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Fungal Nomenclature: Managing Change is the Name of the Game

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Fungal species have undergone and continue to undergo significant nomenclatural change, primarily due to the abandonment of dual species nomenclature in 2013 and the widespread application of molecular technologies in taxonomy allowing correction of past classification errors. These have effected numerous name changes concerning medically important species, but by far the group causing most concern are the *Candida* yeasts. Among common species, *Candida krusei*, *Candida glabrata*, *Candida guilliermondii*, *Candida lusitaniae*, and *Candida rugosa* have been changed to *Pichia kudriavzevii*, *Nakaseomyces glabrata*, *Meyerozyma guilliermondii*, *Clavispora lusitaniae*, and *Diutina rugosa*, respectively. There are currently no guidelines for microbiology laboratories on implementing changes, and there is ongoing concern that clinicians will dismiss or misinterpret laboratory reports using unfamiliar species names. Here, we have outlined the rationale for name changes across the major groups of clinically important fungi and have provided practical recommendations for managing change.

Keywords. *Candida*; clinical fungi; nomenclature; taxonomy.

If we accept that the only constant in life is change, we can begin to understand that fungal name changes always have and always will occur. Fungal nomenclature has been undergoing extensive change for more than a decade. This can largely be attributed to the now commonplace role of molecular-based technologies in taxonomy, diagnostics, and epidemiology. Molecular studies have improved the way in which fungal species are defined and identified, permitting refinement of inter- and intraspecies phylogenetic relationships and correction of taxonomical errors arising from the phenotypic classification and identification methods used in the past. For this reason, the long-held convention of fungal species having 2 or more valid names for their teleomorph (sexual) and anamorph (asexual) states was abandoned in 2013 [1]. The subsequent need to rationalize existing names meant that some names in common use have been retained, whereas in other cases they have been replaced by the less commonly used name. Additional impacts of molecular studies include revealing extensive genetic variation within species that were originally ascribed by their morphology, leading to the description of additional species within them. Molecular analyses have shone a light on whether taxonomic groups that have been classified and named on the basis of shared morphological or phenotypic features actually share a single common ancestor (monophyletic) or whether the species have mixed ancestry such that not all species within the group are related (polyphyletic). In the case of polyphyletic genera, transfer of those species that do not share common ancestry into a more appropriate genus is warranted.

These changes form a critical part of an ongoing process of refinement in the way that we understand organisms to have evolved, to interact, and to behave. Changes in fungal species names have been occurring at a rapid pace over the past decade [2–4], and this has led to some heated debate in the arena of social media [5, 6] on the benefits and difficulties caused by such changes in clinical practice. Commonly the name change affects the genus, but the species epithet remains recognizable (eg, *Scedosporium prolificans* became *Lomentospora prolificans*), but this is not always the case (eg, *Candida krusei* became *Pichia kudriavzevii*); anecdotally, it seems to be the latter situation causing most concern. It is important to note that fungal nomenclature changes must strictly follow the International Code of Nomenclature for algae, fungi, and plants [7], and any wish to preserve certain names or parts thereof, is overridden by the nomenclatural priority of previous legitimate names for the species. However, nomenclatural changes are not new or unique to fungi, and numerous species name changes in the past have been accepted and embedded into clinical

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practice. Here we review nomenclature changes in clinically important fungi over the past 20 years and make recommendations on incorporating nomenclature change into laboratory reporting and clinical practice.

YEASTS AND YEAST-LIKE FUNGI

Candida

Arguably the group of fungi undergoing the most reclassification in recent times and causing most concern among clinicians and medical laboratorians is the ascomycetous yeasts, and particularly *Candida*, likely because these are a common cause of invasive and superficial infections encountered in both specialized and nonspecialized microbiology laboratories worldwide. The problem with *Candida* is that it represents a large, highly polyphyletic group of budding, white colony-forming yeasts in the subphylum Saccharomycotina, originally grouped together because of their similar morphology and lack of a defined teleomorph [8–10]. It does not meet the 3 generally accepted criteria of a genus: (1) monophyly, that is, all species within it evolving from a common ancestor; (2) reasonable compactness in terms of the number of species it encompasses; and (3) members of the genus share evolutionarily derived characteristics [11]. Extensive phylogenetic study of species within the *Candida* group has revealed a number of well-supported clades that better fit the definition of a genus [8–10]. Figure 1 provides an overview of the relationship between clades within the *Candida* group. Three of the most common *Candida* pathogens are *Candida albicans*, *Candida parapsilosis*, and *Candida tropicalis*, which fall into the *Lodderomyces* clade; this clade contains generally antifungal-susceptible *Candida* species [10]. Being among the largest clades with demonstrated monophyly, this clade has retained the name *Candida*. However, *Candida glabrata*, along with the closely related species *Candida bracarensis* and *Candida nivariensis*, form part of the *Nakaseomyces* clade, and hence have been transferred to a new genus, *Nakaseomyces*, as *Nakaseomyces glabrata*, *Nakaseomyces bracarensis*, and *Nakaseomyces nivariensis*, respectively, although formal description is still pending [4]. *Candida krusei*, at one point also being known concurrently by *Issatchenckia orientalis*, *Candida glycerinogenes*, and *Pichia kudriavzevii* [12], belongs to the *Pichia* clade and was formally described as *P kudriavzevii* due to the nomenclatural priority of this name over others. *Candida norvegensis* also forms part of the *Pichia* clade, and has been transferred to *Pichia norvegensis* [13]. Both the *Nakaseomyces* and *Pichia* clades include species characterized by decreased susceptibility or intrinsic resistance to azole antifungal drugs [10], such that these reclassified genera now represent specific evolutionary traits, the third criterion for a genus (Figure 1).

Analyses of 18S and internal transcribed spacer ribosomal DNA (rDNA) have determined that *Candida rugosa* represents a complex of highly similar species, including *C rugosa*, *Candida pararugosa*, *Candida neorugosa*, and *Candida pseudorugosa* [14, 15]; these species, along with *Candida catenulata* and *Candida scorzettiae*, form a well-separated clade and were transferred to a new genus as *Diutina* [14]. Other new genera containing former *Candida* species include *Debaryomyces*, *Clavispora*, *Kluyveromyces*, *Meyerozyma*, *Wickerhamomyces*, and *Yarrowia*. Table 1 summarizes nomenclature changes to date in clinically important yeasts.

Several pathogenic *Candida* species have been described in recent years. Without a doubt, *Candida auris*, described in 2009 as part of the *Candida haemulonii* complex, has become the most notorious of these [22]. *Candida auris* has been associated with large healthcare-related outbreaks globally, and comprises 4 major lineages, each having their own antifungal susceptibility characteristics [23, 24]. Other members of this species complex are *Candida duobushaemulonii* and *Candida vulturna* [25, 26]. The latter was indicated as *C vulturna* pro tempore, indicating that "*Candida*" is a temporary solution. In fact, these species all cluster within the *Clavispora* clade [8], suggesting that a name change may be warranted. *Candida blankii* was described in 1968 but has only recently been recognized as a multidrug-resistant human pathogen [27–31]. It does not group in any of the *Candida* clades and may, therefore, be the sole representative of an as yet undescribed genus [9].

Cryptococcus

The basidiomycetous yeasts have also undergone substantial taxonomic change based on large-scale phylogenetic evidence [18, 32]. The revision of the genus *Cryptococcus* coincided with the proposal to elevate the 7 lineages within the *Cryptococcus neoformans* and *Cryptococcus gattii* complexes to species [33], which, while now largely accepted, has not been without robust debate [34, 35]. Besides 3 nonpathogenic *Cryptococcus* species, the genus now contains the major cause of cryptococcosis: *C neoformans* sensu stricto (previously *C neoformans* var *grubii*) and *Cryptococcus deneoformans* (previously *C neoformans* var *neoformans*). Two of 5 pathogenic species within the *C gattii* complex were renamed to a previously published synonym: *C gattii* sensu stricto (genotype AFLP4/VGI) and *Cryptococcus bacillisporus* (AFLP5/VGIII), and *Cryptococcus deuterogattii* (AFLP6/VGII), *Cryptococcus tetragattii* (AFLP7/VGIV), and *Cryptococcus decagattii* (AFLP10/VGVI) were named for their molecular type [33]. Epidemiological studies indicate that various *Cryptococcus* species have a predilection for certain hosts and exhibit differences in antifungal susceptibility [33]. While identification platforms such as matrix-assisted laser desorption/ionization–time of flight mass spectrometry (MALDI-TOF MS) have the capability to differentiate and identify these species using in-house databases, this may not be accessible to many laboratories on a routine basis; in such cases the organism could be reported as *C gattii* complex or *C neoformans* complex as appropriate.

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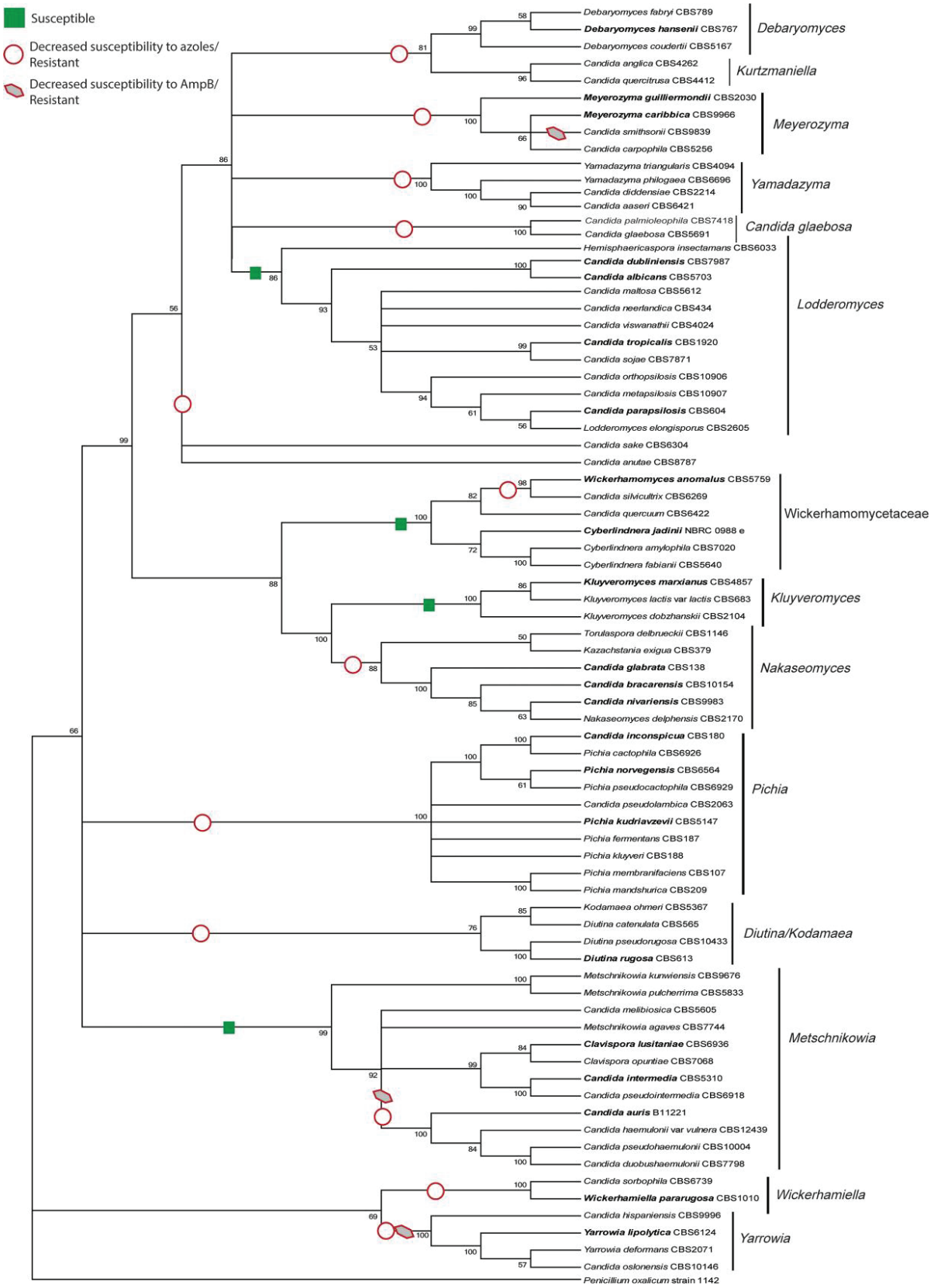

Figure 1. Phylogenetic analysis showing the genetic and antifungal susceptibility relationships between 76 Saccharomycotina yeasts within the 14 recognized clades. The tree was based on ribosomal DNA data (18S, ITS1, 5.8S, ITS2, and D1/D2) and constructed using maximum likelihood analysis. Species names in bold indicate those commonly reported in a clinical setting. General antifungal susceptibility properties have been indicated on the tree. Reproduced from Stavrou et al, *FEMS Yeast Research* 19(4): foz037 [10], with permission from Oxford University Press.

