REVIEW OF THE DEPARTMENT OF LABOR'S SITE EXPOSURE MATRIX DATABASE

Committee on the Review of the Department of Labor's
Site Exposure Matrix (SEM) Database

Board on the Health of Select Populations

INSTITUTE OF MEDICINE
OF THE NATIONAL ACADEMIES

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BOX S-1
Statement of Task

The Institute of Medicine will convene a panel of experts to review the scientific rigor and organization of the Site Exposure Matrix (SEM) database. The committee's focus will be on the occupational disease links to chemical usage/exposure; the National Institutes of Health's (NIH's)/National Library of Medicine's (NLM's) review process with regard to Haz-Map, and the review process used by Haz-Map developer when including information in the Haz-Map database. Haz-Map is an occupational health database about the health effects of exposures to chemicals and biologicals at work; it links jobs and hazardous tasks with occupational diseases and their symptoms. The committee will identify strengths and weaknesses of the SEM and make recommendations for addressing any weakness. Additionally, the following questions, here described as tasks, will be addressed in the report issued by the committee.
    Tasks:

1. What, if any, occupational diseases that might have affected the DOE contractor workforce are missing from SEM?
2. What, if any, links between occupational diseases and toxic substances present at the Department of Energy (DOE) sites are missing from SEM?
3. Is there additional literature (preferably human epidemiological in nature) that might be incorporated into SEM to strengthen or add to the existing links between toxic substances and occupational diseases? Are the existing links sufficiently robust?
4. What, if any, other occupational disease databases might be used to supplement the Haz-Map information in SEM?
5. How scientifically rigorous are the disease links contained in the SEM and Haz-Map?
6. What are the strengths and weaknesses of the NIH/NLM peer review process with regard to Haz-Map? How might this process be improved?
7. Can any known (epidemiologically significant) synergistic effects between chemicals/chemicals or chemicals/radiation be placed in SEM? If so, what are the sources of these links and are they occupational in nature?
8. What consistent process or approach could be used to consider a disease or cancer established when studies are inconclusive, inconsistent, or conflicted in some way?

TABLE 3-2 Selected Missing Links for Toxic Substance–Cancer Based on Sufficient Evidence of Cancer in Humans[a]

SEM Substance	Cancer Site
Arsenic	Urinary Bladder
Asbestos	Ovary
1,3-Butadiene	Hematolymphatic Organs[b]
Coal Tar Pitch Volatiles	Lung[c]
Diesel Exhaust	Lung[d]
Formaldehyde	Leukemia[d]
Hepatitis B Virus	Liver (hepatocellular carcinoma)
Iodine 131	Thyroid
Plutonium	Bone[e]; Liver
Radium	Bone[d]; Mastoid Process; Paranasal Sinus[d]
Radon	Lung[d]
Strontium 90	Leukemia; Solid Cancers
Thorium	Bile Duct, extrahepatic; Gall Bladder; Leukemia (excluding chronic lymphocytic leukemia); Liver (including hemangiosarcoma)
o-Toluidine	Urinary Bladder[d]
Trichloroethylene	Kidney[e]

[a]Except as noted (see footnote d), identified by IARC as sufficient evidence of cancer in humans as described in Cogliano et al. (2011) and IARC (2011). IARC (2012) reclassified diesel exhaust as sufficient evidence of cancer in humans.

[b]Haz-Map identifies "Leukemia" and "Lymphoma, Non-Hodgkin" as the cancer sites linked to 1,3-butadiene.

[c]Scheduled to be added to Haz-Map at the end of 2012 (www.Haz-Map.com). Presumably will be added to SEM when the database is updated.

[d]Listed in Haz-Map. Presumably will be added to SEM when the database is updated.

[e]Identified by EPA as sufficient evidence of cancer in humans by all routes of exposure (EPA, 2011).

links shown in Table 3-2 for arsenic, asbestos, and hepatitis B virus to SEM so that it is transparent to SEM users.

The rationale for not including in SEM the trichloroethylene–kidney cancer link established by EPA may be due to the fact that trichloroethylene has not been identified as a Group 1 carcinogen by IARC (IARC, 1995).[3] As a result, the trichloroethylene-cancer link does not meet the Haz-Map criterion for cancer causality. EPA classified trichloroethylene as carcinogenic in humans by all routes of exposure based on the results of a meta-analysis that included occupational

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[3]In December 2012, a news item was published in the *Lancet* describing IARC's recent reclassification of trichloroethylene as a Group 1 carcinogen with sufficient evidence of carcinogenicity in humans for kidney cancer (Guha et al., 2012).

The committee conducted an exercise to illustrate where toxic substance–disease links might be missing in SEM and to identify reasons for the omissions. Overall, the committee found that links may be missing in SEM for several reasons, including ambiguous criteria for establishing the links in Haz-Map (the source of the SEM links); lack of consistency between the Haz-Map "Diseases" field and the SEM "Specific Health Effects" field for some substances; an inability to deal with complex exposures, such as exposures to mixtures; and delays in updating links in Haz-Map and thus in SEM.

