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EMERGENCY MANAGEMENT ISSUES SPECIAL INTEREST GROUP

Launching Emergency Management Leadership

Chemical Mixture Method Update

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CMM Rev. 27 - Status

- CMM Workbook “Rev. 27” will be published after the SCAPA meeting
- CMM Rev. 27 contains the PAC/TEEL data published in PAC Rev. 27
- CMM and PAC data set are “consistent”
  - CMM analysis uses the most updated PAC values

HCN Update Task - Status

- The HCNs of over 3,300 chemicals have been reviewed and updated (as appropriate) and all the updated HCNs are in CMM Rev. 27
- The HCN review and update activity started in 2008
- The HCN update task was completed in 2011

CMM Rev. 28 Status

- About 500 chemicals will be reviewed annually per NA-41 direction
  - Priorities will be literature review for those chemicals that have not been reviewed in the past 6-7 years
  - 15% independent QA review will be followed
- Explore potential CMM enhancement options by conducting additional testing
- Release CMM Wizard prototype

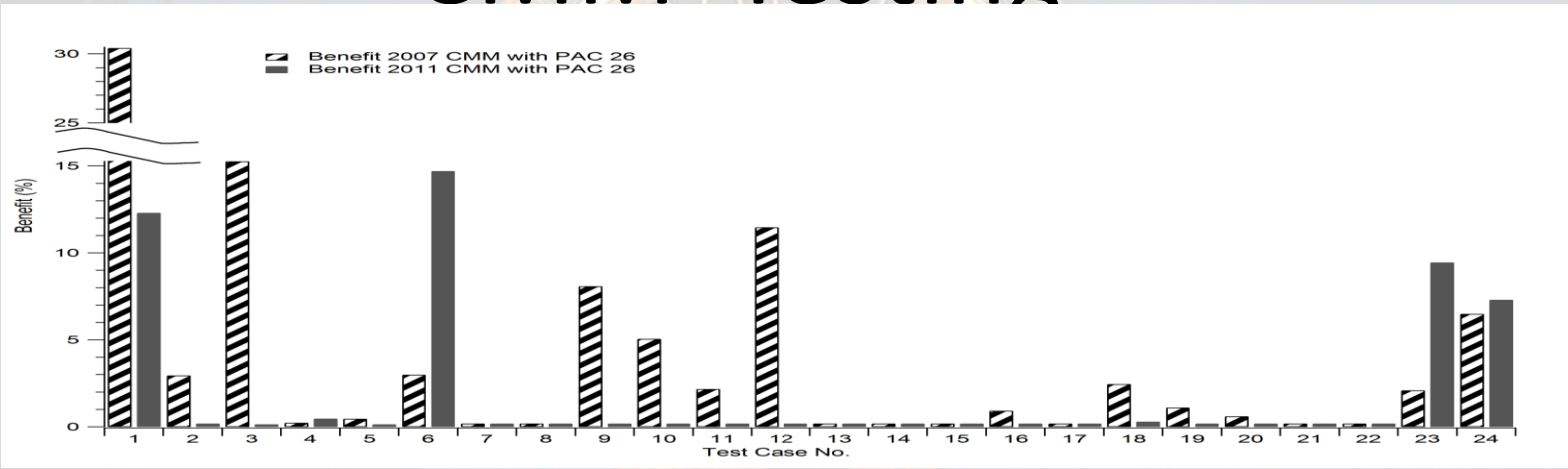
CMM Project Team

- Experienced Intern: Juan Yao (WSU)
- Departing STAR Fellow: Alex Booth (WWU)
- New summer Interns:
  - Sarah Horn (CU), NSF STAR fellow
  - Two undergraduate students, DHS-HS-STEM
- Intern Coordinators: Xiao-Ying Yu and Cliff Glantz
- Senior Mentor: Rocky Petrocchi, ATL

CMM Testing

- The CMM interns conducted a detailed CMM case study involving 24 chemical mixtures
- The CMM's HCN-based approach provides a benefit over the simple summing of all HIs in cases where the significant chemicals affected different target organs.
- Somewhat less benefit is seen in the 2011 version of the CMM then in the 2007 version of the CMM.
- In some cases the 2007 version was non-conservative. In other instances the 2011 version was overly conservative.

CMM Testing



- Differences between 2007 and 2011 versions of the CMM are likely due to:
  - The addition of more than 5 HCNs per chemical
  - Addition of more HCN categories (2011) as opposed to the previous fewer HCN categories (2007) appears to have decreased the benefit of the CMM's Target-Organ analysis.

CMM Enhancement

- It would be beneficial to find a way to reduce the new over conservatism in the CMM.
- Simply returning to using fewer HCNs is not a good answer.
- The consensus is to examine applying weighting factors to the HCNs based on their potential relevance for the threshold limit value (e.g., PAC-2).