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Table 1. Summary of Nomenclature Changes in Clinically Important Yeast-like Fungi

Previous Name(s)	Current Name	Commonly Associated Infections	Reference
Candida bracarensis	*Nakaseomyces bracarensis*[a]	Invasive infections including fungemia	[8]
Candida catenulata	*Diutina catenulata*	Invasive infections including fungemia	[14]
Candida colliculosa	*Torulaspora delbrueckii*	Invasive infections including fungemia	[16]
Candida fabianii	*Cyberlindnera fabianii*	Invasive infections including fungemia	[16]
Candida famata	*Debaryomyces hansenii*	Invasive infections including fungemia	[16]
Candida glabrata	*Nakaseomyces glabrata*[a]	Invasive infections including fungemia	[8]
Candida guilliermondii	*Meyerozyma guilliermondii*	Invasive infections including fungemia	[16]
Candida krusei	*Pichia kudriavzevii*	Invasive infections including fungemia	[16]
Candida kefyr, Candida pseudotropicalis	*Kluyveromyces marxianus*	Invasive infections including fungemia	[16]
Candida lipolytica	*Yarrowia lipolytica*	Invasive infections including fungemia	[16]
Candida lusitaniae	*Clavispora lusitaniae*	Invasive infections including fungemia	[16]
Candida nivariensis	*Nakaseomyces nivariensis*[a]	Invasive infections including fungemia	[8]
Candida neorugosa	*Diutina neorugosa*	Invasive infections including fungemia	[14]
Candida norvegensis	*Pichia norvegensis*	Invasive infections including fungemia	[16]
Candida pararugosa	*Diutina pararugosa*	Invasive infections including fungemia	[14]
Candida pelliculosa, Pichia anomala	*Wickerhamomyces anomalus*	Invasive infections including fungemia	[17]
Candida pseudorugosa	*Diutina pseudorugosa*	Invasive infections including fungemia	[14]
Candida rugosa	*Diutina rugosa*	Invasive infections including fungemia	[14]
Cryptococcus albidus	*Naganishia albida*	Invasive infections including fungemia	[18]
Cryptococcus curvatus	*Cutaneotrichosporon curvatus*	Invasive infections	[18]
Cryptococcus cyanovorans	*Cutaneotrichosporon cyanovorans*	Respiratory infections, especially in cystic fibrosis	[18]
Cryptococcus laurentii	*Papiliotrema laurentii*	Invasive infections including fungemia	[18]
Pseudozyma antarctica	*Moesziomyces antarticus*	Fungemia	[19]
Pseudozyma aphidis	*Moesziomyces aphidis*	Fungemia	[19]
Pseudozyma churashimaensis	*Dirkmeia churashimaensis*	Fungemia	[19]
Pseudozyma crassa	*Triodiomyces crassus*	Fungemia	[19]
Pseudozyma parantarctica	*Moesziomyces parantarcticus*	Fungemia	[19]
Pseudozyma siamensis	*Ustilago siamensis*	Fungemia	[19]
Geotrichum capitatum	*Magnusiomyces capitatus*	Invasive infections including fungemia	[20]
Geotrichum clavatum, Saprochaete clavata	*Magnusiomyces clavatus*	Invasive infections including fungemia	[20]
Pichia ohmeri	*Kodamaea ohmeri*	Invasive infections including fungemia	[21]
Trichosporon cutaneum	*Cutaneotrichosporon cutaneum*	Cutaneous/superficial infections	[18]
Trichosporon dermatis	*Cutaneotrichosporon dermatis*	Cutaneous infections, allergic conditions	[18]
Trichosporon domesticum	*Apiotricum domesticum*	Uncertain pathogenicity	[18]
Trichosporon loubieri	*Apiotrichum loubieri*	Invasive infections including fungemia	[18]
Trichosporon mucoides	*Cutaneotrichosporon mucoides*	Cutaneous/superficial infections	[18]
Trichosporon montevideense	*Apiotrichum montevideense*	Invasive infections including fungemia	[18]
Trichosporon mycotoxinivorans	*Apiotrichum mycotoxinivorans*	Invasive infections including fungemia	[18]

[a]Species is pending formal description.

Other clinically relevant *Cryptococcus* species transferred to other genera were *Filobasidium magnum* (formerly *Cryptococcus magnus*), *Naganishia adeliensis* (formerly *Cryptococcus adeliensis*), *Naganishia albida* (formerly *Cryptococcus albidus*), *Naganishia diffluens* (formerly *Cryptococcus diffluens*), *Naganishia liquefaciens* (formerly *Cryptococcus liquefaciens*), and *Papiliotrema laurentii* (formerly *Cryptococcus laurentii*) [32].

Pseudozyma

Pseudozyma species, which are closely related to smut fungi in the Ustilaginaceae, are emerging as a cause of human fungemia. While reported cases are few, most commonly *Pseudozyma aphidis* has been identified as the cause of infection, but also *Pseudozyma antarctica*, *Pseudozyma parantarctica*, *Pseudozyma alboarmeniaca*, *Pseudozyma churashimaensis*, *Pseudozyma crassa*, *Pseudozyma siamensis*, and *Pseudozyma thailandica* [36, 37]. This genus has been demonstrated as polyphyletic, with many species clustering with other genera within the Ustilaginaceae [19]. *Pseudozyma aphidis*, *P antarctica*, and *P parantarctica* clustered with *Moesziomyces bullatus* and were therefore transferred to this genus as *Moesziomyces aphidis*, *Moesziomyces antarcticus*, and *Moesziomyces parantarcticus*, respectively; a new genus was created for *P churashimaensis*, now known as *Dirkmeia churashimaensis*; *P crassa* was

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transferred to *Triodiomyces* as *Triodiomyces crassus*; *P siamensis* was transferred to *Ustilago* as *Ustilago siamensis*; and the taxonomic status of *P alboarmeniaca* and *P thailandica* remains to be resolved [19].

Trichosporon

Trichosporon was greatly expanded by the addition of novel species prior to the taxonomic revision by Liu and colleagues [18, 32]. Currently, *Trichosporon* includes the clinically relevant species *Trichosporon asahii*, *Trichosporon asteroides*, *Trichosporon coremiiforme*, *Trichosporon dohaense*, *Trichosporon faecale*, *Trichosporon inkin*, *Trichosporon japonicum*, and *Trichosporon ovoides* [18, 32]. *Trichosporon montevideense* and *Trichosporon mycotoxinivorans* were transferred to *Apiotrichum* as *Apiotrichum montevideense* and *Apiotrichum mycotoxinivorans*, respectively. *Trichosporon cutaneum*, *Trichosporon jirovecii*, *Trichosporon dermatis*, *Trichosporon mucoides*, *Cryptococcus curvatus*, and *Cryptococcus cyanovorans* have been accommodated in the new genus *Cutaneotrichosporon*, all retaining their species epithets [18].

Geotrichum

Geotrichum is a genus of arthroconidial yeast-like fungi and an emerging cause of fungemia in immunocompromised patients [38]. Originally species were assigned based upon morphological differences only but have since undergone extensive taxonomic revision [38–42]. Examination of 18S rDNA sequences discerned 2 major groups, the first containing *Geotrichum* species with *Galactomyces* and *Dipodascus* teleomorphs, and the second comprising *Saprochaete* species with *Magnusiomyces* teleomorphs [39]. *Geotrichum clavatum* fell into the second group and was thus renamed as *Saprochaete clavata*, whereas *Geotrichum capitatum* was renamed as *Magnusiomyces capitatus*; more recently a multigene phylogenetic analysis supported transferring *S clavata* to *Magnusiomyces* as *Magnusiomyces clavatus* [20]. Thus, *Geotrichum candidum* remains the only clinically relevant species in this genus.

HYALINE HYPHOMYCETE MOLDS

Aspergillus

Aspergillus species, including the 9 teleomorphic genera associated with them, are among the most common causes of invasive or allergic disease in humans and animals [43, 44], particularly the immunosuppressed, in addition to their devastating impact on agriculture due to mycotoxin production as well as biodiversity and ecological health [45, 46]. The application of "one fungus: one name" to the taxonomy of this group was an area of concern, given the potential for many clinically important *Aspergillus* species to be renamed according to their teleomorphs [47, 48]. However, multigene phylogenetic studies found that *Aspergillus* is broadly monophyletic, without overlapping with its sibling genus *Penicillium* [49, 50]. The monophyly of *Aspergillus* allowed this name to be maintained for most species in the genus, and the clinical importance of its name to be preserved. Those species commonly known by their teleomorphs were renamed within *Aspergillus* (eg, *Neosartorya fischeri* was renamed as *Aspergillus fischeri*).

Many new *Aspergillus* species have been described in the past 2 decades, with molecular studies finding numerous genetically distinct species within those which were originally described based on their morphological characteristics. At least 50 genetically distinct species have been identified within the morphologically circumscribed *Aspergillus fumigatus*, including the pathogenic and antifungal resistant *Aspergillus lentulus*, *A fischeri*, and *Aspergillus udagawae* [51–53]. Molecular investigation of other "morphological species" of *Aspergillus* have also identified "cryptic species" within [54–57]. Table 2 summarizes nomenclature changes in *Aspergillus* and other hyaline hyphomycetes.

Penicillium

A 2011 multigene analysis of *Penicillium* and *Talaromyces* species found the *Biverticillium* subgenus of the former to be monophyletic with the latter; thus, species in the subgenus *Biverticillium* group were transferred to *Talaromyces* [67]. This included the clinically important *Talaromyces marneffei*, the only thermally dimorphic species of *Penicillum*/*Talaromyces*, which is endemic to tropical areas of Southeast and South Asian countries, predominantly seen as systemic infection in human immunodeficiency virus (HIV)–positive individuals [70]. The red diffusible pigment released into semi-solid media is regarded as a typical *T marneffei* phenotype; however, several *Talaromyces* species exhibit this phenotype, including *Talaromyces atroroseus* and *Talaromyces purpureogenus*, both described as industrially relevant pigment producers [71, 72]. Both species have been reported as the cause of infection in patients with and without HIV, or with other underlying conditions [73–76].

