Epidemiological Study Pre-screening Form

Reference:	Ellingsen, D.G., Bast-Pettersen, R., Efskind, J., and Y. Thomassen. 2001. Neurospychological effects of low mercury vapor exposure in chloralkali workers. *Neurotoxicology.* **22**: 249-258.

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 exposure to Hg^o vapour. Duration averaged 13.3 years with a calculated mean concentration of urinary Hg was 9.0 (range: 4.0 - 19.6) nmol/mmol creatinine per year.
Endpoint relevance (renal/neuro/immuno)	Y	Neurological

Secondary Criteria	**(Y/N)**	**Comments**
Study objectives clearly defined	Y	To study the effects on the CNS of chloralkali workers with long-term low level exposure to Hg^o by the use of neuropsychological methods.
Study method described	Y	Methodology well described.
Control(s) Used	Y	47 male referents.
Exposure characteristics described (groups, number of subjects, duration and level)	Y	47 male chloralkali workers exposed to Hg^o vapour for 2.8-34.5 years. Mean cumulative exposure was 123.2 14.5-490.6) nmol/mmol creatinine.
Statistical analysis conducted	Y	ANOVA and multiple linear regression analysis.

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

Epidemiological Study Pre-screening Form

Reference:	Ellingsen, D.G., Efskind, J., Berg, K.N., Gaarder, P.I. , and Y. Thomassen. 2000. *Scand J Work Environ Health* **26**(5): 427-435.

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° in a defined area of a plant for a duration of at least 1-year were assessed.
Endpoint relevance (renal/neuro/immuno)	Y	Renal and immunological endpoints assessed.

Secondary Criteria	**(Y/N)**	**Comments**
Study objectives clearly defined	Y	The purpose of this study was to examine the effect of low-level, long-term exposure to Hg° vapour on renal function and immunologic markers.
Study method described	Y	Methodology well described.
Control(s) Used	Y	Controls were matched with exposed subjects for age.
Exposure characteristics described (groups, number of subjects, duration and level)	Y	47 chronically exposed workers were assessed over 2-days for renal and immunologic biomarkers.
Statistical analysis conducted	Y	Levenes test, ANOVA, factorial analysis

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

Epidemiological Study Pre-screening Form

Reference:	Ellingsen, D.G., Gaarder, P.I., and H. Kjuus. 1994. An immunological study of chloralkali workers previously exposed to mercury vapour. *Apmis* . **102**:170-176.

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 exposure of 77 chloralkali workers to Hg^o vapour. Details regarding exposure (measured uninary Hg) are published in a previous paper.
Endpoint relevance (renal/neuro/immuno)	Y	Immunological

Secondary Criteria	**(Y/N)**	**Comments**
Study objectives clearly defined	Y	Study part of a comprehensive investigation into the adverse health effects of previous Hg^o exposure among former chloralkali workers.
Study method described	Y	Study methodology well described. Design referenced.
Control(s) Used	Y	53 age-matched referents.
Exposure characteristics described (groups, number of subjects, duration and level)	Y	77 male chloralkali workers previously exposed to Hg vapour for a mean duration of 7.9 years (range 1.1 - 36.2) and the exposure had ceased on average 12.3 years (range 1.0 - 35.0) prior to examination. Exposure maximum was greater than 3000 nmol/L cummulative urinary Hg.
Statistical analysis conducted	Y	Mann-Whitney test to assess intergroup differences, Spearman's rank correlation test, Fisher's test were used.

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

Epidemiological Study Pre-screening Form

Reference:	Echeverria, D., Aposhian, H.V., Woods, J.S., Heyer, N.J., Aposhian, M.M., Bittner, A.C.Jr., Mahurin, R.K., and M. Cianciola. 1998. Neurobehavioural effects from exposure to dental amalgam Hg(0): New distinctions between recent exposure and Hg body burden. *FASEB* **12**(11): 971 – 980.

Primary Criteria	**(Y/N)**	**Comments**
Primary literature	Y	Complete study described.
Inhalation exposure	Y	Exposure to Hg^o vapour from application of dental amalgam fillings.
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	Exposure measured by Hg^o urine concentrations for recent exposure and body burden. All subjects had very low Hg^o concentrations (<50 µg/L). Duration of exposure is not identified.
Endpoint relevance (renal/neuro/immuno)	Y	Neuro: evaluation of symptoms, mood, motor function and cognition.

