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TECHNICAL REPORT

Methodology Report for H2SModel

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14. ABSTRACT

Hydrogen sulfide is similar in pathophysiology to cyanide in that it binds to mitochondrial cytochrome oxidase. By blocking oxidative respiration at the cellular level its effects are most evident in tissues with high metabolic demand such as the central nervous system, cardiovascular, and respiratory systems. The onset of signs and symptoms is rapid. Hydrogen sulfide also has local irritant effects, particularly upon the nose and membranes of the upper respiratory tract and the eyes. Physiological manifestations of H2S exposure may be quantified as a time-dependent severity vector described as increased time required to perform tasks owing to H2S-induced performance decrements as well as lethality. The model uses the time integral of agent concentration to calculate an internal "dose", then determines the severity vector based on the dose. Outcome probability can be estimated as the time course till the casualty returns to duty, or else dies. Although H2S has not knowingly been used in warfare, it is a toxic industrial chemical/toxic industrial material that could be used as a terrorist agent.

15. SUBJECT TERMS

Hydrogen sulfide; human performance; casualty estimates; health effects

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CONVERSION TABLE

Conversion Factors for U.S. Customary to metric (SI) units of measurement.

MULTIPLY →	BY →	TO GET
TO GET ←	BY ←	DIVIDE

angstrom	1.000 000 x E -10	meters (m)
atmosphere (normal)	1.013 25 x E +2	kilo pascal (kPa)
bar	1.000 000 x E +2	kilo pascal (kPa)
barn	1.000 000 x E -28	meter^2 (m^2)
British thermal unit (thermochemical)	1.054 350 x E +3	joule (J)
calorie (thermochemical)	4.184 000	joule (J)
cal (thermochemical/cm^2)	4.184 000 x E -2	mega joule/m^2 (MJ/m^2)
curie	3.700 000 x E +1	*giga bacquerel (GBq)
degree (angle)	1.745 329 x E -2	radian (rad)
degree Fahrenheit	$t_k = (t^0f + 459.67)/1.8$	degree kelvin (K)
electron volt	1.602 19 x E -19	joule (J)
erg	1.000 000 x E -7	joule (J)
erg/second	1.000 000 x E -7	watt (W)
foot	3.048 000 x E -1	meter (m)
foot-pound-force	1.355 818	joule (J)
gallon (U.S. liquid)	3.785 412 x E -3	meter^3 (m^3)
inch	2.540 000 x E -2	meter (m)
jerk	1.000 000 x E +9	joule (J)
joule/kilogram (J/kg) radiation dose absorbed	1.000 000	Gray (Gy)
kilotons	4.183	terajoules
kip (1000 lbf)	4.448 222 x E +3	newton (N)
kip/inch^2 (ksi)	6.894 757 x E +3	kilo pascal (kPa)
ktap	1.000 000 x E +2	newton-second/m^2 ($N-s/m^2$)
micron	1.000 000 x E -6	meter (m)
mil	2.540 000 x E -5	meter (m)
mile (international)	1.609 344 x E +3	meter (m)
ounce	2.834 952 x E -2	kilogram (kg)
pound-force (lbs avoirdupois)	4.448 222	newton (N)
pound-force inch	1.129 848 x E -1	newton-meter (N-m)
pound-force/inch	1.751 268 x E +2	newton/meter (N/m)
pound-force/foot^2	4.788 026 x E -2	kilo pascal (kPa)
pound-force/inch^2 (psi)	6.894 757	kilo pascal (kPa)
pound-mass (lbm avoirdupois)	4.535 924 x E -1	kilogram (kg)
pound-mass-foot^2 (moment of inertia)	4.214 011 x E -2	kilogram-meter^2 ($kg-m^2$)
pound-mass/foot^3	1.601 846 x E +1	kilogram-meter^3 (kg/m^3)
rad (radiation absorbed dose)	1.000 000 x E -2	**Gray (Gy)
roentgen	2.579 760 x E -4	coulomb/kilogram (C/kg)
shake	1.000 000 x E -8	second (s)
slug	1.459 390 x E +1	kilogram (kg)
torr (mm Hg, 0^0 C)	1.333 22 x E -1	kilo pascal (kPa)

*The Becquerel (Bq) is the SI unit of radioactivity; 1 Bq = 1 event/s.
**The Gray (Gy) is the SI unit of absorbed dose.

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Table 1: Health effects of hydrogen sulfide at various exposure levels (adapted from [20]).

Concentration (ppm[a])	Effect
0.01 – 0.3	Odor threshold (varies widely)
1 – 5	Mild offensive odor, sometimes associated with nausea; prolonged exposure can result in tearing of eyes, headaches or loss of sleep; however, healthy young male subjects tolerated this level with no decline in maximal physical work capacity
20 – 50	Eye irritation or keratoconjunctivitis and lung irritation. Several days of exposure can result in eye damage; some individuals experience digestive upset and loss of appetite
100	Olfactory paralysis occurs and the odor disappears; eye and lung irritation are more pronounced;
150 – 200	Severe eye and lung irritation; loss of sense of smell
250 – 500	If exposure is prolonged, pulmonary edema occurs
500	Serious eye damage within 30 min; severe lung irritation; amnesia for period of exposure; 'knockdown' or unconsciousness and death within 4 – 8 hours
1,000	Immediate collapse; breathing may stop within seconds

[a] 1 ppm $\approx$ 1.4 mg/m^3 [11].

1 Overview of Health Effects of Hydrogen Sulfide

Hydrogen sulfide (H_2S) is a cellular poison and affects all organs, particularly the pulmonary system and the central nervous system. The signs and symptoms of illness depend on the concentration of H_2S, the route of exposure and the duration of exposure. Inhalation is usually the route of significant H_2S poisoning cases. H_2S has a very high lipid solubility which allows it to penetrate easily through biologic membranes. H_2S effects are similar to cyanide in that it is a mitochondrial poison. It inhibits mitochondrial cytochrome oxidase and thus, the utilization of oxygen by the tissue. It also binds to hemoglobin in red blood cells interfering with oxygen transport [20, 25]

Individuals exposed to low levels of hydrogen sulfide (< 100 ppm) may experience irritation of the eyes and respiratory system, resulting in tearing of the eyes, coughing, headaches and nausea. Continuous low level concentrations or acute exposure to high concentrations of hydrogen sulfide can cause subjects to lose their ability to smell/detect the gas despite its continued presence (olfactory fatigue/paralysis). High-level exposures to hydrogen sulfide result in more neurologic and pulmonary symptoms such as severe coughing, dyspnea, vertigo, confusion, and nausea and vomiting and possible loss of consciousness. Very high concentrations (> 500 ppm) result in brainstem toxicity leading to cardiorespiratory arrest, myocardial infarction, "knockdown" or sudden loss of consciousness, seizure, and

