

To: Atkin John CHBS[john.atkin@SYNGENTA.COM]; Lawrence David CHBS[david.lawrence@SYNGENTA.COM]
Cc: Sullivan Jonathan Dale CHBS[jonathan_dale.sullivan@SYNGENTA.COM]; Nadel Alan USGR[alan.nadel@SYNGENTA.COM]; McFarland Janis USGR[janis.mcfarland@SYNGENTA.COM]
From: Smith Lewis CHBS
Sent: Thur 11/22/2007 2:43:15 PM (UTC)
Subject: FW:
Attachment: Nuerotox Conference.doc

[Please see attachment](#)

[Lewis](#)

From: Burton Judith GBAP
Sent: 20 November 2007 15:01
To: Smith Lewis CHBS
Subject:

Case ID: 220300429

SYNG-PQT-ATR-16987892



Lewis L Smith
Global Head, Regulatory
Sciences

Syngenta
CTL
Alderley Park, Macclesfield
Cheshire SK10 4TJ
United Kingdom
www.syngenta.com

Tel: +44 1625 514848
Fax: +44 1625 590250
Mobile: +44 0780 103 8044
Lewis.Smith@Syngenta.com

Memo

To	John Atkin David Lawrence	Date:	19 November 2007
Copy To	John Sullivan Alan Nadel Janis McFarland	Number of pages:	[PAGE * MERGEFORMAT]/[NUMPAGES * MERGEFORMAT]
Concerning			

John/Dave

I attended a Neurotoxicology Conference last week in San Antonio. The meeting lasted four days and was attended by many senior neurotoxicologists in the USA. It is important to distinguish neurotoxicologists from neuroscientists; the latter may well be studying the same diseases as neurotoxicologists, but they are not necessarily assigning a chemical or drug entity as provoking or contributing to the disease.

There was approximately 160 attendees at the meeting. From the list of attendees I was only able to identify two from industry and one from Crop Life, (the individual from Crop Life did not turn up). The subjects for the conference were autism, Alzheimer's Disease and Parkinson's Disease. The latest twist was the suggestion that Alzheimer's Disease and Parkinson's Disease, although different entities are closely associated by the progressive damage to neuronal cells that in some circumstances, may have a common cause.

Specifically on Parkinson's Disease, recent data was presented (by Dr Tanner), on the American Ag Workers Health Study. This involves 80,000 participants, cost in excess of \$100M and was originally set up to look for the relationship between pesticides and cancer, but now has a significant arm of the study devoted to the relationship between pesticides and Parkinson's Disease. The recent data indicated that there is a progressive increase in the incidence of Parkinson's Disease associated with pesticides, and paraquat in particular. The most recent data did not stay on the screen for long, but the increase appeared to be progressive, although the relative risk was still less than 2. The study has been running for 10 years, and if it continues to run, does have the prospect of providing strong evidence of an association that will be extremely difficult to contradict. This is because it would cost tens of millions to repeat the study and even if this was undertaken, it would take many years before the results were available. It is likely that if industry were to fund the study, we would be accused of bias in the study design and interpretation. Furthermore, Dr DiMonte, who by no means views pesticides as a major cause of Parkinson's, has shown in non-human primates that paraquat increases the level of synuclein in the brain. This protein is strongly associated with Parkinson's Disease in both humans and experimental animals. It is thought to play a role in the severity of the disease and be an indicator of its development. The doses Dr DiMonte used in the monkeys were high, but the study only lasted two months. Therefore, the increase in synuclein may well have continued had the study continued. Data from non-human primates and rodents are providing an increasingly plausible hypothesis that is sustained by epidemiological studies that shows an association between paraquat use and Parkinson's Disease. While it is true to say no causal relationship has been established, had you been at the meeting you

Case ID: 220300429

SYNG-PQT-ATR-16987893



would have been struck by the consensus amongst the broad group of scientists that environmental factors were primarily responsible for Parkinson's Disease. Also, it was taken as a given that pesticides were a major factor which contributed to Parkinson's Disease and that paraquat was a likely culprit in the development of the disease.

It is of concern that so many academic neurotoxicologists seem to accept the likely involvement of paraquat in Parkinson's Disease and that this community is virtually unchallenged on what, from our perspective, is highly unlikely. Unless we are able to generate new data on the mechanism of toxicity of paraquat in the brain and provide evidence of an exaggerated response in the C57B6J strain mouse, we shall not halt or far less reverse the perception that paraquat contributes to some extent to the incidence of Parkinson's disease

Lewis