



INSTITUTE FOR DEFENSE ANALYSES

**2011 Review on the Extension
of the *AMedP-8(C)* Methodology to
New Agents, Materials, and Conditions**

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Executive Summary

In March 2011, the North Atlantic Treaty Organization (NATO) promulgated *Allied Medical Publication 8 (C): NATO Planning Guide for the Estimation of CBRN Casualties*, (*AMedP-8(C)*) as a general methodology for estimating casualties resulting from chemical, biological, radiological, and nuclear (CBRN) attacks against deployed military forces. *AMedP-8(C)* contains parameters and values that can be used to apply the methodology for a limited number of specified CBRN agents or effects. This document is the third annual review by the Institute for Defense Analyses (IDA) of the extent to which information available in published literature can be used: 1) to support the development of quantifiable casualty estimation parameters for additional agents or effects, 2) in response to new research, to update parameters for agents or effects already modeled, and 3) to extend the methodology to allow consideration of conditions not included in *AMedP-8(C)*. The 2011 review focuses on the effort required to meet the priorities evinced in discussions with sponsors within Office of the Surgeon General (OTSG) and the Joint Staff. The recommendations for future work contained herein are based on these priorities.

The review recommends that continued work should be prioritized as follows:

- First, existing human response models should be updated, as required, to take advantage of new data from ongoing medical countermeasure research programs and from recent large-scale disease outbreaks. In particular, new data are starting to emerge from research into bioscavengers, vaccines against botulinum toxin and Ebola/Marburg hemorrhagic fevers, and the recent outbreak of Q fever in the Netherlands. In addition, if the data from experiments involving Military Research Volunteers (MRVs) were to become accessible, the existing human response models for tularemia, Q fever, and staphylococcal enterotoxin B (SEB) should be reviewed.
- Second, current *AMedP-8(C)* models should be extended to fill identified gaps in areas where the Common User Database (CUD) incorporates patient conditions that have no corollary within *AMedP-8(C)*.
- Third, new human response models should be developed for any agents of priority interest to the sponsors of *AMedP-8(C)*. At present, these agents include eastern equine encephalitis (EEE), western equine encephalitis (WEE), Marburg hemorrhagic fever, melioidosis, and ricin.

- Fourth, the chemical human response models developed by Applied Research Associates (ARA) (chlorine, cyanogen chloride, hydrogen cyanide, hydrogen sulfide, and phosgene) should be incorporated into *AMedP-8(C)*.
- Fifth, new human response models should be developed for those remaining agents now incorporated into the CUD, with priority being given to the two agents (cholera and Ebola hemorrhagic fever) that appeared in both the Defense Threat Reduction Agency (DTRA) and OTSG inputs to the CUD program of work.
- Finally, the estimation of psychological casualties resulting from the use of CBRN weapons has long been considered an important requirement, but one that has been either too difficult or of too low priority. IDA's initial investigations in this area have led the IDA study team to conclude that such estimation is feasible within the framework of *AMedP-8(C)*, and the team is prepared to address this problem should it become a priority.

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1. Introduction

A. Objective

In March 2011, the North Atlantic Treaty Organization (NATO) promulgated *Allied Medical Publication 8 (C): NATO Planning Guide for the Estimation of CBRN Casualties*, (*AMedP-8(C)*)¹ as a general methodology for estimating casualties resulting from chemical, biological, radiological, and nuclear (CBRN) attacks against deployed military forces. *AMedP-8(C)* contains parameters and values that can be used to apply the methodology for a limited number of specified agents or effects.

This document is the third annual review by the Institute for Defense Analyses (IDA) of the extent to which information available in published literature can be used to support the development of quantifiable casualty estimation parameters for additional agents, materials, and conditions of current and emerging interest to the United States and NATO. It also identifies areas where new research and data can be used to improve existing parameters.

B. Task Requirements

This document describes work done under Task Order CA-6-3079 “CBRN Casualty Estimation Update of the Medical CBRN Defense Planning and Response Project,” Subtask 2 “Update Agents/Materials into *AMedP-8(C)* Methodology.” It provides a “draft program of work identifying agents, effects, materials, and conditions of interest to the Department of Defense (and NATO and other Federal agencies, as requested), but not currently included in *AMedP-8(C)*.” It is not an addendum to *AMedP-8(C)* but may be considered a supplement to the *AMedP-8(C) Technical Reference Manual*² for U.S. purposes. The IDA study team describes projected work estimates for the various potential components of *AMedP-8(C)* and the basis for making those estimates.

IDA reviewed literature relevant to the extension of *AMedP-8(C)* to include additional CBRN agents and effects, new medical countermeasures, new data emerging from

¹ NATO, *AMedP-8(C): NATO Planning Guide for the Estimation of CBRN Casualties*, (Brussels: NATO, 2011).

