## 1. INTRODUCTION

Methods to verify the alleged use of chemical warfare (CW) agents should be available in order to sustain the credibility of a Chemical Weapons Convention (CWC) banning the production, posession, and use of chemical weapons (1). Presumably, allegations for the use of CW agents will be based primarily on the observation of injuries in supposed CW victims. In view of the far reaching political and military consequences of illegal use of CW agents, unequivocal methods should be available which stand in a court of law to prove, or disprove, the exposure of alleged victims to CW agents. Methods such as survey interviews of supposed victims can at best give circumstantial evidence for alleged use of CW agents (2).

Several incidents in the recent past demonstrated the present lack of reliable methods to verify exposure to CW- agents. The most straightforward case was the use of mustard gas, and possibly also of tabun, in the First Gulf War (3). With severe casualties in hospitals all over Europe, analyses of agents and metabolites had to be improvised. The results were inconclusive (4). The controversies with regard to the use of mycotoxins as an agent ("yellow rain") in Southeast Asia, which arose from the analyses of environmental and biological samples, were widely publicized. These incidents were reviewed (5). Rather recently, rumors were spread on the use of CW agents in Angola. Samples from the casualties were analyzed, with disputable results (6-8). In the more distant past, the alleged use of CW agents in Yemen could not be confirmed, due to lack of adequate methods of analysis (9).

Experience with the above-mentioned incidents learned that urine, blood and other biopsies or autopsies for analysis can often be obtained only several days or even weeks after exposure. Therefore, verification methods for biological samples should be very sensitive and should relate to long lasting, specific effects of the CW agent under investigation. Such methods are not yet available for the common CW agents. For example, intact nerve agents can be analyzed in blood, brain, and muscle tissues at minimum detectable levels in the low picomolar range. However, these levels are exceeded in primates only for a few hours after intoxication at high doses (10). An alternative, the observation of low levels of cholinesterase activity, is not specific for nerve agents. Possibly, development of sensitive methods of analysis for hydrolysis products in urine may provide a more promising approach to retrospective detection of nerve agent exposure (11).

The large scale use of sulfur mustard in the First Gulf War, demonstrated the renewed interest in this agent. Therefore, we selected this agent (12) to develop methods for retrospective detection of exposure. Presently available methods seem unsatisfactory. Recent reports on detection with gas chromatography in combination with mass spectrometry (GC-MS) of intact sulfur mustard in an abdominal fat sample obtained from autopsy of an Iranian soldier who died seven days after exposure to sulfur mustard (13), and in the urine of another soldier seven days after exposure (14,15), need further confirmation. Neither has the older report by Stade (16) been confirmed on the presence of intact agent in skin blisters caused by sulfur mustard. Attempts to verify exposure to sulfur mustard via analysis in blood or urine of its hydrolysis product thiodiglycol (17), and of thiodiglycol derivatives which are (re)converted into sulfur mustard with hydrochloric acid (18,19), were complicated by the presence of these products in samples from non-exposed volunteers. Reports on the identity of further metabolites of sulfur mustard are contradictory and lack spectrometric evidence (20,21). The metabolism of