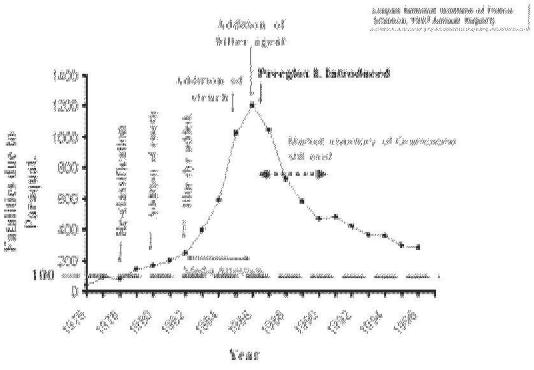
From: Dieterle Roland Mario CHBS <roland_mario.dieterle@syngenta.com>
Sent: Friday, July 06, 2012 10:37 AM
To: Brown Richard Anthony CHBS; Cook Andy GBJH
Subject: emetic effect - initial thoughts

Both

Following our CPTT telecom, I was looking in my files for any useful information we could use to demonstrate the effect of the emetic.

Interestingly, I didn't find a position statement on the emetic so far.

I understood from Martin that we cannot demonstrate the effectiveness of the emetic in real life situations. The JP development of fatal suicides appear to confirm that – the introduction of the emetic has not demonstrated any impact in JP (see below); of course we also don't know whether the situation would be worse without emetic…



A draft PS-TED is available which concluded that in the dog the oral gavage studies had demonstrated that the onset of vomiting, duration, and severity would be dose related. However, the impact on the PQ plasma level from the emetic was not addressed.

Swain/Heylings (2006) extracted data from dog studies conducted at the CTL between 1987 and 1991. Conclusion: This investigation into the effect of increasing the concentration of the emetic agent in Gramoxone on the acute toxicity of paraquat in the dog has demonstrated a measurable improvement in oral toxicity. This has been brought about by causing very rapid emesis. However, even this very prompt emesis was only effective in reducing Gramoxone toxicity by approximately 3-fold.

There are maybe other dog studies we could use to demonstrate that the PQ plasma level is reduced by the emetic – we have just to be very careful not to overclaim a hypothesis…

Any thoughts, useful literature, other data?

Regards,

Roland