sulfur mustard is currently being investigated by CBDE (Porton Down, UK). Based on radioactivity measurements, 80-90% of the metabolites are excreted within 48 hours.

We have chosen to develop immunochemical detection methods of "adducts," i.e., reaction products that are generated by alkylation of DNA bases and proteins by in vivo exposure to sulfur mustard.# This choice is based on extensive experimental evidence which shows that analogous methods of analysis for DNA adducts of cytostatic agents and environmental alkylating agents can be highly selective, detecting one modified base in DNA among $\leq 10^8$ unaltered bases (23). The minimum detectable concentration of modified bases lies in the low femtomolar range. If cells producing monoclonal antibodies to the adducts can be isolated, detection methods based on these antibody-adduct interactions can be performed on a large scale, with quantitative results. Although alkylated bases in DNA can undergo secondary reactions and the damage resulting from adduct formation tends to be repaired, the adducts are detectable for days or even weeks after exposure (23).

In general, methods to detect exposure to alkylating agents based on analysis of protein adducts in biological samples (biomonitoring; for reviews see 24-26) are complementary to methods based on analysis of DNA adducts. In contrast to the immunochemical detection methods for the latter adducts, protein adducts are usually quantified by GC-MS analysis after total hydrolysis of the protein and derivatization of the alkylated amino acid(s). Therefore, relatively few results are available for the immunochemical detection of protein adducts (27,28). A priori, it should be assumed for stoechiometric reasons that in vivo exposure to alkylating agents yields much more adducts to proteins than to DNA, unless the agent reacts specifically with DNA. Moreover, it has been shown that the life span of proteins is not shortened by alkylation. Human hemoglobin, with a biological half life of 16-18 weeks, has been proposed as an easily available protein for biomonitoring exposure to various alkylating agents (24-26).

In recent experiments the degree of alkylation by ethylene oxide of the N-terminal valine in human hemoglobin was determined by means of radioimmunoassay as well as by GC-MS analysis. A good correspondence of the results was found. With ethylene oxide and other directly alkylating agents, a reasonably linear relationship between levels of alkylation of DNA and proteins was also observed (29).

When sulfur mustard is used in chemical warfare, the agent affects the skin in liquid or vapor form, whereas inhalation of vapor or aerosol causes extensive damage of the respiratory tract and lungs. Extensive, long-lasting systemic intoxication is also observed due to rapid penetration of the agent into the general circulation both via inhalation and the skin (12). Therefore, DNA and proteins from various biopsies may serve as samples to monitor exposure to the agent. Primarily, skin biopsies and nucleated blood cells are convenient to assess damage to DNA. Hemoglobin, albumin, and skin biopsies are logical targets for immunochemical detection of sulfur mustard adducts to protein.

The use of immunochemical methods to detect compounds listed in Schedules 1 and 2 at facilities has been suggested (22).
