



January 5, 2007

Via U.S. Mail

Office of Environmental Information (OEI) Docket
Mail Code: 2822T
U.S. Environmental Protection Agency
1200 Pennsylvania Avenue, N.W.
Washington, D.C. 20460-0001

Attention: Docket ID Number EPA-HQ-ORD 2006-0756

Re: Evaluation of the Carcinogenicity of Ethylene Oxide

Dear Sir or Madam:

On behalf of Hospira, Inc., we submit the following comments on the U.S. Environmental Protection Agency (EPA) Office of Research and Development Evaluation of the Carcinogenicity of Ethylene Oxide (Draft Risk Assessment).¹

GENERAL COMMENTS

Completely missing from the Draft Risk Assessment is any evidence that ORD has met its responsibility to explain to its "customers" (e.g., OPP and OAR), much less to us, the regulated industry, what the pure science means *versus* what it doesn't mean, how its (ORD's) scientific judgments can and should be interpreted, how to apply those

¹ 71 Fed. Reg. 55470 (Sept. 22, 2006).

Hospira, Inc.
275 North Field Drive
Lake Forest, IL 60045



judgments properly, what a lack of information means (e.g., no cluster of cancer cases in either manufacturing or user sites, particularly in the last 20 years) and so on.

For example, the real risk(s) associated with exposure to ethylene oxide (EO) is not explained in terms of nor *vis-à-vis* the naturally-occurring background level of the material, nor the occupational exposure levels or environmental exposure levels, pre- or post-regulation. Additionally, post-1987 the lack of any statistically-significant evidence of cancer among the industry's workers or the public² is not even addressed, much less explained. We believe that the long-term safe workplace use of this well-regulated material and the greatly-reduced environmental exposures from industrial emissions should be acknowledged by ORD and the impacts of those facts for both risk assessment and regulatory purposes explained.

In summary, all the factors potentially affecting a regulatory risk/benefit ratio and the cost(s) to society of prospective regulation should be listed and quantified. This will assist all ORD "customers" to understand and properly apply the same information.

² In the 2002 follow-up to the original NIOSH study it is stated in the Abstract that "analyses restricted to the post-1987 data did not show any significant positive trends (exposure levels dropped sharply in the early 1980s)." *Mortality Analysis in a Cohort of 18,235 Ethylene-oxide Exposed Workers: Followup Extended from 1987 to 1998* The National Institute for Occupational Safety and Health (NIOSH), published 2004. These very strong scientific findings must be taken into consideration in the EPA analysis.



SPECIFIC COMMENTS

EO provides unmatched public health benefits to society via its use by the medical community. In the United States alone EO is used to sterilize a staggering 20 billion medical devices every year and 55% of all new medical devices. Indeed, medical, laboratory, and hospital settings rely on EO to sterilize equipment to protect patients from the very real risks of infectious disease from bacteria and viruses. Severe Acute Respiratory Syndrome (SARS) and Tuberculosis (TB) are just two of the more notable diseases effectively controlled by use of EO. Hospira uses ethylene oxide to sterilize approximately 0.28 million cubic feet of medical products annually, ranging from IV administration sets to cardiac catheterization kits. Many of these are products that are not amenable to other sterilization processes due to componentry or materials of construction.

As a user of EO, we are particularly concerned that were the current Draft Risk Assessment adopted there would be profound impacts on the medical community, including unfounded product deselection consequences. EO is of particular value to the medical community because it is the most gentle of sterilization procedures and capable of sterilizing materials at low temperatures. By inappropriately magnifying the risk associated with use of EO, EPA could ultimately force users to switch to less effective, impractical, and more-costly alternatives with severe public health consequences.

Hospira, Inc
275 North Field Drive
Lake Forest, IL 60035

www.hospira.com



From Hospira's perspective there are several potential impacts that would result from the Draft Risk Assessment. Since Hospira is one of the largest manufacturers of medical devices for the U.S. market we believe these impacts would be representative of the industry as a whole.

These potential impacts include, but are not limited to:

1. A dramatic reduction in the use of EO to sterilize medical devices.
2. Increased cost to manufacturers and their customers due to the need to revalidate sterilization procedures converted from EO to other methods.
3. Increased cost to manufacturers and their customers due to the need to redesign products that are not candidates for other methods of sterilization in their current forms.
4. Increased cost to manufacturers and their customers due to the need to decommission EO sterilizers and purchase new capital equipment for sterilization.

We urge EPA to correct the critical scientific deficiencies found throughout the Draft Risk Assessment and offer the following specific observations and recommendations:

- Based on the extensive database of toxicological and epidemiological studies on EO, the cancer risk posed by EO is thousands of times less than portrayed in EPA's risk estimates.

Hospira Inc
275 North Field Drive
Lake Forest, IL 60045

www.hospira.com

EPA's lymphohematopoietic cancer risk estimates for EO are based entirely on a single NIOSH retrospective study whose cohort was large, diverse and consisted of more women than men. While a slight increased risk of lymphohematopoietic cancer was observed in males, no increase was observed in females and all other cancer risks were found to be lower than expected. This discrepancy raises fundamental questions about EPA's exclusive reliance on this study population. EPA should derive its cancer risk estimates from a combination of all valid studies rather than solely on this single NIOSH study.

- The Agency's estimates of extra lifetime cancer incidence and mortality risk assume 85 years of exposure in contrast to the more-generally accepted and already-conservative assumption of 70 years of exposure. This unjustifiable increase of more than 20% adds further uncertainty and considerable increased conservatism into the excess lifetime cancer risk estimates for EO.

- EPA's risk estimates are implausible because they are significantly lower than natural background levels of EO in the atmosphere and the natural biological production of EO in the human body.



- Because EO is both a mutagen and genotoxicant EPA relies exclusively on *linear* dose-response assumptions. However, the Agency draft fails to acknowledge that the multiple, requisite steps in chemical mutagenesis are themselves *non-linear*. While the EPA's Cancer Guidelines encourage the use of linearity in certain circumstances, it must be remembered that these are *guidelines* which need not and should not be relied upon rigidly, especially at the expense of sound science.

- EPA calculates the additional risk posed by early-life exposure to EO because, according to EPA, there is a lack of "chemical-specific data to evaluate differences in susceptibility." The Agency's assertions notwithstanding, adequate data exist to contradict EPA's application of additional risk estimates for early-life exposures.

We urge EPA to revise this Draft Risk Assessment substantially by incorporating the foregoing comments along with those submitted by the American Chemistry Council.

Any questions or comments may be forwarded to:

Deborah Havlik
275 North Field Drive
Dept 097K, Bldg. H3
Lake Forest, IL 60045
T: 224-212-6260
deborah.havlik@hospira.com

Hospira, Inc.
275 North Field Drive
Lake Forest, IL 60045

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Sincerely,

A handwritten signature in cursive script that reads "Deborah Havlik".

Deborah Havlik
Research Investigator, Microbiology, Pharmaceutical R&D
Hospira, Inc.

A handwritten signature in cursive script that reads "LuAnn Pandy".

LuAnn Pandy
Vice President, Device Quality Operations
Hospira, Inc.