REVIEW OF THE ENVIRONMENTAL PROTECTION AGENCY'S DRAFT IRIS ASSESSMENT OF FORMALDEHYDE

Statement of

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and

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Good morning, Mr. Chairman and members of the subcommittee. My name is Jonathan Samet. I am Flora L. Thornton Chair and Professor in the Department of Preventive Medicine at the Keck School of Medicine of the University of Southern California. I am a pulmonary physician and epidemiologist and I have carried out population studies on the health effects of environmental pollutants for over three decades. I served as chair of the Committee to Review EPA's Draft IRIS Assessment of Formaldehyde, a committee of the National Research Council (NRC). The NRC is the operating arm of the National Academy of Sciences and the National Academy of Engineering. I also chair the Clean Air Scientific Advisory Committee (CASAC) of the EPA.

I am pleased to appear before you today to discuss our committee's recent report, *Review of the Environmental Protection Agency's Draft IRIS Assessment of Formaldehyde*, which was released on April 8, 2011. As stated in the policies of the National Academies, the purpose of report review in general is to assist the authors in making their report as accurate and effective as possible, enhancing the clarity, cogency, and credibility of the final document. Our review of the draft assessment was written by a 15-member committee that had a wide range of scientific expertise, appropriate to the task. Our charge primarily focused on specific questions related to the EPA's derivation of reference concentrations (RfCs) for noncancer effects and of unit risk estimates for cancer. Beyond these specific questions, the committee assessed the processes underlying the development of the draft and made suggestions about the process generally followed by EPA in developing the IRIS assessments. Our committee was not charged or constituted to carry out an independent review on the strength of evidence for causation of non-cancer effects and cancer by formaldehyde. We have provided a copy of the report for the Subcommittee and the Executive Summary is attached.

Formaldehyde is widely used and exposure to formaldehyde is ubiquitous, both indoors and outdoors. Consequently, the health effects of formaldehyde exposure have been a topic of research for decades. Past concerns arose because of exposures to people from various indoor sources and because of findings

of worker studies showing increased risks of nasopharyngeal cancer. Recently, one concern has been adverse health effects reported by people displaced by hurricanes who were relocated into trailers provided by the Federal Emergency Management Agency. Published research has also reported an association between leukemia and formaldehyde exposure.

The U.S. Environmental Protection Agency (EPA) has been working to update its assessment of formaldehyde for its Integrated Risk Information System (IRIS) for a number of years. The large amount of new research data on formaldehyde since its original assessment in the early 1990s has made the task challenging and lengthy. Given the complex nature of the IRIS assessment and the knowledge that the assessment will be used as the basis of regulatory decisions, the NRC was asked to conduct an independent scientific review of the draft IRIS assessment. Specifically, the committee was asked to answer questions concerning the EPA's identification of potential noncancer health effects, the toxicological basis for those health effects, and the basis of the determination of uncertainty factors used to derive the reference concentrations (RfCs). The committee was also asked specifically to comment on the scientific rationale provided for the cancer assessment and the quantified risk estimates derived.

To address its task, the committee reviewed the draft IRIS assessment and key literature, and determined whether EPA's conclusions were supported on the basis of that assessment and the literature reviewed. The committee was not charged or constituted to perform its own assessment and therefore did not conduct its own literature searches, review all relevant evidence, systematically formulate its own conclusions regarding causality, or recommend values for the RfC and unit risk. Furthermore, given the committee's statement of task, the committee focused on reviewing and critiquing the draft IRIS assessment, and the majority of the committee's report is directed at providing constructive comments and recommendations on improving specifically the draft IRIS assessment of formaldehyde

That said, the committee found that it could not address its charge without considering the methods and structure of the document as a whole, and in responding to its charge questions, the committee found some recurring methodologic problems that cut across components of its charge. Consequently, the committee commented on the general methodology of the assessment in Chapter 2 of the report and offered general suggestions in Chapter 7 with regard to the processes used by EPA to develop IRIS assessments. It did not review the IRIS Program itself, but rather focused on "lessons learned" from the formaldehyde assessment.