Paecilomyces

Paecilomyces, a genus of cosmopolitan fungi largely known for their biological control applications against bacteria, phytopathogenic fungi, and nematodes [77], are occasional causes of keratitis and onychomycosis, as well as hyalohyphomycosis in immunocompromised patients [78]. A multilocus phylogenetic study of *Paecilomyces* found significant variation [65], and the major pathogenic species *Paecilomyces variotii*, *Paecilomyces lilacinus*, and *Paecilomyces marquandii* were each found to group with different families (the Trichocomaceae, Ophiocordycipitaceae, and Clavicipitaceae, respectively). On this basis, *P lilacinus* and *P marquandii* were each transferred to a new genus as *Purpureocillium lilacinum* and *Marquandomyces marquandii*, respectively [65, 66].

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Table 2. Summary of Nomenclature Changes in Clinically Important Hyaline Hyphomycete Molds

Previous Name(s)	Current Name	Commonly Associated Infections	Reference
Acremonium kiliense	*Sarocladium kiliense*	Fungemia, subcutaneous infections	[58]
Acremonium roseogriseum	*Gliomastix roseogrisea*	Not associated with infection	[58]
Acremonium strictum	*Sarocladium strictum*	Cutaneous, invasive infections	[58]
Arthroderma benhamiae	*Trichophyton benhamiae*	Cutaneous infections	[59]
Cerinosterus cyanescens, Sporothrix cyanescens	*Quambalaria cyanescens*	Peritonitis, pneumonia, postsurgical complications	[60]
Fusarium dimerum	*Bisifusarium dimerum*	Keratitis, invasive infections	[61]
Fusarium falciforme, Acremonium falciforme	*Neocosmospora falciformis*	Keratitis, invasive infections	[61]
Fusarium keratoplasticum	*Neocosmospora keratoplastica*	Keratitis, invasive infections	[61]
Fusarium lichenicola	*Neocosmospora lichenicola*	Keratitis, invasive infections	[61]
Fusarium petroliphilum	*Neocosmospora petroliphila*	Keratitis, invasive infections	[61]
Fusarium solani	*Neocosmospora solani*	Keratitis, invasive infections	[61]
Geosmithia argillacea, Penicillium argillaceum	*Rasamsonia argillacea*	Respiratory infections, especially in cystic fibrosis	[62]
Gibberella fujikuroi	*Fusarium fujikuroi*	Keratitis, invasive infections	[63]
Lecythophora hoffmannii, Phialophora hoffmannii	*Coniochaeta hoffmannii*	Subcutaneous infections	[64]
Microsporum cookei	*Paraphyton cookei*	Cutaneous infections	[59]
Microsporum fulvum	*Nannizzia fulva*	Cutaneous infections	[59]
Microsporum gallinae	*Lophophyton gallinae*	Cutaneous infections	[59]
Microsporum gypseum	*Nannizzia gypsea*	Cutaneous infections	[59]
Microsporum nanum	*Nannizzia nana*	Cutaneous infections	[59]
Microsporum persicolor	*Nannizzia persicolor*	Cutaneous infections	[59]
Neosartorya fischeri, Neosartorya pseudofischeri, Aspergillus thermomutatus	*Aspergillus fischeri*	Respiratory, invasive infections, allergic conditions	[50]
Neosartorya udagawae	*Aspergillus udagawae*	Respiratory, invasive infections, allergic conditions	[50]
Paecilomyces lilacinus	*Purpureocillium lilacinum*	Keratitis, cutaneous infections	[65]
Paecilomyces marquandii	*Marquandomyces marquandii*	Cutaneous infections (rare)	[66]
Penicillium marneffei	*Talaromyces marneffei*	Systemic infections	[67]
Penicillium purpureogenum	*Talaromyces purpureogenus*	Pulmonary infections (rare)	[67]
Trichophyton terrestre	*Arthroderma terrestre*	Doubtful pathogenicity	[59]
Trichophyton ajelloi	*Arthroderma uncinatum*	Cutaneous infections	[59]
Trichophyton mentagrophytes			
var *interdigitale*	*Trichophyton interdigitale*	Cutaneous infections	[68]
var *mentagrophytes*	*Trichophyton mentagrophytes*	Cutaneous infections	[68]
genotype VIII	*Trichophyton indotineae*	Cutaneous infections	[69]

Rasamsonia

Rasamsonia argillacea, often recovered from the airways of patients with cystic fibrosis [79], and a cause of disseminated infections in those with chronic granulomatous disease and immunosuppression [80], bears morphological similarities to *Penicillium* and *Paecilomyces* species. Originally classified as *Penicillium argillaceum* and noted for its thermotolerance, it was transferred to a new genus in 1979, *Geosmithia* (as *Geosmithia argillacea*) with teleomorph *Talaromyces eburneus* [81]. *Geosmithia* was later found to be polyphyletic [82], paving the way to the eventual creation of a new genus of thermotolerant pathogens, *Rasamsonia*, for *Rasamsonia argillacea*, *Rasamsonia aegroticola*, *Rasamsonia eburnea*, and *Rasamsonia piperina*, often referred to as the *R argillacea* complex [62, 83].

Fusarium and Fusarioid Genera

Modern taxonomy of *Fusarium* and related genera is based on multilocus phylogenies, accompanied by genomic data, morphological descriptions, and physiological and ecological data. This caused a significant but necessary revision in classification and nomenclature of these fungi. *Fusarium* and allied fusarioid genera, *Bisifusarium* (formerly the *Fusarium dimerum* species complex), and *Neocosmospora* (formerly the *Fusarium solani* species complex), contain a genetically diverse group of hyaline fungi with global distribution. They are mainly known as ubiquitous soil saprobes, plant pathogens, and mycotoxin producers; however invasive human infections in immunocompromised patients have high mortality despite antifungal therapy. They are also major causes of fungal keratitis and nondermatophyte onychomycosis. Application of

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phylogenetic species recognition revealed that there are nearly 500 species in *Fusarium*. Members of *Fusarium* species complexes are different in morphology, host association, and molecular characteristics [63] (www.fusarium.org). The majority of human infections are caused by the *F solani* species complex (FSSC), which contains numerous phylogenetically distinct species. New formal names within *Neocosmospora* have been proposed for several *F solani* lineages [61]. The most commonly reported species, under recent revised nomenclature, correspond to *Neocosmospora keratoplastica* (formerly *Fusarium keratoplasticum* [FSSC2]), *Neocosmospora petroliphila* (formerly *Fusarium petroliphilum* [FSSC1]), *Neocosmospora falciformis* (formerly *Fusarium falciforme* [FSSC3 + 4]), *Neocosmospora lichenicola* (formerly *Fusarium lichenicola*), and *Neocosmospora solani* (formerly *Fusarium solani* [FSSC5]). Notably, morphological species recognition is unable to distinguish *Fusarium*-like taxa that have been described based on genealogical concordance of phylogenetic species recognition. Thus, the term "fusarioid" was suggested when phenotypic methods are solely used to identify *Fusarium*-like members of Nectriaceae. Accurate species-level identification of *Fusarium* and related genera from clinical specimens requires multigene sequencing with comparison to well-curated databases, which is often beyond the capacity of routine diagnostic mycology laboratories. Thus, there is currently no standard approach in reporting of these fungi in clinical practice.

Dermatophytes

Dermatophytes, a group of keratinophilic hyaline hyphomycetes, have traditionally been classified within 3 asexual genera *Trichophyton*, *Microsporum*, and *Epidermophyton*, whereas species with sexual reproduction were placed in within *Arthroderma* and *Nannizzia*. While this morphological classification is useful in dermatology clinics and routine diagnostic mycology laboratories, it does not capture the true diversity of this group. A recent multilocus phylogenetic analysis of type and reference strains [59] showed that *Trichophyton* is polyphyletic and proposed a generic classification scheme for all dermatophytes containing 7 genera—namely, *Trichophyton*, *Epidermophyton*, *Nannizzia*, *Microsporum*, *Lophophyton*, *Paraphyton*, and *Arthroderma*. Most of the anthropophilic and some zoophilic species remained in 3 older groups of *Trichophyton*, *Microsporum*, and *Epidermophyton*. In contrast, geophilic and some rare zoophilic dermatophytes are now classified in the remaining 4 genera (summarized in Table 2). Under this new scheme, novel geophilic species such as *Arthroderma eboreum* and *Nannizzia aenigmatica* have been described. Some older names used to describe distinct phenotypic variants of dermatophytes are no longer in use (eg, *Trichophyton megninii*, *Trichophyton gourvilii*, *Trichophyton yaoundei*, *Microsporum boullardii*, and *Microsporum equinum*).

Recent additions to the revised classification include 3 novel species causing tinea corporis, *Arthroderma chiloniense* [84], *Nannizzia perplicata* [85], and *Trichophyton indotineae* [69], the latter being of major clinical significance. *Trichophyton indotineae* exhibits a high level of terbinafine resistance due to missense mutations is the squalene epoxidase gene, causing extensive recalcitrant infections, mainly in the Indian subcontinent [86], but also reported from Europe [87] and Canada [88].

THERMALLY DIMORPHIC FUNGI

The thermally dimorphic fungal genera *Blastomyces*, *Emergomyces*, *Histoplasma*, *Paracoccidioides*, and *Sporothrix* have all significant taxonomic changes. The exception is the genus *Coccidioides* that 2 decades ago was expanded from a single representative to 2 species, *Coccidioides immitis* and *Coccidioides posadasii*, and has been stable ever since [89]. Changes and additions for the other genera are described below and summarized in Table 3.

Histoplasma

Histoplasma capsulatum was until recently represented by 3 varieties: *H capsulatum* var *capsulatum*, var *duboisii*, and var *farciminosum*. Multiple large phylogenetic studies observed extensive genetic diversity and potentially several new species within the variety *capsulatum* [98–101]. Using whole genome sequencing, Sepúlveda and colleagues took a first step in revising the genus *Histoplasma*, splitting *H capsulatum* var *capsulatum* into 4 species named *H capsulatum* sensu stricto (known as the Panama or H81 lineage), *Histoplasma mississippiense* (NAm1 lineage), *Histoplasma ohiense* (NAm2 lineage), and *Histoplasma suramericanum* (LAmA lineage) [92].

Blastomyces and *Emmonsia*

A phylogenetic analysis revealed 2 evolutionarily distinct lineages within *Blastomyces dermatitidis*, prompting the recognition of a second species, *Blastomyces gilchristii* [102]. Changes to the genus *Emmonsia* led to it being merged with other genera, including *Blastomyces*; *Emmonsia helica*, *Emmonsia parva*, and *Emmonsia* "species 3" were transferred to *Blastomyces* as *Blastomyces helicus*, *Blastomyces parvus*, and *Blastomyces percursus*, respectively [90, 103, 104]. This was followed by the description of 2 novel species, *Blastomyces silverae*, and *Blastomyces emzantsi*, which has so far only been reported from Southern Africa [90, 105]. The remaining *Emmonsia* species were transferred to *Emergomyces*, with *Emmonsia* "species 5" being renamed *Emergomyces africanus* [91], a major outbreak-associated clinical species [106]. *Emmonsia pasteuriana*, *Emmonsia crescens*, and *Emmonsia soli* were also transferred to *Emergomyces* as *Emergomyces pasteurianus* [91], *Emergomyces crescens*, and *Emergomyces soli* [107], respectively. Novel *Emergomyces* species are

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Table 3. Summary of Nomenclature Changes in Clinically Important Dimorphic Fungi

Previous Name(s)	Current Name	Commonly Associated Infections	Reference
Emmonsia crescens	*Emergomyces crescens*	Adiaspiromycosis	[90]
Emmonsia helica	*Blastomyces helicus*	Systemic infections	[90]
Emmonsia parva	*Blastomyces parvus*	Systemic infections	[90]
Emmonsia soli	*Emergomyces soli*	Not associated with infection	[90]
Emmonsia "species 3"	*Blastomyces percursus*	Systemic infections	[91]
Emmonsia "species 5"	*Emergomyces africanus*	Systemic infections	[91]
Emmonsia pasteuriana	*Emergomyces pasteurianus*	Systemic infections	[91]
Histoplasma capsulatum var *capsulatum*	*Histoplasma capsulatum* sensu stricto *Histoplasma mississippiense* *Histoplasma ohiense* *Histoplasma suramericanum*	Systemic infections	[92]
Lacazia loboi	*Paracoccidioides loboi*	Subcutaneous "lobomycosis"	[93]
Paracoccidioides brasiliensis	*Paracoccidioides brasiliensis* sensu stricto *Paracoccidioides americana* *Paracoccidioides restrepoana*[a] *Paracoccidioides venezuelensis* *Paracoccidioides lutzii*	Pulmonary, cutaneous infections	[94, 95]
Penicillium marneffei	*Talaromyces marneffei* [b]	Systemic infections	[67]
Sporothrix schenckii	*Sporothrix schenckii* sensu stricto *Sporothrix brasiliensis* *Sporothrix globosa* *Sporothrix luriei*	Subcutaneous infections	[96]
Sporothrix pallida	*Sporothrix pallida* sensu stricto *Sporothrix chilensis* *Sporothrix humicola* *Sporothrix mexicana* *Sporothrix stylites*	Doubtful pathogenicity in humans	[96, 97]

[a]Published as *Paracoccidioides restrepiensis*.