² Carl A. Curling et al., *Technical Reference Manual: NATO Planning Guide for the Estimation of Chemical, Biological, Radiological, and Nuclear (CBRN) Casualties, Allied Medical Publication-8(C)*, IDA Document D-4082 (Alexandria, VA: Institute for Defense Analyses, August 2010).

recent disease outbreaks, and psychological casualties. This literature review has identified tentative human response knowledge gaps and enabled estimates of the work levels required to incorporate quantitative casualty estimation parameters for new agents into *AMedP-8(C)*. This review is the third in a series of annual reviews, updated as the scope of *AMedP-8(C)* expands.

C. Background

AMedP-8 has evolved over the past four decades from a strictly nuclear casualty guide to one applicable to a wide range of CBRN agents. *AMedP-8* has included various casualty estimation methodologies for a wide range of nuclear weapon yields, up to 3 different chemical agents, and up to 11 different biological agents.

The purpose of *AMedP-8(C)* is to support the medical planning process by providing a methodology for estimating casualties that occur uniquely because of CBRN attacks against allied targets. The methodology provides the capability to estimate the numbers of casualties over time and the incidence of injury by type and severity. Previous versions of *AMedP-8* provided three separate chemical, biological, and nuclear documents with tabular casualty estimates for specified brigade-size units, postures, and weapons sizes or yields. *AMedP-8(C)* consolidates CBRN agents and effects into a single document and allows the estimation of personnel status within user-specified scenarios.

AMedP-8(C) considers the human response to CBRN agents and effects in terms of injury profiles. Injury profiles describe changing injury severity over time as a function of dose, dosage, or magnitude of insult. Casualty status is then defined as a function of a chosen level of injury severity. *AMedP-8(C)*, while applicable to a wider range of agents and effects than previous *AMedP-8* editions, is still limited in application. The injury profile parameters for implementing the methodology are presented for only a subset of CBRN agents and weapon effects. These agents and effects include the following:

- Acute³ effects of external whole-body irradiation, including irradiation from the prompt radiation emitted by a nuclear detonation, the radiation present from the delayed radiation (fallout) resulting from a nuclear detonation, and the radiation resulting from the release of seven specified radioisotopes (⁶⁰Co, ⁹⁰Sr, ¹³¹I, ¹³⁷Cs, ¹⁹²Ir, ²³⁸Pu, and ²⁴¹Am)
- Acute effects of irradiation or radioactive contamination on the skin
- Acute primary blast injuries (injuries resulting from the direct effects of the blast wave passing through the body)

³ “Acute” is used to differentiate effects and injuries that produce symptoms within the first six to eight weeks after exposure.

- Fatalities from the dynamic pressure (wind) of a nuclear detonation
- Acute primary thermal injuries (flash burns) from the thermal pulse of a nuclear detonation
- Acute injuries from exposures to three chemical agents (Sarin (GB), VX, and distilled mustard (HD))
- Acute illness from exposure to five biological agents (anthrax, botulism, pneumonic plague, smallpox, and Venezuelan equine encephalitis (VEE))

In 2010, the *AMedP-8(C)* methodology was extended to five additional biological agents (brucellosis, glanders, Q fever, staphylococcal enterotoxin B (SEB), and tularemia). These agents had been considered in earlier versions of *AMedP-8* but not in the current version due to constraints on time and resources.

D. Human Response Model Parameters

The methodology incorporated into *AMedP-8(C)* contains a series of submodels describing specific aspects of human response.⁴ The submodels used depend on the nature of the agent or effect being modeled.

1. Chemical, Radiological, and Nuclear (CRN) Models

The human response models for CRN agents and effects are the combination of two submodels:

- Toxicity: to sort each exposure into a dose/dosage/insult range according to the ultimate severity of effects resulting for each exposure type or route of entry
- Injury profile: to map the changing course of injury severity over time

2. Biological Models

The human response models for biological agents are the combination of five submodels:

- Infectivity (or effectivity, for toxins): to estimate the number of individuals who will become ill, given their dose of agent
- Incubation or latency period: to estimate when those individuals will develop signs and symptoms

⁴ NATO, *AMedP-8(C)*, 3-1 to 3-6. The *AMedP-8(C)* human response model is one component of a larger casualty estimation methodology that includes additional components. The first portion of the methodology generates estimates of the dose, dosage, or insult values that are the primary input to the human response model. The final portion of the methodology uses the outputs of the human response model to generate a casualty estimate.

- Duration of illness: to estimate the length of time between the onset of symptoms and death or recovery
- Disease profile: to describe the course of illness or the disease through clinically differentiable stages with the severity of the associated signs and symptoms over time
- Lethality: to estimate the number of ill individuals who die

3. Prophylaxis

For both CRN and biological agents, the human response models were developed in *AMedP-8(C)* without considering the use of any medical intervention that would change the human response to an exposure of interest. For some diseases (specifically, anthrax, pneumonic plague, and smallpox), it was reasonable to expect a significantly different response due to the use of immunization or chemoprophylaxis, and a separate set of prophylaxis parameters was developed for these agents. Therefore, the availability of information on the efficacy of prophylaxis was investigated as a separate submodel of the chemical and biological agents considered in this document. This information was collected only for those agents that had identified vaccination protocols or existing vaccination research programs and for bacterial agents that respond to antibiotics.

