Report on activities for 2017
Summary
GAFFI continues to make progress in its mission to reduce illness and death associated with fungal diseases worldwide. Its achievements in 2017, its fourth year of operation, include:

• **Listing of 3 new antifungals as Essential Medicines**: GAFFI coordinated a successful application to the World Health Organisation for itraconazole, voriconazole and topical natamycin to be included in the adult and paediatric Essential Medicine Lists.

• **Diagnosing lethal AIDS infections in Guatemala**: GAFFI’s demonstration project in Guatemala “Minimising HIV deaths through rapid diagnosis and better care in Guatemala” has its first full year of data. A single GAFFI-supported laboratory enabled diagnostic tests for the commonest fungal infections and TB in 2,394 HIV patients in 2017, with 16% having a life-threatening infection (55% fungal). Of those with life-threatening infection, 282 (79.2%) survived, an estimated additional 53 survivors as a result of the program with an annual cost of <$200,000.

• **Chromoblastomycosis as a Neglected Tropical Disease (NTD)**: Chromoblastomycosis is a very disfiguring deep skin disease of mostly farmers in the world’s poorest and often remote locations. GAFFI’s application to the WHO for chromoblastomycosis be accepted as an NTD was successful, alongside mycetoma.

• **Burden of Fungal Diseases**: GAFFI’s program of mapping the how many fungal diseases there are in each country has now reached 75 countries. In 2017 burden papers were published for Algeria, Bangladesh, Canada, Chile, Ecuador, Egypt, Guatemala, Pakistan, Peru, South Korea, the Philippines, Portugal, Thailand, United Kingdom and Uzbekistan. A revised estimation of the global burden HIV-associated cryptococcal meningitis was published in Lancet Infect Dis, with individual country estimates. Another series of papers are to be published early in 2018 in the Journal of Fungi for another 13 countries.

• **TB-like fungal infections**: A first-in-Africa study from Nigeria found at least 8.7% of HIV positive and HIV negative patients had chronic pulmonary aspergillosis at the end of their TB treatment, >19% in the smear-negative, HIV negative group. This condition is similar to TB, with cough, bringing up blood weight loss and tiredness and only 25% survive 5 years. Usually it is mis-treated as TB. This finding is consistent with >140,000 patients with this disease in Nigeria alone. The key test is *Aspergillus* antibody testing, not yet available in Africa, having been developed in London the 1960’s.

• **AMR and fungal diagnostics**: Antimicrobial resistance (AMR) is a major problem, especially in bacteria, but also fungi. GAFFI’s senior advisors have argued in a perspective piece in the US journal Emerging Infectious Diseases that fungal diagnostics can reduce antibiotic usage and so have a positive impact on antibacterial resistance.

• **GAFFI’s Ambassadors**: Multiple educational programs and awareness have been delivered in Nigeria, Sri Lanka, Pakistan, Mexico, Chile, Iran Denmark, Hungary and the UK.

• **Health professional education**: GAFFI’s senior advisers wrote a series of 8 review papers in Lancet Infectious Diseases. One paper describes how fungal disease diagnosis and management fits into health systems, the first to propose these solutions. GAFFI’s educational partner LIFE-Worldwide has translated its online microscopy course (www.microfungi.net) into Spanish, French and Portuguese and extended the learning to include rare fungal infections. With GAFFI support, LIFE is developing multiple online videos and podcasts on key fungal disease topics (www.LIFE-Worldwide.org/Education).
**GAFFI’s Goals**

GAFFI has 4 primary long term goals, supported by advocacy:

- **Goal 1 - Increase awareness of the impact of fungal disease**
- **Goal 2 - Improve access to diagnostics for fungal disease**
- **Goal 3 - Improve access to appropriate and affordable antifungal therapeutics with a focus on generic agents**
- **Goal 4 - Improve education of health professionals about fungal disease.**

GAFFI 10 year Roadmap ‘95-95 by 2025’ focused and fleshed out these objectives as follows:

- Ensure that 95% of people with serious fungal disease are diagnosed and 95% treated by 2025 (95-95)

- Support the goal of reducing AIDS deaths to under 500,000 by 2020, with a determined focus on the commonest lethal fungal infections cryptococcal meningitis, *Pneumocystis* pneumonia, disseminated histoplasmosis and chronic pulmonary aspergillosis after tuberculosis

To accomplish these goals, it is necessary in each country to:

- Ensure that affordable diagnostic tests for all common and uncommon fungal infections are made available, focused on rapid, non-culture testing

- Develop and maintain at least one laboratory led by an expert in fungal disease diagnostics with a comprehensive diagnostic portfolio and critical mass of healthcare professionals per country

- Develop a network of expert clinicians and ‘train the trainer’ programs, supported by clinical guidelines

- Ensure distribution of antifungal agents on the WHO Essential Medicine List to reach all those who need them

- Establish ongoing surveillance of fungal infections of high burden to inform clinical practice, training and research needs

- Develop local experts in public health mycology
**Goal 1 - Increase awareness of the impact of fungal disease**

A major goal is to achieve increased awareness of fungal disease globally, especially among global health agencies and country medical opinion leaders and decision-makers. GAFFI has approached this by estimating the burden of fungal diseases country by country, identifying and highlighting diagnostic and therapeutic gaps and supporting epidemiological studies to better define fungal disease locally.

**1.1 Burden of fungal disease**

By the end of 2017, burden of fungal disease estimates were published for 57 countries [www.gaffi.org/media/academic-papers/] and presented for another 18 countries. Published papers are now available or in press for Algeria, Argentina, Austria, Bangladesh, Belgium, Brazil, Burkina Faso, Cameroon, Canada, Chile, Colombia, Czech Republic, Denmark, Dominican Republic, Ecuador, Egypt, France, Germany, Greece, Guatemala, Hungary, India (partial), Ireland, Israel, Italy, Jordan, Kazakhstan, Kenya, Malawi, Malaysia, Mexico, Mozambique, Nepal, Nigeria, Norway, Qatar, Pakistan, Peru, Philippines, Portugal, Romania, Russia, Senegal, Serbia, South Korea, Spain, Sri Lanka, Tanzania, Thailand, Trinidad and Tobago, Turkey, Uganda, UK, Ukraine, Uruguay, Uzbekistan and Vietnam. A summary of burden papers published before mid 2017 provided a public critique of the methods used and their weaknesses.

Summary abstracts and posters have or will shortly be presented at international congresses for Australia, Belarus, Benin, China, Congo, Indonesia, Iraq, Iran, Japan, Madagascar, Mongolia, Netherlands, New Zealand, Saudi Arabia, Singapore, Sweden, Venezuela and Zambia [www.gaffi.org/media/news/]

Collaborators have also re-estimated the burden of cryptococcal disease in AIDS by country (Radha Rajasingham et al), histoplasmosis in Africa (Rita Oladele et al, published in 2018), histoplasmosis in AIDS in the Americas (Antoine Adenis et al, submitted for publication) and the prevalence of chronic pulmonary aspergillosis after tuberculosis in Nigeria (Rita Oladele).

**1.2 Chromoblastomycosis accepted as a Neglected Tropical Disease by WHO**

Chromoblastomycosis was approved as an NTD by WHO in May 2017, along with ‘other deep mycoses’. This rare disfiguring disease of the skin and subcutaneous tissue is treatable with antifungal therapy, possibly with enhancement with immunotherapy with imiquinod and is probably partly preventable. GAFFI orchestrated the application to the WHO Strategic Technical Advisory Committee in 2016, with support from the Ministry of Health in Brazil, through PAHO, and the government of Madagascar.

In follow up dialogue with the WHO, a public health definition of chromoblastomycosis was proposed at the ISHAM Working Group meeting in Havana in December 2017: “Chromoblastomycosis is a chronic (>3 months) cutaneous and subcutaneous fungal infection manifesting with verrucous, nodular and plaque lesions, showing muriform fungal cells on microscopy.”

GAFFI has proposed that sporotrichosis and paracoccidioidomycosis are added as NTDS, as fitting the WHO criteria, as the ‘other deep mycoses’. This proposal is in discussion.
Goal 2 - Improve access to diagnostics for fungal disease

Both improved diagnostic tests for low and middle income countries and improved access to diagnostics are critically important GAFFI goals. Fungal disease is often clinically silent and/or mimics other infections and specific diagnostic tests are required for diagnosis. Many hospitals and countries have little or no diagnostic capability. Complex test formats, expense, inadequate laboratory infrastructure and a lack of training are all barriers to diagnostic testing. Accurate assessment of the burden of disease requires accurate diagnosis.