[b]See also section on hyaline hyphomycete molds and Table 2.

Emergomyces canadensis, *Emergomyces europaeus*, and *Emergomyces orientalis* [107, 108].

Paracoccidioides

Paracoccidioides is restricted to endemic areas in South America, and *Paracoccidioides brasiliensis* was considered the only causative agent for >80 years. However, the failure of serology tests to detect some *Paracoccidioides* infections was noted, and molecular studies determined that these cases were caused by a different species, *Paracoccidioides lutzii*, previously known as Pb01-like [94]. In addition, several consistently observed lineages led to the diversification of the *P brasiliensis* species complex into 4 species—*Paracoccidioides americana*, *P brasiliensis* sensu stricto, *Paracoccidioides restrepoana* (*as P restrepiensis*), and *Paracoccidioides venezuelensis*—which are more closely related to each other than to *P lutzii* [95, 109]. Two recently described members of *Paracoccidioides* have to date been unculturable; *Paracoccidioides loboi* (previously *Lacazia loboi*) has been associated with human infections, and *Paracoccidioides ceti* is linked to disease in marine animals [93].

Sporothrix

Sporothrichosis typically presents as subcutaneous infection caused by traumatic implantation of *Sporothrix* species. More than 50 species have been described within this genus, but only a small number are proven causes of infections in humans and animals. Until 2007, *Sporothrix schenckii* was the main causative agent, but molecular investigations showed that this species was highly diverse and 3 new species, *Sporothrix brasiliensis*, *Sporothrix globosa*, and *Sporothrix mexicana*, were subsequently described [96]. *Sporothrix brasiliensis* has been identified as the cause of large-scale and expanding outbreaks of sporothrichosis among cats with transmission from cats to humans in Brazil and sporadic cases in neighboring countries [110]. The clinically relevant *S schenckii*, *S brasiliensis*, *S globosa*, and *Sporothrix luriei* are now considered to form the *S schenckii* complex, while species rarely associated with infection form the *Sporothrix pallida* complex (*S pallida* sensu stricto, *Sporothrix chilensis*, *Sporothrix humicola*, and *S mexicana*) [97, 110].

DEMATIACEOUS (MELANIZED) HYPHOMYCETE MOLDS

Scedosporium

Members of the genera *Scedosporium* and *Pseudallescheria* have undergone extensive review and reclassification [111] based upon evidence of extensive diversity within the *Pseudallescheria boydii* complex [112–114]. Two findings are

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Table 4. Summary of Nomenclature Changes in Clinically Important Dematiaceous Hyphomycetes

Previous Name(s)	Current Name	Commonly Associated Infections	Reference
Bipolaris australiensis	*Curvularia australiensis*	Keratitis, cutaneous infections	[115]
Bipolaris hawaiiensis	*Curvularia hawaiiensis*	Keratitis, cutaneous infections	[115]
Bipolaris spicifera	*Curvularia spicifera*	Keratitis, cutaneous infections	[115]
Ochroconis gallopava	*Verruconis gallopava*	Brain and pulmonary infections	[116]
Phialophora richardsiae	*Pleurostoma richardsiae*	Subcutaneous infections	[117]
Pseudallescheria boydii	*Scedosporium boydii*	Osteoarticular, invasive infections	[114]
Ramichloridium mackenziei	*Rhinocladiella mackenziei*	Brain infections	[118]
Ramichloridium schulzeri	*Myrmecridium schulzeri*	Tongue ("golden tongue" syndrome)	[118]
Scedosporium prolificans	*Lomentospora prolificans*	Osteoarticular, invasive infections	[111]

of particular importance in clinical mycology. First, that *P boydii* and *Scedosporium apiospermum* were found to represent distinct species on the basis of significant molecular and phenotypic differences and were not in fact anamorph and teleomorph states of a single species [114]. Since *Scedosporium* has nomenclatural priority, *P boydii* was transferred into *Scedosporium* as *Scedosporium boydii*. Second, *Scedosporium prolificans* was found to be phylogenetically distinct from all other *Scedosporium* species and was returned to its original name of 1974, as *Lomentospora prolificans* [111]. This transfer to a different genus accounts not only for the taxonomic differences between *L prolificans* and other *Scedosporium* species, but also the pan-antifungal-resistant nature of this species and differences in its clinical management, compared to other *Scedosporium* infections. Other clinically relevant species recognized within this group include *Scedosporium aurantiacum*, *Scedosporium dehoogii*, and *Pseudallescheria angusta* [112, 114]. Table 4 summarizes nomenclature changes in these and other dematiaceous hyphomycetes.

Bipolaris and *Curvularia*

Species within the genera *Bipolaris* and *Curvularia* represent anamorphic forms of the *Cochliobolus* teleomorph, and share many morphological similarities, notwithstanding the characteristic curved conidia of some *Curvularia* species. The taxonomy of this group has long been controversial, and neither genus is monophyletic [119, 120]. Several studies proposed that *Bipolaris* and *Curvularia* were in fact synonymous [121, 122], as there is little more than conidial morphology to differentiate them, and many species have conidia that are intermediate between the 2 [122]. Manamgoda and colleagues [115] resolved the conflict with a multigene phylogenetic analysis of a wide range of species including ex-type cultures, which showed 2 distinct clades. On this basis, several common *Bipolaris* species, including *Bipolaris australiensis*, *Bipolaris hawaiiensis*, and *Bipolaris spicifera*, were transferred into *Curvularia* as *Curvularia australiensis*, *Curvularia hawaiiensis*, and *Curvularia spicifera*, respectively [115].

Ochroconis

The genus *Verruconis* was established to accommodate thermophilic species of *Ochroconis*, which have been isolated from hot springs, thermal soils, sewage from nuclear power plants, and coal waste piles. *Ochroconis gallopava*, *Ochroconis calidifluminalis*, and *Ochroconis verruculosum* were transferred to *Verruconis* as *Verruconis gallopava*, *Verruconis calidifluminalis*, and *Verruconis verruculosum*, respectively [116], supported by a phylogenetic analysis [123]. The type species *V gallopava* is a neurotropic pathogen of humans and other warm-blooded animals, mainly birds [124]. *Ochroconis* species are mesophilic and generally nonpathogenic in mammals, although subcutaneous human infections have been noted by *Ochroconis mirabilis* [125].

Ramichloridium

Ramichloridium was found to be polyphyletic, forming 8 distinct clades across several orders and families of dematiaceous fungi [118]. *Ramichloridium mackenziei*, a pathogen associated with high-mortality cerebral infections and prevalent in the Middle East [126], grouped with the *Rhinocladiella* type species *Rhinocladiella atrovirens* and was therefore transferred to *Rhinocladiella* as *Rhinocladiella mackenziei*. Isolates of *Ramichloridium schulzeri* formed a distinct cluster away from other genera, leading to the creation of a new genus, *Myrmecridium*, among which *Myrmecridium schulzeri* is the only mammalian pathogen. *Rhinocladiella aquaspersa* and *Rhinocladiella similis* are known causes of chromoblastomycosis [127, 128].

COELOMYCETES

Significant nomenclature change has also occurred within coelomycetous fungi, those that produce nonsexual conidia within fruiting bodies (summarized in Table 5). *Neoscytalidium dimidiatum*, formerly *Scytalidium dimidiatum*, is a plant pathogen associated with a broad spectrum of infections in humans, affecting skin and nails in tropical and subtropical continents and invasive diseases mostly in immunocompromised hosts. Nonmelanized mutants, with white colonies and reduced conidiation, were referred to as *Neoscytalidium hyalinum* (*Scytalidium hyalinum*) but have since been synonymized

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Table 5. Summary of Nomenclature Changes in Clinically Important Coelomycetes

Previous Name(s)	Current Name	Commonly Associated Infections	Reference
Leptosphaeria senegalensis	*Falciformispora senegalensis*	Mycetoma	[129]
Leptosphaeria tompkinsii	*Falciformispora tompkinsii*	Mycetoma	[129]
Scytalidium dimidiatum, Scytalidium hyalinum	*Neoscytalidium dimidiatum*	Onychomycosis	[130]
Hendersonula toruloidea	*Nattrassia mangiferae*	Onychomycosis	[131]
Pyrenochaeta romeroi	*Medicopsis romeroi*	Mycetoma	[132]
Pyrenochaeta mackinnonii	*Nigrograna mackinnonii*	Mycetoma	[133]
Madurella grisea	*Trematospheria grisea*	Mycetoma	[129]

with *N dimidiatum* [130]. Furthermore, molecular studies revealed that *N dimidiatum* and its teleomorph, *Nattrassia mangiferae* (formerly *Hendersonula toruloidea*), are 2 distinct species and not closely related [131].

Reclassification of species belonging to *Pleosporales* led to renaming of some of the main etiologic agents of black-grain eumycetoma. Based on the combined DNA sequence data set of the 18S, 28S, *RPB2*, and *TEF1* genes, *Leptosphaeria senegalensis* was renamed *Falciformispora senegalensis* and *Leptosphaeria tompkinsii* as *Falciformispora tompkinsii* [129]. Likewise, based on the rDNA sequence, the taxonomic position of *Madurella grisea* was changed to the order *Pleosporales*, and in 2013 was officially renamed as *Trematosphaeria grisea* [129]. However, the classification of *Madurella mycetomatis*, the most common fungal causative agent of mycetoma, remained unchanged. The main taxonomic change in the genus *Pyrenochaeta* was the reclassification of *Pyrenochaeta romeroi* to *Medicopsis romeroi* [132] and *Pyrenochaeta mackinnonii* as *Nigrograna mackinnonii* [133]. Based on molecular analysis of the rRNA genes, both fungi were distant from the type species of *Pyrenochaeta* and from each other; hence, they have been allocated into different genera. It is important to highlight that most members of *Pleosporales* remain sterile even in prolonged cultures, making their phenotypic identification troublesome. Application of molecular and sequence-based methods are necessary for accurate identification of these fungi.