E. The 2009/2010 Reviews and Subsequent Program of Work

The first report in this annual series, the “2009 Report on the Extension of the *AMedP-8(C)* Methodology to New Agents, Materials, and Conditions,” estimated the level of effort expected to develop the *AMedP-8(C)* parameters for 32 new biological agents and 12 new chemical agents and for the psychological impact of using CBRN weapons. No additional radiological agents or higher order nuclear effects were addressed. In addition, the authors of the 2009 report compiled a list of some 900 chemical and biological agents included on various threat lists published by various organizations within the U.S. Departments of Defense (DoD), Homeland Security (DHS), and Health and Human Services (HHS) and by NATO.

In 2010, IDA published the *AMedP-8(C)* parameters for five biological agents (brucellosis, glanders, Q fever, staphylococcus enterotoxin B, and tularemia).⁵ At the same time, Applied Research Associates (ARA), under contract to the Defense Threat Reduction Agency (DTRA), began the development of similar parameters for five chemical agents (chlorine, phosgene, hydrogen cyanide, cyanogen chloride, and hydrogen sulfide).

⁵ Carl A. Curling et al., *Parameters for Estimation of Casualties from Exposure to Specified Biological Agents: Brucellosis, Glanders, Q Fever, SEB and Tularemia*, IDA Document D-4132 (Alexandria, VA: Institute for Defense Analyses, November 2010).

The second review in this series, the *2010 Review on the Extension of the AMedP-8(C) Methodology to New Agents, Materials, and Conditions*,⁶ described an approach for extending current human response models to consider the effects of medical countermeasures and treatment on casualty estimates and estimated the level of effort required to do so. The 2010 document also reviewed the list of agents and effects now included or proposed for inclusion in the Common User Database (CUD), a collection of CBRN treatment protocols and estimated personnel and materiel requirements developed and maintained by the Defense Medical Standardization Board (DSMB), now called the Defense Medical Materiel Program Office (DMMPO). Both the *AMedP-8(C)* casualty estimation methodology and the CUD would likely be incorporated into any future U.S. military medical planning tool, and alignment of the two is a priority for our sponsors. Because the CUD at present considers a much larger set of CBRN agents and effects, the 2010 review outlined a prioritization scheme for extending *AMedP-8(C)* to encompass agents and effects in the CUD.

In 2011, IDA published a new set of *AMedP-8(C)* parameters that accounted for the effects of treatment on casualty estimates. These parameters were developed for all agents and effects now considered in *AMedP-8(C)* and for the five additional biological agents for which human response models have been developed. In a parallel effort, IDA also reviewed the CUD treatment briefs to determine the extent to which personnel and materiel requirements could be estimated for the range of casualties of varying types and severity estimated by *AMedP-8(C)*.

⁶ Carl A. Curling, Lucas L. LaViolet, and Julia K. Burr, *2010 Review on the Extension of the AMedP-8(C) Methodology to New Agents, Materials, and Conditions*, IDA Document D-4131 (Alexandria, VA: Institute for Defense Analyses, December 2010).

2. The 2011 Review

A. Approach

The 2011 review is not intended to be a restatement of the 2010 review. Rather, this document considers the extension of *AMedP-8(C)* from the perspective of priorities evinced in discussions with sponsors within Office of the Surgeon General (OTSG) and the Joint Staff. The recommendations for future work contained herein are based on these priorities.

Specifically, this document describes several potential modifications and extensions of the current *AMedP-8(C)* designed to improve existing models by taking advantage of new data from ongoing medical countermeasure research programs and from recent large-scale disease outbreaks. It also focuses on continued efforts to align *AMedP-8(C)* with other U.S. DOD medical planning tools, primarily the CUD.

The level-of-effort estimates for each proposed modification consider the familiarity that the researchers at IDA have with the relevant literature and the perceived complexity of the associated analyses. For the extension of *AMedP-8(C)* to additional agents not currently modeled, level-of-effort estimates are taken from the 2009 and 2010 reports. These estimates are derived from an assessment of the availability of required data in the literature and include the development of models with and without treatment.

B. Consideration of Emerging Medical Countermeasures

Medical countermeasures can mitigate the impact of CBRN use in a number of ways. They can reduce the probability of injury given exposure, they can reduce mortality, and they can reduce the duration and severity of injury if it occurs. Because all of these mitigations will change the number, severity, and time-phasing of casualties, the ongoing development of CBRN medical countermeasures should be monitored as part of any ongoing effort to maintain *AMedP-8(C)*'s currency.