2.1 Demonstration project in Guatemala

The second year of GAFFI’s demonstration project in Guatemala is complete: ‘Minimising HIV deaths through rapid fungal diagnosis and better care in Guatemala.” This project has been ably co-ordinated by GAFFI Senior Advisor Prof Juan Luis Rodriguez Tudela and GAFFI Ambassador for Spain Dr Ana Alastrauey-Izquierdo. GAFFI is indebted to the Jylag Foundation for financial support.

In 2016, Guatemala had 2,900 (1,400 – 5,200) new HIV infections and 1,600 (<1,000 – 2,800) AIDS-related deaths. There were 46,000 (31,000 – 65,000) people living with HIV in 2016, among whom only 36% (24% - 50%) were accessing antiretroviral therapy. Additionally, over 50% of the diagnosed patients are in advanced HIV stage which results in long periods of hospitalization and often death. From this perspective a project called "Minimizing HIV deaths through rapid fungal diagnosis and better care in Guatemala” was implemented by Global Action Fund for Fungal Infections (GAFFI) and Asociación de Salud Integral (ASI) (Medical Director Dr Eduardo Arathoon, GAFFI Ambassador for Guatemala). The objectives of this Program include: i) to implement rapid diagnosis for cryptococcal meningitis, disseminated histoplasmosis, Pneumocystis pneumonia and chronic pulmonary aspergillosis; ii) to develop a training program in fungal disease management for health workers in the HIV comprehensive care units of Guatemala and; iii) to develop a national registry for fungal infections. To develop this program, a network of laboratories connected with a central Mycology Laboratory was set-up, as well as trained clinicians in fungal diseases. The network has implemented the following actions: 1) Training activities; 2) Strategic alliances; 3) Development of a website; 4) Diagnostic guidelines and 5) Cohort study. Currently the network comprises 13 HIV units across Guatemala and one Reference Laboratory lead by ASI. Only two HIV units have declined the participation in the network so far, but conversations with them are still ongoing to get them in and cover the whole country.

This year, processes were implemented to improve the coordination of the network as well as to increase the training activities and the diagnostic portfolio in the Reference Laboratory. Activities included: (i) A better use of the website by the network to get all information about clinical samples analysis and patient’s data in the system; (ii) An in-depth analysis of the Reference Laboratory workflow to improve the turnaround time and the delivery of the results to the network; (iii)
An increase in the number and modalities of the training activities for the network including virtual and face to face conferences. Topics covered included epidemiology, diagnosis and treatment of opportunistic infections, focused on fungal diseases and (iv) Incorporation of *Pneumocystis jirovecii* diagnosis to Reference Laboratory diagnostic portfolio.

### 2.1.1 Training activities

Training included the following: (i) A II National workshop attended by 51 participants about opportunistic infections was held in February 2017 in Guatemala City; (ii) A workshop attended by 32 participants about opportunistic infections was held in May 2017 in Guatemala City; (iii) Four meetings in rural hospitals attended by 140 participants were also held; (iv) Three on line conferences to discuss clinical cases were done by means of ZOOM platform.

The diagnostic activities performed in the network during 2017 are as follows. Two thousand, three hundred and ninety-four patients were included in the study. Three hundred and seventy-one patients (15,5 %) had an opportunistic infection, 209 (56.3%) of which were fungal. *H. capsulatum* was diagnosed in 127 patients (34.2%), *C. neoformans* in 79 (21.3%) and other fungal infection in 3 (0.80%). One hundred and forty-seven (39.6%) cases of *M. tuberculosis* and other mycobacterial infections were also diagnosed. Ten cases (2.69%) of co-infection with *M. tuberculosis* and *Histoplasma capsulatum* were detected. Co-infections caused by other pathogens reached 1.34% (5 cases). In comparison with the same period of 2016, when the network was not still implemented, we observed a 110.8% increase in opportunistic infection diagnosis - from 176 to 371 cases. In addition, the network ruled out these infections in 2,023 HIV cases, allowing an earlier start of antiretroviral therapy and therefore the chance of a better outcome.

### 2.1.2 Next steps

- Intensify the training activities
- Facilitate country and government ownership of the project
- Bring the 2 remaining HIV units into the program
- Work with the government to ensure antifungal drug access and no cost to patients or affordable prices, including flucytosine.
- Add more tests to the diagnostic portfolio, including Pneumocystis PCR, Aspergillus IgG, and probably toxoplasma serology and TB antigen (LAM) testing.
- Write up the first year’s results in a scientific journal, including survival outcome.