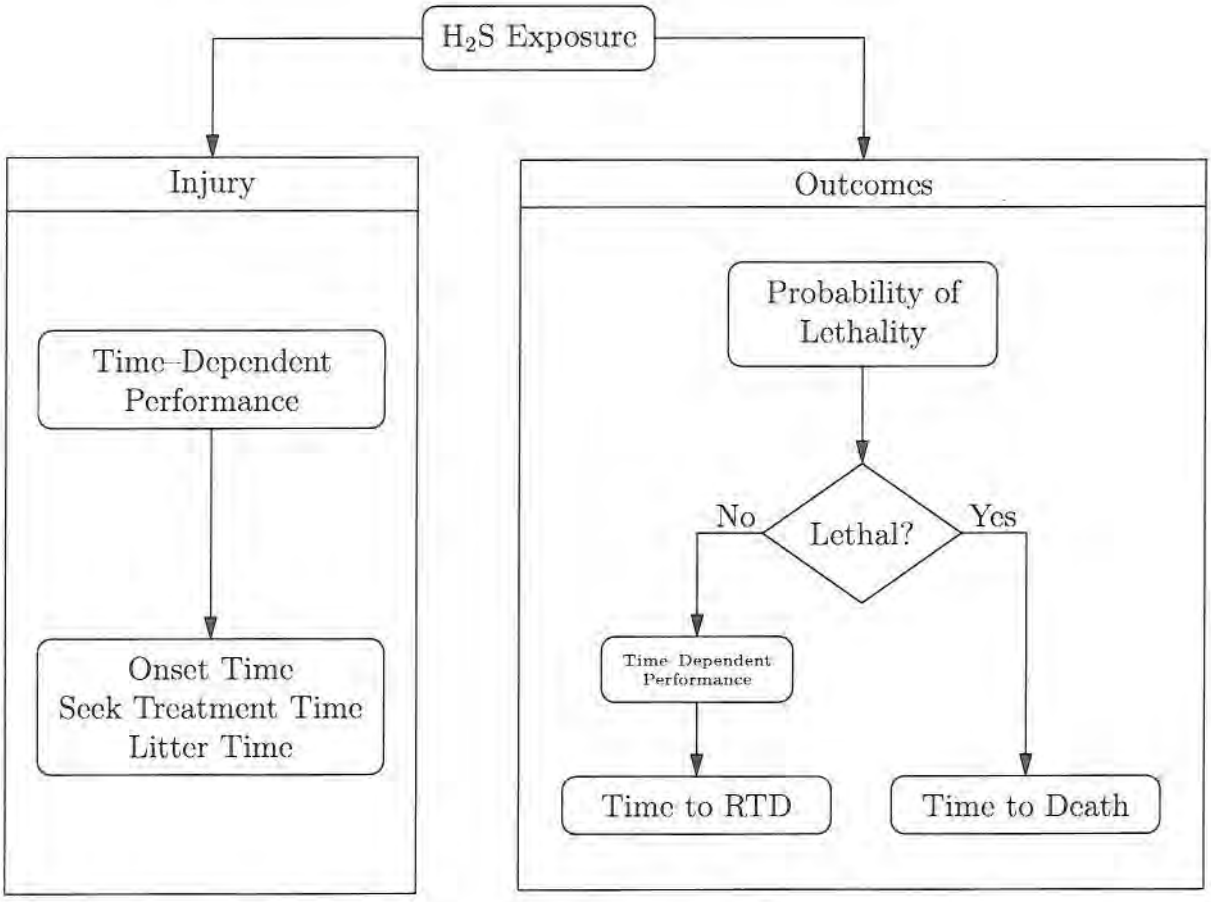

Figure 1: Overview of H2SModel calculations.

cardiopulmonary arrest (see Table 1) [25].

There may be few physical signs of low–level exposure to hydrogen sulfide but those observed include conjunctivitis (even at only 4 ppm), pharyngitis, and wheezing. Physical signs associated with high–level exposure of hydrogen sulfide include bradycardia, tremulousness, agitation, cyanosis, and acute lung injury. Patients may present with acute respiratory distress syndrome [ARDS]) [25].

2 Overview of H2SModel Calculations

The Java class H2SModel models the human health effects of exposure to hydrogen sulfide (H_2S), including human performance capability during and after exposure. H2SModel's methodology for estimating performance decrement is well established [8, 9, 17, 23, 24, 27] and underlies the casualty estimates generated by modules such as HDModel, GBModel, VXModel, ClModel, and CGModel. In this report we describe this methodology and show how we implemented it in H2SModel.

Figure 1 illustrates the key values calculated by H2SModel. Given an H_2S vapor exposure,

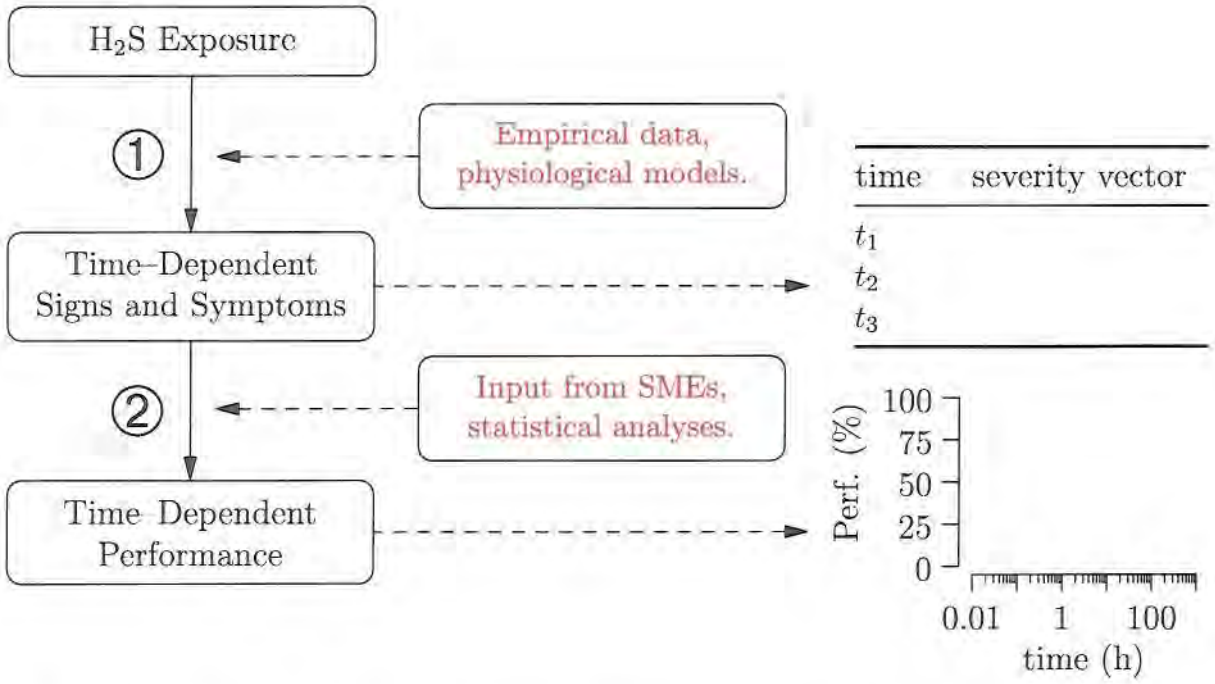

Figure 2: Overview of H2SModel performance calculation. Step ① utilizes empirical data and physiological models. Step ② utilizes SME (Subject Matter Expert) provided performance decrement estimates and statistical analyses. Lower right graph shows performance curves associated with increasingly severe exposures.

H2SModel estimates four time values related to the progression of injury: onset time, seek treatment time, litter time, and either time to return to duty (RTD) or time to death.

Figure 2 illustrates the two main steps in H2SModel's performance calculation. First, H2SModel estimates the severity of the signs and symptoms of injury resulting from exposure to hydrogen sulfide. This estimate, a time–dependent severity vector, represents a quantification of the physiological effects of the exposure. The four components of the severity vector, real numbers between 1 and 5, correspond to four sign/symptom (S/S) categories and describe the severity of the effects associated with each category. In Section 3 we list the S/S categories used by H2SModel, give descriptions of the severity values 1, 2, 3, 4, and 5 (for each S/S category), and describe how H2SModel associates severity vectors with H_2S exposures. Second, H2SModel maps each severity vector to a performance value P, where $0 \leq P \leq 1$. This task–specific mapping models the increase in task time due to H_2S exposure. In Section 4 we give the performance function P and plot performance curves $(100 \cdot P(t))$ for several exposure scenarios. In Section 5 we show how H2SModel uses $P(t)$ to estimate time phased casualties. Finally, in Section 6 we describe how H2SModel estimates time to RTD or time to death.

