Animal Study Pre-screening Form

Reference:	Newland, M.C., Warfvinge, K., and M. Berlin. 1996. Behavioural consequences of *in utero* exposure to mercury vapour: Alterations in lever-press durations and learning in squirrel monkeys. *Toxicol. Appl. Pharmacol.* **139**(2): 374 – 386.

Primary Criteria	**(Y/N)**	**Comments**
Primary literature	Y	Complete study described.
Inhalation exposure	Y	Pregnant squirrel monkeys exposed to mercury vapor.
Dose groups defined	Y	Exposed to 0.5 or 1.0 mg/m^3 of mercury vapor for 4 or 7 hr/day, 5 days/week during gestation. Exposure calculated at 20 to 62 μg/day.
Negative Control(s) Used	Y	Unexposed monkeys born at about the same time served as controls.
Endpoint relevance (renal/neuro/immuno)	Y	Behavioural neurotoxicity.

Secondary Criteria	**(Y/N)**	**Comments**
Study objectives clearly defined	Y	The study was designed to investigate the behavioural neurotoxicity of *in utero* exposure to mercury vapor.
Study method described	Y	Study method is well described for measuring behavioural responses. Articles refers to Warfvinge et al. (1994) for additional details on exposure.
Exposure characteristics described (groups, number of subjects, duration and level)	Y	Six monkeys were exposed to 0.5 or 1.0 mg/m^3 of mercury vapor for 4 or 7 hr/day, 5 days/week during gestation. Exposure calculated at 20 to 62 μg/day. Five monkeys served as controls.
Effect Level Identified or Positive Control Used	N	Presence of an effect was identified but not enough information was available to identify a dose-response relationship. No NOAEL was identified.
Statistical analysis conducted	Y	

Results of Prescreen	**(Y/N)**	**Comments**
Inclusion in Critical Review	N	A dose-response relationship or a NOAEL could not be identified from this study.

Epidemiological Study Pre-screening Form

Reference:	Netterstrom, B., Guldager, B., and J. Heeboll. 1996. Acute mercury intoxication examined with coordination ability and tremor. *Neurotoxicology and Teratology*. **18**(4): 505-509.

Primary Criteria	**(Y/N)**	**Comments**
Primary literature	Y	Complete study described.
Inhalation exposure	Y	Occupationally exposed to Hg vapour.
Exposure Identified Note: May be specific (e.g. concentration and duration of exposure measured for each individual) or more general (e.g. range of exposure, low vs. high).	Y	Workers were exposed to Hg vapour concentrations of up to 0.15 mg/m^3 with no defined duration. Urine [Hg] ranged from 25 - 249 nmol/L two weeks after exposure.
Endpoint relevance (renal/neuro/immuno)	Y	Neurological: examines coordination and tremor.

Secondary Criteria	**(Y/N)**	**Comments**
Study objectives clearly defined	Y	The objectives included the evaluation of two test methods as appropriate assessment in acute Hg intoxication.
Study method described	Y	Study methodology is well described.
Control(s) Used	Y	An unexposed control group (n=15), matched for age, sex and occupation was used.
Exposure characteristics described (groups, number of subjects, duration and level)	Y	Male workers were exposed to Hg vapours after a mercury spill. The duration is not defined, other than that is was over a few days. Workers were examined 2 weeks, 3 months and 16 months after exposure and divided into high (n=7) and low (n=7) exposed groups with an original range of [Hg] in urine of 49.5 - 249 and 25 - 49.5 nmol/L, respectively.
Statistical analysis conducted	Y	Statistical methods were not reported. Study relied heavily on standard deviation.

Results of Prescreen	**(Y/N)**	**Comments**
Inclusion in Critical Review	Y	This study can be considered in the critical review. However, it will need to be considered that the exposure was subacute.

Epidemiological Study Pre-screening Form

Reference:	Moszczynski, P., Slowinski, S., Rutkowski, J., Bem, S., and D. Jakus-Stoga. 1995. Lymphocites, T and NK cells, in men occupationally exposed to mercury vapours. *Int. J. Occup. Med. Environ. Health.* **8**(1): 49-56.