### 2.2 Guidelines for chronic pulmonary aspergillosis

The second Global Fungal Infection Forum in Liverpool on October 26th 2016 developed a
definition of chronic pulmonary aspergillosis for low resource settings. The manuscript was submitted in 2017 and will be published in 2018.

The consensus definition developed comprises 3 elements:
1 - Symptoms for 3 months or longer (haemoptysis and/or persistent cough, and/or weight loss) (other symptoms are common, but not required, notably fatigue, chest pain and sputum production)
AND
2 - Radiological features (progressive cavitation on chest imaging AND/OR intracavitary fungal ball AND/OR pleural thickening or pericavitary fibrosis or infiltrates all adjacent to cavities)
AND
3 - Microbiological evidence of Aspergillus infection (positive Aspergillus-specific IgG and/or sputum microscopy showing hyphae consistent with Aspergillus and/or Aspergillus growth on 2 or more sputum or other respiratory samples)
AND
4. Mycobacterial infection should be ruled out with smear, GeneXpert and/or mycobacterial culture. It is possible for mycobacterial infection and CPA to be present concurrently, but this diagnosis requires characteristic radiological findings on CT scan that are not present with PTB including pleural thickening, a fungal ball or other intra-cavitary material, or marked peri-cavitary infiltrates in addition to a positive Aspergillus IgG antibody test.

2.3 Engage with the manufacturers and distributors of fungal diagnostics worldwide

Numerous interactions with companies providing cryptococcal antigen assays and Aspergillus antibody tests are ongoing.

Chronic pulmonary aspergillosis: commercial Aspergillus antibody testing comparisons of 6 test systems are complete and published (Page, 2016). Two ‘gold standard’ tests have been identified. A separate report (Dummolard, 2016) compared 3 different ELISA tests and introduced a new assay, with high performing characteristics, that may also be a gold standard assay, when replicated by others. Alternative cut-offs have been derived, which need evaluation in a wide spectrum of people. Proposals for European cut-offs have been validated and submitted for publication.

2.4 Kenya – the FIP-Kenya program

GAFFI has been working with several leaders in Kenya and Japan International Co-operation Agency (JICA) to provide much greater capacity for fungal disease and cancer diagnosis in Kenya. The Fungal Infections Program (FIP-Kenya) development program aims to provide all 12 of the major urban centers with excellent radiology, histopathology and fungal disease diagnostics and support leading clinical personnel through training, in combination with networking, quality assurance and surveillance programs. Unfortunately the program stalled in 2017 with the complex elections.

2.5 Uganda – the UFICAD program

In Uganda, GAFFI has developed a similar program with the Ministry of Health and JICA Uganda Fungal Infections and Cancer Diagnostic Program (UFICAD) to provide diagnostic capacity for fungal disease and cancer through mycology (non-culture based testing), imaging and histopathology. The educational elements of the program would be delivered with the Infectious Diseases Institute in Kampala and supported nationally through the National Public Health Laboratory.
Goal 3 - Improve access to appropriate and affordable antifungal therapeutics with a focus on generic agents

Access to affordable antifungal agents remains a critical goal for GAFFI, with considerable progress made in 2016.

3.1 Engagement with generic manufacturers of antifungals.

GAFFI has signed a number of Memoranda of Understanding (MOUs) with generic manufacturers to work together to increase country access of by registering them with the WHO as prequalified medicines (PQ) and directly seeking approval in major countries. WHO PQ would allow rapid approvals in Armenia, Botswana, Burkina Faso, Burundi, Caribbean Community (CARICOM), Cameroon, Côte d'Ivoire, Democratic Republic of the Congo, Eritrea, Ethiopia, Georgia, Ghana, Kenya, Kyrgyzstan, Lao People’s Democratic Republic, Madagascar, Malawi, Mali, Mozambique, Namibia, Nigeria, Philippines, Senegal, Sierra Leone, South Africa, Tanzania, Thailand, Uganda, Ukraine, Zambia, Zanzibar and Zimbabwe. GAFFI is aiming for WHO PQ and/or stringent regulatory approval (SRA) approved products in all countries. GAFFI has modeled potential markets in many country (based on the burden of disease) and a snapshot of several markets is shown on a rotational basis on the website here: https://www.gaffi.org/antifungal-drug-maps/

3.2 Application to the WHO for itraconazole, voriconazole and natamycin 5% ophthalmic solution to be added to the Essential medicines List.