3 Signs and Symptoms

In this section we describe how H2SModel associates a time dependent severity vector with a given exposure to hydrogen sulfide (i.e., Step ① in Figure 2). Before giving details about Step ①, however, we must briefly discuss Step ②. Two key steps in defining Step ② are the following:

1. determine the performance decrements associated with a base set of severity vectors;
2. derive the performance model's regression coefficients (see Equation 11), so that performance predictions can be made for arbitrary severity vectors.

In previous applications of this methodology, the first task mentioned above was accomplished by interviewing SMEs or conducting performance assessment batteries. For this study, however, time constraints necessitated an alternative approach. Therefore, we defined Step ② by adapting performance models from two previously developed human response models [8, 27]. Those models, which describe the effects of exposure to mustard (HD) and sarin (GB), include (among others) the S/S categories and severity levels given in Table 2. Therefore, H2SModel also uses Table 2 to describe symptom severity. In summary, the symptomatology associated with H_2S exposure (which can be regarded as a subset of the symptomatology associated with exposure to HD or GB) can be adequately described using Table 2, so we used Table 2 and regression coefficients derived from previous studies [8, 27] as the basis for Step ②(in section 4 we describe how we derived these regression coefficients).

The S/S categories and severity level descriptions given in Table 2 therefore form the basis of mapping ①, which is outlined in Figure 3. First, the HE/RC Manager passes the total dosage D_{total}, the "Dosage Duration" T, and the "Exposure Duration" t to H2SModel. D_{total}, the time integral of concentration, and T, a measure of the effective duration of the exposure, define the H_2S exposure; t refers to the elapsed time since the beginning of the exposure. From these three variables H2SModel then estimates the dosage $D(t)$ and an "internal dose" $D_{int}(t)$. Finally, H2SModel calculates the severity vector $(S_{ME}, S_{SY}, S_{RE}, S_{OC})$. In the paragraphs below we describe each of these calculations.

Dosage $D(t)$ H2SModel assumes that

$$D(t) = C(t) \cdot t, \tag{1}$$

where

$$C(t) = \begin{cases} \frac{D_{total}}{T}, & t \leq T \\ 0, & t > T \end{cases} \tag{2}$$

(The HE/RC Manager only passes D_{total} and T to H2SModel, so H2SModel uses the average concentration.)

Table 2: H_2S S/S categories and descriptions of severity levels. In previous modeling efforts [8, 27], these signs and symptoms were used to describe the effects of HD exposure and GB exposure.

Mental Distress

1	No effect.
2	Anxious and irritable
3	Hard to remember or concentrate
4	Cannot remember or concentrate
5	Unconscious

Systemic Damage

1	No effect.
2	Nauseated and swallows often.
3	Headache, nauseated, vomited once or twice.
4	Headache and fever, vomited several times and will again.
5	Pounding headache, dry heaves, fatigued from vomiting.

Respiratory Damage

1	No effect.
2	Dry mouth, dry cough, sneezing, and runny nose.
3	Sore throat, continuous coughing, hoarse voice, chest feels tight.
4	Hurts to breathe, hacking cough, cannot speak.
5	Awful chest pain, wheezing and short of breath, coughs up red colored mucus.

Ocular Damage

1	No effect.
2	Eyes sting and tear.
3	Eyes feel gritty and sensitive to light, nonstop tears flood eyes.
4	Eyelids puffy and eyes burn, painful to keep open.
5	Eyelids swollen shut and burning eyes too painful to open.

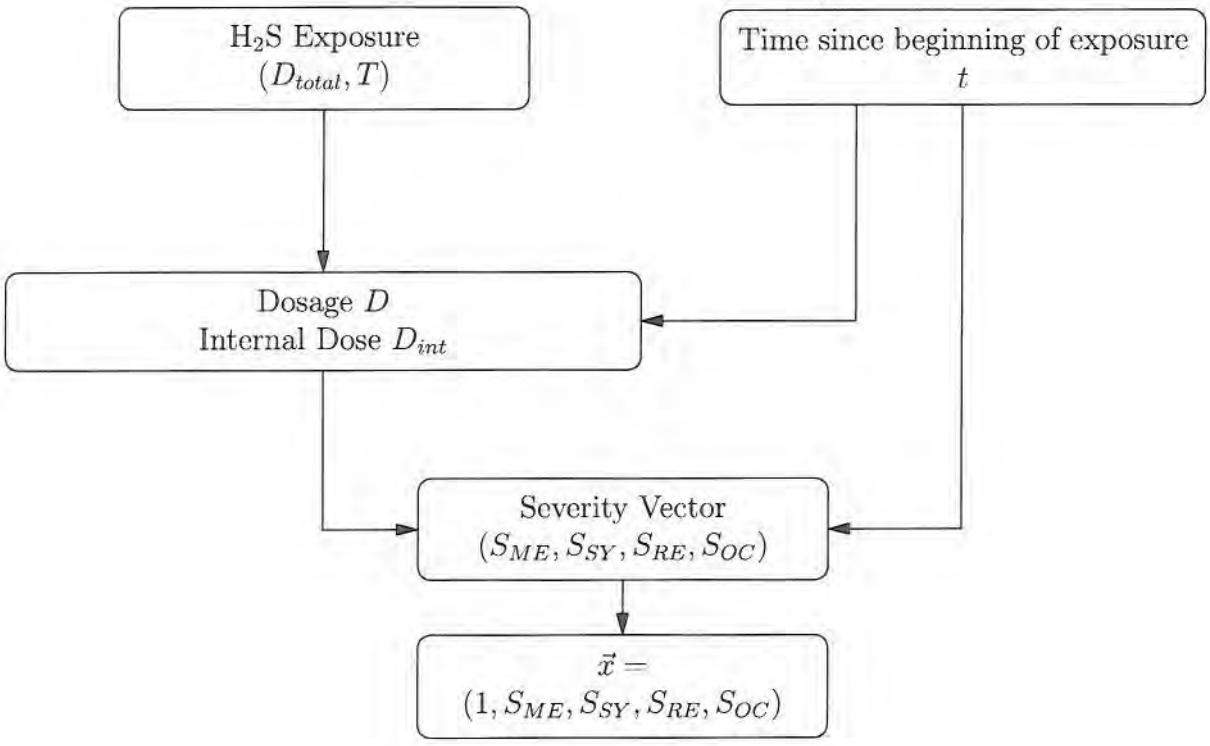

Figure 3: Calculation of the severity vector and the sign/symptom (S/S) complex $\vec{x}$ from a given H_2S exposure and the elapsed time since the beginning of the exposure (corresponds to Step ① in Figure 2).

Internal Dose $D_{int}(t)$ H2SModel estimates an "internal dose" $D_{int}(t)$ using a model similar to the Moore Gates formula quoted by McNamara [28],[1] though we estimate the extraction efficiency (which corresponds to "a" in the formula in [28]) using a model that is based on the MPPD (Multiple Path Particle Dosimetry) model developed by Asgharian ([7, 10]).