MUCORALES

The zygomycetes and their classification within Kingdom Fungi has undergone significant change over the past 15 years. The establishment of a phylogenetic system of fungal classification [134] revealed the polyphyletic nature of what was then recognized as the phylum Zygomycota and has since been abolished. It has been replaced by 2 phyla, the Mucoromycotina and the Zoopagomycota, which include the clinically important subphyla Mucoromycotina and Entomophthoromycotina, respectively [135]. As a flow-on effect, the term "zygomycosis," which described any invasive fungal infection caused by species of the former phylum Zygomycota [136], was replaced by either "mucormycosis" or "entomophthoromycosis." This was supported by their significant clinical, ecological, and epidemiological differences between the diseases caused by these groups.

Mucor

Within the Mucoromycotina, *Mucor* is the largest genus, with close to 80 accepted species [137]. *Mucor circinelloides* is the most clinically important representative of the genus, and a recent in-depth phenotypic and molecular characterization revealed it to be a complex of 16 species [138]. The clinically relevant species in this complex are *M circinelloides*, *Mucor lusitanicus*, *Mucor griseocyanus*, *Mucor velutinosus*, and *Mucor janssenii* [138]. Additionally, *Rhizomucor variabilis* was transferred to *Mucor* as *Mucor irregularis* on the basis of rDNA phylogeny [139], becoming somewhat unique among *Mucor* species due to having rhizoids. Table 6 summarizes nomenclature changes among the clinically important Mucoromycotina.

Absidia and *Lichtheimia*

The genus *Absidia* was investigated on the basis of multiple gene phylogenies, finding that the species *Absidia corymbifera* and 4 other species formed a distinct clade that could also be characterized by thermotolerance; these species were reclassified within the genus *Lichtheimia*, comprising the clinically relevant species *Lichtheimia corymbifera*, *Lichtheimia ramosa*, *Lichtheimia hyalospora*, and *Lichtheimia ornata* [140, 144].

Rhizopus

Rhizopus oryzae and *Rhizopus arrhizus* are known to be synonyms of the same species, representing the most common cause of mucormycosis [145, 146]. There has been long-standing debate over which of these is the valid name, well reviewed by Dolatabadi et al [142], with both names in use for many years. This is now settled, with *R arrhizus* found to be the first valid name [142]. Additional changes in this genus include recognition of *Rhizopus delemar* as a variety of *R arrhizus* (ie, *R arrhizus* var *arrhizus* and *R arrhizus* var *delemar*) and collapse of the varieties within *Rhizopus microsporus* [141, 142].

Saksenaea

Members of the genus *Saksenaea* are rarely seen in the clinic, but the majority of reported cases are due to *Saksenaea vasiformis* and *Saksenaea erythrospora* [143, 147]. Five additional species have been described during the past decade, although not all have been associated with infection: *Saksenaea dorisiae*

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Table 6. Summary of Nomenclature Changes in Clinically Important Mucoromycotina

Previous Name(s)	Current Name	Commonly Associated Infections	Reference
Absidia corymbifera, *Mycocladus corymbifera*	*Lichtheimia corymbifera*	Sinonasal, subcutaneous, systemic infections	[140]
Rhizopus azygosporus	*Rhizopus microsporus*	Sinonasal, subcutaneous, systemic infections	[141]
Rhizopus delemar	*Rhizopus arrhizus* var *delemar*	Sinonasal, subcutaneous, systemic infections	[142]
Rhizopus microsporus var *chinensis* var *oligosporus* var *rhizopodiformis*	*Rhizopus microsporus* (varieties no longer recognized)	Sinonasal, subcutaneous, systemic infections	[141]
Rhizopus oryzae	*Rhizopus arrhizus*	Sinonasal, subcutaneous, systemic infections	[142]
Rhizomucor variabilis	*Mucor irregularis*	Sinonasal, subcutaneous, systemic infections	[139]
Saksenaea vasiformis	*Saksenaea vasiformis* sensu stricto *Saksenaea erythrospora* *Saksenaea oblongispora*	Sinonasal, subcutaneous, systemic infections	[143]

[148], *Saksenaea longicolla* [149], *Saksenaea loutrophoriformis* [150], *Saksenaea oblongispora* [143], and *Saksenaea trapizispora* [151].

MANAGING CHANGES IN FUNGAL NOMENCLATURE

Nomenclature changes are not new or unique to fungi [152–157]. However, in recent years changes in fungal nomenclature have been numerous, and in the age of social media, criticism has been swift [5]. Concerns include pathology reports containing unfamiliar species names that might be dismissed as nonpathogens (ie, colonizers, laboratory or environmental contaminants) and disruption of molecular and literature databases, as well as interruption of local epidemiology and antifungal susceptibility profiles. Although such concerns are valid, there is little evidence to support them. Recent surveys of Australasian laboratory staff and clinicians found a high level of support (71/92 [77%] laboratories and 204/217 [94%] clinicians) for nomenclature change, providing the previous clinically familiar names are included on reports alongside updated names [158]. This support is further demonstrated by the inclusion of updated nomenclature in the recently published global guidelines for diagnosis and management of rare yeast infections [159] and updated Australasian antifungal guidelines [160].

In fact, common fungal pathogens have undergone numerous name changes in the past; *Candida albicans* was known by several names including *Monilia albicans* until 1923, and its associated infection is still sometimes referred to as moniliasis; *Candida glabrata* was known as *Torulopsis glabrata* until 1978, a name that was still in common use until the late 1990s and was included in a clinical case report as recently as 2005 [161]. It is unclear to what extent these changes caused concern at the time; however, safe adaptation to the changes was evidently possible.

Concerns that literature and molecular databases will be disrupted by name changes and flooded by redundant "First case of …" reports, are unwarranted. All National Center for Biotechnology Information (NCBI) databases, which include PubMed and GenBank, are underpinned by a standardized taxonomy database, ensuring that any organism-based search term will retrieve all relevant material, regardless of whether the name is current or obsolete [162, 163]. This permits extraction of all relevant literature to guide management. Publicly accessible resources such as Index Fungorum (http://www.indexfungorum.org) and MycoBank (www.mycobank.org) that serve as repositories for nomenclatural information, including whether names are current or obsolete, can assist those unsure of the status of a fungal species name.

Nomenclature updates in proprietary databases, such as those for MALDI-TOF mass spectrometry, will be critical to the successful adaptation to new species names by clinical microbiology laboratories. Unfortunately, this is hindered by the need for manufacturers to meet the requirements of regulatory bodies, such as the US Food and Drug Administration. At this time, the Vitek MS Expanded V3.2 database (bioMérieux, Marcy l'Étoile, France) uses some updated nomenclature (eg, *Purpureocillium lilacinum*, *Lichtheimia corymbifera*, *Sarocladium kiliense*) but also obsolete nomenclature (eg, various *Candida* species, *Scedosporium prolificans*). In contrast, the recently released MBT Compass Library Revision G (2021) and MBT Filamentous Fungi Library (2021) (Bruker Daltonics, Bremen, Germany, 2021) accommodates the reclassification of many yeasts and molds. As further database updates are rolled out to laboratories, it can be expected that resistance to nomenclature changes will be reduced. Access to database updates may be dependent upon service contracts and regulatory approval in different regions, but broadly speaking, most laboratories utilizing Vitek MS or MALDI Biotyper systems receive annual database updates without cost. However, in-house databases would require laboratory input to update nomenclature.

Critical to the success of adapting to new nomenclature is education of laboratory staff and of clinicians. The experience in

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Australia, New Zealand, and the United Kingdom has demonstrated a clear role for external quality assurance programs and reference laboratories in education. Revised names should be incorporated into formal teaching and training programs as well as examinations; this will be greatly supported by the incorporation of updated names in medical reference texts such as the *Manual of Clinical Microbiology*. The Clinical and Laboratory Standards Institute (CLSI) recently recognized but stopped short of adopting new names in the M27M44S document [164]. There is enormous potential for organizations such as the CLSI, the European Committee on Antimicrobial Susceptibility Testing, the College of American Pathologists, the International Society for Human and Animal Mycoses, the Mycoses Study Group Education and Research Consortium, the European Confederation of Medical Mycology, and the Australia and New Zealand Mycoses Interest Group to play an important role, perhaps through joint working groups, in the education of laboratory staff through workshops, newsletters, and the development of guidelines.

In the absence of endorsed guidelines on adapting to nomenclature change, we make the following recommendations for clinical microbiology laboratories:

1. It is recommended that all microbiology laboratories, regardless of size, geographic location, degree of mycology expertise, or supervision structure, should take steps toward utilization of updated fungal nomenclature as soon as is practical. Ultimately, this will provide consistency in reporting between laboratories nationally and internationally, reducing the potential for confusion and support the education of laboratory staff and clinicians.
2. When reporting an organism using new/updated nomenclature, the previous name must also be included on the report; for example, "Growth of *Pichia kudriavzevii* (*Candida krusei*)" or "Growth of *Pichia kudriavzevii*. This species was formerly known as *Candida krusei*." Depending on the laboratory information system, the above comments may be coded to occur automatically and ensure consistency in the approach.
3. It may be necessary to include the previous names on reports for 5 years, or longer, depending on the range of specimens and requesting clinicians and the perceived level of acceptance of the nomenclature into common use.
4. For taxa where the identification method used is insufficiently sensitive or robust to identify reliably to species level, reporting to species complex level is useful, along with clinically pertinent comments as appropriate; for example, "Growth of *Cryptococcus gattii* complex" or "Growth of *Aspergillus fumigatus* complex. This species complex includes a number of pathogenic species that may have reduced susceptibility to one or more antifungal drugs." In these situations, it may also be important to indicate the method used for identification.
5. The reporting strategy must be consistent, requiring all laboratory staff to be educated. New names should be updated in the laboratory information system and document-controlled procedure manuals and as soon as practicable.

CONCLUSIONS

Change in the nomenclature for any pathogen is an inevitable and necessary part of the scientific process, a result of refinement and correction of past taxonomic errors, and offers possibilities for improved recognition of clinically relevant biological characteristics, such as antifungal resistance or thermotolerance. The real issue is managing change to best serve those who work with these organisms.

Notes

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References

1. Hawksworth DL, Crous PW, Redhead SA, et al. The Amsterdam declaration on fungal nomenclature. IMA Fungus **2011**; 2:105–12.
2. Warnock DW. Name changes for fungi of medical importance, 2012 to 2015. J Clin Microbiol **2017**; 55:53–9.
3. Warnock DW. Name changes for fungi of medical importance, 2016–2017. J Clin Microbiol **2019**; 57:e01183–18.
4. Borman AM, Johnson EM. Name changes for fungi of medical importance, 2018 to 2019. J Clin Microbiol **2021**; 59:e01811–20. Erratum in: J Clin Microbiol 2021; 59.
5. Kidd SE, Halliday CL, McMullan B, Chen SC, Elvy J. New names for fungi of medical importance: can we have our cake and eat it too? J Clin Microbiol **2021**; 59:e02730–20.
6. Borman AM, Johnson EM. Reply to Kidd, et al, "New names for fungi of medical importance: can we have our cake and eat it too?" J Clin Microbiol **2021**; 59: e02896–20.
7. Turland NJ, Wiersema JH, Barrie FR, et al, eds. 2018: International Code of Nomenclature for algae, fungi, and plants (Shenzhen Code) adopted by the Nineteenth International Botanical Congress Shenzhen, China. Regnum Vegetabile 159. **2017**. Glashütten, Germany: Koeltz Botanical Books. https://doi.org/10.12705/Code.2018
8. Daniel HM, Lachance MA, Kurtzman CP. On the reclassification of species assigned to *Candida* and other anamorphic ascomycetous yeast genera based on phylogenetic circumscription. Antonie Van Leeuwenhoek **2014**; 106:67–84.
9. Kurtzman CP, Robnett CJ. Relationships among genera of the Saccharomycotina (Ascomycota) from multigene phylogenetic analysis of type species. FEMS Yeast Res **2013**; 13:23–33.
10. Stavrou AA, Lackner M, Lass-Flörl C, Boekhout T. The changing spectrum of Saccharomycotina yeasts causing candidemia: phylogeny mirrors antifungal susceptibility patterns for azole drugs and amphotericin B. FEMS Yeast Res **2019**; 19:foz037.
11. Gill FB, Slikas B, Sheldon FH. Phylogeny of titmice (Paridae): II. Species relationships based on sequences of the mitochondrial cytochrome-B gene. Auk **2005**; 122:121–43.

