ONE HEALTH INTERAGENCY REPORT ON AZOLE RESISTANCE IN *ASPERGILLUS* SPP.

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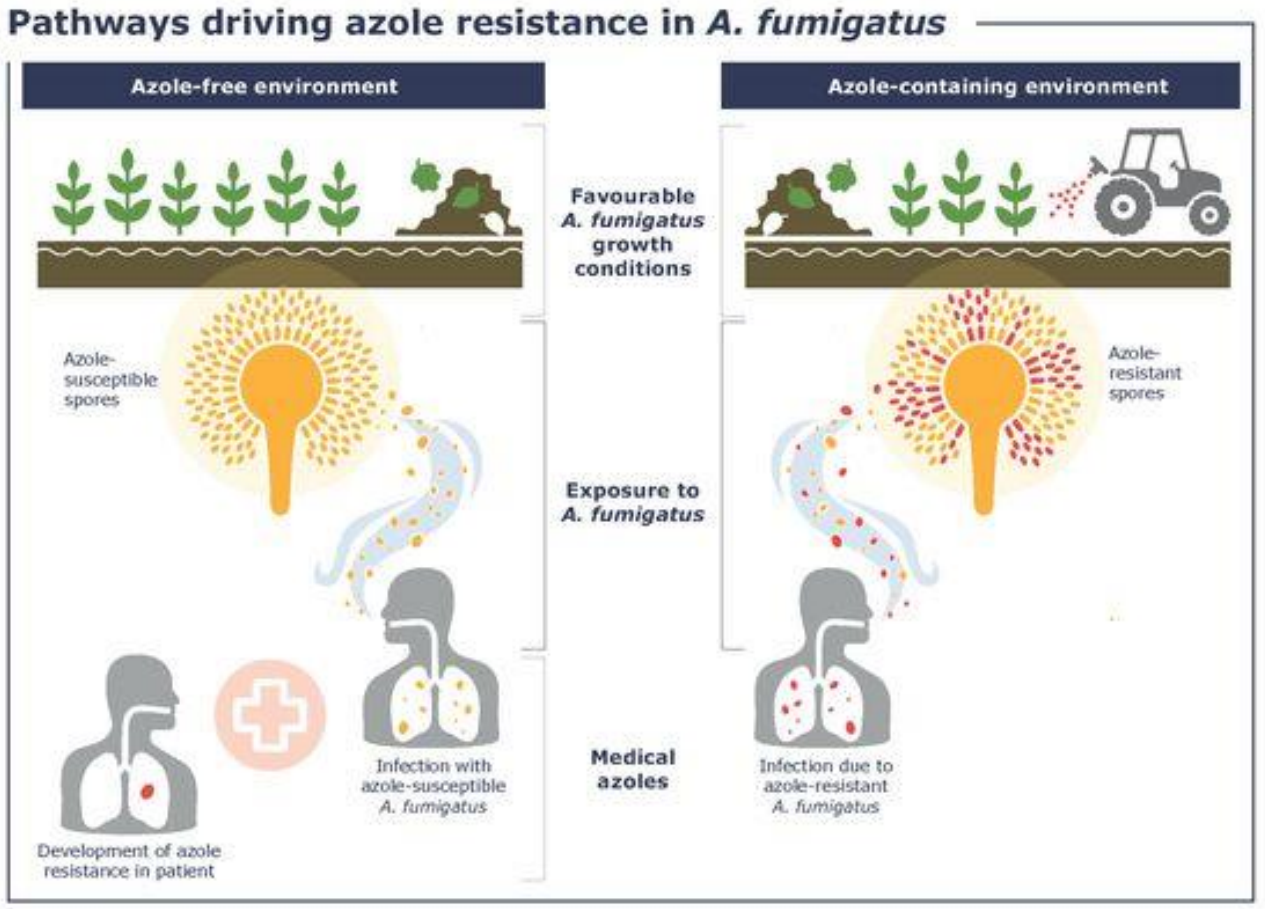
BACKGROUND

Azoles are broad-spectrum antifungals:

Human medicinal products	excluded
Veterinary medicinal products (VMPs)	EMA
Plant protection products (PPPs)	EFSA
Biocidal products (BPs)	ECHA
Industrial chemicals	ECHA



RESISTANCE AND PUBLIC HEALTH

- Azole resistance in *A. fumigatus* high in Europe:

	Invasive aspergillosis	Chronic pulmonary aspergillosis	Allergic bronchopulmonary aspergillosis
Prevalence (ARAF/Af)	0.7 – 63.6%	5.9 – 59.2 %	0.7 – 63.6 %
Mortality	36-100%	less documented	

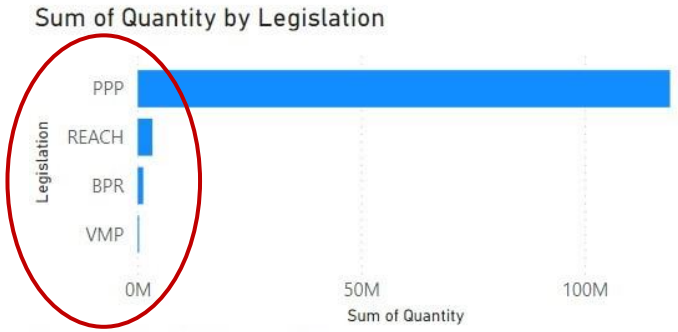
- Substantial evidence supports a **link between azole fungicide exposure in the environment and cross resistance selection to medical azoles** in *Aspergillus* species

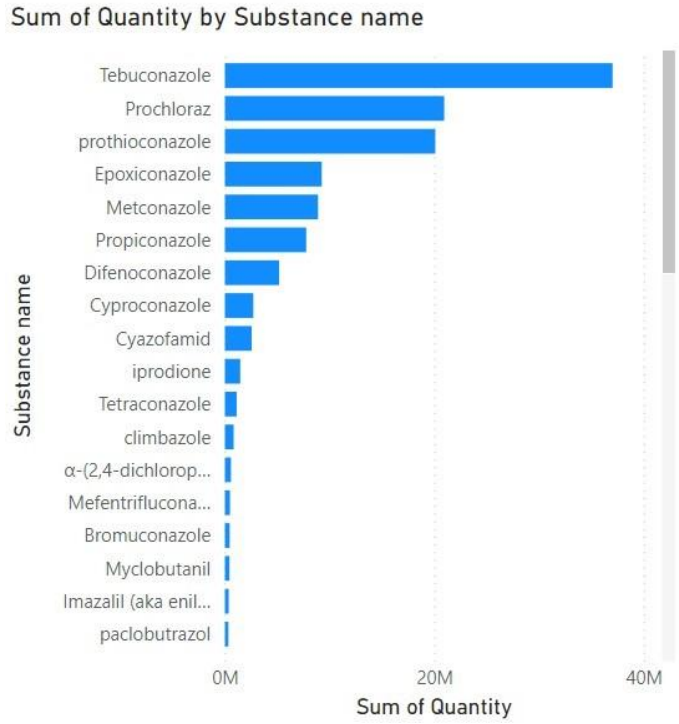
- Evidence supports hypothesis that transmission of ARAf occurs **from the environment to humans**

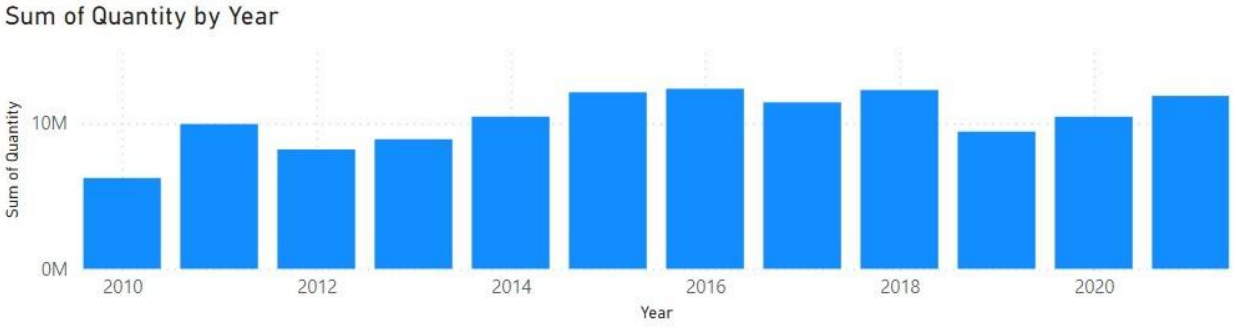
- **Azole usage outside the human domain is likely or very likely to contribute** to the selection of ARAf isolates that could cause severe disease such as IA, but the extent of this contribution needs to be better understood

