



SCIENCE & TECHNOLOGY LADDER (S&T Ladder)
– NOMINATION FORM –
FELLOW

NOMINEE	
Employee name	Andy Cook
Job Title	Global Regulatory & Product Safety lead – bipyridyls
Location	Jealotts Hill
Function	Global CP Regulatory
Line Manager's name	Roland Dieterle
Submission date	30 th September 2018

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EDUCATION and PROFESSIONAL HISTORY	
Curriculum Vitae	CV ANDREW RICHARD COOK 2016

REFERENCES	
Internal Reference (Senior manager)	Phil Botham – Principal Science Advisor
Internal Reference (Peer)	Monty Dixon – US Regulatory Portfolio Lead
Internal Reference (Peer)	Erin McGregor – Regulatory Portfolio Manager Canada
External Reference	Professor Sir Colin Berry
External Reference	Jonathan Sullivan



1. Business Impact

The 2017 combined Syngenta global sales of paraquat and diquat were in excess of US\$525 million, contributing approximately US\$250 million GP (Gross profit) for Syngenta. The 2017 total global sales of paraquat alone were approximately US\$1.2 million. The 2017 total global sales of the bipyridyls was estimated to be US\$1.5 million. Total paraquat sales in Brazil alone equate to a Syngenta 'Blockbuster' (i.e. US\$250 million/annum).

The strong global demand for glyphosate resistance management has been a major driver of recent paraquat demand with global 12% CAGR (compound annual growth rate) in remaining markets between 2012 and 2017, remarkable for a product first commercially introduced in multiple markets in the early 1960s. Syngenta paraquat production capacity limits our global market share, total global production capacity is approximately 100 million tonnes/annum.

Maintenance of the global licence to operate (LTO) for both bipyridyls is almost exclusively dependent on Syngenta R&D. Unlike other major molecules (e.g. glyphosate) or chemical classes (e.g. neonicotinoids) all LTO initiatives are driven by Syngenta rather than by cross-Company or Crop protection industry associations.

In addition to the sales / GP impact the bipyridyls, especially paraquat, are of critical importance to the Syngenta portfolio in several other important respects. Paraquat continues to represent greater than 50% of Syngenta's annual sales in a number of markets and it provides a critical portfolio lever for access to distributor networks in key markets such as the USA. The management of the LTO environment for paraquat has broader impact on Syngenta's Corporate reputation with multiple external stakeholders at the National and International level. Intense regulatory pressure, driven by multiple stakeholders based on high acute toxicity (suicidal, accidental, occupational) and allegations of association with chronic disease outcome.

The paraquat supply and demand strategy is heavily dependent on regulatory events / maintenance of LTO. The Global Regulatory function is a critical partner for the global asset team and the global supply chain team. Critical regulatory judgement is required in assessing the global LTO outlook for both paraquat and diquat to guide the business strategy through my inputs to the global AIM (Asset Management) teams for both molecules. My inputs on, for example, the LTO outlook for both molecules in Brazil and the regulatory outlook for diquat outside the EU were essential inputs for the recent substantial (US\$30 million) business investments in diquat manufacturing assets at Huddersfield.

Maintenance of the LTO of many active substances within the EU is threatened by the current implementation of Regulation 1107/2009. However, the threat to our LTO for paraquat has been sustained (since the 1980s) and is global. This has further intensified following the loss of paraquat in the EU in 2007 and subsequent global losses (e.g. China, Malaysia, South Korea, Sri Lanka, Taiwan) due principally to deliberate gross abuse of the product for the purposes of self-harm.



The 'holy grail' has always been to maintain the agronomic / user benefits of paraquat as the leading contact non-selective herbicide while mitigating the acute toxicity hazard. Syngenta and its Corporate predecessors have collectively spent in excess of US \$200 million over the past 40 years attempting to address this issue. I was the first within the Syngenta Regulatory, Product Safety and Stewardship community to identify and advocate the step change which the development of 'CLKS' (Closed loop Knapsack sprayer) presents in elegantly addressing this issue.

