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Safe Handling Procedures for Compounds Developed by the Petro-Chemical Industry

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THIS PAPER describes the methods used in establishing safe handling procedures for petro-chemical compounds originating in the Shell Development laboratories. Problems concerned with safe handling of chemicals in a research and development laboratory differ from those in a manufacturing company. These differences occur because the number of persons exposed is fewer, the quantity of compounds is smaller, the time of contact is shorter, the number of compounds is greater, procedures are more varied, and information about the toxicity is less complete and frequently lacking.

In the Shell Development Company, it is management's responsibility to see that conditions are as safe as it is practicable to make them, and to insure that persons working with new compounds, processes and applications, know the hazards involved and the precautions to be taken. To meet this responsibility effectively, management depends upon information and recommendations prepared by the following staff groups: (1) the Safety Board, composed of members of management whose decisions delineate policy relating to industrial hygiene and safety matters; (2) the Safety Committee, a group of technical and non-technical personnel appointed by the manager of the laboratories, to study specific safety problems and review recommendations which are made by its subcommittees; (3) Departmental Safety Committees, which are appointed by, and are responsible to, the Department Heads.

In addition, professional personnel, engineers trained in industrial hygiene and safety, and the toxicologist, serve in an advisory capacity. Upon these persons falls the immediate responsibility of evaluating hazards and making recommendations for safe handling procedures. The extent to which each of these groups and persons may participate depends on the magnitude of the problem.

The problem is defined in terms of (1) toxicity of the compound, (2) the number and training of exposed persons, and (3) industrial hygiene aspects of preparation and development.

Requests for investigation into the hazard of a process or the toxicity of a new compound may originate from several sources. The most usual source is by personal request from a chemist or engineer in charge of a project. This exchange of information is usually carried out on an informal basis unless the number of persons involved is sufficiently large, or the toxicity of the compound is sufficiently great, to warrant its investigation by a subcommittee of the Safety Committee. In the latter case, formal recommendations are made by the subcommittee following its interviews with the toxicologist, the industrial hygiene and safety engineers, and following their inspection of the process. Requests for information may also originate from the Market Development Department. This department coordinates and disseminates toxicological information to the other Shell Companies and potential customers. The majority of experimental work in toxicology is coordinated through this department. Reports made to this group are usually more formal and represent a more studied opinion. Occasionally, investigations are origi-

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nated by the toxicologist as a result of his findings of intoxication in exposed personnel. More extensive animal testing may be subsequently undertaken and industrial hygiene practices are reviewed together with existing engineering design and safe handling precautions.

As has been outlined, the first step in establishing safe handling procedures is to define the toxicity of the compound. In the case of older compounds, this may already be established and reference can be made to published data of experimental and clinical nature. However, with new compounds, there are but two approaches: (1) to explore the compound in terms of theoretical, biochemorphology (relation of chemical structure to biological activity) and (2) to apply experimentation. Biochemorphological studies require an intimate knowledge of pharmacology, biochemistry and pathology. This is the method of preference when there is a limited quantity of compound, when it is closely related structurally to well known compounds, or when it is in a stage of embryonic development. Toxicity data of an experimental nature are developed by studying the effects of the compound, usually on laboratory animals and occasionally on man. Since 1936, Shell Development has maintained a research program with a nearby medical school through which toxicological evaluations can be made. The extent of the toxicological investigation depends upon the stage of development of the compound in the research laboratory and the need for additional toxicological information. In the early stages, information of a simple nature as to acute toxicity classes and skin- and eye-irritating properties is generally all that is required. In other words, an attempt is made to integrate the development of toxicological data with the orderly market development of the agent. In preliminary toxicological tests information is obtained on the approximate quantity of the chemical which will kill a laboratory animal. These tests are made by exposing an animal to the vapors, placing the compound on the skin or in the stomach. Having obtained this information, the data are then translated by one of two methods either by reference to procedures similar to those described by Hodge and Sterner (Table I), or by reference to compounds familiar to the chemist through previous experience. In the first method, one defines the toxicity of the compound, using common terms, with reference to the quantity necessary to produce death in a rat or rabbit by a specified route of administration (Table I). As the development of the compound passes to the pilot plant stage, additional information is obtained. Experiments are then designed to determine the effects of repeated exposures to varied concentrations of dusts and vapors, repeated contact with the skin and repeated daily ingestion of small quantities in the diet. By these tests an attempt is made to define the following levels of exposure: (1) those which produce no significant change in behavior, activity and growth of an animal, (2) those which

*Hodge, H. C., and Sterner, J. H.: Tabulation of Toxicity Classes. *Amer. Indust. Hyg. Assn. Quarterly* 10:4, 93 (December), 1949.