USE OF AZOLE FUNGICIDES

- Overall 2010-2021
- Total 120,000 tonnes
- PPPs 119,000 tonnes
- Only indicative, please note data limitations

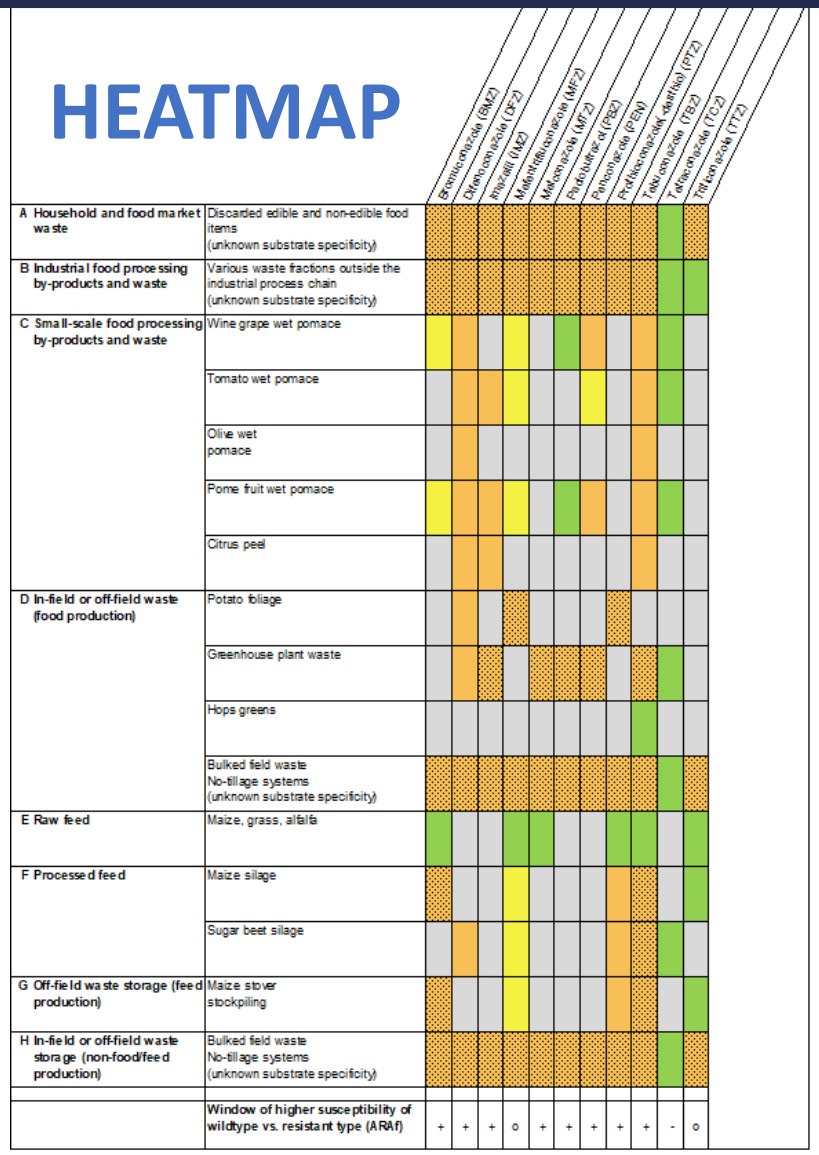






ENVIRONMENTAL HOTSPOTS

HEATMAP



No risk	No authorisation
Low risk potential	Authorisation AND residues not exceeding PNEC_AF100 OR non-relevant by default
Moderate risk potential	Authorisation AND residues exceeding PNEC_AF100, but not exceeding PNEC_AF10
High risk potential	Authorisation AND residues exceeding PNEC_AF10
Non-negligible risk potential	Authorisation and no data on residues

