

Trichloroethylene (TCE):

Comments before the EPA Science Advisory Board TCE Panel

During the Conference Call, September 13, 2010

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Good afternoon. The Panel is to be congratulated for dealing so well with an enormous report in a few brief sessions. I will address two topics today:

The Panel has, effectively, accepted that the Lash estimate of DCVG production in humans is flawed by steering EPA away from giving priority to results that require extrapolation from rodent kidney to man. The suggestion is made that the Lash-Green contrast should be handled “transparently”. We consider that the advice should be stronger and that the Lash estimate should be dropped from practical consideration. The Panel focused on the nature of the analytical techniques. Because, as explained by Prof. Dekant, the problem is peak recognition in the Lash HPLC technique, the measurements are technician- and occasion-specific. For this reason, fresh side-by-side comparison of methods in the lab will not determine the validity of the Lash measurements. A repeat of human volunteer work with improved analytical techniques would take too much time, if it can be done at all. Beyond the simple contrast of analytical procedures, there are reasons to believe that the Lash results are incorrect. For DCVG to be produced in such high amounts in man relative to rat, human liver biochemistry would have to be radically different from that in rat – in reality, biochemical evidence from several sources suggests less DCVG will be produced in man. Urinary output of detoxified downstream products of DCVG in man is low and lower than observed for rats. If the high blood level of DCVG is real, the human kidney would have to have much greater ability to activate and retain DCVG-derived products – again, the biochemistry from several sources indicates that man has a lower capacity to activate DCVG/DCVC than the rat. Thus the Lash results for DCVG levels in humans are highly implausible and a rational explanation for their inaccuracy is found in flawed analytical evaluations. If inter-species extrapolations can be based on the estimates of DCVG production from Green data, so much the better, otherwise an “administered dose” approach might be required. There is no reason for EPA to show the results of extrapolations from rat to man based on the Lash DCVG data.

The Panel emphasizes that the cancer slope factors based on the Charbotel epidemiology study should be given priority. The exposure assessment in that study is a critical element in the development of the cancer slope factors and it should be recognized that the assessment was originally developed to put the subjects into exposure categories and not provide precise estimates for quantitative risk assessment. The NRC TCE Panel report of 2006 advised against the use of epidemiology studies because of the uncertainties of exposure assessments – that warning may also apply to the Charbotel study. Reviewers of the draft report of the Charbotel study (final report listed in the EPA current draft assessment as Charbotel et al 2005) expressed concerns regarding the exposure assessment. Some of those concerns were addressed, but some remain. A reviewer stated that the “...allocation of exposure scores to all 295 job episodes

appears to be overly precise,” and there were concerns about the accuracy of exposure estimates for non-screw cutters. The concern is not whether the exposure study was suitable for application within the epidemiology study, but whether it is sufficiently robust to carry the enormous regulatory burden that the cancer slope factors represent. We would like to see a recommendation that EPA test the robustness of the exposure assessment, perhaps through a sensitivity analysis. We also wonder what effect potential confounding by exposure to cutting oils (and/or other confounding factors) might have on calculations of cancer slope factor – again, a sensitivity analysis might help clarify this.