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Bcc:
Received Date: 2005-05-09 13:44:38 GMT
Subject: Shanghai Health Study

Attached please find the summary relating to the draft manuscript on benzene-induced myelodysplastic syndrome.

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Attachments:

shr-341-05-01memo.ZIP

INTEROFFICE MEMORANDUM

MAY 3, 2005

FROM: CHAIRMAN, HAZARD EVALUATION GROUP

TO: VICE PRESIDENT, HSSE & SUSTAINABLE DEVELOPMENT

SUBJECT: SHR-341-05-01

DATE SHR
RECEIVED: APRIL 18, 2005

DATE 30 DAY
PERIOD
EXPIRES: MAY 17, 2005

I. SUMMARY OF INCIDENT OR INFORMATION

The Original Reporting Person, Stuart Z. Cagen, submitted SHR-341-05-01, which reports results from a draft publication describing a distinct form of myelodysplastic syndrome (benzene-induced myelodysplastic syndrome or BIMDS) related to benzene exposure observed in the Shanghai Health Study.

II. CONSIDERATION AND ANALYSIS OF THE INFORMATION

A. HEG DISCUSSION: APRIL 21 & 28, 2005

Participants:

M. Hulse, HEG Secretary/Chairman
S. Z. Cagen, Toxicologist
S. P. Tsai, Epidemiologist
P. M. Clegg, Product Steward

B. DISCUSSION

BACKGROUND:

The Shanghai Health Study is a joint research project to investigate the effects of benzene exposure on workers. The study is under the direction of investigators from Fudan University, the University of Colorado Health Science Center, and Applied Health Services. Sponsors of the research are Shell Chemical LP, BP, Chevron Texaco, ConocoPhillips, ExxonMobil, and Marathon.

A draft manuscript of a paper to be submitted for publication to a peer reviewed scientific journal was recently provided to sponsors. The investigators observed 23 workers exposed to high levels of benzene with a distinct form of myelodysplastic syndrome (MDS) referred to as benzene-induced myelodysplastic syndrome (BIMDS). The workers were estimated to have full shift exposures averaging between 50 and 300 ppm benzene for varying periods of time ranging from 6 to 22 years. MDS is characterized by a lack of mature circulating blood cells, white blood cells, and platelets. According to the draft manuscript, MDS has a "tendency to

evolve into AML (acute myelogenous leukemia)". The draft manuscript describes several clinical features not previously observed in other forms of MDS that appear to be associated with benzene exposure and concludes that the results indicate that immune-mediated bone marrow injury is an early or predisposing event in the pathogenesis of benzene-induced hematopoietic disease.

FOLLOW UP INFORMATION:

ExxonMobil Refining and Supply transmitted a letter summarizing information contained in the draft manuscript to the EPA on April 14, 2005. Although the letter mentions Shell Chemical LP and other sponsors as funding companies, the ExxonMobil letter does not indicate that it was sent on behalf of the other sponsors. Further, as required by EPA 8(e) guidelines, the ExxonMobil letter does not state that their filing was being specifically submitted under Section 8(e). Finally, the ExxonMobil letter did not provide a copy of the draft manuscript to the Agency.

C. COVERAGE

Benzene is a liquid product used in the manufacture of other chemical products that, in turn, are used to make plastics, paints, nylon, CDs and pharmaceuticals. It is also a naturally occurring constituent of gasoline. Benzene is a carcinogen; its exposure has been associated with acute myelogenous leukaemia (AML). It is readily biodegradable and has a low potential to bioaccumulate. It is toxic to aquatic organisms. Benzene is highly flammable.

On a global scale, just over 34 million tonnes a year of benzene are produced. Shell chemicals companies are the world's second largest producers manufacturing almost 3 million tonnes of benzene a year across ten manufacturing locations world wide: Godorf, Germany; Stanlow, UK; Deer Park, USA; Sarnia, Canada; Scotford, Canada; Yokkaichi, Japan; Kawasaki, Japan; Pulau Ayer Merbau, Singapore; Al Jubail, Saudi Arabia.)