First, transport of H_2S in the lung is modeled by the area-averaged convective–diffusion equation

$$\frac{\partial C_a}{\partial t} + U\frac{\partial C_a}{\partial z} = D_a\frac{\partial^2 C_a}{\partial z^2} - \frac{2}{r}J_R, \tag{3}$$

where C_a is the air phase H_2S concentration, U is the average airflow velocity in an airway, D_a is the diffusion coefficient in the air, and J_R is the H_2S flux lost to the walls. The flux J_R, which depends on the pressure equilibrium between the air and tissue phases, is given by

$$J_R = K_o C_a, \tag{4}$$

where

$$K_o = \frac{1}{\frac{1}{k_g} + \frac{1}{k_t}} \tag{5}$$

and k_g and k_t are the air– and tissue–phase mass transfer coefficients, respectively. We assume that the tissue–phase mass transfer coefficient k_t is given by

$$k_t = \frac{P_{t:a}D_t}{L}, \tag{6}$$

where $P_{t:a}$ is the tissue–to–air partition coefficient and D_t is the diffusion coefficient in the tissue.

The deposition rate of H_2S onto lung airway surfaces is given by

$$\dot{r} = EVC_{a_0}, \tag{7}$$

where E is the extraction efficiency of H_2S, V is the minute ventilation, and C_{a_0} is the exposure concentration of H_2S ($C_{a_0} = D_{total}/T$ for $t \le T$; see Eq. 2). E is found from the solution of Eq. 3 by running MPPD. Lung dose is therefore given by

$$D_{lung}(t) = \begin{cases} EVC_{a_0}t, & t \le T \\ EVC_{a_0}T, & t > T \end{cases} \tag{8}$$

Next, we assume that the entire mass of the absorbed H_2S will pass through the lung tissue to reach the systemic circulation and subsequently be distributed to other tissues and

[1] McNamara applied the Moore–Gates formula to an analysis of hydrogen cyanide (HCN) toxicity. However, the toxicity of H_2S, the primary mechanism through which H_2S causes systemic effects (inhibition of cytochrome oxidase), and the rate at which H_2S causes systemic effects are similar to hydrogen cyanide [11]. Moreover, it appears that (similar to HCN) H_2S is rapidly detoxified [37], and systemic effects are only seen if the rate of H_2S absorption exceeds the detoxification rate [11]. Thus, it seems reasonable to apply the Moore–Gates formula to H_2S.

organs of the body. We assume that the transport rate of H_2S to the lung tissue rises from zero to reach a steady value after several breaths, and that the tissue eventually becomes saturated and the transfer from the tissue to the blood equals the deposition rate from the air space to the tissue. Thus, assuming a constant clearance rate of H_2S from the body, the mass of H_2S in the body can be modeled by[2]

$$\frac{dD_{int}}{dt} = \dot{r} - \lambda, \tag{9}$$

where D_{int} is the internal dose, $\dot{r}$ is the deposition rate of H_2S in the lung, and λ is the clearance rate of H_2S from the body. We assume that $\lambda = 0.1$ mg/min).[3]

For H_2S, MPPD estimates $E = 0.12$, so Equations 9 and 7 imply that $D_{int}(t)$ is given by

$$D_{int}(t) = \begin{cases} \max\{0, 0.12V\frac{D_{total}}{T}t - 0.1t\}, & t \le T \\ \max\{0, 0.12V D_{total} - 0.1t\}, & t > T \end{cases} \tag{10}$$

The toxicity and mechanism through which H_2S causes systemic effects are similar to those of hydrogen cyanide [11], and some methods of treatment of cyanide poisoning can be used in cases of sulfide poisoning [33]. However, H2SModel does not assign a patient condition code at this time.

Finally, we note that D_{int} is measure of overall insult to the body that for small t is similar to an acute intravenous dose of sulfide. However, the severity functions in Fig. 4 were designed to provide S/S severity estimates, based on D_{int} values calculated using Eq. 10, that are consistent with the H_2S LCt_{50} value from the recent work of Sommerville et al [35]. Thus, the D_{int} value associated with 50% probability of lethality may differ somewhat from an internal dose suggested by published estimates of lethal blood sulfide concentration [40].[4]

Severity Vector and S/S Complex H2SModel calculates the severity vector $(S_{ME}, S_{SY}, S_{RE}, S_{OC})$ using the functions given in Fig. 4, 5, 6, and an interpolation algorithm. Finally, the S/S complex $\vec{x}$ is defined by

$$\vec{x} = (1, S_{ME}, S_{SY}, S_{RE}, S_{OC}).$$

The value of the first component of the S/S complex, 1, results from the regression analysis that underlies the performance function in Equation 11.

[2] At physiologic pH (~ 7.4), about one third of absorbed H_2S remains undissociated, about two thirds produces HS^- ions, and very little S^{2-} is produced [11]. We do not model this dissociation.

[3]

[4] The LCt_{50} for a 2 minute exposure to H_2S (15 liter minute volume) is approximately 3,200 mg·min/min^3 [35]. Using $D_{total} = 3,200$, $t = T = 2$, and $V = 0.015$ in Eq. 10, $D_{int} \approx 6$ mg.

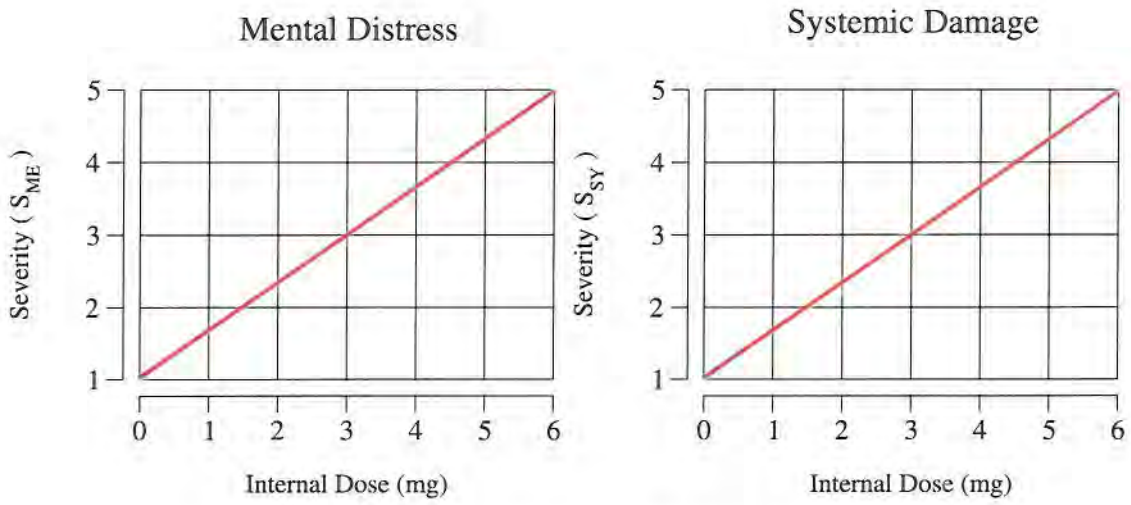

Figure 4: Severity functions $S_{ME}(D_{int})$ and $S_{SY}(D_{int})$.

