
From: Cook Andy GBJH
Sent: 07 November 2011 11:14
To: Lewis Dick GBJH
Cc: Botham Phil GBJH; Pearson Charles USGR; Hertl Peter CHBS
Subject: RE: SynCRAs
Attachments: FW: SynCRAs Guidance for RSF

Dick,

My feedback in relation to the DRAFT GPR Syncra for paraquat ahead of the RSF scheduled for 10th November is as follows:

I believe the agreed global regulatory endpoints have been used. Nevertheless the 'generic' approach to Syncra production ignores the higher tier data we have supporting our current regulatory position. In the absence of that refinement of the risk assessments the document could be misinterpreted.

- I was never informed that there was an intent to produce a SYNCRA for paraquat, neither did anyone from GPR ever indicate that such a document was being worked on. I appear to be by no means unique within PS in this regard. Indeed it appears that some of the GPR regulatory managers themselves were only informed at a stage when drafts already existed. This lack of transparency is disappointing to say the least.
- We are already in pre-litigation and must consider any document not created under legal privilege to be subject to external scrutiny in a Court of Law. I do not believe the global or US litigation teams (effectively Jonathan Sullivan and Alan Nadel) would have agreed to or sanctioned the creation of such a document by the GRTMs who are unfamiliar with the specific threats and are not listed in or currently subject to the global Data Preservation Notice.
- Notwithstanding the 'Note for User' statement the language in the document is unhelpful, as illustrated in the passages below and displayed visually in Figs. 4-1 and 5-2. The document could be interpreted as implying significant human dietary exposure to paraquat residues in food and / or drinking water. This is simply not true.

Note for User:

As a general guidance document, this SynCRA does not:

- determine the registrability of the AI or product in the context of specific regulatory frameworks.**
- demonstrate that a registered uses is unsafe to humans or the environment**

This document provides a broad risk assessment for the above AI. The assessment is based on a wide range of varying parameters including, but not limited to crops, rates, application methodologies, and exposure scenarios. As such, it is intended to provide guidance on relative risks of use patterns when compared to Syngenta's endpoints. The analyses herewith may identify potential areas of concern for which discipline experts can build refined models and / or suggest risk mitigation measures to ensure safe use. Such targeted refinements / mitigations are outside the scope of this document. More information on the correct use of the document is described in the "Guidance document on SynCRAs".

For paraquat estimated operator exposure for the given typical and worst-case GAPs was above the AOEL for all application techniques but for handheld applications (typical GAP) when in addition to current label requirements the use of gloves during application is considered (see following graph). Based on existing experience, higher tier risk assessments are expected to lead to favorable results.

Further considerations are needed for acute intake of paraquat residues in root and tuber vegetables and watermelon. For those crops, a refined risk analysis and/or mitigations are needed before initiation of new projects or any changes in existing GAPs.

The Tier-1 surface water assessment indicates a risk of contamination at concentrations that may raise a toxicological concern.

Results of the operator exposure estimations are summarized below.

Application technique	Application rate [g ai/ha]	Model/scenarios used	Total systemic exposure [% of AOEL]			
			No PPE/ clothes	Clothes	PPE	PPE+
Worst-case GAP (PPE+)						
Tractor boom sprayer	1800 (150 ha)	PHED 3 (m/l) + 13 (appl)	15654	14342	2791	2790
	(1800 (50 ha))		5218	4781	930	930
Aerial (plane)	1800	PHED 3 (m/l) + 7 (appl)	48580	44639	6134	6096
Handheld: Backpack sprayer	1800	PHED 3 (m/l) + 20 (appl)	21563	-	-	-
Handwand°		PHED short clothes	-	399	-	-
		PHED 34	-	-	-	339
		German model	-	4464	1669	1540
		PHED 32 (m/l + appl)	3056	-	-	283
		PHED short clothes	-	3012		
Typical-use GAP (PPE+)						
Tractor boom sprayer	600 (50 ha)	PHED 2 (m/l) + 13 (appl)	1739	1594	310	310
	(600 (150 ha))		5218	4781	930	930
Aerial (plane)	600	PHED 2 (m/l) + 7 (appl)	16193	14880	2045	2032
Handheld: Backpack sprayer	600	PHED 3 (m/l) + 20 (appl)	7188	-	-	-
Handwand°		PHED short clothes	-	133	-	-
		PHED 34	-	-	-	113
		German model	-	1488	556	513
		PHED 32 (m/l + appl)	1019	-	-	94.4
		PHED short clothes	-	1004	-	-