Approaches explored so far

- Four weighting approaches were tested:
  - "Generic" – base weighting on the rank order of the HCNs listed for a chemical
  - "Percentile" – base weighting on generic tables listing all the HCNs
  - "Exposure Routes" – base weighting on toxic effects on target organ or mode of action induced by primary or the most common routes of exposure in an emergency
  - "Combined" – base weighting on both percentile and exposure routes induced primary target organ and route of exposure

Weighting factors: an example using tri(2-ethylhexyl) phosphate

HCN Priority Ranking	HCNs	Approach 1 Generic Weighting Factor	Approach 2-Alpha Percentile Weighting Factor	Approach 2-Beta Stepwise Weighting Factor	Approach 3		
					Exposure Weighting Factor		Stepwise Weighting Factor
1	15.01	0.5[a]	0.5	1.0[b]	1	×	0.8
2	15.02	0.5[a]	0.5	0.8	1	×	0.8
3	7.11	0.8	0.5	0.4	1	×	0.4
4	10.00	0.7	0.5	0.4	1	×	0.4
5	3.09	0.6	0.5	0.4	1	×	0.4
6	3.02	0.5	0.5	0.4	0.75	×	0.4
7	3.10	0.4	0.5	0.4	0.75	×	0.4
8	3.07	0.3	0.5	0.4	0.75	×	0.4
9	3.01	0.2	0.5	0.4	1	×	0.4
10	3.11	0.1	0.25	0.2	0.75	×	0.2

Annual Meeting • May 14 – 17, 2012 • Marriott Renaissance Seattle Hotel • Seattle, Washington

What we learned,

- The approach employing a priority ranking of the HCNs based on their potential impact to an individual's ability to take protective actions provides the most appropriate balance during initial testing and it warrants further study by our new interns.
- The approach incorporating exposure route information underwent limited testing and it warrants further study by our new interns.
- Enhancements to the CMM can provide more accurate estimates of health effects and make appropriate and cost effective emergency planning decisions.

In the near future,

- The interns will conduct further testing to explore ways to improve the CMM
- The interns will examine a new focus on target organ and specific target organ systems in this round of testing. This looks like a promising new approach that will improve the technical defensibility of the CMM and provide a greater benefit to users.
- Invited article reporting recent testing of the CMM was submitted to the journal "Toxicology" in April

CMM Wizard

- The CMM Wizard is an on-line version of the CMM with additional features to enhance usability.
- This is an effort supported by our NSF STAR interns Kimberly Schutte and Alex Booth
- The new CMM Wizard will be presented in the next talk…

Thank you!

- Questions?
- Comments?

Weighting factors for Approaches 2-Alpha and 2-Beta.

2a. Approach 2-Alpha						
Rank	HCN	WF		Rank	HCN	WF
1	17.00	1		31	1.02	0.5
2	18.00	1		32	2.00	0.5
3	13.00	1		33	2.01	0.5
4	6.00	1		34	2.02	0.5
5	14.01	1		35	3.05	0.5
6	14.00	1		36	7.11	0.5
7	15.01	0.5[a]		37	7.10	0.5
8	15.00	0.5[a]		38	10.00	0.5
9	4.01	1		39	9.00	0.5
10	11.01	1		40	3.09	0.5
11	14.02	1		41	3.02	0.5
12	15.02	0.5[a]		42	3.04	0.5
13	4.00	1		43	3.10	0.5
14	4.08	1		44	3.07	0.5
15	4.05	1		45	3.01	0.5
16	7.01	0.75		46	3.03	0.25
17	8.00	0.75		47	3.06	0.25
18	7.00	0.75		48	12.00	0.25
19	11.00	0.75		49	5.00	0.25
20	4.02	0.75		50	5.10	0.25
21	4.09	0.75		51	4.11	0.25
22	4.06	0.75		52	3.11	0.25
23	4.04	0.75		53	4.12	0.25
24	4.10	0.75		54	3.12	0.25
25	4.07	0.75		55	3.00	0.25
26	4.03	0.75		56	16.01	0.25
27	4.13	0.75		57	16.00	0.25
28	3.08	0.75		58	16.02	0.25
29	1.00	0.75		59	19.00	0.25
30	1.01	0.75		60	20.00	0.25

2b. Approach 2-Beta						
Rank	HCN	WF		Rank	HCN	WF
1	17.00	1		31	10.00	0.4
2	18.00	1		32	9.00	0.4
3	11.01	1		33	7.11	0.4
4	11.00	1		34	7.10	0.4
5	7.01	1		35	12.00	0.4
6	7.00	1		36	3.01	0.4
7	8.00	1		37	3.02	0.4
8	14.01	1		38	3.03	0.4
9	4.08	1		39	3.04	0.4
10	4.05	1		40	3.05	0.4
11	4.01	1		41	3.06	0.4
12	6.00	1		42	3.07	0.4
13	14.00	1		43	3.08	0.4
14	14.02	1		44	3.09	0.4
15	13.00	1		45	3.10	0.4
16	15.01	0.8[b]		46	3.00	0.4
17	15.00	0.8[b]		47	1.00	0.4
18	15.02	0.8[b]		48	1.01	0.4
19	4.00	0.8		49	1.02	0.4
20	4.02	0.8		50	2.00	0.4
21	4.03	0.8		51	2.01	0.4
22	4.06	0.8		52	2.02	0.4
23	4.07	0.8		53	16.01	0.2
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26	4.10	0.6		56	5.10	0.2
27	4.11	0.6		57	3.11	0.2
28	4.12	0.6		58	3.12	0.2
29	4.13	0.6		59	19.00	0.1
30	5.00	0.6		60	20.00	0.1

Priority order of the literature used to identify exposure routes in Approach 3

Order	References*
1	AEGL[a]: toxicity data
2	ERPG[b]: toxicity data
3	HSDB[c]: toxicity data
4	RTECS[d]: toxicity data
	TLVs and BEIs[e]: toxicity data
5	NIOSH[f]: toxicity data
6	CHRIS[g]: symptoms
7	SAX[h]: safety profile
8	MSDS[i]: toxicity data

Weighting factors used in Approach 3 for evaluation of exposure routes

Exposure Routes	Weighting Factor
Inhalation	1
Skin and /or eye contact	1
Oral	0.75
Other exposure routes but primary target organ	0.5
Other unspecified routes but not primary target organ	0.25