Secondary Criteria	**(Y/N)**	**Comments**
Study objectives clearly defined	Y	Dentists and dental assistants (49 total) were exposed to relatively low concentrations of Hg^o vapor through working with dental amalgam fillings. Chelation was used to evaluate CNS functions in relation to both recent exposure and Hg body burden.
Study method described	Y	The study methodology is well described.
Control(s) Used	N	Only investigated pre and postchelation of the 49 subjects.
Exposure characteristics described (groups, number of subjects, duration and level)	Y	34 practicing dentists and 15 dental assistants were studied. Exposure was based on Hg^o urine concentration, both before and after chelation with DMPS to represent recent exposure and body burden, respectively.
Statistical analysis conducted	Y	Multiple regression analysis, paired t-tests and beta coefficients were used to assess relationships and significance.

Results of Prescreen	**(Y/N)**	**Comments**

Inclusion in Critical Review	Y	The study found significant dose-effect relationships with both pre and post chelation urinary Hg^o levels. A NOAEL/LOAEL may be identified as concentrations of Hg^o in urine were measured.

Epidemiological Study Pre-screening Form

Reference:	Echeverria, D., Heyer, N., Martin, M., Naleway, C., Woods, J. and A. Bittner. 1995. Behavioral effects of low-level exposure to elemental Hg° among dentists. Neurotoxicol. Teratol. 17:161-168.

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	Recent exposure identifed through urinary mercury concentrations. Chronic measures of exposure included porphyrin concentrations in urine and work histories.
Endpoint relevance (renal/neuro/immuno)	Y	Neurological effects determined through behavioural tests.

Secondary Criteria	**(Y/N)**	**Comments**
Study objectives clearly defined	Y	An evaluation among dentists of sensitive measures of effect (symptoms, mood and behaviour) and measures of exposure (Hg and poryphrins in urine), in an effort to identify if potential adverse effects are associated with urinary mercury levels below 50 μg/L.
Study method described	Y	
Control(s) Used	Y	Twenty (20) dentists with nondetectable levels of mercury in their urine were used to represent an unexposed group.
Exposure characteristics described (groups, number of subjects, duration and level)	Y	Nineteen (19) dentists with urinary mercury concentrations greater than 19 μg/L represented the exposed group for the study.
Statistical analysis conducted	Y	Multivariate regression techniques were used to evaluate possible associations between recent and chronic measures of mercury exposure and adverse changes in symptoms, mood and behavioral function.

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

Epidemiological Study Pre-screening Form

Reference:	Discalzi, G., Fabbro, D., Meliga, F., Mocellini, A., and F. Capellaro. 1993. Effects of occupational exposure to mercury and lead on brainstem auditory evoked potentials. *Int. J. Psychophysiol.* **14**: 21-25.

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 exposure to Hg^{o}.
Endpoint relevance (renal/neuro/immuno)	Y	Neurological - brainstem auditory evoked potentials

Secondary Criteria	**(Y/N)**	**Comments**
Study objectives clearly defined	Y	Examination of the effects of industrial exposure to mercury (and lead) on the brainstem auditory pathway by recording brainstem auditory evoked potentials.
Study method described	Y	Methodology described.
Control(s) Used	Y	8 age matched controls (6 male) with no previous exposure to neurotoxic substances.
Exposure characteristics described (groups, number of subjects, duration and level)	Y	8 workers (6 males) exposed to Hgo with a mean duration of 11.7 years. Urinary mercury levels were taken once before test day (mean: 325 µg/g creatinine).
Statistical analysis conducted	Y	Linear regression and ANOVA.

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

Epidemiological Study Pre-screening Form

Reference:	DeRouen, T.A., Leroux, B.G., Martin, M.D., Townes, B.D., Woods, J.S., Leitao, J.L., Castro-Caldas, A., and N. Braveman. 2002. Issues in design and analysis of a randomized clinical trial to assess the safety of dental amalgam restoration in children. *Cont Clin Trial* **23**: 301-320.

Primary Criteria	**(Y/N)**	**Comments**
Primary literature	N	Paper discusses study design issues related to an on-going 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).		
Endpoint relevance (renal/neuro/immuno)		

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	Article examines design-related issues associated with an on-going study. Results not presented.

Epidemiological Study Pre-screening Form

Reference:	Chang, Y.C., Yeh, C.Y, and J.D. Wang. 1995. Subclinical neurotoxicity of mercury vapor revealed by a multimodality evoked potential study of chloralkali workers. *Am J Ind Med* **27**: 271-279.