GAFFI’s application to the WHO for inclusion on the Essential Medicine List (EML) of itraconazole (capsules and oral suspension), voriconazole (capsules and intravenous solution) and natamycin 5% ophthalmic solution was successful. This was a collaboration between GAFFI and the Instituto de Salud Carlos III, International Foundation for Dermatology, London School of Hygiene of Tropical Medicine and The University of Manchester. These antifungal agents join fluconazole, amphotericin B and flucytosine on the EML.

3.3 Global mapping of current availability of voriconazole and topical natamycin

GAFFI has mapped availability and price of oral voriconazole. Voriconazole is not available in Senegal, Sudan and Uzbekistan and data on most African countries is missing. The price of voriconazole varies substantially, partly because it is off patent in many countries, ranging from a high of $400 per day in Peru to $19 in India and $2 in Iran. The prices should fall as generic drug becomes more established.
Goal 4 - Improve education of health professionals about fungal disease

Health professionals need to have fungal disease at the front of their mind when dealing with patients with complex health problems. Laboratory training is critical for building diagnostic capability. Antifungal prescribing can be complex and pharmacists need to be aware of drug interactions and dose adjustments. GAFFI, in concert with many others, is committed to improving health professional competence related to fungal diseases. In addition to its ‘Fact sheets’: http://www.gaffi.org/media/fact-sheets/ GAFFI also has a twitter account with >1,000 followers.

4.1 Lancet Infectious Diseases series published – “Recovery from serious fungal diseases should be realizable for everyone”

GAFFI senior advisers were instrumental in writing a series of papers for the prestigious journal Lancet Infectious Diseases, and published in August 2017 (see reference section). These included an up to date summary of the lethal infections in AIDS, critical care, transplant recipients and leukaemia, a comprehensive summary of all fungal infections of the lungs and sinuses in those with immune defects, a summary of key neglected fungal infections including mycetoma, chromoblastomycosis and sporotrichosis, an optimistic summary of the options for immunotherapy to support antifungal therapy and surgery for treatment, the problems of antifungal resistance, an a remarkable catalogue of fungal disease outbreaks. The final paper in the series is the first attempt to describe how fungal disease diagnosis and management fits into a health systems framework, with 4 country examples (India, Mozambique, South Africa and Kenya).

- Fungal infections in HIV/AIDS by Andrew H Limper, Antoine Adenis, Thuy Le, Thomas S Harrison
- Candida and invasive mould diseases in non-neutropenic critically ill patients and patients with haematological cancer by Arnaldo L Colombo, J N de Almeida Júnior, Monica A Slavin, Sharon C-A Chen and Tania C Sorrell
- Pulmonary and sinus fungal diseases in non-immunocompromised patients by David W Denning and Arunaloke Chakrabarti
- Neglected endemic mycoses by Flavio Queiroz-Telles, Ahmed Hassan Fahal, Diego R Falcí, Diego H Caceres, Tom Chiller and Alessandro C Pasqualotto
- Immunotherapeutic approaches to treatment of fungal diseases by Darius Armstrong-James, Gordon D Brown, Mihai G Netea, Teresa Zelante, Mark S Gresnigt, Frank L van de Veerdonk and Stuart M Levitz
- The global problem of antifungal resistance: prevalence, mechanisms, and management by David S Perlin, Riina Rautemaa-Richardson and Ana Alastrauey-Izquierdo
- Emerging issues, challenges, and changing epidemiology of fungal disease outbreaks by Kaitlin Benedict, Malcolm Richardson, Snigdha Vallabhaneni, Brendan R Jackson and Tom Chiller
- Improvement of fungal disease identification and management: combined health systems and public health approaches by Donald C Cole, Nelesh P Govender, Arunaloke Chakrabarti, Jahit Sacarlal and David W Denning
- And an Editorial - Recovery from serious fungal diseases should be realizable for everyone by Juan Luis Rodríguez Tudela and David W Denning
4.2 Online microscopy and histology training program translated

LIFE-Worldwide has translated its online microscopy and histology course (www.microfungi.net) into Spanish, French and Portuguese and extended the learning to include rare fungal infections. With GAFFI support, LIFE is developing a series of short online videos and podcasts on key fungal disease topics (www.LIFE-Worldwide.org/Education).

