

**ACTION NOTES FROM ATLANTA EPIDEMIOLOGY MEETING
15 FEBRUARY 2008**

Attendees:

Dr LL Smith

Dr J Mandel (Atlanta)

Dr M Wilks

Dr J Cole (Alabama)

Dr C Breckenridge

Dr J Simpkin (Florida)

Mr DJ Berry

For an epidemiology study to have sufficient scientific and legal rigor, it would have to be a *persuasive negative* - difficult to achieve and requires a large number of cases. The strong implication is therefore that we require a case control study.

ACTION – MFW to compile a list of known pq PD epidemiology papers and current studies

It was recognised that epidemiology studies have a publication bias for positive results and that studies which demonstrate no associations with PD are unlikely to be published.

ACTION- JM to establish what pq PD studies are ongoing (or have been completed but not reported) in the US

ACTION – CB to copy the Berry, Pierluigi, Schapira and Louchetti review paper to JM and PC

Governance

Subject to approval, Syngenta want to convene a panel to conduct a review of PD risk factors; this panel would also advise on the design, conduct and reporting of studies/ analyses that were undertaken. Syngenta would also encourage the panel members to be prepared testify as expert witnesses on our behalf.

There was general agreement that there should be a Steering Committee (members to include at least JM, PC, Adami and Thichopoulos); Syngenta would insist on the inclusion of at least one epidemiologist in the PD field; the inclusion of a neurophysiologist/pathologist (eg Schapira) was also recommended.

ACTION - JM to consider the inclusion of Checkoway, or another leading PD epidemiologist.

Reporting to, and commissioned by, the Steering Committee would be an *ad hoc* Advisory Group to include (say) an exposure specialist, a biologist (Jim Simpkin), possibly the neurophysiologist/pathologist and others.

Case ID: 220300429

CONFIDENTIAL AND ATTORNEY CLIENT PRIVILEGED COMMUNICATION

The Steering Committee would need to be clear from the outset as to the remits for the teams and contributors (eg, contributions, authorship, costs etc).

Critical review of PD Risk Factors

JM considers that 18 months is sufficient time for the completion of a review from commission to publication.

ACTION – JM to provide cost and timings

Case Control Study

A Case Control study, once given the go-ahead from Syngenta, would be commissioned through the Steering Committee. The study would be conducted as a number of academic institutions; Syngenta's involvement would be to agree the protocol and have an opportunity to comment on any scientific points in a draft report, but would have no say on the interpretation of the study.

- Would need estimated 300-400 cases per group depending on required power - would need to have tight limits on the power calculation for the outcome to be a persuasive negative.
- Challenge will be to establish exposure estimates – though the mapping work from CB looks encouraging
- Need to look in 3-4 centres of known pq use; aim would be to set up the work through a co-ordinating centre/university.
- Definition of control population important; by increasing the size of the control group we could reduce the number of cases in the “treated” grp – this would save time but be less cost efficient. Controls would be matched for age, gender and geological location – other factors need to be considered.
- May be difficulties in obtaining agreement from patients and physicians to participate.
- If we need to collect and store biological samples (blood, saliva, urine) this can be done but at additional costs, including storage.
- Collection of data would be based on a questionnaire with patients describing symptoms; the current proposal is that these findings would then be checked back with a panel of physicians to characterise as definite, possible, probable and negative PD/ Parkinsonism associations.
- Will need to conduct a feasibility study to ensure the protocol can be adopted.

ACTION- LLS to confirm by Easter whether or not Syngenta will to commission the feasibility study, with a proviso to also conduct the main study, recognising there would be some cost penalties if Syngenta decided not to proceed.

- As a ballpark figure, assuming 2 grps of 400 at \$1000 to \$2000 per patient, the cost will be in the region of \$2m to \$3m. Estimated time = 2 to 3 years.

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ACTION - JM to provide best cost and time estimates for feasibility and main studies.

Cohort Studies

JM believes we are obligated to conduct studies on plant workers – although the answer would not be a persuasive negative, it is the question we are bound to be asked.

If commissioned, Syngenta would be seeking advice from the Steering Grp on how best to analyse the data; we also need to be conscious that Syngenta Occupational Health need to agree for any such work to be undertaken, and that any analysis is compatible with work that has been done previously on the same cohort.

There may already be data available on the

- US AgHealth and California Surveys.
- France is also setting up a study similar to the US AgHealth survey
- CB also mentioned the US (war) veterans database which, although likely to be low on pq exposure data, may be useful for information on risk factors.
- Lori Nelson is running a cohort/ case control study at Stanford.

ACTION – JM to try and find out what data are available.

It may also be possible to conduct a cohort study on survivors of paraquat suicide attempts (UK and Korea) – though the team envisaged ethical and practical difficulties in achieving this.

GENERAL ACTIONS –

- ***CB to send copies of OHs to JM and PC***
- ***CB to arrange for lawyers to call and discuss directly with JM the drawing up of contracts.***

Circulation

Those Present
Mr A Nadel
Mr J Sullivan
Ms B Quarls
Mr J Wolff