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HANDLING CYTOTOXIC DRUGS

THESIS

Robert J. Kennie, B.S., M.S.
Captain, USAF

AFIT/GLM/LSM/86S-66

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AFIT/GLM/LSM/86S-66

HANDLING CYTOTOXIC DRUGS

THESIS

Presented to the Faculty of the School of Systems and Logistics

of the Air Force Institute of Technology

Air University

In Partial Fulfillment of the

Requirements for the Degree of

Master of Science in Logistics Management

Robert J. Rennie, B.S., M.S.

Captain, USAF

September 1986

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Preface

The purpose of this research was three fold. The first was to examine the applicable federal laws and regulations that govern the shipping, handling, distribution and labeling of cytotoxic drugs. The second was to examine the medical literature regarding the deficiency of existing regulations to adequately protect personnel from injury when handling cytotoxic drugs, and the third was to identify the level of knowledge that medical supply officers in Department of Defense Air Force hospitals have about cytotoxic drugs (CD's).

To determine the cytotoxic drug level of knowledge of the medical supply service, a survey instrument and measurements were established. Evaluation criteria were designed and the experimental and control populations were identified. The findings revealed that medical supply officers in facilities which treated patients with CD's did have a basic knowledge about the drugs. References distributed to the field during CY 1985 did help to educate some personnel. Supply officers in facilities that did not treat patients with CD's or those officers who did not know if their facility treated patients with CD's demonstrated a level of knowledge equal to that of the control group which received no information concerning CD's. This finding appears to indicate that unless there is an immediate need-to-know, medical supply officers are ignoring reference material provided in the Air Force Medical Logistics Letter (AFMLL). In light of recent OSHA publications and Veterans Administration action regarding the labeling and handling of CD's, the Air Force is re-evaluating current policies and practices.

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Abstract

Cytotoxic drugs which are used throughout the health care system to treat cancer, have not been classified in a manner that requires special Department of Transportation labeling even though there is clinical evidence that the drugs are potentially dangerous to humans if the drug material (liquid, powder) accidentally touches the skin, is inhaled, or is ingested.

A field (AF hospital medical supply officer) level of knowledge determination was conducted in order to show that the lack of a labeling requirement contributes significantly to the medical supply health care worker's lack of knowledge about the potential hazard to humans associated with these drugs. The findings indicate that medical supply officer's whose facility handled cytotoxic drugs failed to demonstrate a basic knowledge about cytotoxic drugs, particularly in key areas such as environmental protection, spill response, and internal control of the drugs. Those officer's whose facility did not handle cytotoxic drugs demonstrated a level of knowledge equal to the control group. This is significant because during CY 1985 an education effort had been undertaken by the Air Force Office of Medical Support to inform all supply officers about cytotoxic drugs.

The Department of Labor, Office of Occupational Safety and Health, in January 1986, issued a comprehensive guideline for handling cytotoxic drugs which exceeds all existing regulations regarding the labeling, storing, issuing, and handling of cytotoxic drugs. The Veterans Administration has initiated its own labeling and handling procedures that ensure a higher degree of safety for logistics personnel. The Air Force is re-considering its own policies and practices in light of these actions and has submitted a labeling policy program to the Defense Medical Standardization Board for concurrence.

HANDLING CYTOTOXIC DRUGS

I. Problem Statement

General Issue

The Department of Transportation (DOT) regulates the packaging, labeling, and shipment of chemicals (including chemical compounds, such as drugs) manufactured and/or distributed in the United States. The designation of a chemical requiring special DOT labeling procedures is the responsibility of either the Environmental Protection Agency (EPA) or the National Institute for Occupational Safety and Health (NIOSH). Cytotoxic drugs, which are used extensively throughout the health care system to treat cancer, have not been classified in such a manner by the EPA or NIOSH that would require special DOT labeling even though there is clinical evidence that the drugs are potentially hazardous to humans if the drug material (liquid, powder) accidentally touches the skin, is inhaled, or is ingested.

Specific Problem

In order to show that the existing laws, policies and directives are the direct cause of a medical supply health care worker's lack of knowledge about the potential hazard to humans associated with these drugs, a field (AF hospital) "level of knowledge" determination is required. If the "level of knowledge" about these drugs is inadequate, this evidence will be used as the basis for attempting to have the Defense Logistics Agency (DLA) unilaterally implement a cytotoxic drug labeling policy. DLA ships medical supplies to all Air Force medical treatment facilities.

Investigative Question

Are medical supply officers adequately informed about the potential hazards associated with handling cytotoxic drugs and have they instituted appropriate work practices to ensure worker safety?

Hypothesis One: Medical supply officers in 1986 have a higher "level of knowledge" about cytotoxic drugs (CD's) than medical supply officers who vacated similar positions prior to the treatment period, defined as CY 1985.