Primary Criteria	**(Y/N)**	**Comments**
Primary literature	Y	
Inhalation exposure	Y	
Exposure Identified Note: May be specific (e.g. concentration and duration of exposure measured for each individual) or more general (e.g. range of exposure, low vs. high).	Y	81 males occupationally exposed to Hgo for under or over a period of 10 years. Urine and blood Hg concentrations ranged from 0 - 240 µg/L and 0 - 30 µg/L, respectively.
Endpoint relevance (renal/neuro/immuno)	Y	Immunological

Secondary Criteria	**(Y/N)**	**Comments**
Study objectives clearly defined	Y	Comparison of lymphocytes, T and NK cell counts in occupationally exposed males to those of non-exposed.
Study method described	Y	Methodology described.
Control(s) Used	Y	36 non-exposed males
Exposure characteristics described (groups, number of subjects, duration and level)		Exposed were divided into two groups: exposure duration of under 10 years (mean 3.35 +/- 1.77) and exposure duration of 10 to 31 years (mean 19.9 +/- 5.8).
Statistical analysis conducted	Y	Shapiro-Wilk Caussian decomposition test, ANOVA, Cochran-Cox test and Student's t-test.

Results of Prescreen	**(Y/N)**	**Comments**
Inclusion in Critical Review	Y	Endpoint and exposure relevant.

Epidemiological Study Pre-screening Form

Reference:	Mathiesen, T., Ellingsen, D.G., and H. Kjuus. 1999. Neuropsychological effects associated with expsoure to mercury vapor among former chloralkali workers. *Scand. J. Work Environ. Health.* **25**(4): 342-350.

Primary Criteria	**(Y/N)**	**Comments**
Primary literature	Y	
Inhalation exposure	Y	
Exposure Identified Note: May be specific (e.g. concentration and duration of exposure measured for each individual) or more general (e.g. range of exposure, low vs. high).	Y	Chronic occupational expsosure to Hg^o vapour. The mean exposure time was 7.9 years, with an annual mean urinary Hg concentration of 539 (41 - 2921) nmol/L year.
Endpoint relevance (renal/neuro/immuno)	Y	Neuropsychological - cognitive function, motor and psychomotor function, attention, memory and learning.

Secondary Criteria	**(Y/N)**	**Comments**
Study objectives clearly defined	Y	To investigate possible neuropsychological effects associated among fromer chloralkali workers with past exposure to Hg^o vapour.
Study method described	Y	Methodology well described.
Control(s) Used	Y	52 referents frequency matched for age.
Exposure characteristics described (groups, number of subjects, duration and level)	Y	75 formerly exposed workers. The mean time since exposure cessation was 12.7 (1 - 35) years. See above.
Statistical analysis conducted	Y	ANOVA. Significance was set at 0.05.

Results of Prescreen	**(Y/N)**	**Comments**
Inclusion in Critical Review	Y	Exposure and endpoints relevant.

Epidemiological Study Pre-screening Form

Reference:	Lim, H.E., Shim, J.J., Lee, S.Y., Lee, S.H., Kang, S.Y., Jo, J.Y., In. K. H., Kim, H.G., Yoo, S.H., and K.H. Kang. 1998. Mercury inhalation poisoning and acute lung injury. *Korean Journal of Internal Medicine.* **13**(2):127-130.

Primary Criteria	**(Y/N)**	**Comments**
Primary literature	Y	Case study.
Inhalation exposure	Y	
Exposure Identified Note: May be specific (e.g. concentration and duration of exposure measured for each individual) or more general (e.g. range of exposure, low vs. high).	Y	Acute exposure to Hg^o vapour.
Endpoint relevance (renal/neuro/immuno)	Y	Neurological

Secondary Criteria	**(Y/N)**	**Comments**
Study objectives clearly defined	N	Presentation of a case study.
Study method described	N	
Control(s) Used	N	
Exposure characteristics described (groups, number of subjects, duration and level)	N	One 72 year old male acutely exposed. Urine Hg concentrations were measured on addmitance to the hospital (6402 µg/L) and 7 days later (25 µg/L).
Statistical analysis conducted	N	Presentation of a case study.