4.2 Educational presentations of GAFFI’s work and fungal disease management for health professionals

4.2.1 Nigeria
February 2017 saw 3 days training program organized by GAFFI Ambassador for Nigeria Dr Rita Oladele for a targeted audience of specialist that manage the groups of patients at risk of serious fungal infections. There were formal lectures, hands-on practical radiology and microbiology sessions for two days. Local facilitators and experts together with Prof David Denning and Prof Malcolm Richardson (GAFFI Senior Advisor) were the main facilitators both for lectures and practicals. The meetings were highly successful (shown twice on our national news network station). The feedback from participants have also been very encouraging and has reflected on how the patient groups at risk are being managed.

The Medical Mycology Society of Nigeria was inaugurated under the supervision of Prof Richardson.

4.2.2 Sri Lanka
GAFFI Ambassador in Sri Lanka Primali I. Jayasekera Delivered a guest lecture on 'Laboratory Diagnosis of Candidaemia – an update' in 'Candidaemia – bridging the gaps' symposium, at Sri Lanka Medical Association on 23rd November 2017, by Dr. Primali I. Jayasekera, Consultant Medical Mycologist, Head / Department of Mycology, Medical Research Institute, Colombo, Sri Lanka

Other mycological research in the country was well received:


4.2.3 Pakistan
The problem of fungal diseases was highlighted at a 2 day conference in November 2017 in Karachi where the growing problem antifungal resistance was real and narrowing treatment options for patients and leaving patients little choice beyond very expensive drugs. This 1st International Collaborative Mycology (ICM) Conference was jointly organised by GAFFI, the Medical Microbiology and Infectious Diseases Society of Pakistan and Aga Khan University (AKU). Candida auris, was focussed on as outbreaks have been problematic in Pakistan and several speakers noted the poor availability of medicines, leading to delays in treatment. Experts from various disciplines of medicine, veterinary medicine, agriculture, food and pharmaceutical industry were present at the two-day event. The conference was followed by a day of workshops at AKU’s Centre for Innovation in Medical Education.

Dr Kauser Jabeen, Associate Professor in the Department of Pathology and Laboratory Medicine at AKU, GAFFI Ambassador for Pakistan was chair of the conference. She and other faculty members at the AKU have launched a new Practical Guide and Atlas of the Diagnosis of Fungal Infections https://ecommons.aku.edu/books/62/
4.2.4 Mexico
From late 2015 and until December 2017, amphotericin B deoxycholate was out of stock in Mexico. This drug is widely used in Mexico as Liposomal AMB is too costly to buy for most of the public hospitals. So all patients with cryptococcal disease, histoplasmosis, and neutropenic fever were treated with drugs other than AMBD and LAMB (high fluconazole doses or echinocandins or voriconazole or weekly low doses of AMBD). Mucormycosis became untreatable and so was simply not treated in some cases or delayed treatments until the patient or the hospital could pay for LAMB or posaconazole.

Ongoing work with four Mexican hospitals will estimate incidence rates of invasive fungal infections and costs of antifungal drugs. The aim of this project is to call the attention of scientific community and health authorities on the cost and need of anti fungal drugs supply, not only for AMBD but for LAMB, posaconazole (IV) and isavuconazole (which is not available in Mexico).

4.2.5 Chile
GAFFI’s work was profiled in several meetings in Chile:
• August 25, 2017; “Serious fungal infections in Chile” Mycology Symposium in IX Latin American Congress of Mycology, Lima, Peru.
• August 08, 2017; III Course in Diagnostic in Medical Mycology, National Health Institute, Santiago de Chile.
• October 12, 2017; Serious Fungal Burden in the World: GAFFI actions; II Meeting in Medical Mycology, Universidad de Chile, Santiago de Chile
• December 12-15, 2017; IV Course of Medical Mycology, Public Health Institute of Chile, Santiago de Chile

Dr Eduardo Alvarez-Duarte, GAFFI’s Ambassador in Chile also notes that their lab have detected 12 cases of histoplasmosis in 2017; all in immigrants which is a "new scenario" in Chile.