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LCY Biotechnology Holding, Inc.
Ex. 1039
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12. Douglass AP, Offei B, Braun-Galleani S, et al. Population genomics shows no distinction between pathogenic *Candida krusei* and environmental *Pichia kudriavzevii*: one species, four names. PLoS Pathog **2018**; 14:e1007138.
13. Leask BG, Yarrow D. *Pichia norvegensis* sp. nov. Sabouraudia **1976**; 14:61–3.
14. Khunnamwong P, Lertwattanasakul N, Jindamorakot S, Limtong S, Lachance MA. Description of *Diutina* gen. nov., *Diutina siamensis*, f.a. sp. nov., and reassignment of *Candida catenulata*, *Candida mesorugosa*, *Candida neorugosa*, *Candida pseudorugosa*, *Candida ranongensis*, *Candida rugosa* and *Candida scorzettiae* to the genus *Diutina*. Int J Syst Evol Microbiol **2015**; 65:4701–9.
15. Ming C, Huang J, Wang Y, et al. Revision of the medically relevant species of the yeast genus *Diutina*. Med Mycol **2019**; 57:226–33.
16. Kurtzman CP, Fell JW, Boekhout T. The yeasts: a taxonomic study. 5th ed. Amsterdam, The Netherlands: Elsevier Science, **2011**.
17. Kurtzman CP. Phylogeny of the ascomycetous yeasts and the renaming of *Pichia anomala* to *Wickerhamomyces anomalus*. Antonie Van Leeuwenhoek **2011**; 99: 13–23.
18. Liu XZ, Wang QM, Göker M, et al. Towards an integrated phylogenetic classification of the *Tremellomycetes*. Stud Mycol **2015**; 81:85–147.
19. Wang QM, Begerow D, Groenewald M, et al. Multigene phylogeny and taxonomic revision of yeasts and related fungi in the Ustilaginomycotina. Stud Mycol **2015**; 81:55–83.
20. Kaplan E, Al-Hatmi AMS, Ilkit M, et al. Molecular diagnostics of arthroconidial yeasts, frequent pulmonary opportunists. J Clin Microbiol **2018**; 56:e01427–17.
21. Yamada Y, Suzuki T, Matsuda M, Mikata K. The phylogeny of *Yamadazyma ohmeri* (Etchells et Bell) Billon-Grand based on the partial sequences of 18S and 26S ribosomal RNAs: the proposal of *Kodamaea* gen. nov. Saccharomycetaceae). Biosci Biotechnol Biochem **1995**; 59:1172–4.
22. Satoh K, Makimura K, Hasumi Y, Nishiyama Y, Uchida K, Yamaguchi H. *Candida auris* sp. nov., a novel ascomycetous yeast isolated from the external ear canal of an inpatient in a Japanese hospital. Microbiol Immunol **2009**; 53: 41–4.
23. Chow NA, Muñoz JF, Gade L, et al. Tracing the evolutionary history and global expansion of *Candida auris* using population genomic analyses. mBio **2020**; 11: e03364–19.
24. de Jong AW, Hagen F. Attack, defend and persist: how the fungal pathogen *Candida auris* was able to emerge globally in healthcare environments. Mycopathologia **2019**; 184:353–65.
25. Cendejas-Bueno E, Kolecka A, Alastruey-Izquierdo A, et al. Reclassification of the *Candida haemulonii* complex as *Candida haemulonii* (*C. haemulonii* group I), *C. duobushaemulonii sp. nov*. (*C. haemulonii* group II), and *C. haemulonii* var. *vulnera var. nov*.: three multiresistant human pathogenic yeasts. J Clin Microbiol **2012**; 50:3641–51.
26. Sipiczki M, Tap RM. *Candida vulturna* pro tempore sp. nov., a dimorphic yeast species related to the *Candida haemulonis* species complex isolated from flowers and clinical sample. Int J Syst Evol Microbiol **2016**; 66:4009–15.
27. Nobrega de Almeida J Jr, Campos SV, Thomaz DY, et al. *Candida blankii*: an emergent opportunistic yeast with reduced susceptibility to antifungals. Emerg Microbes Infect **2018**; 7:1–3.
28. Al-Haqqan A, Al-Sweih N, Ahmad S, et al. Azole-resistant *Candida blankii* as a newly recognized cause of bloodstream infection. New Microbes New Infect **2018**; 26:25–9.
29. Chowdhary A, Stielow JB, Upadhyaya G, Singh PK, Singh A, Meis JF. *Candida blankii*: an emerging yeast in an outbreak of fungaemia in neonates in Delhi, India. Clin Microbiol Infect **2020**; 26:648.e5–8.
30. Kollu VS, Kalagara PK, Islam S, Gupte A. A report of *Candida blankii* fungemia and possible endocarditis in an immunocompetent individual and the review of literature. Cureus **2021**; 13:e14945.
31. Mirchin R, Czeresnia JM, Orner EP, Chaturvedi S, Murphy K, Nosanchuk JD. The continuing emergence of *Candida blankii* as a pathogenic fungus: a new case of fungemia in a patient infected with SARS-CoV-2. J Fungi (Basel). **2022**; 8:166.
32. Liu XZ, Wang QM, Theelen B, Groenewald M, Bai FY, Boekhout T. Phylogeny of tremellomycetous yeasts and related dimorphic and filamentous basidiomycetes reconstructed from multiple gene sequence analyses. Stud Mycol **2015**; 81:1–26.
33. Hagen F, Khayhan K, Theelen B, et al. Recognition of seven species in the *Cryptococcus gattii/Cryptococcus neoformans* species complex. Fungal Genet Biol **2015**; 78:16–48.
34. Kwon-Chung KJ, Bennett JE, Wickes BL, et al. The case for adopting the "species complex" nomenclature for the etiologic agents of cryptococcosis. mSphere **2017**; 2:e00357-16.
35. Hagen F, Lumbsch HT, Arsic Arsenijevic V, et al. Importance of resolving fungal nomenclature: the case of multiple pathogenic species in the *Cryptococcus* genus. mSphere **2017**; 2:e00238-17.
36. Telles JP, Ribeiro VST, Kraft L, Tuon FF. *Pseudozyma* spp. human infections: a systematic review. Med Mycol **2021**; 59:1–6.
37. Chowdhary A, Sharada K, Singh PK, et al. Outbreak of *Dirkmeia churashimaensis* fungemia in a neonatal intensive care unit, India. Emerg Infect Dis **2020**; 26: 764–68.
38. Graeff L Durán, Seidel D, Vehreschild MJ, et al; FungiScope Group. Invasive infections due to *Saprochaete* and *Geotrichum* species: report of 23 cases from the FungiScope Registry. Mycoses **2017**; 60:273–9.
39. de Hoog GS, Smith MT. Ribosomal gene phylogeny and species delimitation in *Geotrichum* and its teleomorphs. Stud Mycol **2004**; 50:489–515.
40. de Hoog GS, Smith MT. Chapter 45, *Magnusiomyces* Zender (1977). In: Kurtzman CP, Fell JW, Boekhout T, eds. The yeasts, a taxonomic study. 5th ed. Amsterdam, The Netherlands: Elsevier Science, **2011**:565–74.
41. de Hoog GS, Smith MT. Chapter 91, *Geotrichum* Link: Fries (1832). In: Kurtzman CP, Fell JW, Boekhout T, eds. The yeasts, a taxonomic study. 5th ed. Amsterdam, The Netherlands: Elsevier Science, **2011**:1279–86.
42. de Hoog GS, Smith MT. Chapter 97, *Saprochaete* Coker & Shanor ex D.T.S. Wagner & Dawes (1970). In: Kurtzman CP, Fell JW, Boekhout T, eds. The yeasts, a taxonomic study. 5th ed. Amsterdam, The Netherlands: Elsevier Science, **2011**:1317–27.
43. Thompson GR 3rd, Young JH. *Aspergillus* infections. N Engl J Med **2021**; 385: 1496–509.
44. Seyedmousavi S, Guillot J, Arné P, et al. *Aspergillus* and aspergilloses in wild and domestic animals: a global health concern with parallels to human disease. Med Mycol **2015**; 53:765–97.
45. Shabeer S, Asad S, Jamal A, Ali A. Aflatoxin contamination, its impact and management strategies: an updated review. Toxins (Basel) **2022**; 14:307.
46. Fisher MC, Henk DA, Briggs CJ, et al. Emerging fungal threats to animal, plant and ecosystem health. Nature **2012**; 484:186–94.
47. Pitt JI, Taylor JW. *Aspergillus*, its sexual states and the new International Code of Nomenclature. Mycologia **2014**; 106:1051–62.
48. Taylor JW, Göker M, Pitt JI. Choosing one name for pleomorphic fungi: the example of *Aspergillus* versus *Eurotium*, *Neosartorya* and *Emericella*. Taxon **2016**; 65:593–601.
49. Houbraken J, Samson RA. Phylogeny of *Penicillium* and the segregation of Trichocomaceae into three families. Stud Mycol **2011**; 70:1–51.
50. Kocsubé S, Perrone G, Magistà D, et al. *Aspergillus* is monophyletic: evidence from multiple gene phylogenies and extrolites profiles. Stud Mycol **2016**; 85: 199–213.
51. Hong SB, Go SJ, Shin HD, Frisvad JC, Samson RA. Polyphasic taxonomy of *Aspergillus fumigatus* and related species. Mycologia **2005**; 97:1316–29.
52. Katz ME, Dougall AM, Weeks K, Cheetham BF. Multiple genetically distinct groups revealed among clinical isolates identified as atypical *Aspergillus fumigatus*. J Clin Microbiol **2005**; 43:551–5.
53. Badali H, Cañete-Gibas C, McCarthy D, et al. Species distribution and antifungal susceptibilities of *Aspergillus* section fumigati isolates in clinical samples from the United States. J Clin Microbiol **2022**; 60:e0028022.
54. Zoran T, Sartori B, Sappl L, et al. Azole-Resistance in *Aspergillus terreus* and related Species: an emerging problem or a rare phenomenon? Front Microbiol **2018**; 9:516. Erratum in: Front Microbiol 2019; 9:3245.
55. Takeda K, Suzuki J, Watanabe A, et al. The accuracy and clinical impact of the morphological identification of *Aspergillus* species in the age of cryptic species: a single-centre study. Mycoses **2022**; 65:164–70.
56. Imbert S, Cassaing S, Bonnal C, et al. Invasive aspergillosis due to *Aspergillus* cryptic species: a prospective multicentre study. Mycoses **2021**; 64:1346–53.
57. Nargesi S, Jafarzadeh J, Najafzadeh MJ, et al. Molecular identification and antifungal susceptibility of clinically relevant and cryptic species of *Aspergillus* sections *Flavi* and *Nigri*. J Med Microbiol **2022**; 71. doi:10.1099/jmm.0.001480
58. Summerbell RC, Gueidan C, Schroers HJ, et al. *Acremonium* phylogenetic overview and revision of *Gliomastix*, *Sarocladium*, and *Trichothecium*. Stud Mycol **2011**; 68:139–16.
59. de Hoog GS, Dukik K, Monod M, et al. Toward a novel multi-locus phylogenetic taxonomy for the dermatophytes. Mycopathologia **2017**; 182:5–31.
60. de Beer ZW, Begerow D, Bauer R, Pegg GS, Crous PW, Wingfield MJ. Phylogeny of the *Quambalariaceae* fam. nov., including important *Eucalyptus* pathogens in South Africa and Australia. Stud Mycol **2006**; 55:289–98.
61. Sandoval-Denis M, Crous PW. Removing chaos from confusion: assigning names to common human and animal pathogens in *Neocosmospora*. Persoonia **2018**; 41:109–29.
62. Houbraken J, Spierenburg H, Frisvad JC. *Rasamsonia*, a new genus comprising thermotolerant and thermophilic *Talaromyces* and *Geosmithia* species. Antonie Van Leeuwenhoek **2012**; 101:403–21.
63. Crous PW, Lombard L, Sandoval-Denis M, et al. *Fusarium*: more than a node or a foot-shaped basal cell. Stud Mycol **2021**; 98:100116.