Environmental hotspots identified:

PPPs

stockpiling of agricultural waste and their possible use as soil amendment or fertiliser for several agricultural crops

BPs

freshly cut wood

PREVENTION AND CONTROL

Agriculture

- thoughtful use of azole fungicides
- promoting best practices for waste management and soil fertilization as well as further research

Biocides use

- optimise concentrations of azole fungicides when treating wood
- ensure proper wood waste management

Human medicine

- enhanced disease diagnostics
- surveillance
- increased awareness of this topic

Research and development

- developing new antifungals with novel mechanisms of action

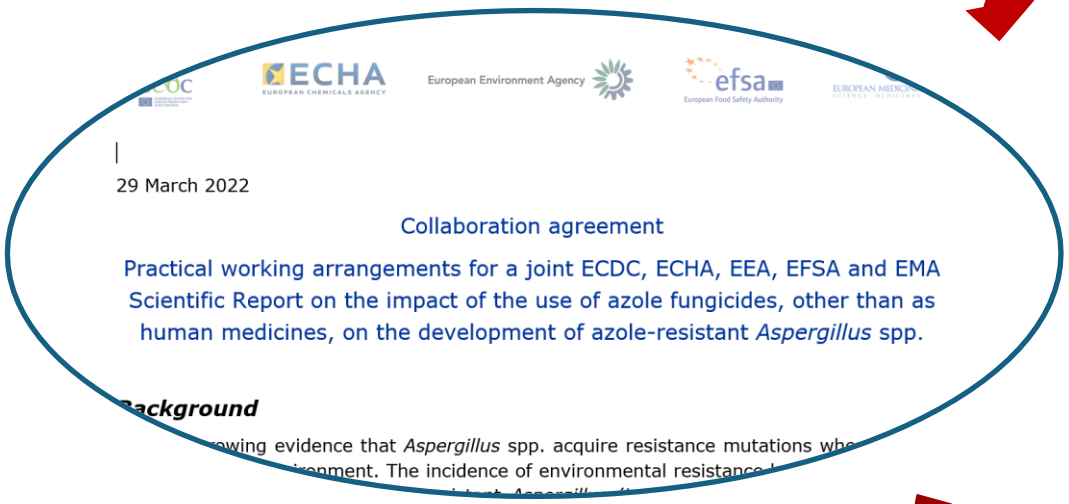
Approval process

- assess potential for cross-resistance with antifungals used in human medicine before approving new fungicides

DATA GAPS

Areas	Possible actions to address gaps
Use of azole fungicides	Establishment of a **mandatory reporting system** at national level with the appropriate level of detail related to the substance/product used and its specific application (e.g. crop of application) **Overcoming confidentiality issues** that limit dissemination and analysis of the data collected and double reporting
Epidemiology of ARAf	Standardised prevalence studies, strengthen **genomic testing**, screening of different environments
Spread of ARAf	Investigations on **pathways for spread** including cross-border
Hazard-related data	Investigations of resistance mechanisms, effect of other substances, **combined exposure**, other ***Aspergillus*** species
Residues in the environment	Investigate **fate and persistence** in environment, levels in crops/wood waste, waters/soil, human exposure
Environmental hotspots	Investigate growth conditions in specific substrates, waste management practices, **field studies**
Risk assessment methodology	To provide technical specifications for specific studies to be submitted within approval procedures, **refine** preliminary framework for risk assessment