In the work environment, the occupational exposure limit for benzene globally ranges from 0.5 – 10 ppm, with 1 ppm being used across most of the world.

The benzene product fact sheet and MSDS provide additional information.

III. PRIOR KNOWLEDGE OF INFORMATION

Shell Chemical LP was not previously aware of the information contained in this SHR. While EPA is in receipt of the information from ExxonMobil's letter, in our judgment it does not constitute a formal notification under 8(e) nor does it address Shell Chemical LPs cognition of the information as 8(e) reportable information.

M. Hulse, Chairman HEG

Conclusion:

The reported information should be submitted to the EPA TSCA 8(e) Administrator, since it is believed that the Administrator has not been adequately informed of the information.

S. Smolik

Date

May 9, 2005

CERTIFIED MAIL – RETURN RECEIPT REQUESTED

Document Processing Center (7407M)
(Attn: TSCA 8(e) Coordinator)
Office of Pollution Prevention and Toxics
U.S. Environmental Protection Agency
1200 Pennsylvania Ave., NW
Washington, DC 2046-0001

Attn: 8(e) Coordinator

SUBJECT: A DISTINCT FORM OF MYELODYSPLASTIC SYNDROME (MDS) ASSOCIATED WITH HIGH LEVELS OF BENZENE (CAS Registry Number 71-43-2) EXPOSURE

Shell Chemical LP is submitting the following information under TSCA 8(e), since it may constitute substantial health risk information not previously known to the Administrator.

On April 14, 2005, ExxonMobil Refining and Supply Company submitted the following summary to the Agency from a draft manuscript for publication arising from the Shanghai Health Study of which Shell Chemical LP is one of several sponsors:

“The investigators identified a form of myelodysplastic syndrome (MDS) in 23 workers who had been exposed to high concentrations of benzene (CAS RN 71-43-2) earlier in their work history. While benzene has been associated with MDS, the characterization of this disease may be different than seen in previous studies. The distinguishing features of benzene-induced MDS (BIMDS) include eosinophilic dysplasia, abnormal cytoplasmic granulation, hematophagocytosis, stromal degeneration and bone marrow hypoplasia. In a subset of cases, bone marrow dysplasia occurred in the absence of significant reductions in peripheral blood cell counts (CBC); this was frequently accompanied by clonal or oligoclonal T cell expansion and alterations in T lymphocyte subsets. Susceptibility to BIMDS appeared to be influenced by a relatively rare genetic polymorphism in the inflammatory cytokine TNF- α (-238) as this was found to be significantly increased in the BIMDS cases and suggested that an inflammatory process was involved.”

Shell Chemical LP received the information on April 20, 2005 and has reviewed the draft manuscript. Shell Chemical LP believes that the Administrator was previously not aware of all of the information. In addition to the above, the investigators note:

“In contrast to prevailing assumptions that cytogenetic injury plays an initiating role in MDS, no clonal cytogenetic abnormalities were observed. These results indicate that immune-mediated bone marrow injury is an early or predisposing event in the pathogenesis of benzene-induced hematopoietic disease.”

The full draft manuscript is attached.

Shell Chemical LP will review its current hazard communication practices with regards to benzene in light of this information to determine what actions are required.

This report is filed to provide information EPA may find useful. In no way is it intended as a waiver of any rights or privileges belonging to Shell Chemical LP as the reporting corporation, its agents or employees. The reporting corporation, its agents and employees, reserve the right to object to this report's use or admissibility in any subsequent judicial or administrative proceeding against the corporation, its agents or employees.

This report has been compiled based on information available as of the date of filing. The corporation, its agents and employees reserve the right to supplement the data contained in this report, and to revise and amend any conclusions drawn therefrom.

This report contains no Confidential Business Information.

The following person should be contacted if you have questions or a need for discussion:

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Very truly yours,

Sam Smolik, Vice President
HSSE and Sustainable Development
Shell Chemical LP

Attachment

bc w/o attachment:

P. M. Clegg
S. Z. Cagen
S. P. Tsai
M. Hulse
D. R. Steup
R. H. Dickehuth (SHR 341-05-01)