The general problems identified by the present committee are not unique and have been reported over the last decade by other NRC committees tasked with reviewing EPA's IRIS assessments for other chemicals. Problems with clarity and transparency of the methods appear to be a repeating theme over the years, even though some of the documents are very lengthy. In the roughly 1,000-page formaldehyde draft reviewed by the present committee, little beyond a brief (two page) introductory chapter could be found on the methods for conducting the assessment. In fact, the introductory chapter of formaldehyde is nearly identical to that used in other IRIS assessments. Numerous EPA guidelines are cited, but their role in the preparation of the assessment is not clear. In general, the committee found that the draft was not prepared in a consistent fashion; it lacks clear links to an underlying conceptual framework; and it does not contain sufficient documentation on methods and criteria for identifying evidence from epidemiologic and experimental studies, for critically evaluating individual studies, for assessing the weight of evidence, and for selecting studies for derivation of the RfCs and unit risk estimates. The critical summary sections that synthesize the evidence are variable and too often brief or not present, and strength of evidence is not characterized with standardized descriptors.

As noted, the committee's report provides many comments and recommendations specific to topics of its charge; additionally, the committee offered six concluding recommendations that were considered as critical to completion of the draft IRIS assessment. First, rigorous editing is needed to reduce the volume

of the text substantially and address the redundancies and inconsistencies; reducing the text could greatly enhance the clarity of the document. Second, Chapter 1 of the draft assessment needs to discuss more fully the methods used to develop the assessment. The committee is not recommending the addition of long descriptions of EPA guidelines but rather clear concise statements of criteria used to exclude, include, and advance studies for derivation of the RfCs and unit risk estimates. Third, standardized evidence tables that provide the methods and results of each study are needed for all health outcomes; if appropriate tables were used, long descriptions of the studies could be moved to an appendix or deleted. Fourth, all critical studies need to be thoroughly evaluated for strengths and weaknesses by using uniform approaches; the findings of these evaluations could be summarized in tables to ensure transparency. Fifth, the rationales for selection of studies that are used to calculate RfCs and unit risks need to be articulated clearly. Sixth, the weight-of-evidence descriptions need to indicate the various determinants of "weight." Readers of the draft need to be able to understand what elements (such as consistency) were emphasized in synthesizing the evidence.

The committee's review of the EPA's draft IRIS assessment of formaldehyde identified both specific and general problems with the document. The persistence of the problems encountered with the IRIS assessment methods and reports concerned the committee, particularly in light of the continued evolution of risk-assessment methods and the growing societal and legislative needs to evaluate many more chemicals in an expedient manner. On the basis of the "lessons learned" from the formaldehyde assessment, the committee offered some suggestions for changes in the IRIS development process that might help EPA improve its approach. The committee recognized that EPA has initiated a plan to revise the overall IRIS process and that it issued a memorandum in 2009 giving a brief description of the steps. However, the focus of the revision as indicated in the 2009 memorandum appears to be on the steps taken after the assessment has been generated (that is, the multiple layers of review). The committee's focus was on the completion of the draft IRIS assessment (that is, the development phase).

The committee offered a several-page roadmap for changes in the development process. The term *roadmap* was used because the topics that need to be addressed are set out, but detailed guidance was not provided because that was seen as beyond the committee's charge. Thus, the committee provided general guidance for the overall process and some more specific guidance on the specific steps of evidence identification, evidence review and evaluation, weight-of-evidence evaluation, selection of studies for derivation of RfCs and unit risk, and calculation of RfCs and unit risks. For each of these steps, there are underlying processes that would need to examined and reconsidered. The report provides further detail.

The committee recognized that any revision of the approach would involve an extensive effort by EPA staff and others and consequently, it did not recommend that EPA delay the revision of the formaldehyde assessment while revisions of the approach are undertaken. In fact, we provided specific guidance as to the steps needed to revise the existing draft. Models for conducting IRIS assessments more effectively and efficiently are available, and the committee provided several examples in the present report. Thus, EPA might be able to make changes in its process relatively quickly by selecting and adapting existing approaches, as it moves towards a more state-of-art process.