TESTING OH COLLABORATION



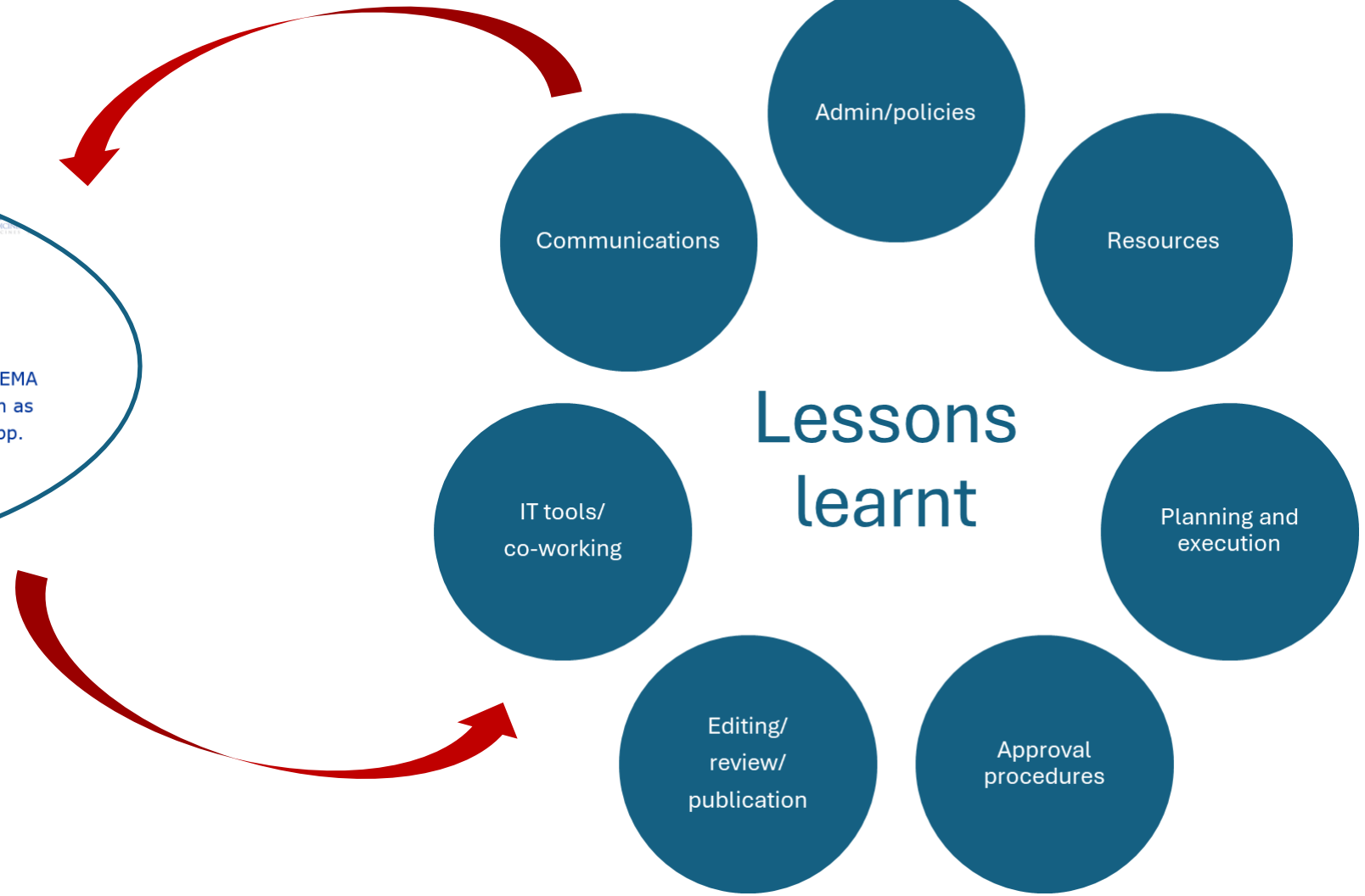
29 March 2022

Collaboration agreement

Practical working arrangements for a joint ECDC, ECHA, EEA, EFSA and EMA Scientific Report on the impact of the use of azole fungicides, other than as human medicines, on the development of azole-resistant *Aspergillus* spp.

Background

owing evidence that *Aspergillus* spp. acquire resistance mutations whe
ronment. The incidence of environmental resistance



JOINT COMMUNICATIONS