Testimony on H.R. 4805
Committee on Energy and Commerce
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"Formaldehyde Emissions and Formaldehyde Risk Assessment"

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Introduction: Good morning. I am Dr. Melvin E. Andersen, Director, Program in Chemical Safety Sciences, The Hamner Institutes for Health Sciences, Research Triangle Park, NC. I am very pleased to be here today to offer brief personal comments on the science used to assess the risk of inhaled formaldehyde by the State of California. The California risk assessment, dating from 1992, provided the rationale for decisions about acceptable formaldehyde emission rates from various building materials. These acceptable emission rates have found their way into H.R. 4805 - the bill under consideration. The 1992 California risk assessment used methods that date back to the 1970's when our knowledge of cancer biology and of the steps in cancer causation were very primitive. Their approach over-estimates cancer risks of formaldehyde at low exposure levels.

My Background: My professional career, spanning nearly 40 years, has focused on understanding how chemicals enter the body, how they make their way into cells and tissues, and how they affect tissues to cause toxicity. My resume' lists nearly 400 published papers and book chapters. The goal of my work has been to make the best use of contemporary science in improving chemical health risk assessments. I am regarded as an international expert in the area of pharmacokinetic (PK) modeling, i.e., a discipline describing the processes by which chemicals reach tissues at sufficient concentrations to cause toxicity. Among my papers are six that describe aspects of toxicology and risk assessment challenges with formaldehyde. In addition, in 1998 I served on a multi-stakeholder panel – US EPA, Health Canada, CIIT and TERA - convened in Ottawa, Canada to peer-review an alternative formaldehyde risk assessment that more adequately considered the extensive toxicological data base on formaldehyde and nasal cancer. CIIT here refers to the Chemical Industry Institute of Toxicology – the organization that developed the alternative risk assessment. TERA - Toxicology Excellence for Risk Assessment – organized the peer-review process. Aspects of the CIIT risk assessment were published in 2003 and 2004.

Current Hamner Research with Formaldehyde: CIIT was the predecessor organization to the Hamner where I have worked since 2002. Scientists at CIIT first discovered the nasal carcinogenicity of formaldehyde in rats about 30 years ago and have conducted a diverse array of studies to understand the changes in nasal tissues caused by inhalation of various concentration of formaldehyde and the role these changes play in nasal cancer. Over the past 5 years, The Hamner has been involved in research supported by the Formaldehyde Council to look at the changes in expression of genes in the rat nose after formaldehyde exposures and especially to see the differences in gene expression for different levels of exposure. Gene expression patterns differed markedly for concentrations causing nasal cancer in rats, above 6000 ppb, and those where no nasal cancers occur, 2000 ppb and below. Two papers from this research, by me and by my colleague Dr. Russell Thomas, received awards from the Risk Assessment Specialty Section of the US Society of Toxicology. Over the last 3 months, we have extended our formaldehyde research program at The Hamner to examine the manner in which inhaled formaldehyde enters nasal tissues and increases concentrations of formaldehyde in epithelial cells at the front of the nose. This newest portion of our formaldehyde research, focusing on pharmacokinetics, has not been supported by the Formaldehyde Council. It has been self-funded by The Hamner. It also bears some emphasis that today I am representing myself and my professional opinions. I am neither representing the Formaldehyde Council nor The Hamner.

You, me and formaldehyde: Formaldehyde is not simply a commercial chemical. It is present in every cell in our bodies –your cells and mine - at substantial concentrations. Formaldehyde is formed during normal metabolism and participates in important cellular functions. Cells in the body have specialized chemical processes to deal with formaldehyde, keep its free cellular concentration low, and stay healthy. Formaldehyde toxicity occurs when inhaled concentrations lead to a significant increase of tissue formaldehyde in the epithelial cells in the front portion of the nasal airways. Our current studies, in an area called pharmacokinetic modeling, show that formaldehyde inhaled at concentrations of 100 ppb or below would not increase cellular formaldehyde in cells in the nose significantly over physiological concentrations. This aspect of formaldehyde biology, i.e., its presence in all cells as a natural metabolite, was not considered in either the 1992 California assessment or in the 1998 CIIT-assessment. Table 1 compares the relationship between exposure levels in ambient and indoor air with inhaled concentrations that lead to specific biological or pharmacokinetic responses.

Formaldehyde and Nasal Cancer in Rats: Formaldehyde unquestionably has the potential to cause toxicity when inhaled concentrations become sufficiently large. When people breathe formaldehyde at 1000 ppb, it causes burning and irritation of the eyes and tissues in airways. The American Conference of Governmental Industrial Hygienists (ACGIH) has recommended an

