

graphite furnace atomic absorption spectrometry (GFAA) with Zeman background correction as found on a Perkin-Elmer instrument model 5100. Standard laboratory tests (SMA-12, CBC, routine urinalysis) will be performed at the clinical laboratories serve the JHH-HPLC and the UM-PAC. A figure in Appendix F summarizes performance of the KKI-TML in the Centers for Disease Control's external proficiency testing program for blood lead determinations. Performance data is for analysis by anodic stripping voltammetry during the period July 1989 to September 1992.

Safety Monitoring:

We expect that safety monitoring will be a joint effort between the clinical center and the Coordinating Center. At the clinical sites the focus of the clinical monitoring will be on side effects of drug therapy and of evidence of continued exposure to environmental lead. Should the need arise (e.g. evidence of significant drug toxicity or extreme elevations of blood lead) to break the code on an individual patient, the Coordinating Center will alone have access to the treatment allocation scheme (see above) and therefore will need to provide a safety officer available on a 24-hour basis in case of emergency.

The duplicate blood leads (analyzed at KKI-TML and the central study laboratory) and other selected laboratory tests specified above will facilitate clinical monitoring and enable prompt remediation of any adverse situations that occur. Individual treatment decisions may need to be made at the clinical center on an emergency basis (see below). It will be the responsibility of the Steering Committee to define stop points for the entire study and it will be the responsibility of the Coordinating Center to monitor for circumstances that could cause the trial to be stopped prematurely.

- Removal from trial/breaking the code

It is expected that some patients will experience increasing blood lead levels during the course of the trial. This could occur when a patient continues to experience exposure to one or more sources of environmental lead or when the endogenous lead burden is very high. The blood lead level at which chelation therapy is universally recommended is 45 $\mu\text{g}/\text{dL}$. Therefore, if a subject reaches or exceeds 40 $\mu\text{g}/\text{dL}$, chelation therapy may be instituted in accordance with our usual medical practice, i.e. in the in-patient setting to assure removal from further sources of environmental lead. This occurrence will also necessitate reinstitution of a search for the lead sources in the child's environment. It should not necessitate removal of the child from the trial for methodological reasons, as analysis by 'intention to treat' is the preferred mode of analysis for randomized clinical trials. However, it is important to recognize that such an occurrence may be perceived as an adverse outcome by the subject's family, resulting in voluntary withdrawal from the trial.