TABLE I.
COMBINED TABULATION OF TOXICITY CLASSES

		Various Routes of Administration			
Toxicity Rating	Commonly Used Term	LD50 Single Oral Dose Rats	Inhalation 4 Hr. Vapor Expos. Mortality of 2/6-4/6 Rats	LD50 Skin Rabbits	Probable Lethal Dose for Man
1	Extremely Toxic	1 mgm. or less/kg	<10 ppm	5 mgm. or less/kg	A taste, 1 grain
2	Highly Toxic	1-50 mgm.	10-100	5-43 mgm.	1 teaspoon 4 cc.
3	Moderately Toxic	50-500 mgm.	100-1000	44-340 mgm.	1 oz. 30 Gm.
4	Slightly Toxic	0.5-5 Gm.	1000-10,000	.35-2.81 Gm./kg	1 pint 250 Gm.
5	Practically non-toxic	5-15 Gm.	10,000-100,000	2.82-22.59 Gm./kg	1 quart
6	Relatively harmless	15 Gm. and more	>100,000	22.6 or more Gm./kg	>1 quart

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LD50 Skin Rabbits	Probable Lethal Dose for Man
mgm. or less/kg	A taste, 1 grain
43 mgm.	1 teaspoon 4 cc.
340 mgm.	1 oz. 30 Gm.
2.81 Gm./kg	1 pint 250 Gm.
2-22.59 Gm./kg	1 quart
or more Gm./kg	>1 quart

will just produce abnormal organ weight changes, minimal tissue damage or minimal change in the function of an organ, and (3) that which is incompatible with survival of a considerable portion of the test species. These tests may run from 30 to 90 days. Compounds which are assured of commercial production will be given even more critical evaluation in terms of levels producing different types of injury over extended periods of time. In addition to defining the relative toxicity of a compound, an attempt is also made to ascertain its mechanism of action, probable detoxication and rate of storage and elimination from the body. This information serves as a basis for developing rational antidoting procedures. At an early date, information is made available to the Company's nursing staff as to suitable first aid measures and to the attending panel of physicians as to desirable methods of treatment of exposed personnel. In addition to the methods of animal experimentation, at times controlled experiments are carried out with human volunteers. By such direct measures, information may be obtained relative to the minimal quantity of vapors required to produce threshold sensory changes, such as, olfactory stimulation, eye and mucous membrane irritation, central nervous system effects (or possible skin-irritating and sensitizing properties). Such information is useful in helping establish suitable maximum allowable concentrations for the compound (and in defining the potential dermatological problem).

The second approach is to analyze the problem in terms of the number and qualifications of personnel; for example, is it a laboratory, an intermediate scale or a semi-plant problem? Initial studies are usually conducted or directed by a few skilled professionals working under excellent laboratory conditions. Consequently, exposures at this level are minimal. These persons are expected to familiarize themselves with the hazard of their operation and to take commensurate precautions. If they desire consultation on safe handling, the services of the health conservation group are available. Regulatory measures for this group are largely unnecessary. When a larger number of persons becomes involved in a problem, the degree of supervision from the health and safety standpoint must be increased. For example, if requests are made of other departments for investigation of the physical and chemical properties of the compound, some information must be transmitted with the sample as to its toxicity, skin-irritating properties and explosibility. When the compound progresses to the pilot plant stage, a study is made by both the departmental Safety Committee and, if requested, by subgroups of the Safety Committee as well.