1. Bioscavengers

Bioscavengers have demonstrated some potential for protecting humans against the effects of organophosphate chemical warfare agents. A number of these drugs are in advanced development and have reached various stages of clinical trials. Used prophy-

lactically, bioscavengers may alter the dose-response to nerve agents for some period of time.

Consideration of bioscavengers within the *AMedP-8(C)* methodology would require the development of the best possible estimates of the efficacy of these drugs. This estimation of efficacy could be done through a review of existing literature, a survey of ongoing bioscavenger development programs, and discussions with program participants and subject matter experts (SMEs). Such consideration would also need to incorporate a discussion of potential side effects and regulatory issues. This process is fairly straightforward and is estimated to require approximately three person-months. In addition, subsequent analysis would be required to revise the dose or dosage ranges for each exposure type or route of entry for GB and VX. This analysis is estimated to require an additional person-month for analysis and review, for a total of four person-months.⁷

2. Vaccines and Therapeutics

In 2011, IDA prepared a paper⁸ on the impact of medical countermeasures and treatment on the parameters and values now used to estimate casualties with the *AMedP-8(C)* methodology. The literature review conducted in support of that analysis highlighted a number of ongoing efforts to develop vaccines and therapeutics to prevent or mitigate biological agent-induced illness. Several of these efforts are nearing fruition, with new vaccines and therapeutic drugs becoming available over the next several years. These vaccines include but are not limited to new botulism candidates and anthrax human immune globulin.

To maintain currency in *AMedP-8(C)*, continued interactions with SMEs in this area and intermittent reviews of newly published literature would be required. The results of this activity would be documented and published as part of the planned 2012 Addendum to *AMedP-8(C)*. The associated level of effort is estimated to require approximately one person-month.

C. Incorporate New Human Response Data

To maintain currency in *AMedP-8(C)*, newly published studies and analyses of various aspects of CBRN human response should be reviewed regularly. As judged appropriate, these data could be used to update existing *AMedP-8(C)* human response models.

⁷ As bioscavenger development continues to advance, corresponding policy, doctrine, and operational concepts for use will also need to be developed. The level of effort estimated herein is restricted to that required to extend the *AMedP-8(C)* casualty estimation methodology to consideration of bioscavengers and does not include the level of effort needed for analysis to support resolution of these other issues.

⁸ Carl A. Curling et al., *The Impact of Medical Care on Casualty Estimates from Battlefield Exposure to Chemical, Biological and Radiological Agents and Nuclear Weapon Effects*, IDA Document D-4465 (Alexandria, VA: Institute for Defense Analyses, May 2012). Draft Final.

1. Q Fever in the Netherlands

From 2007 through 2010, a large outbreak of Q fever in the Netherlands sickened over 4,000 individuals and resulted in 18 fatalities. Early reports tend to support many of the human response model parameter values incorporated into the proposed *AMedP-8(C)* model of Q fever, including duration and severity of illness and mortality rate. However, more rigorous studies of the outbreak are now being published and should be reviewed to refine these parameters, as appropriate. For example, current parameters for the duration of illness with treatment are based on limited data that describe the effectiveness of antibiotics in truncating the febrile period. The persistence of other symptoms, however, is not well characterized, and the data emerging from this outbreak might help. More importantly, the prevalence of chronic fatigue following the acute phase of illness seems to be significantly higher in The Netherlands than in earlier outbreaks elsewhere, and our Dutch colleagues have suggested that we consider adding a second phase to our model of Q fever to capture the extended period of convalescence experienced by a significant percentage of individuals in their recovery from the illness.

Updating the proposed *AMedP-8(C)* model of Q fever is estimated to require approximately one person-month for literature review, correspondence with SMEs, and documentation in the planned 2012 Addendum to *AMedP-8(C)*.

2. Experiments with Military Research Volunteers

In earlier versions of *AMedP-8(C)*, human response models for Q fever, tularemia, and SEB relied heavily on a large set of human experimental data involving Military Research Volunteers (MRVs). As part of IDA's 2010 effort to extend the current *AMedP-8(C)* methodology to these three agents, IDA actively tried to gain access to the MRV data but was unable to do so. While the study team used some of the submodel parameters included in the earlier human response models, we were unable to reproduce them and cannot confirm whether they are correct. Moreover, since MRV data are by far the most comprehensive set of controlled human data available for these agents, these data could be extremely useful for refining other parameters (e.g., duration of illness with treatment) not included in the earlier models.

If the MRV data were to become available, approximately three person-months would be needed to compile and analyze these data and make appropriate changes to the *AMedP-8(C)* human response models. The results would be documented in the planned 2012 Addendum to *AMedP-8(C)*.

