





# 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 interand 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to rationalize existing names meant that some names in common use have been retained, whereas in other cases they have been replaced by the less commonly used name.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

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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 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).

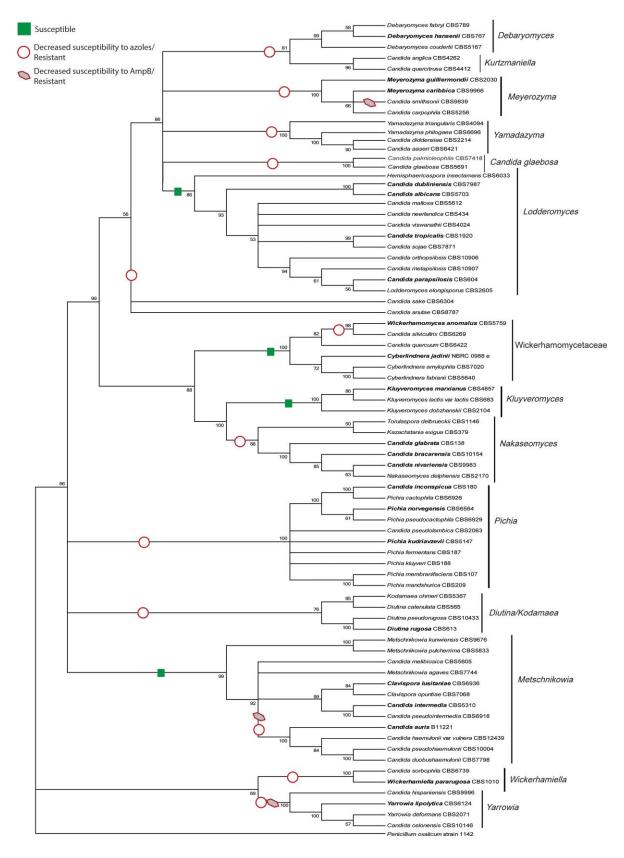
Analyses of 18S and internal transcribed spacer ribosomal DNA (rDNA) have determined that *Candida rugosa* represents a complex of highly similar species, including *C rugosa*,

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.



**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.

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 <sup>a</sup>	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 <sup>a</sup>	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 Iusitaniae	Clavispora Iusitaniae	Invasive infections including fungemia	[16]
Candida nivariensis	Nakaseomyces nivariensis <sup>a</sup>	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]

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

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].

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

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

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 <sup>a</sup> Paracoccidioides venezuelensis Paracoccidioides lutzii	Pulmonary, cutaneous infections	[94, 95]
Penicillium marneffei	Talaromyces marneffei <sup>b</sup>	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]

<sup>&</sup>lt;sup>a</sup>Published as *Paracoccidioides restrepiensis*.

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

### Paracoccidioides 4 8 1

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

bSee also section on hyaline hyphomycete molds and Table 2.

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

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, N attrassia mangiferae (formerly H endersonula t oruloidea), 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* 

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

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 documentcontrolled 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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