WAC 296-62-07346 Appendix C—Medical surveillance guidelines for DBCP. (1) Route of entry.

(a) Inhalation;

(b) Skin absorption.

(2) Toxicology. Recent data collected on workers involved in the manufacture and formulation of DBCP has shown that DBCP can cause sterility at very low levels of exposure. This finding is supported by studies showing that DBCP causes sterility in animals. Chronic exposure to DBCP resulted in pronounced necrotic action on the parenchymatous organs (i.e., liver, kidney, spleen) and on the testicles of rats at concentrations as low as 5 ppm. Rats that were chronically exposed to DBCP also showed changes in the composition of the blood, showing low RBC, hemoglobin, and WBC, and high reticulocyte levels as well as functional hepatic disturbance, manifesting itself in a long prothrombin time. Reznik et al., noted a single dose of 100 mg produced profound depression of the nervous system of rats. Their condition gradually improved. Acute exposure also resulted in the destruction of the sex gland activity of male rats as well as causing changes in the estrous cycle in female rats. Animal studies have also associated DBCP with an increased incidence of carcinoma. Olson, et al., orally administered DBCP to rats and mice five times per week at experimentally predetermined maximally tolerated doses and at half those doses. As early as ten weeks after initiation of treatment, DBCP induced a high incidence of squamous cell carcinomas of the stomach with metastases in both species. DBCP also induced mammary adenocarcinomas in the female rats at both dose levels.

(3) Signs and symptoms.

(a) Inhalation: Nausea, eye irritation, conjunctivitis, respiratory irritation, pulmonary congestion or edema, CNS depression with apathy, sluggishness, and ataxia.

(b) Dermal: Erythema or inflammation and dermatitis on repeated exposure.

(4) Special tests.

(a) Semen analysis: The following information excerpted from the document "Evaluation of Testicular Function," submitted by the Corporate Medical Department of the Shell Oil Company (exhibit 39-3), may be useful to physicians conducting the medical surveillance program. In performing semen analyses certain minimal but specific criteria should be met:

(i) It is recommended that a minimum of three valid semen analyses be obtained in order to make a determination of an individual's average sperm count.

(ii) A period of sexual abstinence is necessary prior to the collection of each masturbatory sample. It is recommended that intercourse or masturbation be performed 48 hours before the actual specimen collection. A period of 48 hours of abstinence would follow; then the masturbatory sample would be collected.

(iii) Each semen specimen should be collected in a clean, wide-mouthed, glass jar (not necessarily pre-sterilized) in a manner designated by the examining physician. Any part of the seminal fluid exam should be initialed *only after liquifaction* is complete, i.e., 30 to 45 minutes after collection.

(iv) Semen volume should be measured to the nearest 1/10 of a cubic centimeter.

(v) Sperm density should be determined using routine techniques involving the use of a white cell pipette and a hemocytometer chamber.

The immobilizing fluid most effective and most easily obtained for this process is distilled water.

(vi) Thin, dry smears of the semen should be made for a morphologic classification of the sperm forms and should be stained with either hematoxalin or the more difficult, yet more precise, Papanicolaou technique. Also of importance to record is obvious sperm agglutination, pyospermia, delayed liquifaction (greater than 30 minutes), and hyperviscosity. In addition, pH, using nitrazine paper, should be determined.

(vii) A total morphology evaluation should include percentages of the following:

(A) Normal (oval) forms,

(B) Tapered forms,

(C) Amorphous forms (include large and small sperm shapes),

(D) Duplicated (either heads or tails) forms, and

(E) Immature forms.

(viii) Each sample should be evaluated for sperm *viability* (percent viable sperm moving at the time of examination) as well as sperm *motility* (subjective characterization of "purposeful forward sperm progression" of the majority of those viable sperm analyzed) within two hours after collection, ideally by the same or equally qualified examiner.

(b) Serum determinations: The following serum determinations should be performed by radiommuno-assay techniques using National Institutes of Health (NIH) specific antigen or antigen preparations of equivalent sensitivity:

(i) Serum follicle stimulating hormone (FSH),

(ii) Serum luteinizing hormone (LH), and

(iii) Serum total estrogen (females only).

(5) Treatment. Remove from exposure immediately, give oxygen or artificial resuscitation if indicated. Contaminated clothing and shoes should be removed immediately. Flush eyes and wash contaminated skin. If swallowed and the person is conscious, induce vomiting. Recovery from mild exposures is usually rapid and complete.

(6) Surveillance and preventive considerations.

(a) Other considerations. DBCP can cause both acute and chronic effects. It is important that the physician become familiar with the operating conditions in which exposure to DBCP occurs. Those with respiratory disorders may not tolerate the wearing of negative pressure respirators.

(b) Surveillance and screening. Medical histories and laboratory examinations are required for each employee subject to exposure to DBCP. The employer should screen employees for history of certain medical conditions (listed below) which might place the employee at increased risk from exposure:

(i) Liver disease. The primary site of biotransformation and detoxification of DBCP is the liver. Liver dysfunctions likely to inhibit the conjugation reactions will tend to promote the toxic actions of DBCP. These precautions should be considered before exposing persons with impaired liver function to DBCP.

(ii) Renal disease. Because DBCP has been associated with injury to the kidney it is important that special consideration be given to those with possible impairment of renal function.

(iii) Skin disease. DBCP can penetrate the skin and can cause erythema on prolonged exposure. Persons with preexisting skin disorders may be more susceptible to the effects of DBCP.

(iv) Blood dyscrasias. DBCP has been shown to decrease the content of erythrocytes, hemoglobin, and leukocytes in the blood, as well as increase the prothrombin time. Persons with existing blood disorders may be more susceptible to the effects of DBCP.

(v) Reproductive disorders. Animal studies have associated DBCP with various effects on the reproductive organs. Among these effects are atrophy of the testicles and changes in the estrous cycle. Persons with preexisting reproductive disorders may be at increased risk to these effects of DBCP.

(7) References.

(a) Reznik, Ya. B. and Sprinchan, G. K.: Experimental Data on the Gonadotoxic effect of Nemagon, *Gig. Sanit.*, (6), 1975, pp. 101-102, (translated from Russian).

(b) Faydysh, E. V., Rakhmatullaev, N. N. and Varshavskii, V. A.: The Cytotoxic Action of Nemagon in a Subacute Experiment, *Med. Zh. Uzbekistana*, (No. 1), 1970, pp. 64-65, (translated from Russian).

(c) Rakhmatullaev, N. N.: Hygienic Characteristics of the Nematocide Nemagon in Relation to Water Pollution Control, *Hyg. Sanit.*, 36(3), 1971, pp. 344-348, (translated from Russian).

(d) Olson, W. A. *et al.:* Induction of Stomach Cancer in Rats and Mice by Halogenated Aliphatic Fumigants, *Journal of the National Cancer Institute*, (51), 1973, pp. 1993-1995.

(e) Torkelson, T. R. *et al.:* Toxicologic Investigations of 1,2-Dibromo-3-chloropropane, *Toxicology and Applied Pharmacology, 3, 1961 pp. 545-559.*

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