Recognition of the unique situation of paraquat within the current Syngenta CP portfolio previously led to the establishment of the global Paraquat Issues Leadership Team (PILT) under the leadership of John Atkin and, more recently, Jon Parr. Membership included the Head of R & D (Trish Malarkey) and the Head of Global Product Safety and Regulatory Affairs (Peter Hertl). This body has now been replaced by a much more focussed global governance team of four, comprising Jon Parr, Roman Mazzotta, Dave French and myself. In addition, paraquat and diquat, like atrazine, the mectins and thiamethoxam continues to be subject to additional global DeCo (Development Committee) governance given the corporate reputational and litigation dimensions.

The long-standing allegations of a causal association between exposure to paraquat and Parkinson's disease represent a significant threat, not only to Syngenta's reputation, but to the existence of the Company as the anticipated US class action lawsuit has now become a reality.



2. Innovation

EU Review of the bipyridyls

Critical to the approval of crop protection products is the balance between the agronomic benefit and the risk. All too often the entire focus is placed on the latter. The global trend to move the accountability for product registration from Agriculture to Health or Environment results in significant dilution of the appreciation for the 'benefit' case. As an example, for the first EU level Review of the bipyridyls under EU Directive 91/414 (submission deadline April 1995) an innovative approach was adopted specifically for the bipyridyls in which, as the Regulatory lead for both active substances, complimentary 'benefits' dossiers focusing on both agronomic and environmental benefits were commissioned and complemented by multiple supporting positions by external stakeholders. This was a novel and highly effective approach with both actives ultimately receiving EU approvals despite some pre-existing National bans.

CLKS (Closed loop Knapsack sprayer)

The Chinese government required paraquat products to be reformulated as solids or gels to reduce their deliberate gross abuse for the purposes of self-harm. There is significant Corporate history of the development and limited commercialization of both solid (granular) and gel formulations of paraquat. However, there are multiple human safety and cost challenges in successfully commercializing such products. A novel granular formulation in a water soluble bag was developed for China but ultimately was not supported on the basis of formulation plant costs. During the evolution of solutions for China the concept of a closed system for backpack / knapsack sprayers was developed. Unfortunately this was not developed for China and, as a result of personal advocacy and perseverance up to and including with the Syngenta Board, is being taken forward in a new design phase with significant human health and regulatory input for still greater utility as a novel and significant patentable innovation with significant benefits for human safety and global maintenance of paraquat LTO in backpack / knapsack markets. The technology also has broad applicability across the Syngenta CP portfolio.

Closed mixing / loading for tractor-mounted sprayers

Canada: the conclusion of the 'Special Review' of paraquat by the Canadian PMRA (Pest Management Regulatory Agency) triggered by the loss of paraquat registration in the EU was a request for a more dilute and less irritant formulation based on a review of human health incidents in North America. There are significant cost and development timeframes for new formulation developments (in addition to technical challenges relating to 'low irritancy').



Therefore I proposed an alternative and novel (for Canada) approach to address the same underlying technical drivers. This required advocacy with commercial colleagues and challenged the existing PMRA regulatory framework. A team was assembled and the proposed system described and physically shown to PMRA to obtain their critical buy-in. This practical demonstration of this novel development generated great interest and engagement with the entire staff of the Division being invited into the meeting by the PMRA Director at the conclusion of the meeting.

