INTERNATIONAL LEAD ZINC RESEARCH ORGANIZATION, INC.

POST OFFICE BOX 12036
RESEARCH TRIANGLE PARK, N.C. 27709-2036
TELEPHONE: (919) 361-4647
FACSIMILE: (919) 361-1957

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Dr. C.W. Jameson
National Toxicology Program
Report on Carcinogens
MD EC-14
P.O. Box 12233
Research Triangle Park, NC 27709

Dear Dr. Jameson:

This brief note is submitted in response to the November 6, 2003 Federal Register summary of seven nominations proposed for listing in the Report on Carcinogens, 11th Edition. Lead and lead compounds were reviewed for listing and the NTP Board Subcommittee subsequently recommended listing as "reasonably anticipated to be human carcinogens" by a unanimous vote of 11 to 0.

ILZRO has filed comments regarding carcinogenicity studies of lead on several occasions in recent years. Our detailed review of the extensive literature available will not be repeated here. In essence, several soluble lead compounds have produced neoplastic lesions in rats and mice. Human epidemiology studies have generally been negative, with occasional reports of modest tumor excesses at various sites. Suggestions of excess human cancer have lacked consistency and statistical associations are usually not strengthened by considerations of exposure duration or intensity. The nature of this profile is such that a causal relationship between lead exposure and human cancer is doubtful. Indeed, in a limited number of lead cohort mortality studies, adequate information has been available for evaluation of potential confounder impact (e.g. ethnicity or arsenic exposure) upon patterns of cancer mortality via case control strategies. These latter studies have consistently suggested that occasional observations of cancer excess are related to confounder impacts and not to lead exposure.

Within the context of the listing criteria for the report on carcinogens, there is sufficient evidence of effects in laboratory animals, but little evidence of carcinogenicity in humans. On a mechanistic basis it is further doubtful that responses observed in laboratory animals are applicable to humans. Although ILZRO doubts that lead poses any risk of carcinogenicity for humans, the proposed listing as "reasonably anticipated to be human carcinogens" is the listing category utilized by NTP that is most concordant with the available data.

Whereas earlier internal review group deliberations suggested that "known to be human carcinogens" might be appropriate, these evaluations demonstrated a progressive shift away from listing as a known human carcinogen with subsequent review sessions. ILZRO notes that the external non-government subcommittee that recommended listing as "reasonably anticipated"

included individuals with extensive expertise in both epidemiological methods and metals toxicology. The unanimous recommendation of this Board Subcommittee is, accordingly, significant.

Please do not hesitate to contact me should you have questions or comments regarding this brief submission.

Best regards,

Craig J. Boreiko, Ph.D.
Manager, Environment and Health

CJB:acw