D. Align *AMedP-8(C)* Models with the Common User Database (CUD)

As part of IDA's ongoing efforts to support the alignment of *AMedP-8(C)* and the CUD, IDA recently reviewed the list of CUD patient conditions to determine the extent to which the range of casualties now estimated by *AMedP-8(C)* have associated patient

conditions. The study team also identified areas where the CUD incorporated patient conditions that had no corollary within *AMedP-8(C)* for agents already considered. The team then developed recommendations for future work to extend current *AMedP-8(C)* models to fill the identified gaps. All of the cases where the team determined augmentation would be beneficial were nuclear related.

1. Whole-Body Radiation

Whole-body radiation injuries progress in severity over time as a function of dose. Both *AMedP-8(C)* and the CUD derive their definitions of casualties from this dose-dependent progression of illness, but they do so differently and for different purposes. *AMedP-8(C)* defines casualties in terms of the severity of their injuries at the time they enter the medical system. This approach allows users to derive a patient stream from the progression of injury. For whole-body radiation, casualties may be mild, moderate, or severe. The CUD defines whole-body radiation casualties by the dose of radiation received. For example, patient condition 130567 is “radiation injury at level R2 (0.7–1.25 Gy) without other physical injury.” Assuming that the progression of injury is the same for all patients in this dose range, the CUD definition allows calculation of treatment requirements from the point of injury forward, regardless of how severe that injury is at the time of presentation.

The injury profiles used by *AMedP-8(C)* to determine the time at which severity reaches a defined level are associated with specific dose ranges. Consequently, aligning the definition of casualty between the two models can be accomplished simply if *AMedP-8(C)* reports dose information as part of its output.

At the same time, *AMedP-8(C)* incorporates injury profiles for five dose ranges, while the CUD calculates resource requirements for seven dose ranges. Further review and assessment will be needed to determine whether the CUD dose ranges capture clinically relevant variations in treatment requirements or whether they can be reasonably collapsed. If the former, the *AMedP-8(C)* dose ranges should be expanded to consider these variations.

Updating the proposed *AMedP-8(C)* model of whole-body radiation to better align it with the CUD is estimated to require approximately one person-month for analysis, review, and documentation in the planned 2012 Addendum to *AMedP-8(C)*.

2. Blast

At present, *AMedP-8(C)* and the CUD are completely misaligned with regard to blast injuries from nuclear weapons. *AMedP-8(C)* only considers the primary blast injuries (PBIs) that occur when the blast wave acts directly upon the human body. Rapid compression and decompression result in the transmission of pressure waves through the

tissues. These waves can be quite severe and will result in damage primarily at junctions between tissues of different densities (bone and muscle) or at the interface between tissue and air spaces. Lung tissue and the gastrointestinal system, both of which contain air, are particularly susceptible to injury. The resulting tissue disruptions can lead to severe hemorrhage or to air embolism, either of which can be rapidly fatal. Perforation of the eardrums would be a common, but a minor, blast injury.

At the same time, *AMedP-8(C)* currently ignores higher order blast effects such as missileing (secondary blast injury), whole-body translation (tertiary blast injury), or crushing from building collapse (quaternary blast injury). Historically, the study team has considered it difficult to model the nature and frequency of these effects in a population at risk due to the large uncertainties in predicting the actual environment or the posture of exposed individuals.

The CUD does not include patient conditions for primary blast injury. It does, however, include a limited number of patient conditions that could be used broadly to estimate the resource requirements for higher order blast injuries, specifically “perforation or other disorders of the tympanic membrane” and “injury due to war operations by other explosions.”

For the consideration of nuclear blast injuries to be comprehensive, significant work would need to be done (1) within the CUD to add patient conditions for primary blast injuries and to expand those for higher order blast injuries and (2) within *AMedP-8(C)* to allow estimation of wounded in action (WIA) casualties suffering from secondary, tertiary, or quaternary blast injuries.

Updating the proposed *AMedP-8(C)* model of blast injury to account for higher order effects will require (1) literature reviews to identify prior research and data sources that correlate the blast (and blast damage) levels anticipated around a nuclear detonation with injuries and (2) further analysis that identifies the specific parameters for use in the modified *AMedP-8(C)* CBRN casualty estimation methodology. This review and analysis is estimated to require approximately 20 person-months.

3. Burns

There is an apparent misalignment of the *AMedP-8(C)* casualty categories and CUD patient condition codes for burn injuries. The CUD defines burn-patient condition codes on the basis of the part of the body injured, while *AMedP-8(C)* burn-casualty categories are expressed as a function of the severity of the injuries.

Alignment of a casualty category to a specific patient condition code is problematic because *AMedP-8(C)* does not entail any information on which part of the body is burned and does not, at present, consider any inputs from which this information could be derived. Assuming that burns of equal size on different parts of the body have different

treatment requirements, it is desirable for the CUD to retain its broad range of burn patient condition codes and for *AMedP-8(C)* to be expanded to provide the information needed as inputs to the CUD.