Results of Prescreen	**(Y/N)**	**Comments**
Inclusion in Critical Review	N	The high, acute exposure identified in this case study is not appropriate for the establishment of a RfC.

Epidemiological Study Pre-screening Form

Reference:	Kobal, A.B., Flisar, Z., Miklavcic, V., Dizdarevic, T., and A., Sesek-Briski. 2000. Renal function in miners intermittently exposed to elemental mercury vapour. *Arh. Hig. Rada. Toksikol.* **51**: 369-380.

Primary Criteria	**(Y/N)**	**Comments**
Primary literature	Y	
Inhalation exposure	Y	
Exposure Identified Note: May be specific (e.g. concentration and duration of exposure measured for each individual) or more general (e.g. range of exposure, low vs. high).	Y	TWAs averaged 0.36 (0.05-0.73) mg/m^3. Mean duration of exposure was 37 days (range 6-82 days).
Endpoint relevance (renal/neuro/immuno)	Y	Renal (biochemical).

Secondary Criteria	**(Y/N)**	**Comments**
Study objectives clearly defined	Y	Evaluation of the potential renal damage under conditions of relatively short and low-level occupational exposure to Hg^o vapour.
Study method described	Y	Methodology well described.
Control(s) Used	Y	Note: urinary Hg concentrations were measured before and after exposure; not a separate group of workers.
Exposure characteristics described (groups, number of subjects, duration and level)		45 workers were occupationally exposed to Hg vapours (see above exposure). Urinary proteins and Hg concentrations were measured before (mean 18.5 µg/g creatinine) and after (69.9 µg/g creatinine) exposures.
Statistical analysis conducted	Y	x2 test, t-test, Pearson's correlation coefficient and ANOVA.

Results of Prescreen	**(Y/N)**	**Comments**
Inclusion in Critical Review	Y	Endpoint and exposure relevant.

Animal Study Pre-screening Form

Reference:	Jonker, D., Jones, M.A., van Bladeren, P.J., Woutersen, R.A., Til, H.P. and V.J. Feron. 1993. Acute (24 hr) toxicity of a combination of four nephrotoxicants in rats compared with the toxicity of the individual compounds. *Food Chemical Toxicol.* **31**(1): 45 - 52.

Primary Criteria	**(Y/N)**	**Comments**
Primary literature	Y	Complete study described.
Inhalation exposure	N	Exposure by oral gavage.
Dose groups defined	Y	
Negative Control(s) Used	Y	
Endpoint relevance (renal/neuro/immuno)	Y	

Secondary Criteria	**(Y/N)**	**Comments**
Study objectives clearly defined		
Study method described		
Exposure characteristics described (groups, number of subjects, duration and level)		
Effect Level Identified or Positive Control Used		
Statistical analysis conducted		

Results of Prescreen	**(Y/N)**	**Comments**
Inclusion in Critical Review	N	This study is not recommended for inclusion in the critical review as administration was by oral gavage and the form of mercury used was mercuric chloride.

Epidemiological Study Pre-screening Form

Reference:	Hsu, L.F., Lee, H.S., Chia, S.E., and K.N. Sin Fai Lam. 1999. Acute mercury poisoning in a shipyard worker - a case report. *Ann. Acad. Med. Singapore.* **28**(2): 294-298.