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LCY Biotechnology Holding, Inc.
Ex. 1039
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64. Khan Z, Gené J, Ahmad S, et al. *Coniochaeta polymorpha*, a new species from endotracheal aspirate of a preterm neonate, and transfer of *Lecythophora* species to *Coniochaeta*. Antonie Van Leeuwenhoek **2013**; 104:243–52.
65. Luangsa-Ard J, Houbraken J, van Doorn T, et al. *Purpureocillium*, a new genus for the medically important *Paecilomyces lilacinus*. FEMS Microbiol Lett **2011**; 321:141–9.
66. Mongkolsamrit S, Khonsanit A, Thanakitpipattana D, et al. Revisiting *Metarhizium* and the description of new species from Thailand. Stud Mycol **2020**; 95:171–251.
67. Samson RA, Yilmaz N, Houbraken J, et al. Phylogeny and nomenclature of the genus *Talaromyces* and taxa accommodated in *Penicillium* subgenus *Biverticillium*. Stud Mycol **2011**; 70:159–83.
68. Gräser Y, Kuijpers AF, Presber W, De Hoog GS. Molecular taxonomy of *Trichophyton mentagrophytes* and *T. tonsurans*. Med Mycol **1999**; 37:315–30.
69. Kano R, Kimura U, Kakurai M, et al. *Trichophyton indotineae* sp. nov.: a new highly terbinafine-resistant anthropophilic dermatophyte species. Mycopathologia **2020**; 185:947–58.
70. Cao C, Xi L, Chaturvedi V. Talaromycosis (penicilliosis) due to *Talaromyces* (*Penicillium*) *marneffei*: insights into the clinical trends of a major fungal disease 60 years after the discovery of the pathogen. Mycopathologia **2019**; 184:709–20.
71. Frisvad JC, Yilmaz N, Thrane U, Rasmussen KB, Houbraken J, Samson RA. *Talaromyces atroroseus*, a new species efficiently producing industrially relevant red pigments. PLoS One **2013**; 8:e84102.
72. Bhatnagar S, Kobori T, Ganesh D, Aoyagi H. Fungal pigment-assisted silver nanoparticle synthesis and their antimicrobial and cytotoxic potential. Methods Mol Biol **2022**; 2469:65–78.
73. Atalay A, Koc AN, Akyol G, Cakir N, Kaynar L, Ulu-Kilic A. Pulmonary infection caused by *Talaromyces purpurogenus* in a patient with multiple myeloma. Infez Med **2016**; 24:153–7.
74. Li L, Chen K, Dhungana N, Jang Y, Chaturvedi V, Desmond E. Characterization of clinical isolates of *Talaromyces marneffei* and related species, California, USA. Emerg Infect Dis **2019**; 25:1765–8.
75. Surja SS, Adawiyah R, Houbraken J, et al. *Talaromyces atroroseus* in HIV and non-HIV patient: a first report from Indonesia. Med Mycol **2020**; 58:560–3.
76. Aboutalebian S, Mahmoudi S, Okhovat A, Khodavaisy S, Mirhendi H. Otomycosis due to the rare fungi *Talaromyces purpurogenus*, *Naganishia albida* and *Filobasidium magnum*. Mycopathologia **2020**; 185:569–75.
77. Moreno-Gavíra A, Huertas V, Diánez F, Sánchez-Montesinos B, Santos M. *Paecilomyces* and its importance in the biological control of agricultural pests and diseases. Plants (Basel) **2020**; 9:1746.
78. Antas PR, Brito MM, Peixoto É, Ponte CG, Borba CM. Neglected and emerging fungal infections: review of hyalohyphomycosis by *Paecilomyces lilacinus* focusing in disease burden, in vitro antifungal susceptibility and management. Microbes Infect **2012**; 14:1–8.
79. Abdolrasouli A, Bercusson AC, Rhodes JL, et al. Airway persistence by the emerging multi-azole-resistant *Rasamsonia argillacea* complex in cystic fibrosis. Mycoses **2018**; 61:665–73.
80. Stemler J, Salmanton-García J, Seidel D, et al. Risk factors and mortality in invasive *Rasamsonia* spp. infection: analysis of cases in the FungiScope registry and from the literature. Mycoses **2020**; 63:265–74.
81. Pitt J. *Geosmithia* gen. nov. for *Penicillium lavendulum* and related species. Can J Bot **1979**; 57:2021–30.
82. Ogawa H, Yoshimura A, Sugiyama J. Polyphyletic origins of species of the anamorphic genus *Geosmithia* and the relationships of the cleistothecial genera: evidence from 18S, 5S and 28S rDNA sequence analyses. Mycologia **1997**; 89: 756–71.
83. Giraud S, Favennec L, Bougnoux ME, Bouchara JP. *Rasamsonia argillacea* species complex: taxonomy, pathogenesis and clinical relevance. Future Microbiol **2013**; 8:967–78.
84. Brasch J, Beck-Jendroschek V, Voss K, Yurkov A, Gräser Y. *Arthroderma chiloniense* sp. nov. Isolated from human stratum corneum: description of a new *Arthroderma* species. Mycoses **2019**; 62:73–80.
85. Borman AM, Szekely A, Fraser M, Lovegrove S, Johnson EM. A novel dermatophyte relative, *Nannizzia perplicata* sp. nov., isolated from a case of tinea corporis in the United Kingdom. Med Mycol **2019**; 57:548–56.
86. Tang C, Kong X, Ahmed SA, et al. Taxonomy of the *Trichophyton mentagrophytes*/*T. interdigitale* species complex harboring the highly virulent, multiresistant genotype *T. indotineae*. Mycopathologia **2021**; 186:315–26.
87. Jabet A, Brun S, Normand AC, et al. Extensive dermatophytosis caused by terbinafine-resistant *Trichophyton indotineae*, France. Emerg Infect Dis **2022**; 28:229–33.
88. Posso-De Los Rios CJ, Tadros E, Summerbell RC, Scott JA. Terbinafine resistant *Trichophyton indotineae* isolated in patients with superficial dermatophyte infection in Canadian patients. J Cutan Med Surg **2022**; 26:371–6.
89. Fisher MC, Koenig GL, White TJ, Taylor JW. Molecular and phenotypic description of *Coccidioides posadasii* sp. nov., previously recognized as the non-California population of *Coccidioides immitis*. Mycologia **2002**; 94:73–84.
90. Jiang Y, Dukik K, Muñoz JF, et al. Phylogeny, ecology and taxonomy of systemic pathogens and their relatives in *Ajellomycetaceae* (*Onygenales*): *Blastomyces*, *Emergomyces*, *Emmonsia*, *Emmonsiellopsis*. Fung Div **2018**; 90:245–91.
91. Dukik K, Muñoz JF, Jiang Y, et al. Novel taxa of thermally dimorphic systemic pathogens in the Ajellomycetaceae (Onygenales). Mycoses **2017**; 60:296–309.
92. Sepúlveda VE, Márquez R, Turissini DA, Goldman WE, Matute DR. Genome sequences reveal cryptic speciation in the human pathogen *Histoplasma capsulatum*. mBio **2017**; 8:e01339–17.
93. Vilela R, Huebner M, Vilela C, et al. The taxonomy of two uncultivated fungal mammalian pathogens is revealed through phylogeny and population genetic analyses. Sci Rep **2021**; 11:18119.
94. Teixeira MM, Theodoro RC, Oliveira FF, et al. *Paracoccidioides lutzii* sp. nov.: biological and clinical implications. Med Mycol **2014**; 52:19–28.
95. Turissini DA, Gomez OM, Teixeira MM, McEwen JG, Matute DR. Species boundaries in the human pathogen *Paracoccidioides*. Fungal Genet Biol **2017**; 106:9–25.
96. Marimon R, Cano J, Gené J, Sutton DA, Kawasaki M, Guarro J. *Sporothrix brasiliensis*, *S. globosa*, and *S. mexicana*, three new *Sporothrix* species of clinical interest. J Clin Microbiol **2007**; 45:3198–206.
97. Rodrigues AM, Della Terra PP, Gremião ID, Pereira SA, Orofino-Costa R, de Camargo ZP. The threat of emerging and re-emerging pathogenic *Sporothrix* species. Mycopathologia **2020**; 185:813–42.
98. Jofre GI, Singh A, Mavengere H, et al. An Indian lineage of *Histoplasma* with strong signatures of differentiation and selection. Fungal Genet Biol **2022**; 158:103654.
99. Rodrigues AM, Beale MA, Hagen F, et al. The global epidemiology of emerging *Histoplasma* species in recent years. Stud Mycol **2020**; 97:100095.
100. Teixeira MM, Patané JS, Taylor ML, et al. Worldwide phylogenetic distributions and population dynamics of the genus *Histoplasma*. PLoS Negl Trop Dis **2016**; 10:e0004732.
101. Theodoro RC, Scheel CM, Brandt ME, Kasuga T, Bagagli E. *PRP8* Intein in cryptic species of *Histoplasma capsulatum*: evolution and phylogeny. Infect Genet Evol **2013**; 18:174–82.
102. Brown EM, McTaggart LR, Zhang SX, Low DE, Stevens DA, Richardson SE. Phylogenetic analysis reveals a cryptic species *Blastomyces gilchristii*, sp. nov. within the human pathogenic fungus *Blastomyces dermatitidis*. PLoS One **2013**; 8:e59237.
103. Schwartz IS, Kenyon C, Feng P, et al. 50 years of *Emmonsia* disease in humans: the dramatic emergence of a cluster of novel fungal pathogens. PLoS Pathog **2015**; 11:e1005198.
104. Schwartz IS, Wiederhold NP, Hanson KE, Patterson TF, Sigler L. *Blastomyces helicus*, a new dimorphic fungus causing fatal pulmonary and systemic disease in humans and animals in western Canada and the United States. Clin Infect Dis **2019**; 68:188–95.
105. Maphanga TG, Birkhead M, Muñoz JF, et al. Human blastomycosis in South Africa caused by *Blastomyces percursus* and *Blastomyces emzantsi* sp. nov., 1967 to 2014. J Clin Microbiol **2020**; 58:e01661–19.
106. Kenyon C, Bonorchis K, Corcoran C, et al. A dimorphic fungus causing disseminated infection in South Africa. N Engl J Med **2013**; 369:1416–24.
107. Jiang Y, Tsui CKM, Ahmed SA, et al. Intraspecific diversity and taxonomy of *Emmonsia crescens*. Mycopathologia **2020**; 185:613–27.
108. Wang P, Kenyon C, de Hoog S, et al. A novel dimorphic pathogen, *Emergomyces orientalis* (Onygenales), agent of disseminated infection. Mycoses **2017**; 60: 310–19.
109. Roberto TN, de Carvalho JA, Beale MA, et al. Exploring genetic diversity, population structure, and phylogeography in *Paracoccidioides* species using AFLP markers. Stud Mycol **2021**; 100:100131.
110. Rodrigues AM, de Hoog GS, de Camargo ZP. *Sporothrix* species causing outbreaks in animals and humans driven by animal-animal transmission. PLoS Pathog **2016**; 12:e1005638.
111. Lackner M, de Hoog GS, Yang L, et al. Proposed nomenclature for *Pseudallescheria*, *Scedosporium* and related genera. Fungal Divers **2014**; 67:1–10.
112. Gilgado F, Cano J, Gené J, Guarro J. Molecular phylogeny of the *Pseudallescheria boydii* species complex: proposal of two new species. J Clin Microbiol **2005**; 43: 4930–42.
113. Zeng JS, Fukushima K, Takizawa K, et al. Intraspecific diversity of species of the *Pseudallescheria boydii* complex. Med Mycol **2007**; 45:547–58.
114. Gilgado F, Cano J, Gené J, Sutton DA, Guarro J. Molecular and phenotypic data supporting distinct species statuses for *Scedosporium apiospermum* and *Pseudallescheria boydii* and the proposed new species *Scedosporium dehoogii*. J Clin Microbiol **2008**; 46:766–71.