Hypothesis Two: Current medical supply officers (1986) "level of knowledge" about handling CD's is inadequate, despite AF directives issued in CY 1985. The "treatment" is defined as a December 1984 HQ AFCOMS/SGPC directive and a Air Force Medical Logistics Letter publication, numbered 2385, both of which the medical supply officer should have read and acted upon. The objective is to demonstrate the ineffectiveness of the directives and infer that labeling is the only available means of increasing the "level of knowledge" about these drugs. The rationale for this premise relies on the existing procedures and handling regulations that are in effect as a result of other special DOT labeling procedures for medical supply items such as poisons, flammables, and corrosives.

Background/Scope

The danger to hospital personnel from handling a cytotoxic drug is a combination of its inherent toxicity and the extent to which workers are directly exposed to the drug in the course of carrying out their duties. This exposure may be through inadvertent ingestion of the drug on foodstuffs, inhalation of drug dusts or droplets, or direct skin contact (1:31).

An antineoplastic drug is a cytotoxic chemical substance that is administered orally or intravenously to a person for the treatment of various types of cancerous tumors. Their mechanism of action involves interaction with DNA, RNA, or protein synthesis in living cells, normal or cancerous. The potential for mutagenic, carcinogenic, or teratogenic effects are possible"(2:1)

Furthermore:

The variables that determine the occupational hazard of a drug to an individual include the following: (1) the drug's chemical properties, (2) the susceptibility of the individual, (3) "co-factors such as dietary habits, smoking, other natural/man-made environmental contaminants, (4) the number of exposures, magnitude of any one exposure, or cumulative amount of exposure, and (5) type of exposure, such as skin or inhalation (e.g. absorbable vs non-absorbable drug)(1:131).

Logistics personnel should be concerned about the handling of cytotoxic drugs for two reasons. The first reason relates to the medical material distribution function of their logistics job and the second reason relates to the other hospital or clinic responsibilities of the medical logistics department which normally includes facility management. Medical logistics personnel, on occasion, are utilized within the plant management, housekeeping and refuse management areas, where the potential risk of contamination from exposure to cytotoxic drug waste products is a distinct possibility.

USAF Supply Manual, AFM 67-1, Vol V Chapter 1.4.g. states:

The director of medical logistics management ... is responsible for ... (2) management and operation of the base medical logistics activity. This includes procurement, receipt, storage, issue control, turn-in, disposition, safeguarding, reporting and accounting for property according to AF directives, ... (3) establishing effective quality control program for medical material, ... (4) delivery of all supplies, equipment and linens to using activities ... (3:1-2).

Furthermore, Chapter 16.3.b. states "local purchase is the normal source of supply and replacement as appropriate, for all nonstock listed items and certain stock listed items ... "(3:16-2).

This regulation gives the medical logistics officer broad authority to purchase medical supplies from civilian sources that are unobtainable through depot channels when the need for such items is immediate. Approximately 40% of the medical supply items purchased annually by the MTF's (in the USAF) are commercially procured. The significance of this fact will be addressed later.

Cytotoxic drugs purchased by the depot or the MTF's come directly to the hospital in packaging that does not adequately distinguish the contents therein. It is common practice to open damaged boxes and salvage unbroken items. Typically during the summer months unrefrigerated surface vehicles haul medical supply items all over the country through arid conditions exposing those drugs to temperatures in excess of their listed safe temperatures, resulting in breakage. During the winter months those same surface transport companies subject medical supply drug items to frigid outside temperatures and unheated warehouses that result in frozen goods and breakage. The Defense Personnel Support Center (DPSC) is aware of the problem which regularly occurs at northern tier bases. Furthermore, medical supply items are commonly stored on warehouse shelving in "loose" form. It is not uncommon for an occasional item to fall to the floor and break open when a cart with bulky items is being moved down an aisle when other items are being retrieved for issue. Medical logistics personnel who handle these dangerous cytotoxic drugs are at an increased risk of accidental gross contamination because these drugs are not marked as hazardous and look quite similar to any other small packaged drug.

A related issue is the incongruity that exists between the HMTA, which defines cytotoxic drugs as non-hazardous poisons and the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA) that identifies cytotoxic drug wastes as hazardous. Cytotoxic drug wastes are diluted cytotoxic drugs. The Department of Transportation regulations allow the shipment of 65 lbs of CD's as non-hazardous cargo. The CERCLA Act defines one pound of cytotoxic drug wastes as hazardous material. Both the EPA and the Department of Transportation could not explain the rationale behind what appears to be a double standard in the classification of cytotoxic drugs and drug wastes.

The Air Force policies and practices used in conjunction with the above federal guidelines and laws will be examined.

