

## **GUIDING AGRICULTURAL R&D TOWARDS SUSTAINABLE POSITIONING OF FUNGICIDES POTENTIALLY CROSS-RESISTANT WITH ANTIFUNGALS USED IN HUMAN MEDICINE.**

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### **INTRODUCTION**

Fungicidal chemistry is important for both agriculture and human health. Fungicides are important guarantors of food security: the crop protection industry continuously searches for new modes of action (MoA) for the integrated management of crop disease. In medicine, human-pathogenic fungi present a global public health threat, with limited treatment options: here too, the efficacy of some medical antifungals has diminished in recent years due to the emergence of resistant isolates.

In the case of the human pathogen *A. fumigatus* (ASPEFU), there are indications that, under certain conditions, agricultural and environmental uses of DMI (“azole”) fungicides and biocides could allow the selection of isolates that are resistant to structurally-similar medical DMIs, which are used to treat human infection. The role of DMIs in certain agronomic settings – and crop waste management in particular - in the inadvertent selection of DMI-resistant ASPEFU isolates and their dispersal into the air is currently under assessment. The ASPEFU case shows that where active substances with a common MoA are used in more than one discipline, the potential for cross-resistance would benefit from an assessment in a OneHealth context.

### **METHODOLOGY**

Pharmaceutical and agricultural research streams have historically provided each other with ideas for lead molecules in developing new antifungals/fungicides to combat human infections & plant-pathogenic fungi alike. As this innovation process continues, the possibility cannot be excluded that new molecules brought to commercial development by the two disciplines are completely cross-resistant. To address this potential issue, scientific experts from CropLife member companies are in the process of reviewing the scientific literature and consulting industry-external researchers in order to develop guidance on the matter. The aim is to establish a basis for the scientific assessment of the potential risk that the use of new MoA as fungicides in specific agronomic settings could select and amplify resistance in relevant human-pathogenic fungi, to the extent that the use of related compounds in medicine is then compromised.

### **RESULTS**

Guidance is under development that aims to support the positioning of new fungicidal modes of action in crop protection where there is an identified risk of complete cross-resistance with compounds intended for use in human medicine. The DMI/ASPEFU findings indicate that the potential risk of selecting for resistance in human-pathogenic fungi through the use of agricultural fungicides is subject to many influencing factors such as, the environmental niche of the human pathogen concerned and the individual agronomic setting, including the specific use pattern (dose, frequency of application) of the fungicide. Individual agronomic settings differ in terms of the risk of selecting resistant isolates.

## DISCUSSION

The guidance under discussion aims to propose a structure for the scientific evaluation of the intended multi-disciplinary use of future cross-resistant molecules. Overall, the aim is to provide greater clarity in the face of scientific complexity. The guidance could help to safeguard the effectiveness of new MoA for both crop protection and medical uses within a “One Health” context. It will also inform the dialogue between the crop protection and pharmaceutical communities to address future potential cross-resistance issues.