Primary Criteria	**(Y/N)**	**Comments**
Primary literature	Y	Presentation of a case study.
Inhalation exposure	Y	
Exposure Identified Note: May be specific (e.g. concentration and duration of exposure measured for each individual) or more general (e.g. range of exposure, low vs. high).	Y	Acute occupational exposure to Hg^o vapour.
Endpoint relevance (renal/neuro/immuno)	Y	Neurological

Secondary Criteria	**(Y/N)**	**Comments**
Study objectives clearly defined	N	Presentation of a clinical case study.
Study method described	N	
Control(s) Used	N	
Exposure characteristics described (groups, number of subjects, duration and level)	Y	48 year old man admitted to hospital 24 hours after exposure. Urine Hg concentration was 284.8 and 63.3 µg/L several days and 18 days after exposure, respectively.
Statistical analysis conducted	N	

Results of Prescreen	**(Y/N)**	**Comments**
Inclusion in Critical Review	N	The high acute exposure addressed in this case study is not appropriate for the development of a RfC.

Epidemiological Study Pre-screening Form

Reference:	Ho, B.S.J., Lin, J.L., Huang, C.C., Tsai, Y.H., and M.C. Lin. 2003. Mercury vapour inhalation from Chinese Red (Cinnabar). *J. Toxicol. Clin. Toxicol.* **41**(1): 75-78.

Primary Criteria	**(Y/N)**	**Comments**
Primary literature	Y	Presentation of a case study.
Inhalation exposure	Y	
Exposure Identified Note: May be specific (e.g. concentration and duration of exposure measured for each individual) or more general (e.g. range of exposure, low vs. high).	N	Air, blood or urine concentrations were not identified.
Endpoint relevance (renal/neuro/immuno)	N	Pulmonary

Secondary Criteria	**(Y/N)**	**Comments**
Study objectives clearly defined		
Study method described		
Control(s) Used		
Exposure characteristics described (groups, number of subjects, duration and level)		
Statistical analysis conducted		

Results of Prescreen	**(Y/N)**	**Comments**
Inclusion in Critical Review	N	Endpoint not relevant and exposure not identified.

Epidemiological Study Pre-screening Form

Reference:	Haut, M.W., Morrow, L.A., Pool, D., Callahan, T.S., Haut, J.S., and M.D. Franzen. 1999. Neurobehavioral effects of acute exposure to inorganic mercury vapor. *Appl. Neuropsychol.* **4**: 193-200.

Primary Criteria	**(Y/N)**	**Comments**
Primary literature	Y	
Inhalation exposure	Y	
Exposure Identified Note: May be specific (e.g. concentration and duration of exposure measured for each individual) or more general (e.g. range of exposure, low vs. high).	Y	Occupational Hg^o vapour exposure over a 2-4 week period. Air Hg^o concentration to which the workers were exposed was up to 80 $\mu g/m^3$.
Endpoint relevance (renal/neuro/immuno)	Y	Neurological - neuropsychological test battery.

Secondary Criteria	**(Y/N)**	**Comments**
Study objectives clearly defined	Y	Examination of the neuropsycological performance of 13 individuals with mercury exposure of 2-4 weeks.
Study method described	Y	Methodology well described.
Control(s) Used	Y	13 non-exposed males matched for age and education.
Exposure characteristics described (groups, number of subjects, duration and level)	Y	13 males occupationally exposed. Urine Hg levels ranged from 21-84 µg/L. See above exposure for more information.
Statistical analysis conducted	Y	Multivariate analyses, omnibus and univariate F.

Results of Prescreen	**(Y/N)**	**Comments**
Inclusion in Critical Review	Y	Exposure and endpoints are relevant.

Epidemiological Study Pre-screening Form

Reference:	Frumkin, H., Letz, R., Williams, P.L., Gerr, F., Pierce, M., Sanders, A., Elon, L., Manning, C.C., Woods, J.S., Hertzberg, V.S., Mueller, P. and B. Brooks Taylor. 2001. Health effects of long-term mercury exposure among chloralkali plant workers. *Am J Indust Med* **39**: 1-18.