4.2.6 Iran
The annual research festival of Mazandaran University of Medical Sciences was held in December 2017. This festival is an assembly of 6 universities from the northern region of Iran. During the festival each of universities present their improvements and achievements in health system and related researches. As the director of Invasive Fungi Research Center (IFRC) Professor Mohammad Hedayati presented the translated GAFFI brochure in Persian.
4.2.7 Denmark
Professor Maiken Arendrup from the Serum Statens Institute (SSI) in Copenhagen has been finding increasing numbers of azole resistant \textit{Aspergillus fumigatus}. She delivered a hard-hitting interview for the national TV broadcast Danish Radio (DR) on azole resistant \textit{A. fumigatus} and the link to environmental azole use. It was on primetime Sunday evening 21:00 the 11 Feb 2018. It was followed by another radio 7 min bit the following morning that was on air several times. This led to a series of questions raised to the ministers of health and food/agriculture in the Danish parliament and many articles in various journals and papers, and on social media. The government is now keen on demonstrating action. A nationwide surveillance programme on azole resistance is planned as well as including Aspergillus PCR which detects TR34/L98H and TR46/Y121F/T289A will be offered for free for BAL as well being more widely adopted in other hospitals.

4.2.8 Hungary
In addition to numerous local, national and regional postgraduate educational events mentioning GAFFI’s work, Dr Janos Sinko has set up a Working group of Key Opinion Leader Experts to negotiate with the National Health Insurance Fund for better financial coverage of serious infections (IFI included). Proposals have been put forward and decisions are awaited.

4.2.9 UK
In addition to publishing the burden of fungal diseases in the UK with Public Health England (a major step forward in awareness), GAFFI’s work was highlighted in multiple educational for a. In July 2017, GAFFI and fungal diseases was represented in Parliament at the Parliamentary and Scientific Committee.

News items and newsletter distributed by GAFFI’s educational partner LIFE

LIFE-Worldwide \([\text{http://life-worldwide.org}]\) focuses on health professional education and provides summaries of pivotal literature which has the potential to change clinical practice and focused on public health on a weekly basis, together with major strategic developments in the area. These posts are posted every 7-10 days. The quarterly LIFE newsletter is emailed to over 14,000 health professionals around the world. In the past 12 months (Jan 2017-Jan 2018), LIFE Worldwide had 212,000 unique visitors, who made a total of 318,000 visits to the site, where they viewed a total of 810,000 individual pages.
Advocacy supporting the above 4 goals

Advocacy is a key continuing mission for GAFFI. In addition to in country advocacy

5.1 Antimicrobial Resistance (AMR).

In a perspective paper published in February 2017 in CDC’s journal Emerging Infectious Diseases, GAFFI Senior Advisors argue that implementing fungal disease diagnostics will contribute to reductions in anti-bacterial usage and therefore control of AMR. They cite 4 examples:

- Candidaemia and invasive candidiasis in critical care
- Pneumocystis pneumonia, especially in AIDS
- Chronic pulmonary aspergillosis versus smear-negative TB
- Treatment of fungal asthma with anti-bacterials instead of asthma control with antifungals

This paper and press release achieved an Altimetric score of 199.

5.2 Neglected Tropical Diseases

The inclusion of Mycetoma and then Chromoblastomycosis onto the WHO NTD listing has enabled a dialogue with WHO and PAHO on addressing these and related disorders. The 10th anniversary meeting of the NTD coalition in May 2017 in Geneva was a remarkable event, even if fungal diseases were not explicitly mentioned. GAFFI is arguing that the acceptance of ‘Chromoblastomycosis and other deep mycoses’ is best served by explicit inclusion of sporotrichosis and paracoccidioidomycosis onto the NTD listing.

5.3 New WHO Guidelines on advanced HIV disease

While GAFFI was not directly involved in the process, GAFFI’s direct advocacy with WHO senior leadership its advocacy partners lead the WHO HIV department to convene a meeting in Geneva to develop broad guidelines on the recognition and management of Advanced HIV Disease. These were published in July 2017. [www.who.int/hiv/pub/guidelines/advanced-HIV-disease/en/](http://www.who.int/hiv/pub/guidelines/advanced-HIV-disease/en/) While they are broader than fungal disease alone, they do address many of the issues that GAFFI has been advocating for.

5.4 Nigeria

Professor David Denning and Dr Rita Oladele (on behalf of GAFFI) met with representatives of the Minister of Health, the Director General of Federal Ministry of Health, Nigeria and Director General of the National Agency for Food and Drug Administration and Control (NAFDAC) to advocate for diagnostics and antifungal registrations for serious fungal infections. Further engagement has focused on cryptococcal meningitis and improving the simplest elements of care, including cryptococcal antigen testing, lumbar puncture and delivering amphotericin B.
**Year 5 plans and aspirations**

GAFFI’s project in Guatemala has developed real traction in the country and is attracting positive attention from the Guatemala government, the CDC and PAHO. Expansion of the testing portfolio to include Pneumocystis pneumonia and complete country coverage and data collection will further demonstrate the value of the work. Analyses of survival and other benefits are ongoing.