Brazil: the conclusion of the 'Special Review' of paraquat by the Brazilian Health Agency, Anvisa, in 2015 was problematic with a proposed ban on the grounds of the lack of a paraquat-specific antidote, a view that paraquat is mutagenic and that exposure is associated with the development of Parkinson's disease. Any one of these elements would provide the basis for a complete product ban. A huge amount of techno-regulatory advocacy was devoted to resolution of this as Brazil is not only the single largest paraquat market (approximately \$250 million in annual sales across multiple suppliers) but is also a key regulatory reference country for the remainder of Latin America. I prepared a comprehensive techno-regulatory response to the original Anvisa technical evaluation. Several innovative steps were taken, an on-line public consultation took place in which key stakeholders were effectively mobilized and which directly resulted in Anvisa convening a scientific seminar with invited National and International scientists. It was however clear that scientific advocacy alone would be unlikely to result in a successful regulatory outcome. Fall-back risk mitigation options were jointly developed with the Ministry of Agriculture, including the use of a novel mixing-loading tractor system to safeguard the critical product uses for pre-plant burn down (weed control) and desiccation in soybeans. Additional techno-regulatory advocacy included a week of high intensity meetings in Brasilia at the political level (the Minister of Agriculture, members of the Brazilian Congress – the latter including Brazilian TV interviews) and further science meetings with Anvisa toxicologists and a regulatory meeting with Anvisa Directors). The final result was an unprecedented 3-year regulatory extension for paraquat with interim mitigation measures, a request for a limited number of additional studies and a move to exclusive use via closed mixing / loading systems by September 2020.

Right-hand shift (RHS)

Sustainability of the future Crop Protection portfolio was a driver for the Development focus on the so-called 'left hand shift' in chemical selection and development. Much more recently similar thinking has been applied to the existing CP portfolio through the formal 'right hand shift' for selected active substances. The approach to diquat was a direct precursor to this generic portfolio approach. The Global strategy for diquat formulation and label extensions was formulated in 2014, developed with the global product biology and assets teams, presented to and endorsed by the global 'Paraquat Issues Leadership Team' (PILT) led by John Atkin in May 2014.



3. Knowledge sharing

Knowledge sharing across multiple functions and across multiple external stakeholders is a fundamental part of what we do within both Global Regulatory Affairs and Product Safety. Knowledge interpretation and adapting complex science to be appropriate for different external stakeholders is vital to the successful operation of the Regulatory function.

Communication management

One of my specific proactive knowledge-sharing initiatives is to raise awareness of the critical importance of the language used in regulatory or safety communications whether internal or external. The primary driver for this activity was a recognition of the Corporate reputational risks which can arise from poorly worded or ambiguous statements which may later be taken out of context due to later deliberate (e.g. as a result of receipt of a Freedom of Information request to a Regulator or a request for document disclosure during litigation proceedings) or inadvertent release outside the Company. Two training modules were developed in conjunction with colleagues in Legal Affairs and shared as a mandatory training module with the entire Syngenta global regulatory and product safety community. The materials have also been shared and used by other functions, including the global asset team in Basel.

Syngenta regulatory processes for EU re-registration

There are several other examples of initiatives taken to gain multi-functional agreement and share the resulting knowledge across the techno-regulatory functions. One example of this is the senior level steering team I established in my former role as EU Regulatory Leader for the EU active substance reviews under the 'old' (91/414) Regulatory Directive. I led the team and authored the report of the recommendations from a cross functional group (Andy Cook, Mike Skidmore, Patrick Rose, Enrico Kiefer, Fraser Lewis and Felix Meier-Manz representing European Regulatory Affairs, Global Regulatory Affairs and HAES) for the effective management of the list 3 EU review process, developed and delivered the global communication of the new processes.

Science publications

Paraquat is one of the most studied crop protection chemicals and has been the subject of numerous science publications for decades. Over the past decade the rate of new science publications is approximately 250 / annum or one for every working day of the year. Monitoring and management of that volume of scientific information is extremely challenging. Some of these studies are low impact while others may challenge Syngenta's science and warrant further investigation. I lead the Syngenta communications management team charged with monitoring new science publications on paraquat (or diquat), making an initial assessment and determining the global Product Safety recommendation. A range of responses exists, including production of an internal critical review, production of a letter to the editor or production of a reactive media statement through to direct contact with the authors of the study or commissioning our own studies. The approach used for the bipyridyls formed the model subsequently communicated and adopted for thiamethoxam.