II. Literature Review

Introduction

The applicable federal regulations and state laws, and regulations coupled with the executive agencies that exercise jurisdiction in the manufacture, distribution and disposal of antineoplastic or cytotoxic drugs are numerous. There is no single federal law, agency or regulation that dominates or controls these items. Briefly, the Food and Drug Administration (FDA- Department of Health and Human Services-HHS) regulates the manufacture and licensing of drugs; the Department of Transportation (DOT) regulates the shipping and packaging of these drugs; the Occupational, Safety, and Health Administration (OSHA-Department of Labor-DOL) regulates the effects of these drugs and their component parts on the human environment; the National Institute for Occupational Safety and Health (NIOSH-HHS) determines what chemical and combinations of chemicals that go into manufacturing the drugs are hazardous; and the Environmental Protection Agency (EPA) regulates the effects of these items and their components "on the environment."

There are five federal laws that have jurisdiction concerning hazardous substances. They are section 112 of the Clean Air Act, sections 307(a) and 311(b)(2)(A) of the Federal Water Pollution Control Act, section 3001 of the Solid Waste Disposal Act, the Hazardous Materials Transportation Act and the Toxic Substances Control Act. For years the various executive agencies had pursued regulating their respective areas and generated regulations that did not complement the rules and regulations of the other agencies. The CERCLA and the Resource Conservation and Recovery Act

(RCRA) attempt to coordinate the activities of all four agencies in regulating a myriad of hazardous substances (DOT; EPA;HHS, specifically the FDA and Dept of Labor, specifically the OSHA).

Existing Laws and Code of Federal Regulations Governing Cytotoxic Drugs

In order to examine the federal regulatory climate that impacts cytotoxic drugs the following interlocking agency areas and/or laws are reviewed and explained:

National Institute for Occupational Safety and Health Agency (NIOSH)
Solid Waste Disposal Act (SWDA)
Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA)
Hazardous Materials Transportation Act (HMTA)

National Institute for Occupational Safety and Health Agency (NIOSH).

The designation of a drug or chemical or combination of chemicals as hazardous is the responsibility of the National Institute for Occupational Safety and Health (NIOSH), a department of the HHS. Both NIOSH and the EPA (under CERCLA, section 102, 40CFR§302) may designate additional hazardous substances to be added to the official list of hazardous substances, which is contained in section 101(14) of CERCLA and contains 698 substances. The NIOSH standard for classifying hazardous substances excludes "a carcinogen mixture, liquid or solid compositions, which contains less than 1% by weight or volume the following hazardous substances: 1-NA, MOCA, DCB, BPL, EI, 2-AAF, DAB, DMN, CMME, BCME, 2-NA, 4-ADP, or 4NBP" (4:19). This exclusion is the specific regulation that permits cytotoxic drugs to be commercially transported and distributed without any warning labels on the outside of the shipping containers.

The risk associated with handling cytotoxic drugs to hospital personnel cannot be quantitatively measured at this time.

The long range effects of continued exposure to very small amounts of such drugs remain a questionmark. Exposure is defined as skin contact, inhalation, or inadvertent ingestion of small amounts of drug dusts, liquids, or aerosols. Contaminated materials are defined as any object to be discarded that is or presumed to be contaminated with cytotoxic substances, including but not limited to, disposable gloves and gowns, syringes, vials, ampules, IV bags and bottles, IV tubing, and all materials used to clean up spills of the drug. Beyond problems in technique, however, contamination also will occur from inevitable spills and breakage of cytotoxic drug solutions. ASHP believes that the occupational dangers of cytotoxic drugs can be summarized as follows: (1) being handled as other less hazardous substances - resulting in contamination, (2) exposure/absorption of drug - amount of drug absorbed by any one individual on any given day probably is very small except for rare and unusual instances of gross contamination, (3) long exposure e.g., cumulative exposure leads to damage, puts at risk oncology and pharmacy personnel, ... (4) consider the above, procedures, equipment and materials that actually or theoretically prevent exposure to cytotoxic drugs in the hospital workplace are necessary (1:131).

Whether exposure is from spills or long handling association, the effects of such exposure cannot be readily determined because "no method currently exists for routinely monitoring personnel for evidence indicative of cytotoxic drug exposure" (1:133). It would appear that the unmeasurability issue is one of the key facts that undermines the reasoning behind the 1% by weight or volume NIOSH standard for classifying substances as hazardous.

Both the USAF Occupational and Environmental Health Laboratory (OEHL) and the National Study Commission of Cytotoxic Exposure (a group from the American Society of Hospital Pharmacists) recommend the following policy in cleaning up spills:

2.0 Spills; 2.1. All personnel involved in the cleanup of a spill should wear protective clothing (e.g., gloves, gowns, etc.). All clothes and other materials used in the process should be treated or disposed of properly; 2.2. Double gloving should be used in the cleanup of spills (2:19).