The final step in definition is to survey the industrial hygiene aspects of preparation and development. This is the responsibility of the supervisor of safety and industrial hygiene. His responsibilities in the initial phase of an investigation are usually to suggest what protective clothing is suitable and whether the process demands a barricade or special ventilation. In intermediate and pilot stage operations, additional methods for control are investigated and recommendations made. These may include techniques for waste disposal, procedures for decontamination, and selection of additional protective equipment. At present, air analyses for special contaminants are not carried out on a routine basis; however, determinations of this type can be performed in instances where there have been specific complaints or when physical examination through the Company's health conservation program has uncovered evidence of intoxication.

General compulsory health appraisals are not conducted on a Company-wide basis; however, all personnel in the semi-plant areas and those exposed to unusually hazardous substances are covered in our health conservation program. As a part of this program, a preliminary assessment of the individual's status is made prior to his period of exposure, and re-examinations are conducted at intervals commensurate with the degree of hazard. When possible, data obtained from these examinations are coordinated with environmental findings.

The clinical laboratory examinations which are a part of this health evaluation program usually include routine blood and urine analysis, bleeding and clotting time and icterus indices determinations. Liver and kidney function tests are done whenever indicated. Biochemical tests which indicate the quantity of toxin in a body fluid or

excreta, or alterations in normal biochemistry, are utilized more rarely. These examinations also provide a check on the engineering design and prescribed protective measures. Another method which has been found useful in early assessment of possible intoxication is to require all personnel with complaints associated with chemical exposure to report immediately to the toxicologist for interview and examination. A record of these complaints and findings is crossfiled under the suspected agent. This facilitates determination of the number and kind of complaints associated with any particular chemical or process. We usually describe the number of complaints and the cases of alterations in physical and laboratory findings in terms of man hours of exposure. In computing rates, we find the potential hours of exposure can easily be ascertained by reference to payroll cards, since cost accounting is kept in terms of man hours expended on a particular project.

So far, methods of determining the degree of hazard encountered in particular processes or from handling specific chemical substances and the methods used in recognition of resulting altered physiology have been presented. To establish safe handling procedures, it is necessary to establish engineering control and adequate medical supervision and care; however, this is not enough.

The individuals concerned must be cognizant of specific precautionary methods and impressed with the necessity for applying these at all times. This is accomplished by formal and informal discussions. The most common method of disseminating information is by interview with the Department Head and those persons who will be directly concerned in the project. Close liaison is maintained with the head of Experimental Plants so that as new compounds are scheduled for manufacture the Safety Engineer and the First Aid group may be alerted to the necessity for carrying out their functions. Occasionally, discussions may take a more formal turn and a group meeting will be held on a conference basis with discussion augmented by demonstration of toxic effects in animals. At the request of certain department heads, their Safety Committees have received lectures on the general aims of the health conservation program and the methods for establishing safe handling of compounds, to better acquaint their staff with this activity.

A safety manual has been prepared for general use and it is the responsibility of every employee who is in laboratory or development work to become familiar with the procedures outlined in this manual. This is a general section on chemical hazards and background information on toxicity; this includes a list of the maximum allowable concentrations for a number of compounds found in the laboratory. Certain compounds are designated as being so hazardous that they require a Hazardous Work Permit prior to their use. In this way, it is possible for the Safety Engineer to inspect any extremely hazardous process, or one involving very toxic chemicals, before any exposure has occurred. The final method of dissemination of information is by circulation of current abstracts pertaining to safety, industrial hygiene and toxicological matters among all professional personnel. These abstracts are prepared from current literature by a rotating committee, reviewed by the toxicologist, and disseminated as an addendum to the lists of new material available in the library.

The results of this program have been most satisfactory. No fatalities have occurred from chemical exposure in the entire history of the Shell Development Company. Intoxications from exposure to compounds have been kept to a minimum, as has lost time due to injury. Finally, a background of know-how in handling compounds safely has been developed, which can be transmitted to the manufacturing companies and to potential users of the compounds.

THE NEW YORK UNIVERSITY, Post-Graduate Medical School, Department of Industrial Medicine together with the College of Engineering presented a course in Air Pollution, May 10 to 21. This comprehensive two-week training period included lectures on all phases of Air Pollution, presented by recognized authorities in the field.

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The work here reported was don
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*This includes all small particula
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