occupational exposure for formaldehyde of 300 ppb as a ceiling – a concentration that is not to be exceeded in the workplace. In rats that breathe formaldehyde for 6 hrs per day every week day for two years, higher concentrations, 6000 ppb and above, caused squamous cell cancer in the front of the nose. At 15000 ppb, over half of the exposed rats developed nasal cancer. It is my professional judgment that formaldehyde is likely to be a 'high dose' human carcinogen: it would cause cancer if you or I were exposed to 15000 ppb, which is a highly irritating, locally corrosive concentration, every day for most of our life. However, a large body of research now shows that nasal cancer from formaldehyde in rats is closely associated with epithelial cell toxicity and with the recurrent scarring and healing processes that go on in these two-year exposures. The CIIT-risk assessment was based on a better understanding of the relationship between cellular toxicity of formaldehyde, the repeated damage and healing, and cancer. My professional judgment, similar in principle to the conclusions of the CIIT assessment and shared by many other toxicologists/risk assessors, is that formaldehyde only poses a cancer risk if concentrations are high enough, above 1000 ppb, to kill cells in the nose. Differences in the estimated risks based on the older methodology versus the CIIT risk assessment are captured in Figure 1. The California risk assessment, similar to the EPA assessment dating to 1987, indicated that 100 ppb exposures over a lifetime would result in 700 cancers in a million exposed individuals. The CIIT assessment indicated a risk of only 0.33 cases in the same size population.

Recommendations: The proposed legislation sets limits on emission rates from building products. Setting the limits based on reductions of off-gassing compounds into breathing zones is a good public health practice. As a certified industrial hygienist, it makes sense to me to follow good manufacturing practices to keep emission rates low. However, it is highly objectionable to take this decision based on an out-dated, biologically-deficient risk assessment – an assessment that neglects a broad body of research on formaldehyde carcinogenicity and toxicity, ignores key attributes of the biochemistry of cellular formaldehyde, and creates an impression that formaldehyde at concentrations of only several ppb poses a substantial, quantifiable cancer risk in people. The legislation should endorse the reduction in emissions without endorsing the questionable risk assessment.

Some References:

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Exposure Category	Concentration Range
Ambient Air	1-5 ppb
Indoor Air	10-50 ppb
FEMA Trailers	77 ppb (Geometric mean)
PK - No Increase in Tissue Concentration	~ 100 ppb
Occupational Standard TLV-Ceiling	300 ppb
Genomic Threshold	~ 700 ppb
Genomic Oxidative Stress Markers	~ 2000 ppb
Rat Nasal Cancer	~ 6000 ppb

Table 1: Comparisons of human formaldehyde exposures, including the occupational exposure limit of 300 ppb, with the formaldehyde concentrations associated with increases in tissue formaldehyde in the nose, alteration in gene expression in nasal tissues, and rat nasal cancer. **PK** stands for pharmacokinetics; **TLV** is Threshold Limit Value, a trademark of the American Conference of Governmental Industrial Hygienists.

Upper-Bound Excess Cancer Risk at 100 ppb formaldehyde

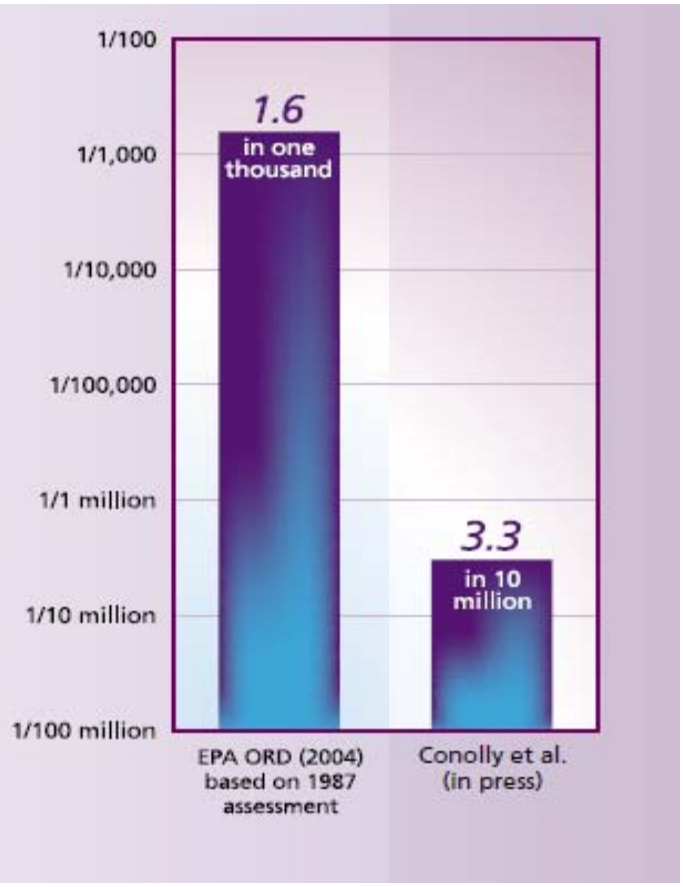

Figure 1: The graph shows the *estimated upper-bound excess lifetime cancer risk levels* for continuous long-term exposure to **100 ppb** formaldehyde in the air. At this exposure level, EPA's published assessment from 2004 predicted an additional cancer risk of 1.6 in one thousand people. The CIIT assessment estimates the cancer risk level to be 3.3 in ten million people. The 1992 California assessment estimated a risk of about 0.7 in one thousand, close to the EPA ORD assessment. This figure was adapted from the ACC-LRI Perspective- September 2004.