

# GAFFI POLICY BRIEF



## Antifungal drug resistance – a dramatic global problem

Resistance to antifungals is now as grave a problem as antibacterial resistance. Many serious fungal infections are untreatable and patient survival is compromised.

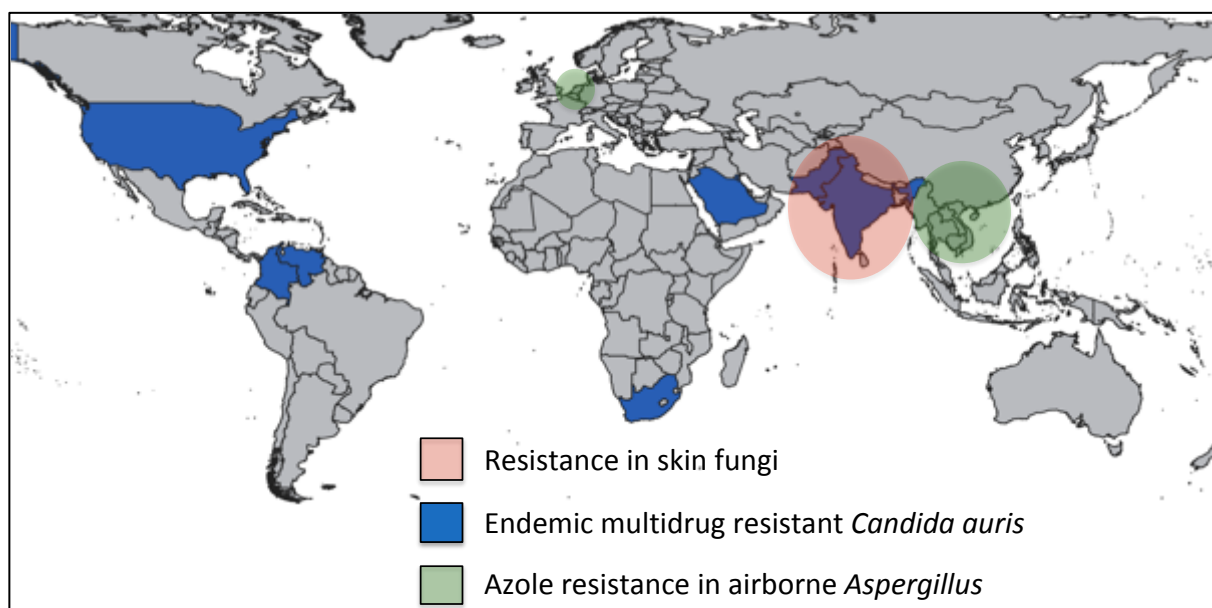
The main causes include:

- Extensive antifungal use by humans is one driver of antifungal resistance.
- Lack of access to diagnosis of Fungal Disease results in broad spectrum, and often wrong, treatment.
- Empirical therapy (i.e. best guess) using combinations of antibacterial and antifungal drugs to cover most infection possibilities, puts pressure on microbial communities to select for resistant clones or species.
- Environmental exposure to antifungals is the other driver. Crop applications of azole antifungals and fish farm usage both have bystander effects on human pathogenic fungi which result in resistant strains.

Without proper access to fast fungal disease diagnosis, the antifungal drugs now available will soon be useless for many fungal infections. This policy paper outlines the GAFFI recommended steps that health organisations across the globe should take to address antifungal resistance.

The World Health Organization (WHO) is soon to formally announce its Fungal Priority Pathogen List. The list will highlight numerous untreatable fungi and those for which clinical outcomes are poor. In addition to the need for new antifungals, it will emphasise the need for better diagnosis and early detection of antifungal resistance.

The map below shows areas of major concern, with extensive resistance documented. Antifungal susceptibility testing to identify resistant strains requires experienced technical expertise, currently not available everywhere.



## **GAFFI's recommendations for addressing Antifungal Resistance:**

### A. Clinical practice

1. Healthcare systems should include Fungal Disease diagnostics, as they strive to enable speedy and accurate diagnosis and decrease the use of antimicrobial empiricism in clinical practice.
2. Antimicrobial stewardship programs should integrate rapid diagnostic testing for Fungal Disease based on best practice guidance and clinical experience.
3. Isolates of *Candida* spp. causing life-threatening infections or all those not responding to treatment should be identified to the species complex level<sup>1</sup> and susceptibility tested, with results reported to clinicians within 24 hours.
4. Isolates of *Aspergillus* spp. causing severe infection or not responding to treatment should be identified to the species complex level and susceptibility tested, with results reported to clinicians as soon as possible.
5. Culture of clinical samples to isolate fungal strains is a critically important diagnostic, recognized by the WHO as 'Essential' and the only realistic means of tracking resistance to antifungals.

### B. Environmental bystander effects

6. Azole fungicide use on crops, flowers, fish farms and non-food products should be minimized, based on international recommendations.
7. Periodic environmental surveillance of resistance in *Aspergillus fumigatus* should be undertaken in each country to assess trends.
8. For each new chemical class of a new crop or seed dressing fungicide also used or planned for use in humans, regulatory authorities should require studies of the potential for resistance induction in human fungal pathogens. Alternatively, such products should not be approved, until they have been demonstrated to not induce resistance as a 'bystander' effect.

### C. Surveillance and public health

9. All countries should accurately track antifungal resistance to major fungal pathogens, notably *Candida* spp., *Aspergillus* spp and *Trichophyton* spp. National reporting on at least an annual cycle is recommended, with tracking over time.
10. Considering the alarming rates of *Aspergillus fumigatus* resistance to azole drugs in some settings, the WHO Global Antimicrobial Resistance and Use Surveillance System (GLASS) program should add this fungal pathogen to *Candida* spp. in its annual data collection about national resistance rates.
11. Antifungal resistance country data and trends must be used by antimicrobial resistance (AMR) guardians, national societies, public health authorities, Ministries of Health and other sectors in awareness campaigns to promote better antifungal use for human, animal and crop health.

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<sup>1</sup> Fungal taxonomy and nomenclature can be complicated. This recommendation is to ensure species names are both accurate and their significance is understood by clinicians.