebsiella aerogenes*
Enterobacter gergoviae	*Pluralibacter gergoviae*
Enterobacter amnigenus	*Lelliottia amnigena*
Eubacterium lentum	*Eggerthella lenta*
Klebsiella pnuemonaie ATCC 700603	*K. quasipneumoniae subsp. similipneumoniae*
Peptostreptococcus micros	*Parvimonas micra*
Propionibacterium acnes	*Cutibacterium acnes*
Streptococcus tigurinus	*S. oralis subsp. tigurinus*
Wolinella rectus	*Camplyobacter rectus*

4. Practical relevance of taxonomical changes

After the official recognition and acknowledgement of taxonomic alterations or a revised nomenclature, significant changes may occur in the everyday practice of physicians and microbiologists dealing with infectious diseases, epidemiologists, university educations and other relevant stakeholders [47]. Changes in bacterial taxonomy, and nomenclature is usually greeted with conservatism and resistance among taxonomists, microbiologists, healthcare-professionals and scientist alike, for the simple reason that nobody likes change [1-3,21,47]. The applications of taxonomic changes can be broad ranging: they may impact the clinical care of patients, through variations in choosing the appropriate antimicrobial susceptibility testing standards or data interpretation, or even their clinical relevance and epidemiology (commensal/colonizer/pathogen). These changes also affect companies supplying laboratories with testing equipment and software (i.e. the laboratory information system or LIS) and even administrative stakeholders (e.g., accreditation services, conformity with legal documentation); of course, the clinical relevance of these changes is also relative to the isolation frequency and invasiveness of the abovementioned bacteria [33,36,37,43,44,47]. Some recent changes of interest in bacterial taxonomy are discussed below and presented in *Table III*.

Gram-negative bacteria (especially ones representing gut bacteria) have seen a plethora of taxonomic revisions since the beginning of the 21st century. Among other things, some *Vibrio* species have been reclassified into the genera *Photobacterium* (e.g., *P. damselae*) and *Grimontia* (*G. hollisae*), and the phylogenetically heterogenous members of the *E. cloacae* complex has been reassigned to the genera *Kosakonia*, *Lelliottia*, and *Pluralibacter* [54-56]. Another relevant change was the one affecting the genus *Salmonella*, where only *Salmonella enterica* strains remained in the species status, while other serovariants (e.g., Enteritidis, Typhimurium, Typhi) are no longer recognized on the species level, therefore their names should no longer be italicized [6,57]. However, one of the major taxonomical changes affecting Gram-negative bacteria (and subsequently, the medical community) is the recent reclassification of the family *Enterobacteriaceae* into the order *Enterobacterales*, containing seven distinct families (namely *Enterobacteriaceae*, *Erwiniaceae*, *Pectobacteriaceae*, *Yersiniaceae*, *Hafniaceae*, *Morganellaceae* and *Budviciaceae*) based on recent phylogenetic analyses [58]. Other suggestions include the differentiation of all *Burkholderia* species into two distinct groups: the genus *Burkolderia* would contain the human pathogenic species, while a newly designated genus *Paraburkholderia* would hold the non-pathogenic species to humans [59]. In contrast, it was proposed that the genera *Chlamydia* and *Chlamydophila* (containing *C. pneumoniae* and *C. psittaci*) should be fused together, eliminating the latter genus in the process [60].

Pronounced taxonomic changes have also occured regarding anaerobic bacteria in the last 30-40 years [16]. The restriction of the genus *Bacteroides* to *B. fragilis* and related species has led to the relclassification and transfer of numerous species to the genera *Prevotella* and *Porphyromonas* (based on pigmentation, bile-sensitivity and saccharolytic properties) and the introduction of novel genera [61-64]. Marked changes have also occured in the field of Gram-positive anaerobic cocci with the introduction of novel species, such as *Finegoldia*, *Parvimonas* and *Peptinophilus*, based on phylogenetic analysis [16,65-66]. *Eubacterium* species were also subject to taxonomic revisions, leading to the introduction of novel genera, such as *Slackia*, *Pseudoramibacter*, *Mogibacterium*, *Eggerthella* and *Cryptobacterium* [16,65]. Perhaps the most controversial taxonomic revision occured regarding the causative agent of antibiotic-associated diarrhoea and pseudomembranous enterocolitis, namely *Clostridium* (*Clostridioides*) *difficile*, which may be considered as the prime example why taxonomic changes have to be carefully considered [67-68]. After the proposal to restric the genus *Clostridium* to *C. butyricum* and other related species, it was found that *C. difficile* was phylogenetically closest to *C. mangenotii* with a 94.7% similarity, however, this species was located in the family *Peptostreptococcaceae* [69]. This would have lead to a nomenclature revision of *C. difficile* as *Peptoclostridium difficile*; however, due to the significance of this pathogen in nosocomial infection and as a public health threat, a lot of energy, time and money was put into the education of the public and healthcare professionals around the globe, regarding the dangers of "C. diff" (as it is colloquially known) and CDD/CDAD (*C. difficile*-associated diarrhea), with educational campaigns, fliers, books and so on [16, 67-69]. The proposed taxonomic change would have put forth issues in this educational

campaign (a sudden change of "*C. diff*" to "*P. diff*" and CDAD to PDAD and so on); for this reason, the reclassification as *P. difficile* was rejected, instead, a novel genus *Clostridioides* gen. nov. was proposed for *C. difficile* (now *Clostridioides difficile*) and *C. magnerotii* was also reclassified to this new genus; therefore previously used, colloquial designations for this pathogen (*C. diff*, CDD/CDAD) also remained valid [70,71].

5. Conclusions

Taxonomy is concerned with the classification of living organisms, which operates in three distinct domains, namely classification, nomenclature and identification. Compared to the taxonomic trends in the 19th century, current methods and technologies allow for more detailed phylogenetic analyses, leading to the description of a tremendous amount of novel bacterial species and the re-classification of several already described bacteria. This 'explosion' in microbial taxonomy (further aided by the developments in bacterial systematics) presents an everyday challenge to medical professionals (e.g., clinical pharmacists, physicians and nurses), pharmaceutical scientists and stakeholders in healthcare. However, the up-to-date knowledge on bacterial taxonomy is important as it may significantly impact the everyday practice of these healthcare professionals. This is especially true for scientists who use various bacterial strains for screening of antimicrobial activity of various compounds or utilizing any kind of bacterial model system during laboratory assays. The aim of this paper was to aid the abovementioned healthcare professionals to navigate through the 'maze' of bacterial taxonomy, to aid in finding authentic information regarding the description of taxonomic changes and to present some examples of changes in bacterial taxonomy which proven to be clinically significant.

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7. Competing interests

The author declares no conflict of interest, monetary or otherwise.

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