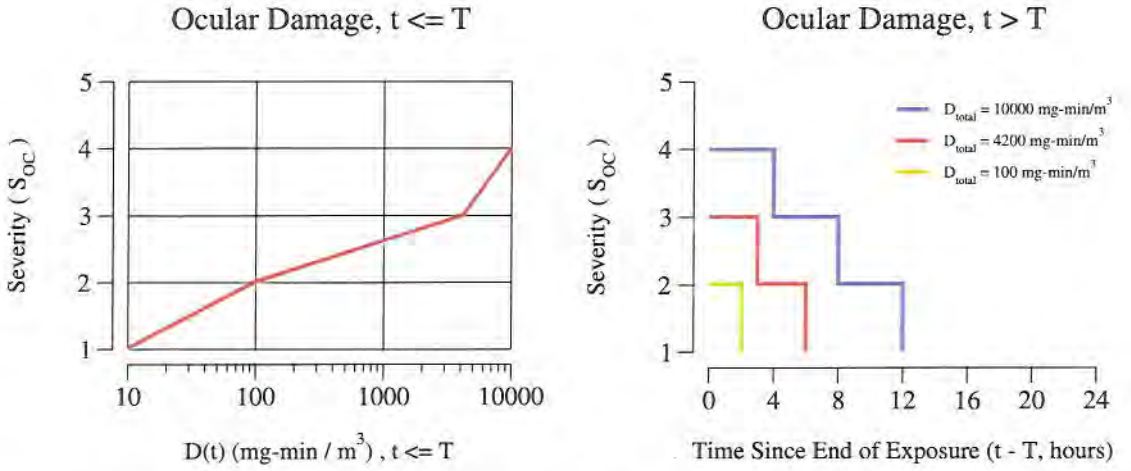

Figure 5: Ocular Damage severity values. Post exposure curves correspond to three dosage bands: [1, 1000], [1000, 10000], [10000, 50000] mg·min/m^3. Note: graph on right defines severity functions for the D_{total} values $G_1 = \sqrt{1 \cdot 1000}$, $G_2 = \sqrt{1000 \cdot 10000}$, $G_3 = \sqrt{10000 \cdot 50000}$. An interpolation algorithm is used to estimate time dependent severity values for other values of D_{total}.

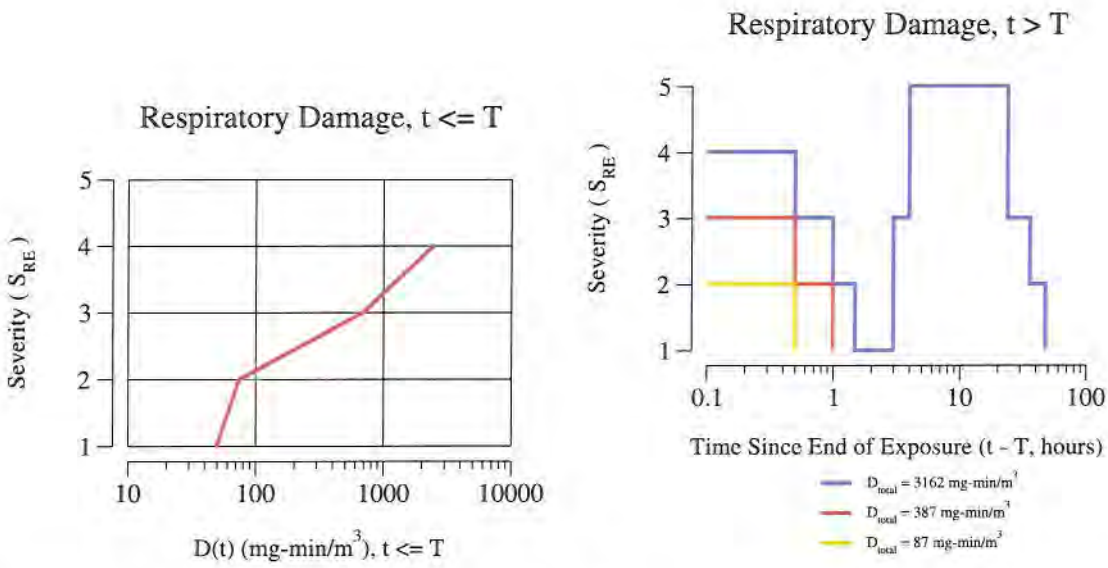

Figure 6: Respiratory Damage severity values. Post exposure curves correspond to three dosage bands: [50, 150], [150, 1000], [1000, 10000] mg·min/m^3. Note: graph on right defines severity functions for the D_{total} values $G_1 = \sqrt{50 \cdot 150}$, $G_2 = \sqrt{150 \cdot 1000}$, $G_3 = \sqrt{1000 \cdot 10000}$. An interpolation algorithm is used to estimate time dependent severity values for other values of D_{total}.

4 Performance

H2SModel uses the following performance function to map S/S complexes $\vec{x}$ to performance values P ($0 \leq P \leq 1$; this is mapping ② in Fig. 2):

$$P = \frac{1}{1 + \exp\left(-\vec{x} \cdot \vec{\beta}\right)} \tag{11}$$

The vector of regression coefficients, $\vec{\beta}$, was derived from a previous study [8]. In [8], performance values were obtained for S/S complexes for a number of chemical agents, based on questionaires given to subject matter experts, for a tasks with variety of degrees of physical exertion.

The S/S categories we have assumed for H_2S exposure are identical to the Systemic Damage (SY), Respiratory Damage (RE), and Ocular Damage (OC) symptom categories used for HD (Sulfur Mustard) and the Mental Distress (ME) category used for GB (Sarin) in [8]. We have therefore used the regression coefficients derived for these agents as the starting point for our calculation.

To develop a performance model for H_2S which uses this combination of S/S categories derived for different agents, we have used the regression procedure detailed in [8] and a restricted set of data from that work. Performance values were calculated for each of the GB ME and HD SY, RE, and OC categories assuming all other S/S categories were equal to

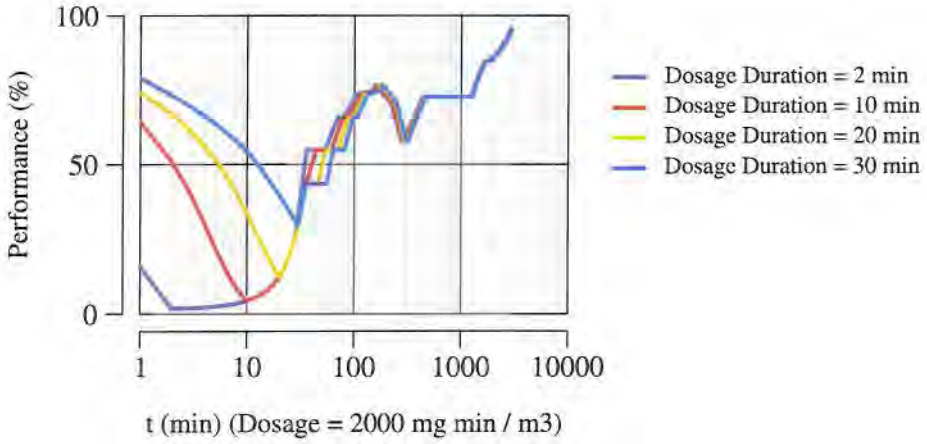

Figure 7: Performance curves $(100 \cdot P(t))$ for several exposure scenarios.

1 (no effect), using the published regression coefficients for the "No. 1 Cannoneer (loader)" task. This is a strenuous task assigned to a crew member of a M119 towed howitzer. These performance data were used as the dependent variable in a regression of the performance against the ME, SY, RE, and OC S/S categories. The independent variables therefore consist of the set of values obtained by considering each of the four S/S category separately ranging from 1-5 while holding all other S/S categories equal to 1 (no effect). An additional set of data for the regression was obtained by noting that the GB Upper Gastrointestinal Distress (UG) symptom category severity level 3 is similar to the HD SY symptom category severity level 2. Therefore, performance values can be obtained for HD SY equals 2, GB ME in the range 1-5, all other S/S categories equal to 1, using only the GB regression coefficients for the UG equals 3, ME equals 1-5 severity levels. The full data set used in the regression is shown in Table 3.