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	Occupationally exposed workers in a chloralkali factor were examined. Exposure level determined from physiological Hg^0 levels.
Endpoint relevance (renal/neuro/immuno)	Y	Neurological effects assessed

Secondary Criteria	**(Y/N)**	**Comments**
Study objectives clearly defined	Y	The purpose of this study was to assess effects on multimodal somatosensory evoked potential (EP) in exposed workers
Study method described	Y	
Control(s) Used	Y	Controls matched to exposed subjects
Exposure characteristics described (groups, number of subjects, duration and level)	Y	Number of workers defined and divided into 'high', 'medium' and 'low' exposure groups
Statistical analysis conducted	Y	Mann-Whitney's test, ANOVA, and Scheffes procedure employed

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

Epidemiological Study Pre-screening Form

Reference:	Cardenas, A., Roels, H., Bernard, A.M., Barbon, R., Buchet, J.P., Lauwerys, R.R., Rosello, J., Hotter, G., Mutti, A., Franchini, I., Fels, L.M., Stolte, H., De Broe, M.E., Nuyts, G.D., Taylor, S.A., and R.G. Price. 1993. Markers of early renal changes induced by industrial pollutants. I. Application to workers exposed to mercury vapor. *Br J Ind Med* **50**: 17-27.

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	Exposed workers (to lead, cadmium or Hg^0) were examined. Duration of Hg^0 exposure ranged from 1.5-25 years.
Endpoint relevance (renal/neuro/immuno)	Y	Renal endpoints assessed.

Secondary Criteria	**(Y/N)**	**Comments**
Study objectives clearly defined	Y	The purpose of this study was to examine various biological markers of nephrotoxicity in several cohorts of workers.
Study method described	Y	Methodology well described.
Control(s) Used	Y	Controls were selected from unexposed areas of the same plant.
Exposure characteristics described (groups, number of subjects, duration and level)	Y	Exposure to three agents examined in three cohorts.
Statistical analysis conducted	Y	Multivariate regression analysis, Pearsons' correlation, Student's t-test, Duncan's test, 2x2 Fisher's exact test and logistic regression analyses were conducted.

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

Epidemiological Study Pre-screening Form

Reference:	Boogaard, P.J., Houtsma, A.T.A.J., Journee, H.L., and N.J. van Sittert. 1996. Effect of exposure to elemental mercury on the nervous system and the kidneys of workers producing natural gas. *Arch. Environ. Health.* **51**(2): 108-115.

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 were exposed to Hg^o vapour over a period of years. Air concentrations were measured occasionally throughout the study (10 - 1500 µg/m^3). Urine, cummulative urine mercury and blood samples were also taken.
Endpoint relevance (renal/neuro/immuno)	Y	Neurological tests and renal biochemistry.

Secondary Criteria	**(Y/N)**	**Comments**
Study objectives clearly defined	Y	1. To investigate any neurological or biochemical differences among the groups of workers. 2. To determine whether any of the neurological or renal parameters correlated with the occupational
Study method described	Y	Methodology well described.
Control(s) Used	Y	Workers from the same company.
Exposure characteristics described (groups, number of subjects, duration and level)	Y	Three groups were created based on exposure level: HIGH, LOW1 and LOW2 groups were exposed for an average of 5.7, 9.7 and 10.3 years, respectively.
Statistical analysis conducted	Y	Fisher's test, Wilcoxon's rank-sum test and multivariate regression analysis.

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

Epidemiological Study Pre-screening Form

Reference:	Bittner, A.C. Jr., Echeverria, D., Woods, J.S., Aposhian, H.V., Naleway, C., Martin, M.D., Mahurin, R.K., Heyer, N.J., and M. Cianciola. 1998. Behavioural effects of low-level exposure to Hg0 among dental professionals: A cross-study evaluation of psychomotor effects. *Neurotoxicol. Teratol.* **20**(4): 429 – 439.

Primary Criteria	**(Y/N)**	**Comments**
Primary literature	Y	Complete study described. A cross-study of six individual studies.
Inhalation exposure	Y	Exposure through dental amalgam application.
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	Exposure was measured through urine [Hg^o] and ranged from 1 - 148 µg/L. Exposure was classified as low-level and was less than or equal to 55 µg/L.
Endpoint relevance (renal/neuro/immuno)	Y	Neurological: Psychomotor test battery used to determine CNS effects.

