

Dick

I am enclosing some
of my thoughts on the
proposed Paraguard study
protocol. Besides some of
the points I've raised here,
I have some other reservations.

Should you want some
further input, please feel
free to call.

Will

7/26/18

Dictz

Below I've tried to point-out a few or the more significant questions or drawbacks I feel exist in the Paraguet Study protocol. Needless to say, there isn't much information to go on, either they've failed to consider a number of things or decided not to elaborate. In any event, my overall impression is that it's a weak study design and the following are some of the reasons:

1. A cross-sectional study design implies studying the existence or prevalence of disease (or whatever) at a specified point in time - is this really the best way to study the effect of paraguet exposure? Why not use a case-control design and study the entire incidence of disease since first exposure to paraguet.
- ✓ 2. The study population and controls are very ambiguous. Are the sprayers considered "exposed" and the tappers and general workers "unexposed"? Why not consider each of these groups ~~as~~ as

subgroups of the study population with varying degrees of exposure to paraquat and study differences between the occurrence of observable disease or clinical abnormalities? In this manner, the entire work force can be studied. If, on the other hand, they are in fact using sprayers as study subjects and ~~tappers~~ and general workers as controls, both groups should be selected randomly after matching for age, sex and race. Is there a large enough workforce to do this? Selecting-out persons with certain diseases of known non-occupational etiology is biasing the results unless this is carried-out in both the study and control groups (I personally don't agree with this technique because in many cases it may be impossible to differentiate).

- ✓3. I take it the whole purpose for carrying-out measurements of paraquat exposure (dermal and inhalation) is to establish (quantify) total exposure for each sprayer. Will this exposure data be used in the analysis in terms of establishing dose-response relationships or is it purely to document exposure to paraquat? Why not sample both groups of controls?

4. The proposed questionnaire is poorly designed. First of all, a specified minimum exposure (person-hours) should be set before inclusion into the study cohort (otherwise many sprayers could be included with only minimal exposure). The information on previous employment tells nothing about exposure to other pesticides or chemicals. Why is information on pesticide exposure only ascertained on the sprayers? Medical history data should be obtained from medical records - you can't rely on the person to supply this info - especially with any high degree of credibility. Also, as I pointed out before, a cross-sectional design is studying disease at a certain point in time, therefore the dates of occurrence of disease can only be considered for study if they occur within this time frame. If someone had a liver or lung problem prior to the study, and has since recovered, he should not be included in the calculation of disease rates.

✓ 5. What statistical tests are to be applied to the data?

✓ 6. No consideration for differences in smoking habits