A logistic model was used to calculate the regression coefficients for the H_2S model. This model is given by

$$\ln\left(\frac{P}{1-P}\right) = \vec{x} \cdot \vec{\beta} + c$$

where P is the performance as a function of S_{ME}, S_{SY}, S_{RE} and S_{OC}, $\vec{x}$ is a vector of real numbers representing severity levels in the ME, SY, RE, and OC S/S categories, given by

$$\vec{x} = (1, S_{ME}, S_{SY}, S_{RE}, S_{OC})$$

(i.e., the S/S complex) and $\vec{\beta}$ is the vector of regresssion coefficients. Once the regression coeffients have been determined, the peformance values can be derived for any values of S_{ME}, S_{SY}, S_{RE}, S_{OC}. The regression coefficients are given in Table 4.

Fig. 7 illustrates $100 \cdot P(t)$ for several exposure scenarios.

Table 3: Data points (from a previous study) upon which H_2S performance model is based [8].

Sign/Symptom Severity				
Mental Distress	Systemic Damage	Respiratory Damage	Ocular Damage	Performance
1	1	1	1	0.8222998
2	1	1	1	0.7262866
3	1	1	1	0.6034160
4	1	1	1	0.4659465
5	1	1	1	0.3334618
1	1	1	1	0.9483361
1	2	1	1	0.8931952
1	3	1	1	0.7921039
1	4	1	1	0.6344849
1	5	1	1	0.4416072
1	2	1	1	0.6293681
2	2	1	1	0.4933411
3	2	1	1	0.3582929
4	2	1	1	0.2425178
5	2	1	1	0.1551104
1	1	1	1	0.9483361
1	1	2	1	0.9076138
1	1	3	1	0.8402020
1	1	4	1	0.7378112
1	1	5	1	0.6009713
1	1	1	1	0.9483361
1	1	1	2	0.8817691
1	1	1	3	0.7518740
1	1	1	4	0.5518067
1	1	1	5	0.3334358

Table 4: H_2S performance model coefficients ($\vec{\beta}$).

Intercept	ME	SY	RE	OC
5.17100	-0.89509	-0.69679	-0.45379	-0.72934

Table 5: Performance thresholds.

Time	Performance Threshold
Onset (τ_{onset})	0.995
Seek Treatment (τ_{seek})	0.75
Litter (τ_{litter})	0.25

Table 6: Calculation of work efficiency for the case in which $\min\{P\} \leq 0.75$.

Case	Work Efficiency
$\tau < \tau_{onset}$	100
$\tau_{onset} \leq \tau < \tau_{seek}$	$100 \cdot P$
$\tau_{seek} \leq \tau < \tau_{RTD}$	0
$\tau \geq \tau_{RTD}$	80

5 Onset Time, Seek Treatment Time, Litter Time, Work Efficiency

H2SModel uses $P(t)$ to calculate onset time (τ_{onset}), seek treatment time (τ_{seek}), and litter time (τ_{litter}). The onset time equals the first value of t at which $P(t) = 0.995$. The seek treatment time and litter time are calculated in a similar manner (see Table 5).

H2SModel calculates work efficiency according to Tables 6 and 7 (see Sec. 6 for the definition of τ_{RTD}).

Table 7: Calculation of work efficiency for the case in which $\min\{P\} > 0.75$.

Case	Work Efficiency
$\tau < \tau_{onset}$	100
$\tau_{onset} \leq \tau$	$100 \cdot P$

6 Outcomes: Time to RTD, Time to Death

Time to Death H2SModel estimates the probability of lethality P_L to be

$$P_L = \Phi\left(PS \log_{10} \frac{K}{K_{50}}\right) \tag{12}$$

where

$$K = \left(\frac{D_{total}}{T}\right)^n T \tag{13}$$

is the toxic load, n is the toxic load exponent, PS is the probit slope, K_{50} is the toxic load for 50% probability of lethality, and Φ is the cumulative distribution function of the standard normal distribution. Values for these parameters are given in Table 8.[5,6]

H2SModel then determines the lethality of the exposure based on a random number $Ran \in [0, 1]$ that is passed to H2SModel. If $Ran \leq P_L$, the exposure is considered lethal and the time to death is set equal to either the time at which the internal dose equals the maximum internal dose (T, if $0.12V\frac{D_{total}}{T} > 0.1$) or the time at which the internal dose equals 6 mg, whichever is earlier:

$$\tau_{death} = \begin{cases} \min\{T, \frac{6}{0.12V\frac{D_{total}}{T} - 0.1}\}, & 0.12V\frac{D_{total}}{T} > 0.1 \\ 10, & 0.12V\frac{D_{total}}{T} \leq 0.1 \end{cases} \tag{14}$$

If $Ran > P_L$, the exposure is considered nonlethal and H2SModel calculates τ_{RTD}.

Time to RTD If the exposure is nonlethal and τ_{seek} is defined (i.e., minimum performance is less than or equal to 0.75), H2SModel uses $P(t)$ to calculate τ_{RTD}, the time to RTD. If t^*

[5] The data in [35] (dosage unit: mg · min/m^3, time unit: min) imply

$$\begin{aligned} K_{50} &= \left(\frac{LCT_{50}}{\tau}\right)^n \tau \\ &= \left(\frac{3200}{2}\right)^{5.7} \cdot 2 \\ &\approx 1.8 \times 10^{18} \end{aligned}$$

[6] If PS_{TL} represents the probit slope with respect to toxic load and PS_C represents the probit slope with respect to concentration,

$$\begin{aligned} PS_{TL} &= \frac{PS_C}{n} \\ &= \frac{18}{5.7} \\ &\approx 3.2 \end{aligned}$$

[35].

Table 8: Probability of lethality probit model parameters.

Parameter	Description	Value	Reference
K_{50}	toxic load for 50% probability of lethality	1.8×10^{18}	[35]
PS	base 10 probit slope with respect to toxic load	3.2	[35]
n	toxic load exponent	5.7	[35]

equals the time at which P returns to 0.75,

$$\tau_{RTD} = \max\{\tau^*, \tau_{seek} + 24 \text{ hours}\}. \tag{15}$$

Time to RTD is not defined if the minimum performance is greater than 0.75.

7 Assumptions and Limitations

- There was a limited amount of quantitative data on which to base our estimates of time dependent severity
- H2SModel only models acute inhalation exposures
- H2SModel assumes that protection is unavailable
- H2SModel does not model ventilation response

8 Appendix A: Summary of Literature Search

Tables 9 16 summarize the data that was used to construct the severity functions in Figs. 4, 5, and 6. Our literature search focused on collecting four pieces of information about H_2S exposures: magnitude, the effects of the exposure, the time at which the effects begin (T_{begin}), and the time at which the effects end (T_{end}). Usually only a subset of this information was available, however, and therefore many of the entries in Tables 9 16 are empty (indicated by " "). Moreover, in many cases this information was given only in qualitative or semi quantitative terms. Tables 9 16 thus provide only general guidance for constructing the severity functions shown in Figs. 4, 5, and 6.

Table 9: Data from literature search: H_2S Exposure.