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Ex. 1039
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115. Manamgoda DS, Cai L, McKenzie EHC. A phylogenetic and taxonomic re-evaluation of the *Bipolaris–Cochliobolus–Curvularia* complex. Fungal Divers **2012**; 56:131–44.
116. Samerpitak K, Van der Linde E, Choi H-J, et al. Taxonomy of *Ochroconis*, genus including opportunistic pathogens on humans and animals. Fungal Divers **2014**; 65:89–126.
117. Réblová M, Miller AN, Rossman AY, et al. Recommendations for competing sexual-asexually typified generic names in Sordariomycetes (except Diaporthales, Hypocreales, and Magnaporthales). IMA Fungus **2016**; 7:131–53.
118. Arzanlou M, Groenewald JZ, Gams W, Braun U, Shin HD, Crous PW. Phylogenetic and morphotaxonomic revision of *Ramichloridium* and allied genera. Stud Mycol **2007**; 58:57–93.
119. Berbee ML, Pirseyedi M, Hubbard S. *Cochliobolus* phylogenetics and the origin of known, highly virulent pathogens, inferred from ITS and glyceraldehyde-3-phosphate dehydrogenase gene sequences. Mycologia **1999**; 91:964–77.
120. Manamgoda DS, Cai L, Bahkali AH. *Cochliobolus*: an overview and current status of species. Fungal Divers **2011**; 51:3–42.
121. Von Arx JA, Luttrell ES. Whole fungus (Kendrick B, ed.). Ottawa: National Museum of Natural Sciences and the Kananaskis Foundation; **1979**; 1:260–1.
122. Goh KT, Hyde KD, Lee KLD. Generic distinction in *Helminthosporium* complex based on restriction analysis of the nuclear ribosomal RNA gene. Fungal Divers **1998**; 1:85–1.
123. Giraldo A, Sutton DA, Samerpitak K, et al. Occurrence of *Ochroconis* and *Verruconis* species in clinical specimens from the United States. J Clin Microbiol **2014**; 52:4189–201.
124. Revankar SG, Sutton DA. Melanized fungi in human disease. Clin Microbiol Rev **2010**; 23:884–928. Erratum in: Clin Microbiol Rev 2012; 25:720.
125. Shi D, Lu G, Mei H, et al. Subcutaneous infection by *Ochroconis mirabilis* in an immunocompetent patient. Med Mycol Case Rep **2016**; 11:44–7.
126. Mohammadi R, Mohammadi A, Ashtari F, et al. Cerebral phaeohyphomycosis due to *Rhinocladiella mackenziei* in Persian Gulf region: a case and review. Mycoses **2018**; 61:261–5.
127. Badali H, Bonifaz A, Barrón-Tapia T, et al. *Rhinocladiella aquaspersa*, proven agent of verrucous skin infection and a novel type of chromoblastomycosis. Med Mycol **2010**; 48:696–703.
128. Santos DWCL, de Azevedo CMPES, Vicente VA, et al. The global burden of chromoblastomycosis. PLoS Negl Trop Dis **2021**; 15:e0009611.
129. Ahmed SA, van de Sande WWJ, Stevens DA, et al. Revision of agents of black-grain eumycetoma in the order *Pleosporales*. Persoonia **2014**; 33:141–54.
130. Crous PW, Slippers B, Wingfield MJ, et al. Phylogenetic lineages in the Botryosphaeriaceae. Stud Mycol **2006**; 55:235–53.
131. Huang S-K, Tangthirasunun N, Phillips AJL, et al. Morphology and phylogeny of *Neoscytalidium orchidacearum* sp. nov. (*Botryosphaeriaceae*). Mycobiology **2016**; 44:79–84.
132. de Gruyter J, Woudenberg JHC, Aveskamp MM, Verkley GJM, Groenewald JZ, Crous PW. Redisposition of *Phoma*-like anamorphs in Pleosporales. Stud Mycol **2013**; 75:1–36.
133. Shaw JJ, Spakowicz DJ, Dalal RS, et al. Biosynthesis and genomic analysis of medium-chain hydrocarbon production by the endophytic fungal isolate *Nigrograna mackinnonii* E5202H. Appl Microbiol Biotechnol **2015**; 99:3715–28.
134. Hibbett DS, Binder M, Bischoff JF, et al. A higher-level phylogenetic classification of the fungi. Mycol Res **2007**; 111:509–47.
135. Spatafora JW, Chang Y, Benny GL, et al. A phylum-level phylogenetic classification of zygomycete fungi based on genome-scale data. Mycologia **2016**; 108: 1028–46.
136. Ajello L, Dean DF, Irwin RS. The zygomycete *Saksenaea vasiformis* as a pathogen of humans with a critical review of the etiology of zygomycosis. Mycologia **1976**; 68:52–62.
137. Walther G, Wagner L, Kurzai O. Updates on the taxonomy of Mucorales with an emphasis on clinically important taxa. J Fungi (Basel) **2019**; 5:106.
138. Wagner L, Stielow JB, de Hoog GS, et al. A new species concept for the clinically relevant *Mucor circinelloides* complex. Persoonia **2020**; 44:67–97.
139. Alvarez E, Cano J, Stchigel AM, et al. Two new species of *Mucor* from clinical samples. Med Mycol **2011**; 49:62–72.
140. Hoffmann K, Walther G, Voigt K. *Mycocladus* vs. *Lichtheimia*, a correction (Lichtheimiaceae fam. nov., Mucorales, Mucoromycotina). Mycol Res **2009**; 113:277–8.
141. Dolatabadi S, Walther G, Gerrits van den Ende AHG, de Hoog GS. Diversity and delimitation of *Rhizopus microsporus*. Fung Div **2014**; 64:145–63.
142. Dolatabadi S, de Hoog GS, Meis JF, Walther G. Species boundaries and nomenclature of *Rhizopus arrhizus* (syn. *R. oryzae*). Mycoses **2014**; 57(Suppl 3):108–27.
143. Alvarez E, Garcia-Hermoso D, Sutton DA, et al. Molecular phylogeny and proposal of two new species of the emerging pathogenic fungus *Saksenaea*. J Clin Microbiol **2010**; 48:4410–6.
144. Alastruey-Izquierdo A, Hoffmann K, de Hoog GS, et al. Species recognition and clinical relevance of the zygomycetous genus *Lichtheimia* (syn. *Absidia* pro parte, *Mycocladus*). J Clin Microbiol **2010**; 48:2154–70.
145. Schipper MAA. A revision of the genus *Rhizopus*. 1. The *Rhizopus stolonifer*-group and *Rhizopus oryzae*. Stud Mycol **1984**; 25:20–34.
146. Ellis JJ. Species and varieties in the *Rhizopus arrhizus–Rhizopus oryzae* group as indicated by their DNA complementarity. Mycologia **1985**; 77:243–7.
147. Prakash H, Chakrabarti A. Global epidemiology of mucormycosis. J Fungi (Basel) **2019**; 5:26.
148. Labuda R, Bernreiter A, Hochenauer D, et al. *Saksenaea dorisiae* sp. nov., a new opportunistic pathogenic fungus from Europe. Int J Microbiol **2019**; 2019: 6253829.
149. Nam B, Lee DJ, Choi YJ. High-temperature-tolerant fungus and Oomycetes in Korea, including *Saksenaea longicolla* sp. nov. Mycobiology **2021**; 49:476–90.
150. Crous PW, Wingfield MJ, Burgess TI, et al. Fungal planet description sheets: 558–624. Persoonia **2017**; 38:240–384.
151. Crous PW, Wingfield MJ, Burgess TI, et al. Fungal planet description sheets: 469–557. Persoonia **2016**; 37:218–403.
152. Munson E, Carroll KC. An update on the novel genera and species and revised taxonomic status of bacterial organisms described in 2016 and 2017. J Clin Microbiol **2019**; 57:e01181–18.
153. Janda JM. Proposed nomenclature or classification changes for bacteria of medical importance: taxonomic update 5. Diagn Microbiol Infect Dis **2020**; 97: 115047.
154. Mathison BA, Bradbury RS, Pritt BS. Medical parasitology taxonomy update, January 2018 to May 2020. J Clin Microbiol **2021**; 59:e01308–20.
155. Loeffelholz MJ, Fenwick BW. Taxonomic changes for human and animal viruses, 2018 to 2020. J Clin Microbiol **2021**; 59:e01932–20.
156. Panda A, Islam ST, Sharma G. Harmonizing prokaryotic nomenclature: fixing the fuss over phylum name flipping. mBio **2022**; 13:e0097022.
157. Walker PJ, Siddell SG, Lefkowitz EJ, et al. Changes to virus taxonomy and to the International Code of Virus classification and nomenclature ratified by the International Committee on Taxonomy of Viruses (2021). Arch Virol **2021**; 166:2633–48.
158. Kidd SE, Halliday CL, Haremza E, Gardam DJ, Chen SCA, Elvy JA. Attitudes of Australasian clinicians and laboratory staff to changing fungal nomenclature: has mycological correctness really gone mad? Microbiol Spectr **2022**; 10: e0237721.
159. Chen SC, Perfect J, Colombo AL, et al. Global guideline for the diagnosis and management of rare yeast infections: an initiative of the ECMM in cooperation with ISHAM and ASM. Lancet Infect Dis **2021**; 21:e375–86. Erratum in: Lancet Infect Dis 2021; 21:e363.
160. Chang CC, Blyth CC, Chen SC, et al. Introduction to the updated Australasian consensus guidelines for the management of invasive fungal disease and use of antifungal agents in the haematology/oncology setting, 2021. Intern Med J **2021**; 51(Suppl 7):3–17.
161. Brickey TW, Trotter JF, Johnson SP. *Torulopsis glabrata* fungemia from infected transjugular intrahepatic portosystemic shunt stent. J Vasc Interv Radiol **2005**; 16:751–2.
162. Federhen S. The NCBI taxonomy database. Nucleic Acids Res **2012**; 40(database issue):D136–43.
163. Schoch CL, Ciufo S, Domrachev M, et al. NCBI taxonomy: a comprehensive update on curation, resources and tools. Database (Oxford) **2020**; 2020:baaa062.
164. Clinical and Laboratory Standards Institute (CLSI). Performance standards for antifungal susceptibility testing of yeasts. 3rd ed. CLSI guideline M27M44SEd3. Wayne PA: CLSI; **2022**.

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