One way to do align these casualty categories is to develop a probability distribution function for each category, similar to the “patient condition occurrence frequency” (PCOF) used in medical analysis tools. This approach would allow the medical planner to assign the casualties in a given severity category among the various relevant patient condition codes.

Updating the proposed *AMedP-8(C)* model of burn injury to estimate the distribution of the extent and portions of the body burned during a nuclear detonation will require (1) literature reviews to identify prior research and data sources that correlate the thermal fluence (and individual exposure) anticipated around a nuclear detonation with injuries and (2) further analysis that identifies the specific parameters for use in the modified *AMedP-8(C)* CBRN casualty estimation methodology. This review and analysis is estimated to require approximately 18 person-months.

E. Extend *AMedP-8(C)* To Consider Additional Agents

The extension of the *AMedP-8(C)* methodology to additional agents would have two objectives: to respond to the interests and priorities of sponsors and to promote further the alignment of *AMedP-8(C)* with the CUD, which considers a much larger number of CBRN agents and effects.

The list of chemical and biological agents included in the CUD program of work is the result of a process of nomination and prioritization from two organizations: OTSG and DTRA. Both organizations submitted their prioritized chemical and biological agent lists in document form:

- Office of the Surgeon General (OTSG) Guidance to Defense Medical Standardization Board (DMSB) Common User Database (CUD)—handout to authors, 3 September 2009
- Defense Threat Reduction Agency (DTRA) Guidance to Defense Medical Standardization Board (DMSB) Common User Database (CUD)—handout to authors, 3 September 2009

At present, IDA has implemented the *AMedP-8(C)* methodology for 13 of the agents included in the CUD program of work, as described in preceding sections. This implementation includes 11 of the 12 agents designated as priority agents by OTSG and DTRA during the selection process. ARA, with funding from DTRA, has developed human response models for five chemical agents (chlorine, cyanogen chloride, hydrogen cyanide, hydrogen sulfide, and phosgene). Phosgene is the final agent designated as a priority by OTSG and DTRA.

1. Extension of *AMedP-8(C)* To Meet Sponsor Priorities

Discussions with sponsors in OTSG and the Joint Staff have revealed that five biological agents (ricin, melioidosis, Marburg hemorrhagic fever, eastern equine encephalitis (EEE), and western equine encephalitis (WEE)) have engendered enough interest to place them at the top of the list when prioritizing the extension of *AMedP-8(C)*. All five of these agents are included in the CUD program of work. Table 1 summarizes the estimated level of effort required for IDA to develop human response models for each of these agents and notes whether the agent is currently considered within the CUD.

Table 1. Biological Agents of Priority Interest, 2011

Agent Class (CBRN)	Agent Name	Included in CUD?	Level of Effort (Person-Months)
Biological	Ricin	Yes	9
Biological	Eastern Equine Encephalitis	Yes	6
Biological	Western Equine Encephalitis	Yes	6
Biological	Melioidosis	Yes	6
Biological	Marburg Hemorrhagic Fever	Yes*	11

* Within the CUD, unless otherwise specified, all hemorrhagic fever viruses are considered generally within the categories of mild, moderate, and severe viral hemorrhagic fevers.

For melioidosis, EEE, and WEE, the estimated level of effort is the minimum required to develop parameter values and injury profiles for a given agent. All three of these agents are well described in the literature and, to some extent, are analogous to agents already considered (VEE and glanders), meaning that IDA researchers have prior knowledge of the behavior of the organism, the mechanism of action within the body, and the general human response associated with that agent.

Although ricin poisoning via ingestion or injection is documented in the literature, aerosol exposure in humans has never been reported. Because clinical manifestation and progression of illness vary by route of exposure for biological toxins, existing cases studies of ricin poisoning may not provide sufficient information, and additional work will be required to develop various submodels. Consequently, extending the *AMedP-8(C)* methodology to consider ricin is estimated to require three additional person-months of effort.

Finally, the estimated level of effort to consider Marburg is significantly higher than that for other agents on this list. In general, consideration of contagious diseases is more complex and requires a substantial modeling effort to derive the parameter values used in contagious disease modeling.