RECOMMENDATIONS

The committee found that focusing on information in only one SEM field, "Specific Health Effects," as imported from the Haz-Map "Diseases" field, without consideration of the EEOICPA claims process was difficult because its review lacked context. Furthermore, the "Specific Health Effects" field did not permit consideration of many aspects of occupational health, including level of exposure (concentration, frequency, and duration), strength of association, and exposure to more than one chemical at a time. Nevertheless, the committee came to three overarching recommendations for improving the toxic substance–disease links in SEM:

1. Add supplemental information sources to the health effects information imported from Haz-Map.
2. Improve the structure and function of SEM, including the addition of available exposure information.
3. Use an external advisory panel to review the health effects information in SEM.

Although those three recommendations focus on improving SEM, recommendations 1 and 3 and portions of recommendation 2 are also applicable to Haz-Map. The committee believes that establishing a formal oversight and review process for the Haz-Map database and using a weight-of-evidence approach are critical for both maintaining and expanding the Haz-Map database and for its use in SEM. Expansion of the information used in Haz-Map and inclusion of citations for all the information in each of its fields would greatly enhance its utility not only for SEM but also for other users. Peer review of the database would also increase public confidence in its accuracy and comprehensiveness and help ensure that it contains the most current information available, irrespective of its use for SEM.

Each of these recommendations is discussed in greater detail in the following sections.

time that such a panel has been suggested and there is a precedent for such a panel as required in Part B of EEOICPA. Furthermore, the proposed EEOICPA Amendment Act of 2011(H.R. 1030) would have required the President to establish an Advisory Board on Toxic Substances and Worker Health to review and approve the SEM database.

An expert advisory panel could perform several important functions with regard to the SEM. This IOM committee recommends that the expert advisory panel be broad based, external to DOL and its current SEM contractor, and include a variety of expertise such as epidemiology, occupational medicine, toxicology, and industrial hygiene. The committee also recommends that the advisory panel include representation of the claimants and their advocacy organizations.

The expert advisory panel would have several immediate tasks:

- Establish the criteria for the evidence base for causal links between exposure to a toxic substance and an occupational disease; criteria might be expanded to include a category of "evidence of no association" as is used by IOM and IARC.
- Determine the information sources that might be reviewed to identify information on possible links.
- Develop a worksheet or other documentation to capture the evidence taken from each information source, including Haz-Map.
- Oversee revisions of SEM to add appropriate fields for capturing supplemental information (such as, chemical interactions, route of exposure, and IARC 2A designations), supplemental information sources (such as NTP, ATSDR toxicological profiles, and IRIS), and update information (such as the date of the last revision of the record and the fields revised).

The expert advisory panel would also have several ongoing responsibilities in support of EEOICPA, Part E:

- Peer review of all new links in SEM that are based on both Haz-Map and the supplemental information described earlier. This might include determining whether the appropriate references are screened and the data are accurately cited.
- Assessment of occupational diseases that might result from complex exposures.
- Identification of potential new links and tracking them for possible future inclusion in SEM, including those suggested by external sources.
- As time permits, review of existing causal links in SEM that are based solely on Haz-Map.
- Periodic review of a sample of the toxic substance–disease links from both accepted and rejected claims to determine whether SEM links are actually assisting in the claims process and, if not, what improvements

could be made in the toxic substance–disease links or what other information might be added to the SEM that would help claimants and claims examiners, such as available monitoring information, disease terminology, or results of cohort studies of DOE workers.

The committee recognizes that peer review is not a simple task, but it is critical if the SEM is to provide both DOL claims examiners and claimants with comprehensive, accurate, and understandable information. The committee also acknowledges that several approaches may be used to institute a peer review process for SEM, all of which have advantages and disadvantages. These approaches might include having the expert advisory panel review contractor assessments of the evidence available on toxic substance, having the expert advisory panel review the available evidence on a substance that was gathered by a contractor, or having the available evidence assessed by an internal expert advisory panel and then having the assessments reviewed by external experts. A major feature of each option is that all information and actions are documented so that the evidence base used to make decisions about the links between toxic substances and occupational diseases is transparent.

In summary, the committee recognizes the pressing need for SEM and the urgency with which it was developed and understands its inherent dynamic nature and the need to be able to adapt to updated and new information. However, as the EEOICPA claims process has evolved and new claims have continued to be submitted to DOL, the need for peer review of SEM (as well as Haz-Map) has increased. The committee believes that implementation of the recommendations in this report will make it possible for the DOL claims process to be improved for both claims examiners and claimants.

STATEMENT OF TASK QUESTIONS AND RESPONSES

In addition to offering recommendations to improve SEM, the committee provides here concise responses to the eight questions in its Statement of Task.

1. **What, if any, occupational diseases that might have affected the DOE contractor workforce are missing from SEM?**
    The committee examined the list of diseases in SEM and found that some diseases such as those of the cardiovascular system and ovarian cancer are not listed in it. Occupational diseases are listed in SEM only if they are associated with exposure to a toxic substance, so diseases associated with a particular job or worker population may not be included. Such organizations as IARC also look at associations between specific occupations (including painters and welders) and diseases in those workers without reference to exposure to specific toxic substances. DOL should consider those types of associations to identify other occu-