FUNGICIDE DEVELOPMENT FOR THE 21\textsuperscript{ST} CENTURY

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Today as we move well into the second decade of the 21\textsuperscript{st} Century we find ourselves at an interesting and challenging time with respect to the development of new fungicide solutions. Plant pathogens have the potential to cause significant crop losses in both pre- and post-harvest situations and fungicides remain a critical tool for protecting yield and quality. The UN estimates that by 2050 the world will need 70\% more food to meet projected population growth and this increase will largely need to be covered by increased efficiency of production from the current finite area of agricultural land. Fungicides will play a key role in attempting to meet this challenging goal and it is critical that industry continues to bring new solutions to market whilst maintaining the registrations of important existing chemistries. The challenges facing R&D companies engaged in this endeavour are numerous. Ever more stringent regulatory safety margins make the identification of new fungicidally active molecules which have a high probability of being registered more difficult, whilst important existing chemistries such as the triazoles face uncertainty about their long term future in certain regions of the globe. One impact of increasing regulatory complexity is that the cost of development of new actives, approximately US $256 million according to a 2010 European Crop Protection Association (ECPA) analysis, and maintenance of existing registrations continues to rise. Fungicide resistance continues to be a major challenge with a real need for new novel modes of action (MOAs). This is particularly acute in the context of the potential loss of some key chemistries in the future due to regulatory challenges thus further limiting the number of effective MOAs available to growers for integration into resistance management strategies. A further challenge is the uncertainty around how the drive towards sustainable crop protection will shape the future landscape for agrochemical development along with the potential impact of climate change on the prevalence and geographic spread of plant pathogens. Sources of new leads for fungicide development include natural products, compound collections from various institutions, combinatorial chemistry libraries and competitor chemistry. Traditional _in vivo_ and _in vitro_ screening of hits and their subsequent optimisation via classical Structural Activity Relationship (SAR) testing remain and important facet of new molecule discovery although the crop protection industry has also seen the introduction of structure based design. The characteristics which must be exhibited by a new fungicide are excellent efficacy and crop selectivity, a clean toxicological and environmental profile, freedom to operate and a synthetically accessible structure which can be manufactured at scale cost effectively. Additional desirable features include physiochemical properties allowing formulation flexibility and effective redistribution in or on the target crop as well as physiological effects on the crop such as greening and drought tolerance. Combining all the above characteristics into a single molecule remains an enormous technical challenge but one we must continue to achieve if we are to meet our needs for a sustainable increase in agricultural productivity as we move towards the middle of this Century.