Primary Criteria	**(Y/N)**	**Comments**
Primary literature	Y	
Inhalation exposure	Y	
Exposure Identified Note: May be specific (e.g. concentration and duration of exposure measured for each individual) or more general (e.g. range of exposure, low vs. high).	Y	Workers occupationally exposed to Hg^0 for a duration of at least one year in a chloralkali plant within the period spanning 1956-1994. Mean cumulative and maximum exposure assessed.
Endpoint relevance (renal/neuro/immuno)	Y	Renal and neurological effects

Secondary Criteria	**(Y/N)**	**Comments**
Study objectives clearly defined	Y	The purpose of this study was to test the association between mercury and neurological, renal and reproductive effects, and to assess the utility of chelation/dimercaptosuccinic acid administration as a biomarker for chronic mercury exposure.
Study method described	Y	Methodology well described.
Control(s) Used	Y	Controls selected from nearby plants and stratified for age, sex and race.
Exposure characteristics described (groups, number of subjects, duration and level)	Y	Workers occupationally exposed to Hg^0 for a duration of at least one year in a chloralkali plant within the period spanning 1956-1994. Mean cumulative and maximum exposure assessed.
Statistical analysis conducted	Y	Spearmans coefficient analysis, chi square, Fisher's exact test, polytomous logistic regression, Hosmer-Lemeshow, Bonferroni

Results of Prescreen	**(Y/N)**	**Comments**
Inclusion in Critical Review	Y	Endpoints and exposure relevant. Also examines reproductive effects.

Animal Study Pre-screening Form

Reference:	Fredriksson, A., Dencker, L., Archer, T., and B.R.G. Danielsson. 1996. Prenatal coexposure to metallic mercury vapour and methylmercury produce interactive behavioural changes in adult rats. *Neurotoxicol. Teratol.* **18**(2): 129 – 134

Primary Criteria	**(Y/N)**	**Comments**
Primary literature	Y	Complete study described.
Inhalation exposure	Y	Preganant rats exposed to metallic mercury vapour.
Dose groups defined	Y	Only one dose level adiministered (0.1 mg Hg°/kg/day).
Negative Control(s) Used	Y	Control group placed in exposure chamber without Hg° vapour.
Endpoint relevance (renal/neuro/immuno)	Y	Behavioural effects were measured as an indication of effects on the nervous system during development.

Secondary Criteria	**(Y/N)**	**Comments**
Study objectives clearly defined	Y	The purpose of the study was to examine a possible additive effect of coexposure to Hg° and a relatively low dose of MeHg on the developing central nervous system.
Study method described	Y	The study method is well described.
Exposure characteristics described (groups, number of subjects, duration and level)	Y	Four groups of pregnant rats, 12 animals per group, were exposed as follows: 1) MeHg group received oral doses of MeHg (2 mg/kg/day) over gestation days 6-9 and vehicle treatment during days 14-19; 2) Hg° vapour group exposed by inhalation to 1.8 mg/m^3 for 1.5 h/day during gestation days 14-19 and vehicle treatment during days 6-9; 3) MeHg and Hg coexposure group received oral doses of MeHg (2 mg/kg/day) over gestation days 6-9 and Hg° vapour by inhalation at 1.8 mg/m3 for 1.5 h/day during gestation days 14-19; and, 4) control group received vehicle treatment during days 6-9 and placement in exposure chamber for 1.5 h/day during gestation days 14-19.
Effect Level Identified or Positive Control Used	N	Only one exposure level was administered which resulted in behavioural effects. As such, a NOAEL or LOAEL cannot be identified.
Statistical analysis conducted	Y	ANOVA and Tukey HSD tests used with a 1% level of significance.

Screening by: Cindy Smith, GTIC
Date Screened: February 5, 2004

Results of Prescreen	(Y/N)	Comments
Inclusion in Critical Review	N	Although this study addresses the effects of Hg°, it only used one dose level. The main objective of the study was to assess the possible additive effect of Hg and MeHg coexposure. Given that a NOAEL or LOAEL cannot be identified, this study is not recommended for inclusion in the critical review.

Screening by: Cindy Smith, GTIC
Date Screened: February 5, 2004