Relative Doses of 2,3,7,8-Tetrachlorodibenzo-p-dioxin (TCDD)
Using Alternative Dosimetrics:
Comparison of the the NIOSH and Ranch Hand Populations

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Abstract
We present an analysis and extrapolation of the serum sampling data for the NIOSH and
Ranch Hand populations using area-under-the-curve (AUC) of serum lipid TCDD concentration
and peak and average serum lipid TCDD concentration. Compared to the NIOSH cohort, Ranch
Hand members have experienced much lower biological exposures to TCDD, with many of the
Ranch Hand members demonstrating TCDD exposures indistinguishable from background.
Cancer epidemiology from the two populations is discussed in light of the relative exposure
information.

Introduction
We previously presented a comparative analysis of the cancer dose-response for TCDD­
induced carcinogenesis in rats and in workers in the NIOSH cohort of occupationally exposed
persons using dosimetrics based upon the area-under-the-curve (AUC) of serum dioxin.¹ The
NIOSH cohort exhibited elevations in mortality from all cancers combined and for respiratory
cancers. In order to add to our understanding of the carcinogenic dose-response for TCDD in
humans, we are extending this analysis to data for two additional exposed populations: the
United States Air Force "Ranch Hand" population and a subset of the Seveso population. We
describe our preliminary analysis of the Ranch Hand data in this paper.

Methods
Members of the United States Air Force who served in Vietnam in units spraying
herbicides (Ranch Hands) were exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin and carry elevated
body burdens of TCDD compared to the general population.² The health status and mortality
rates of the Ranch Hands compared to a control population of Air Force personnel who served in
southeast Asia in the same time period are being tracked in an ongoing study using periodic
medical examinations and mortality ascertainment.

We analyzed the biological dose of TCDD in this population using three biologically-
based dosimetrics: peak serum lipid TCDD concentration (C_peak), lifetime area-under-the-curve
(AUC), and lifetime average calculated using measured concentrations. The Ranch Hand population and C_peak were calculated for each individual using a three-part concentration model.

Briefly, the measured level at time of last exposure for elimination at 50% of body weight per
day for TCDD exposure, regardless of subgroup. The most recent December 31, 1993 was
December 31, 1993 for the nonfliers. Because this number of cancer deaths noted that more than 20

Results and Discussion
Figures 1A, B are respectively, for the four groups. Table I present the Ranch Hand data. Table I
presents the number of cancer deaths noted that more than 20

Acknowledgements
This work was: Manufacturers Associa
Ranch Hand data.

References
(1) Aylward, L.L.; 1996, 30, 3534
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References

Acknowledgements
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Results and Discussion
Figures 1A, B and C present the distribution of the calculated AUC, C_{peak}, and C_{avg}, respectively, for the four Ranch Hand subgroups compared to the NIOSH exposure duration groups. Table I presents the SMRs for all cancer mortality for the Ranch Hand population as a whole and for the subgroups described above from the most recent analysis.

The all-cancer SMR was elevated only in the nonflying officer group, but this elevation was based on a single death from cancer. Compared to the NIOSH cohort, the Ranch Hand population experienced much lower TCDD exposure, regardless of dose measure used; many of the Ranch Hand cohort appear to have experienced TCDD exposures that are indistinguishable from background. This low exposure and the low number of deaths experienced to date due to cancer make a quantitative cancer dose-response comparison between these two groups of little value.

Briefly, the measured serum level from 1987 was back-extrapolated to an estimated peak level at time of last exposure (end of last tour of duty in the Ranch Hand unit) using a 7.5 year half-life for elimination and simple first-order kinetics. We assumed a constant rate of exposure for each individual during the tour(s) of duty sufficient to result in the estimated peak. Finally, we assumed that serum levels before exposure were constant at 5 ppt. These assumptions resulted in a three-part concentration time curve (time before, during, and after exposure) which we used to estimate AUC, C_{peak}, and C_{avg} for each individual. If the measured serum level from the 1987 sample was below 10 ppt, the individual was assumed to have had a constant serum level of 5 ppt through his entire life. This assumption may have underestimated exposure for some individuals, while overestimating exposure for others.

The most recent mortality analysis for the Ranch Hand cohort includes follow-up through December 31, 1993. The mortality data in this study are reported for the Ranch Hands as a group and for subgroups defined by rank (officer, enlisted) and military occupation (flyer, nonflyer). Because this is a relatively young population (average age 58 in 1993), the expected number of cancer deaths are low. Although the average age of this population is low, it should be noted that more than 20 years have passed since last exposure for nearly the entire cohort.

References
Dioxin '97, Indianapolis, Indiana, USA

Table 1: All cancer SMRs and 95% confidence intervals for Ranch Hands (mortality through Dec. 31, 1993)3)

<table>
<thead>
<tr>
<th>Exposure Group</th>
<th>All Cancer SMR (Obs/Expected)</th>
<th>95% C.I.</th>
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<tbody>
<tr>
<td>Flying officer</td>
<td>87 (10/11.48)</td>
<td>44-155</td>
</tr>
<tr>
<td>Flying enlisted</td>
<td>102 (8/7.85)</td>
<td>47-194</td>
</tr>
<tr>
<td>Nonflying officer</td>
<td>173 (1/0.58)</td>
<td>9-850</td>
</tr>
<tr>
<td>Nonflying enlisted</td>
<td>83 (11/13.32)</td>
<td>44-155</td>
</tr>
<tr>
<td>All Ranch Hands</td>
<td>90 (30/33.22)</td>
<td>58-125</td>
</tr>
</tbody>
</table>

Figure 1: Box plot comparing Ranch Hand populations, by exposure group, to expected values. Bars correspond to exposure designation (flying, nonflying), rank (officer, enlisted), and flight status (FL, nonFL). SMR's for officers, nonflying officers, nonflying enlisted, and all Ranch Hands are shown.

Figure B: Estimated lifetime area under the peak serum lipid TCDD concentration curve for Ranch Hands.
Figure 1: Box plot comparisons of serum lipid TCDD dosimetrics for the NIOSH and Ranch Hand populations, by exposure duration for the NIOSH cohort (groups N1, N2, N3, and N4 correspond to exposure durations of <1, 1 to <5, 5 to <15, and ≥ 15 years, respectively) and by rank and flight status for Ranch Hands (groups RH12, RH3, RH4, and RH5 correspond to flying officers, nonflying officers, flying enlisted, and nonflying enlisted, respectively). Figure A: Estimated lifetime area under the curve (AUC) of serum lipid TCDD concentration (ppt-ys). Figure B: Estimated lifetime average serum lipid TCDD concentration (ppt). Figure C: Estimated peak serum lipid TCDD concentration (ppt).