2. Extension of *AMedP-8(C)* to Align with the CUD

Extending *AMedP-8(C)* to consider all of the agents already in the CUD would require a great deal of effort. Priority should be given to those agents that are of particular current interest to the sponsors of the work, as described previously. Beyond that, a number of criteria could be used to prioritize additional work. These criteria include those agents for which human response models now exist but would require adaptation for use in *AMedP-8(C)*; those agents that have been a high priority previously, as demonstrated by inclusion on both the OTSG and DTRA inputs to the CUD program of work; and the remaining agents now considered within the CUD.

a. ARA Chemical Human Response Models

In 2010, ARA developed human response models for five chemical agents (chlorine, cyanogen chloride, hydrogen cyanide, hydrogen sulfide, and phosgene). Treatment narratives and task and resource lists have been completed under the CUD program of work for all five of these agents. IDA reviewed and commented on this work in its early stages, with the objective of facilitating the integration of this work into *AMedP-8(C)*. Although the work remains unpublished, we believe that integrating these five chemical human response models will be straightforward and is estimated to require approximately three person-months of effort in total for data and algorithm review, reproduction of outputs, and derivation of specific parameters.

b. OTSG/DTRA Priorities Used To Direct the CUD Program of Work

Some 14 agents appeared on both the OTSG and DTRA lists used to develop the CUD program of work. Of these, 10 agents have already been considered in *AMedP-8(C)*. Of the remainder, one of these agents, Marburg, is on our list of agents of interest, and another agent, phosgene, is on the list of chemical agent human response models developed by ARA. Two additional agents, cholera and Ebola hemorrhagic fever, have not yet been addressed. Table 2 summarizes the estimated level of effort required for IDA to develop human response models for each of these agents, and notes the status of that agent vis-à-vis the CUD.

Table 2. Common User Database Agents on Both OTSG and DTRA Lists, Not Otherwise Considered

Agent Class (CBRN)	Agent Name	Included in CUD?	Level of Effort (Person-Months)
Biological	Cholera	Yes	9
Biological	Ebola Hemorrhagic Fever	Yes	11

* Within the CUD, unless otherwise specified all hemorrhagic fever viruses are considered generally within the categories of mild, moderate, and severe viral hemorrhagic fevers.

Cholera is a common disease worldwide, and many characteristics of the disease have been well documented in the literature. However, it is not traditionally considered or modeled as a biological warfare agent, and many of the specific parameters (e.g., infectious dose as a function of route of entry and incubation period) may not have been assessed with the rigor needed to support *AMedP-8(C)* submodels.

As with Marburg, the level of effort required to consider Ebola hemorrhagic fever virus is driven largely by the need to derive parameter values to allow modeling of the contagious aspects of the disease. Because Ebola and Marburg are genetically similar viruses with similar clinical manifestations, significant overlap between these two diseases exist. Consideration of both viruses would allow some consolidation of effort.

c. Remaining Agents Considered in the CUD

In addition to the 13 agents for which *AMedP-8(C)* human response models now exist, 12 agents are discussed previously as being priorities for further work because of sponsor interest, data availability, and CUD program prioritization. Beyond that, 26 other agents are now considered within the CUD. Table 3 (biological agents) and Table 4 (chemical agents) summarize the estimated level of effort required for IDA to develop human response models for each of these agents.

As with the agents discussed previously, the estimates for level of effort for each proposed modification consider the familiarity that IDA researchers have with the relevant literature and the perceived complexity of the associated analyses. For the extension of *AMedP-8(C)* to additional agents not currently modeled, estimates of level of effort are taken from the 2009 and 2010 reports. These estimates are derived from an assessment of the availability of required data in the literature and include the development of models with and without treatment.

Table 3. Estimated Level of Effort for Other Biological Agents Considered within the CUD

Agent Class (CBRN)	Agent Name	Level of Effort (Person-Months)
Biological	Argentine Hemorrhagic Fever*	10
Biological	Bolivian Hemorrhagic Fever*	10
Biological	Brazilian Hemorrhagic Fever*	10
Biological	Crimean-Congo Hemorrhagic Fever*	8
Biological	Cryptosporidiosis	9
Biological	Escherichia coli O157:H7 (E. Coli)	15
Biological	Korean Hemorrhagic Fever*	8
Biological	Kyasanur Forest Disease*	13
Biological	Lassa Fever	10
Biological	Omsk Hemorrhagic Fever*	13
Biological	Psittacosis	15
Biological	Rift Valley Fever	9
Biological	Shiga Toxin (Shigellosis)	12
Biological	T-2 Toxin	13
Biological	Tick-Borne Encephalitis	10
Biological	Typhoid Fever	
Biological	Typhus Fever	15

* Within the CUD, unless otherwise specified all hemorrhagic fever viruses are considered generally within the categories of mild, moderate, and severe viral hemorrhagic fevers.