m/l = mixing/loading, appl = application

Clothes: handheld: short clothes; all other: long clothes

PPE: long clothes, gloves for m/l

PPE+: long clothes, gloves for m/l and application

^o low pressure handwand sprayer

- Generically there is recognition that the internal Tier I Syncra approach has the potential to identify potential for further operator exposure mitigation (following additional data generation and/or risk assessment refinement) in territories with less rigorous regulatory regimes. However this is also potentially the case in North America and non-EU countries within EAME in which adjustment of an oral NOAEL for the extent of oral absorption is not part of the local regulatory practise when establishing an AOEL. This issue is most acute for the bipyridyls but may also be significant for chlorothalonil.
- The specific legal status of paraquat is one reason why the agreed EASY support model for PQ is different to that of other active substances in the portfolio – all technical support is (should be) requested directly from PS, not from the GRM. This was put in place in recognition of the need to manage the specific complexity of the current external environment for this a.i.
- I do not believe it is appropriate to finalise the Syncra for paraquat in its current form without reference to elements of the extensive higher tier data (inhalation of coarse spray droplets not possible in normal use, operator exposure and health monitoring surveys, market basket dietary residue survey, etc.) which underpin our overall assessment of the safety of paraquat in normal use.

I appreciate that much of this may be seen as being specific to paraquat but there is a broader point here in that we can never be sure what external challenges we may be subject to and a document considering uses registered and on sale for decades should, in my view, leave the reader in no doubt as to where the Company actually stands on the issues potentially highlighted by the lower tier regulatory assessments through appropriate reference to the existing higher data which support our position. There needs to be a recognition that the one size fits all approach to the portfolio may not be appropriate for the final version of a Syncra.

Regards.

Andy

From: Lewis Dick GBJH
Sent: 20 October 2011 15:16
To: Hill Simon GBJH; Cook Andy GBJH
Subject: FW: SynCRAs

See the note below which is self explanatory. Can you check that the endpoints used are those agreed in the relevant endpoints documents

Dick

From: Botham Phil GBJH
Sent: 20 October 2011 11:51
To: Pearson Charles USGR; Lister Neil GBJH; Lewis Dick GBJH; Lewis Fraser GBJH; Hadfield Steve GBJH; Meyer Linda USRE
Cc: Hertl Peter CHBS; Malarkey Trish USRE; Payan Luis USGR; Kelly Christine SGSG; French Dave CHBS
Subject: FW: SynCRAs

Dear Platform Leads

Ahead of the November RSF discussion on SYNCRAs, Peter and I agreed in separate conversations with Dave French and with the Platform Leads and Neil Lister that we really needed to have two things in place:-

1. An opportunity for the Platforms to review the 9 SYNCRAs which have been prepared by the GRTMs so that we were not discussing the technical content of the documents at the meeting
2. A clear understanding of the purpose of the RSF discussion

Following a discussion with Steve Maund yesterday, I've now been sent two of the SYNCRAs by Kersten. I'll need to follow up with them why they've only sent two, as I believe that the Platforms have still not received any of the 9 directly (please let me know if this is not true).

Steve's view on the purpose of the RSF is to ensure that we have global safety and regulatory buy-in to the concept of these "simplified" SYNCRAs before further work is done on the remaining a.i.'s, and to decide on the next steps that would be needed, for example to manage the "red risks" which have been identified through this process.

I've cc'd Dave French into this as a "sanity check" on my interpretations.

Phil

From: Mewes Kersten CHBS
Sent: 20 October 2011 10:40
To: Botham Phil GBJH
Cc: Maund Steve CHBS
Subject: SynCRAs

Dear Phil,

Steve told me yesterday that he had a discussion with you on the SynCRA project. Please find attached two SynCRA proposals – one for paraquat and the other for azoxystrobin. I hope these two examples will help to understand how we visualized the results of the Syngenta RA modules.

Please feel free to forward these two SynCRA proposals to the PS platform leads.

Best regards,
Kersten

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