Lethality

Ref.	Exposure	Comments
[11, 32]	700-1400 mg/m^3 (Air)	Acts primarily as a systemic poison causing unconsciousness and death through respiratory paralysis
[11]	970-1250 mg/m^3 (Air)	Rapidly produces unconsciousness, cessation of respiration, and death
[11]	$>$ 1250 mg/m^3 (Air)	Exposure at these concentrations may mean instant death
[20]	1400 mg/m^3 (Air)	Breathing may stop within one or two breaths, immediate collapse
[6]	106 mg/m^3 (Air)	10 minute AEGL-3 value
[6]	85 mg/m^3 (Air)	30 minute AEGL-3 value
[6]	71 mg/m^3 (Air)	30 minute AEGL-3 value
[2]	140 mg/m^3 (Air)	NIOSH IDLH level (immediately dangerous to life or health)

Table 10: Data from literature search: H_2S Exposure.

Nausea and Vomiting

Ref.	Exposure	T_{begin}	T_{end}	Comments
[20]	1-7 mg/m^3 (Air)	—	—	Moderate offensive oder, may be associated with nausea with prolonged exposure
[3]	350-700 mg/m^3 (Air)	—	—	Nausea, vomiting
[26]	140-700 mg/m^3 (Air)	—	—	Nausea, vomiting

Table 11: Data from literature search: H_2S Exposure.

Vertigo, Dizziness, Headache

Ref.	Exposure	T_{begin}	T_{end}	Comments
[3]	350-700 mg/m^3 (Air)	—	—	Headache, dizziness, vertigo
[26]	2 mg/m^3 (Air)	—	—	Headache

Table 12: Data from literature search: H_2S Exposure.

Confusion, Anxiety

Ref.	Exposure	T_{begin}	T_{end}	Comments
[32]	700 mg/m^3 (Air)	—	—	Anxiety
[3]	350-700 mg/m^3 (Air)	—	—	Confusion

Table 13: Data from literature search: H_2S Exposure.

Weakness

Ref.	Exposure	T_{begin}	T_{end}	Comments
[3]	350-700 mg/m^3 (Air)	—	—	Weakness

Table 14: Data from literature search: H_2S Exposure.

Eye Irritation

Ref.	Exposure	T_{begin}	T_{end}	Comments
[20]	700 mg/m^3 (Air)	30 min.	—	Serious damage to eyes
[32]	70 mg/m^3 (Air)	—	—	Conjunctival irritation
[11]	13 mg/m^3 (Air)	—	—	Sore eyes
[11]	67 mg/m^3 (Air)	—	—	Conjuntival irritation is first noticelable
[11]	270 mg/m^3 (Air)	—	—	Stings eyes
[1]	70 mg/m^3 (Air)	1 hr	—	Conjunctivitis with ocular pain, lacrimation, and photophobia; this can progress to kerato-conjunctivitis and vesiculation of the corneal epithelium

Table 15: Data from literature search: H_2S Exposure.

Respiratory Irritation

Ref.	Exposure	T_{begin}	T_{end}	Comments
[20]	30-70 mg/m^3 (Air)	—	—	Lung irritation
[20]	130 mg/m^3 (Air)	—	—	Lung irritation, olfactory paralysis, odor disappears
[20]	200-270 mg/m^3 (Air)	—	—	Sense of smell paralyzed, severe lung irritation
[11]	70 mg/m^3 (Air)	—	—	Marked irritant action on respiratory tract
[11]	130 mg/m^3 (Air)	—	—	Loss of smell in 3-15 minutes, stings throat
[11]	500 mg/m^3 (Air)	0.5 hr	1 hr	Respiratory failure
[11]	940-1200 mg/m^3 (Air)	—	—	Rapidly produces cessation of respiration
[2]	$<$ 67mg/m^3 (Air)	—	—	Rapidly produces irritation of nose, throat and lower respiratory tract
[1, 41]	3-7 mg/m^3 (Air)	15 min	—	coughing and throat irritation

Table 16: Data from literature search: H_2S Exposure.

Pulmonary Edema

Ref.	Exposure	T_{begin}	T_{end}	Comments
[11]	330 mg/m^3 (Air)	—	—	Prolonged exposure may cause pulmonary edema
[11]	400-670 mg/m^3 (Air)	—	—	Pulmonary edema, imminent threat to life
[20]	330-670 mg/m^3 (Air)	—	—	Pulmonary edema may occur, especially if exposure is prolonged
[32, 36]	350-700 mg/m^3 (Air)	—	—	Pulmonary edema

9 Definitions, Acronyms, and Abbreviations

Dosage Duration A measure of the effective duration of an exposure (this value is calculated elsewhere and passed to H2SModel).

Exposure Duration Time elapsed since the beginning of an exposure. This quantity, defined elsewhere and passed to H2SModel, continues to increase even after the cessation of exposure. It should not be confused with dosage duration, which does not increase after the cessation of exposure.

Litter Time (τ_{litter}) First time since the beginning of an exposure at which $P = 0.25$. The exposed person is presumed to require assistance to reach medical care after this time.

Onset Time (τ_{onset}). First time since the beginning of an exposure at which $P = 0.995$. Indicates the time of first occurrence of signs or symptoms of injury.

PPM Parts per million (e.g., of hydrogen sulfide gas) in air by volume.

RTD Return to Duty.

Seek Treatment Time (τ_{seek}) First time since the beginning of an exposure at which $P = 0.75$. The time at which an individual seeks treatment for his or her symptoms.

SME Subject Matter Expert.

S/S Sign/Symptom.

Time to Death If (and only if) the exposure is lethal, equal to either the time at which the internal dose equals the maximum internal dose or the time at which the internal dose equals (X) mg, whichever is earlier.

Time to RTD (τ_{RTD}) If the exposure is nonlethal, the minimum performance is less than or equal to 0.75, and τ^* equals the time at which P returns to 0.75, $\tau_{RTD} = \max\{\tau^*, \tau_{seek} + 24 \text{ hours}\}$. This RTD time is different than that used in AMedP–8, where it was assumed that no treatment was available. In the context of the software that uses H2SModel, the lower bound ($\tau_{seek} + 24$ hours) on τ_{RTD} models time in the medical care system. Time to RTD is not defined if the minimum performance is greater than 0.75.

References

[1] Acute toxicity summary: Hydrogen sulfide. http://oehha.ca.gov/air/acute_rels/pdf/7783064A.pdf.

[2] ATSDR - MMG: hydrogen sulfide. http://www.atsdr.cdc.gov/MHMI/mmg114.html (accessed May 2010).

[3] Hydrogen Sulfide - national library of medicine HSDB database. http://toxnet.nlm.nih.gov (accessed May 2010).

[4] Hydrogen sulfide (Cicads 53, 2003). http://www.inchem.org/documents/cicads/cicads/cicad53.htm (accessed March 2010).

[5] Hydrogen sulfide (EHC 19, 1981). http://www.inchem.org/documents/ehc/ehc/ehc019.htm (accessed June 2010).

[6] Hydrogen sulfide interim acute exposure guideline levels (AEGLS). Technical report, November 2002. http://www.epa.gov/oppt/aegl/pubs/hydrogen_sulfide_interim_nov_2002.pdf.

[7] Anjilvel, S., and B. Asgharian. A multiple path model of particle deposition in the rat lung. *Fundam. Appl. Toxicol.* 28: 41 50, 1995.

[8] Anno, G. H., et al. Predicted performance of infantry and artillery personnel following acute radiation or chemical agent exposure. Technical Report DNA TR 93 174, Defense Nuclear Agency, Alexandria, VA, 1994.