GAFFI has been planning to setup a whole country diagnostic program in Kenya and has applied to do the same in Uganda. It is anticipated that these will be initiated in 2018.

An international Essential Diagnostics meeting is being held in Kampala in April 2018 to develop consensus on which fungal diagnostics should be listed by the WHO as essential, in their new process.

The arguments have been made to extend Neglected [Fungal] Tropical Diseases to include sporotrichosis and paracoccidioidomycosis. Further advocacy will be necessary to achieve this. A consensus statement on the whole diagnostic process (journey) for patients with suspected chromoblastomycosis and mycetoma is underway and should report in 2018.

Further advocacy to ensure that antifungals (especially flucytosine) are available to everyone is necessary and will be addressed.

**Glossary of terms, organisations and abbreviations:**

AKU – Aga Khan University
AMBD – conventional amphotericin B (deoxycholate)
AMR – Antimicrobial Resistance
BAL – bronchoalveolar lavage
CDC – US Centers for Disease Control and Prevention
DNDi – Drugs for Neglected Diseases initiative
EDL – Essential Diagnostics List
EML – Essential Medicines List
FIP-Kenya – Fungal Infections Program Kenya
Gates Foundation – Bill and Melinda Gates Foundation
Global Fund – Global Fund to fight AIDS, Tuberculosis and Malaria
JICA – Japan International Co-operation Agency
LAMP – Liposomal amphotericin B
LIFE – Leading International Fungal Education
MOU – Memorandum of Understanding
MSF – Medicines Sans Frontieres
PEPFAR – President’s Emergency Program For AIDS Relief
PAHO – Pan-American Health Organization
SRA – stringent regulatory approval
SSI – Serum Statens Institute
UFICAD – Uganda Fungal Infections and Cancer Diagnostic Program
UNAIDS – WHO-affiliated and co-located organization focused on AIDS
UNICEF – United Nations Children’s Fund
UNITAID – Agency hosted by WHO in Geneva.
WHO – World Health Organisation
Publications

**Burden of disease papers:**


**Reviews and position papers**


**Press releases and GAFFI news items:**

**GAFFI opens UK sister foundation and Oddi Aasheim joins as Director**

Posted January 6, 2017

**Delivering on Antimicrobial Resistance Agenda (AMR) Not Possible without Improving Fungal Diagnostic Capabilities**


**Fight back against fungal infections started in Lagos today**

Posted February 17, 2017.

**The burden of fungal disease: new evidence to show the scale of the problem across the globe**

Posted February 28, 2017.

**New model for saving millions of lives from fungal disease is being implemented**

Posted March 8, 2017.

**Ruling by World Health Organisation delights Doctors**

Posted April 5, 2017.

**Burden of fungal diseases in Belarus, Cameroon, Indonesia and Italy presented at ECCMID Vienna**

Posted April 25, 2017.

**Fungal meningitis still killing over 180,000 people each year despite drugs available to save lives**


**Poor farmer’s fungal skin condition gets approval from who as ‘neglected’ after lobbying by gaffi**


**Randomised trial establishes amphotericin B as best immediate therapy for Talaromyces marneffei infection in AIDS**

Posted June 29, 2017.
Major clinical trial shows flucytosine a critical component of reducing deaths from cryptococcal meningitis
Posted July 24, 2017.

Call for global action on life-threatening fungal infections
Posted August 1, 2017.

Professor Matthew Burton of the London School of Hygiene & Tropical Medicine appointed as a GAFFI Senior Adviser
Posted August 18, 2017.

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Posted October 1, 2017.

Burden of fungal diseases in Turkey, Norway, Malawi and Argentina presented at TIMM, Belgrade
Posted October 12, 2017.

How precise are country estimates of fungal disease burden? An updated analysis
Posted October 23, 2017.

As the true extent of fungal diseases in Pakistan is revealed, scientists launch a new book aimed at improving the diagnosis and treatment of life threatening fungal infections which affect 3.28 million Pakistanis
Posted December 4, 2017.

Havana meeting on the Neglected Tropical Fungal Disease Chromoblastomycosis, calls on Public Health authorities to take action