Table 4. Estimated Level of Effort for Other Chemical Agents Considered within the CUD

Agent Class (CBRN)	Agent Name	Level of Effort (Person-Months)
Chemical	3-Quinuclidinyl Benzilate (BZ)	17
Chemical	Ammonia	9
Chemical	Cyclosarin (GF)	8
Chemical	Hydrogen Chloride	8
Chemical	Lewisite (L,L-1,L-2,L-3)	8
Chemical	Nitric Acid	8
Chemical	Nitrogen Mustard (HN-1, HN-2, HN-3)	8
Chemical	Soman (GD)	8
Chemical	Sulfur Dioxide	8

F. Psychological Casualties

An adversary's use of CBRN agents might cause significant numbers of psychological casualties, although none of this class of casualties is presently considered in *AMedP-8(C)*. Extension of the *AMedP-8(C)* methodology to estimate psychological casualties would require the following:

- Psychological casualties must be appropriately characterized to differentiate those that would impact the acute casualty estimate from those that might be delayed beyond the period of interest. From the literature review already performed, it is clear that definitions of psychological casualties are continuing to evolve, and arriving at a consensus on terminology and development of a clear problem statement and approach is estimated to require six person-months of effort.
- It would be necessary to develop a correlation of the types of psychological casualties of interest to the different classes of CBRN agent and, potentially, to the populations at risk. To the extent possible, data would need to be collected to characterize that response within the CBRN class or agent models. If no data are available, a review and analysis of related studies and modeling efforts in the literature would have to be used to extrapolate this correlation. Examples include estimates of the psychological impact of nuclear attacks made during the Cold War and more recent assessments of the psychological impact of terrorist attacks, natural disasters, large-scale accidents (e.g., Bhopal), and combat stress. Developing this correlation would require a considerable analytic effort that is estimated to require approximately 18 person-months.
- Planning factors and rules of thumb for modifying *AMedP-8(C)* casualty estimates would have to be derived and accredited. Given that the previous steps had been completed successfully, this work is primarily a requirement for analysis, documentation, and presentation and is estimated to require another six person-months of effort.

3. Nomination of Additional Agents

The sponsors of this effort within OTSG and the Joint Staff have stated that their 2012 priorities for the development of *AMedP-8(C)* are to maintain currency of the underlying data, to address agents of specific interest, and to continue the process of aligning *AMedP-8(C)* human response models with the treatment protocols and associated personnel and materiel requirements delineated in the CUD.

To that end, the IDA study team suggests that *AMedP-8(C)* human response modeling work be prioritized as follows:

- First, existing human response models should be updated, as required, to take advantage of new data from ongoing medical countermeasure research programs and from recent large-scale disease outbreaks. In particular, new data are starting to emerge from research into bioscavengers, vaccines against botulinum toxin and Ebola/Marburg hemorrhagic fevers, and the recent outbreak of Q fever in the Netherlands. In addition, if the data from experiments involving MRVs were to become accessible, the existing human response models for tularemia, Q fever, and SEB should be reviewed.
- Second, current *AMedP-8(C)* models should be extended to fill identified gaps in areas where the CUD incorporates patient conditions that have no corollary within *AMedP-8(C)*.
- Third, new human response models should be developed for any agents of priority interest to the sponsors of *AMedP-8(C)*. At present, these agents include EEE, WEE, Marburg hemorrhagic fever, melioidosis, and ricin.
- Fourth, the chemical human response models developed by ARA (chlorine, cyanogen chloride, hydrogen cyanide, hydrogen sulfide, and phosgene) should be incorporated into *AMedP-8(C)*.
- Fifth, new human response models should be developed for those remaining agents now incorporated into the CUD, with priority being given to the two agents (cholera and Ebola hemorrhagic fever) that appeared in both the DTRA and OTSG inputs to the CUD program of work.
- Finally, the estimation of psychological casualties resulting from the use of CBRN weapons has long been considered an important requirement but one that

has been either too difficult or of too low priority. IDA's initial investigations in this area have led us to conclude that such estimation is feasible within the framework of *AMedP-8(C)*, and we are prepared to address this problem should it become a priority.

Appendix A

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Appendix B

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- Curling, Carl A., Lucas L. LaViolet, and Julia K. Burr. *2010 Review on the Extension of the AMedP-8(C) Methodology to New Agents, Materials, and Conditions*. IDA Document D-4131. Alexandria, VA: Institute for Defense Analyses, December 2010.
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Appendix C

Abbreviations

<i>AMedP-8(C)</i>	NATO Allied Medical Publication 8(C)
ARA	Applied Research Associates
CBRN	Chemical, Biological, Radiological, and Nuclear
CRN	Chemical, Radiological, and Nuclear
CUD	Common User Database
DHS	Department of Homeland Security
DMSB	Defense Medical Standardization Board
DoD	Department of Defense
DTRA	Defense Threat Reduction Agency
EEE	Eastern Equine Encephalitis
GB	Sarin
GD	Soman
GF	Cyclosarin
HD	Distilled Mustard
HHS	Department of Health and Human Services
IDA	Institute for Defense Analyses
MRV	Military Research Volunteer
NATO	North Atlantic Treaty Organization
OTSG	Office of the Surgeon General
PBI	Primary Blast Injury
PCOF	Patient Condition Occurrence Frequency
SEB	staphylococcal enterotoxin B
SME	Subject Matter Expert
VEE	Venezuelan Equine Encephalitis
WEE	Western Equine Encephalitis
WIA	Wounded in Action

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