[9] Anno, G. H., D. B. Wilson, and M. A. Dore. Nuclear weapons effect research at PSR, 1983: Acute radiation effects on individual crewmember performance. Technical Report DNA TR 85 52, Defense Nuclear Agency, Washington, D.C., 1984.

[10] Asgharian, B., et al. Multiple Path Particle Dosimetry Model (MPPD v 2.0). http://www.ara.com/products/mppd.htm.

[11] Beauchamp, R. O., Jr., J. S. Bus, J. A. Popp, C. J. Boreiko, and D. A. Andjelkovich. A critical review of the literature on hydrogen sulfide toxicity. *CRC Critical Reviews in Toxicology* 13(1): 25 97, 1984.

[12] Burnett, W. W., E. G. King, M. Grace, and W. F. Hall. Hydrogen sulfide poisoning: review of 5 years' experience. *Canadian Medical Association Journal* 117(11): 1277 1280, 1977.

[13] Chaturvedi, A. K., D. R. Smith, and D. V. Canfield. A fatality caused by hydrogen sulfide produced from an accidental transfer of sodium hydrogen sulfide into a tank containing dilute sulfuric acid. Final Report DOT/FAA/AM-00/34, Civil Aeromedical Institute, Federal Aviation Administration, Oklahoma City, Oklahoma, November 2000.

[14] Chou, S., M. Fay, S. Keith, L. Ingerman, and L. Chappell. Toxicological profile for hydrogen sulfide. Technical report, Agency for Toxic Substances and Disease Registry (ATSDR), July 2006. http://www.atsdr.cdc.gov/toxprofiles/tp114.pdf.

[15] Collins, J., and D. Lewis. Hydrogen sulfide: evaluation of current california air quality standards with respect to protection of children. Technical report, 2000. Report of the Air Toxicology and Epidemiology Section, California Office of Environmental Health Hazard Assessment.

[16] Couch, L., L. Martin, and N. Rankin. Near death episode after exposure to toxic gases from liquid manure. *NZ Med J* 118, 2005.

[17] Deverill, A. P., and D. F. Metz. Defense Nuclear Agency Improved Casualty Estimation (DICE) chemical insult program acute chemical agent exposure effects. Technical Report DNA TR 93 162, Defense Nuclear Agency, Alexandria, VA, 1994.

[18] Evans, C. L. The toxicity of hydrogen sulphide and other sulphides. *Quart. J. Experimental Physiology* 52(3): 231 248, 1967.

[19] Famini, G., L. Roszell, and R.Gooding, . Chemical Security Analysis Center Chemical Infrastructure Risk Assessment, April 2009. Presentation, Department of Homeland Security (FOUO).

[20] Guidotti, T. L. Hydrogen sulphide. *Occupational medicine* 46(5): 367 371, 1996.

[21] Haggard, H. W., and T. J. Charlton. The fate of sulfides in the blood. *Journal of Biological Chemistry* 49(2): 519 529, 1921.

[22] Jäppinen, P., and R. Tenhunen. Hydrogen sulphide poisoning: blood sulphide concentration and changes in haem metabolism. *British Journal of Industrial Medicine* 47(4): 283 285, 1990.

[23] Levin, S. G. The effect of combined injuries from a nuclear detonation on soldier performance. Technical Report DNA TR 92 134, Defense Nuclear Agency, Alexandria, VA, 1993.

[24] Levin, S. G., and J. W. Fulton. Consolidated Human Response Nuclear Effects Model (CHRNEM). Technical Report DNA TR 93 45, Defense Nuclear Agency, Alexandria, VA, 1993.

[25] Mandavia, S. Toxicity, hydrogen sulfide. http://emedicine.medscape.com/article/815139-overview (accessed June 2010).

[26] Marshall, T., D. Dorman, D. Gardner, and F. Adeshina. Provisional advisory levels (PALs) for hydrogen sulfide. *Inhalation Toxicology* 21(s3): 56 72, 2009.

[27] McClellan, G. E., G. H. Anno, and L. N. Matheson. Consequence analytic tools for NBC operations, vol. 3: Chemical agent exposure and casualty estimation. Technical Report DSWA TR 97 61 V3, Defense Special Weapons Agency, Alexandria, VA, 1998.

[28] McNamara, B. P. Estimates of the toxicity of hydrocyanic acid vapors in man. Technical Report EB TR 76023, Edgewood Arsenal, Aberdeen Proving Ground, August 1976.

[29] Muehling, A. J. Gases and odors from stored swine wastes. *Journal of Animal Science* 30(4): 526 531, 1970.

[30] Policastro, M. A., and E. J. Otten. Case files of the university of cincinnati fellowship in medical toxicology: Two patients with acute lethal occupational exposure to hydrogen sulfide. *Journal of Medical Toxicology* 3(2): 73 81, 2007.

[31] Prior, M. G., A. K. Sharma, S. Yong, and A. Lopez. Concentration time interactions in hydrogen sulphide toxicity in rats. *Canadian Journal of Veterinary Research* 52(3): 375 379, 1988.

[32] Reiffenstein, R. J., W. C. Hulbert, and S. H. Roth. Toxicology of hydrogen sulfide. *Annual review of pharmacology and toxicology* 32(1): 109 134, 1992.

[33] Smith, R. P., and R. E. Gosselin. Current concepts about the treatment of selected poisonings: Nitrite, cyanide, sulfide, barium, and quinidine. *Annual review of pharmacology and toxicology* p. 189 199, 1976.

[34] Snyder, J. W., E. F. Safir, G. P. Summerville, and R. A. Middleberg. Occupational fatality and persistent neurological sequelae after mass exposure to hydrogen sulfide. *The American Journal of Emergency Medicine* 13(2): 199 203, 1995.

[35] Sommerville, D. R., S. R. Channel, and J. Bray. Proposed provisional human toxicity estimates for military Operations-Hydrogen sulfide. Technical report, September 2009.

[36] Strickland, J., A. Cummings, J. III Spinnato, J. Liccione, and G. Foureman. Toxicological review of hydrogen sulfide. Technical Report EPA/635/R-03/005, U.S. Environmental Protection Agency, Washington, DC, June 2003.

[37] Subcommittee on Hydrogen Sulfide, Committee on the Medical and Biologic Effects of Environmental Pollutants, National Research Council, National Academy of Sciences, . Hydrogen sulfide. Technical Report EPA-600/1-78-018, U.S. Environmental Protection Agency, Research Triangle Park, N.C., February 1978.

[38] for Toxic Substances, Agency, and Disease Registry (ATSDR). ToxGuide for hydrogen sulfide, July 2006. http://www.atsdr.cdc.gov/toxguides/toxguide-114.pdf?id=1088&tid=67.

[39] U.S. Army Center for Health Promotion and Preventive Medicine. Chemical exposure guidelines for deployed military personnel. USACHPPM Reference Document 230, Aberdeen Proving Ground, May 2003. Version 1.3.

[40] Winek, C. L., W. W. Wahba, C. L., Jr. Winek, and T. W. Balzer. Drug and chemical blood level data 2001. *Forensic Science International* 122(2-3): 107 123, November 2001. http://fscimage.fishersci.com/webimages_FSC/downloads/winek.pdf.

[41] Woodall, G. M., Jr., R. L. Smith, and G. C. Granville. Proceedings of the hydrogen sulfide health research and risk assessment symposium october 31–November 2, 2000. *Inhalation Toxicology* 17(11): 593 639, 2005.

[42] World Health Organization, . *Air Quality Guidelines for Europe.* Number 91 in WHO regional publications. World Health Organization, Regional Office for Europe, Copenhagen, 2nd ed., 2000.

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