Secondary Criteria	**(Y/N)**	**Comments**
Study objectives clearly defined	Y	The primary purpose of the study was to compare the relative sensitivities of five psychomotor tests for detection of adverse preclinical psychomotor effects attributable to low-level Hg^o exposure.
Study method described	Y	The study methodology is well described.
Control(s) Used	N	
Exposure characteristics described (groups, number of subjects, duration and level)	Y	A total of 230 dental professionals (81% male) with a mean age of 50 from 6 studies were studied. Actual exposure was not measured or estimated, only urine [Hg^o] were analysed (1 - 148 µg/L, with the majority (93%) of subjects below 55 µg/L). Exposure duration was not defined.
Statistical analysis conducted	Y	Multivariate analysis, principle factor analysis (PFA) and evaluation of patterns of correlation between the psychomotor tests employed. Statistical significance (p values) are stated in the results.

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

Epidemiological Study Pre-screening Form

Reference:	Bhattacharya, B., Banerjee, S., and S. Singhi. 1997. Acute mercury vapour poisoning in an infant. *Ann. Trop. Paediatr.* **17**:57-60.

Primary Criteria	**(Y/N)**	**Comments**
Primary literature	Y	Case study.
Inhalation exposure	Y	Acutely exposed to Hg^o 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).	N	Neither air or urine concentrations were measured.
Endpoint relevance (renal/neuro/immuno)		

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	Exposure was acute and not quantified.

Animal Study Pre-screening Form

Reference:	Batora, I., Marazova, J., Ulicna, O., Plackova, S., Kresanek, J. and E. Urbanova. 2000. Abstracts of the European Association of Poisons centres and Clinical Toxicologist XX International Congress (Intravenous elemental mercury intoxication in a drug addict). *Journal of Toxicology, Clinical Toxicology* . **38**:254.

Primary Criteria	**(Y/N)**	**Comments**
Primary literature	N	Case study abstract.
Inhalation exposure	N	Exposure is intravenous.
Dose groups defined		
Negative Control(s) Used		
Endpoint relevance (renal/neuro/immuno)		

Secondary Criteria	**(Y/N)**	**Comments**
Study objectives clearly defined		
Study method described		
Duration of exposure indicated		
Number of subjects indicated		
Effect Level Identified or Positive Control Used		
Statistical analysis conducted		

Results of Prescreen	**(Y/N)**	**Comments**
Inclusion in Critical Review	N	

Epidemiological Study Pre-screening Form

Reference:	Aydin, N., Karaoglanoglu, S., Yigit, A., Keles, M.S., Kirpinar, I., and N. Seven. 2003. Neuropsychological effects of low mercury exposure in dental staff in Erzurum, Turkey. *Int. Dent. J.* **53**: 85-91.

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	Dental staff who had worked with dental amalgam daily for an average of 10 years were assessed.
Endpoint relevance (renal/neuro/immuno)	Y	Neurological

Secondary Criteria	**(Y/N)**	**Comments**
Study objectives clearly defined	Y	Evaluate possible adverse neurological effects in dental personnel.
Study method described	Y	Methodology well described.
Control(s) Used	Y	43 age and education matched hospital employees with no known Hgo exposure.
Exposure characteristics described (groups, number of subjects, duration and level)	Y	43 Hgo vapour exposed dental staff. Blood (mean 2.18 nmol/L) and urine (mean 1.17 nmol/mmol creatinine) Hg levels were measured. Subjects were exposed everyday for an average of 10 years (range: 4-27 years).
Statistical analysis conducted	Y	T-test, Spearman's correlation coefficient and stepwise regression analysis.

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

Animal Study Pre-screening Form

Reference:	Aschner, M., Lorshceider, F.L., Cowant, K.S., Conklin, D.R., Vimy, M.J. and L.H. Lash. 1997. Metallothionein induction in fetal rat brain and neonatal primary astrocyte cultures by in utero exposure to elemental mercury vapor (Hg°). *Brain Research* . **778**: 222 - 232.

Primary Criteria	**(Y/N)**	**Comments**
Primary literature	Y	
Inhalation exposure	Y	
Dose groups defined	Y	Dams exposed to Hg° for 4 h/day at 300µg Hg°/m^3
Negative Control(s) Used	Y	
Endpoint relevance (renal/neuro/immuno)	N	This study addressed the increase of metallothioneins due to Hg° exposure for the purpose of identifying biomarkers.

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 addressed that use of MT as useful biomarkers of intrauterine exposure to Hg°.

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