Review of the literature to this point has shown that cytotoxic exposure is non-measurable at small levels of exposure, that pharmacy professionals fear such exposure is hazardous to one's health, and lastly, that due to the small quantities involved with such spills in the hospital environment, that the federal government has taken no action.

Solid Waste Disposal Act (SWDA). Seven cytotoxic drug wastes are identified as hazardous substances under the provisions of section 3001 of the Solid Waste Disposal Act. The DOT, Hazardous Materials Transportation Act (HMTA) states that "contract carriers may be liable under the CERCLA (section 306(b)) for the release of a 'hazardous substance' as defined in the act" (5:166).

A hazardous waste is defined in the Solid Waste Disposal Act as:

a solid waste, or combination of solid wastes, which because of its quantity, concentration, or physical, chemical, or infectious characteristics may- (A) cause, or significantly contribute to an increase in mortality or an increase in serious irreversible, or incapacitating reversible illness; or (B) pose a substantial present or potential hazard to human health or the environment when improperly treated, stored, transported, or disposed of, or otherwise managed ... (6:180).

The seven hazardous cytotoxic drug wastes are shown in Table I along with all existing CD's. The SWDA does not explain why the pre-waste state of these drugs (powder, liquid, or semi-solid) are not classified as hazardous.

TABLE I

Hazardous and Non-hazardous Cytotoxic Drug Wastes as Defined by CERCLA

<u>CD Name</u>	<u>RCRA ID No.</u>	<u>H/N-h*</u> <u>Wastes</u>	<u>NSN</u>
asparaginase	None	N-h	6505011539650
azathioprine	None	N-h	No NSN
bleomycin	None	N-h	6505010604278
carmustine	None	N-h	F0015301297
chlorambucil	U035	H	6505011456378
cisplatin	None	N-h	No NSN
cyclophosphamide	U058	H	6505007335246
cytarabine	None	N-h	6505004340733
dacarbazine	None	N-h	6505010526672
dactinomycin	None	N-h	6505009021222
daunomycin	U059	H	6505011594570
doxorubicin	None	N-h	6505010182728
etoposide	None	N-h	F0015309597
fluorouracil	None	N-h	6505009608383
melphalan	U150	H	6505009127457
methotrexate	None	N-h	6505010202367
mitomycin c	U010	H	6505010057327
mustargen	None	N-h	6505011452629
plicamycin	None	N-h	No NSN
streptozotocin	U206	H	No NSN
thiopeta	None	N-h	6505010473872
uracil mustard	U237	H	No NSN

*H-Hazardous, N-h-Non-hazardous drug waste

Comprehensive Environmental Response, Compensation, and Liability

Act (CERCLA). The quantities of these items (wastes or drugs) that concern the government is defined in this act.

A reportable quantity of one pound for all hazardous substances .. and ... the primary purpose of notification is to ensure that releasers notify the federal government so that the federal government personnel can assess the need to respond to the release (7:13456).

A release is defined as "spills from tanks or valves ... open to the outside air, ... into lagoons or ponds, or any other discharges that are not wholly contained within buildings or structures as defined in CERCLA section 101 (22)" (7:13462). No reporting is required if the quantity involved is less than one pound and the substance does not leave the structure and "enter the environment." There is no mention for concern about the item entering the worker. However, the EPA has proposed new ceiling limits (to be effective March 1986) to the Hazardous and Solid Waste Amendments of 1984 to lower the quantity that requires organizations to register with the Federal Government under RCRA as generators of hazardous waste. This is a positive step in controlling the amount of hazardous wastes being introduced into the environment. The limit is being reduced from 1000 kg/month to 100 kg/month. For hospitals, this equals treating 254 cancer patients (254 lbs - 254 cancer treatments, e.g. weight of the IV bag, needles, and other medical supply items) per month. The effect of this limit will be to increase the awareness of the plant management and housekeeping staff of the toxicity of these chemicals (drugs) and ensure that disposal occurs within existing regulations or by licensed low-level refuse solid waste management companies.

When a spill occurs that involves large enough quantities, notification

of the appropriate federal agency is required under the CERCLA and RCRA laws. An example of this just recently occurred in a Dayton, Ohio community. A cytotoxic manufacturing facility had an industrial accident which, due to the volume involved, qualified the incident for OSHA and EPA involvement. A newspaper article reported the following:

Chemical Mixup Hospitalizes 19: An accidental mixing of chemicals at the Monsanto Research Corp. plant ... Tuesday afternoon created a vapor like 'tear gas' sending 16 workers, one Dayton firefighter and two paramedics to the hospital. A spokesman from the Miami Valley Hospital said none of the victims was seriously injured. They suffered skin and membrane irritation from exposure to the fumes. Monsanto officials said the incident occurred about 3:30PM when workers were preparing to mix chemicals to produce an anti-cancer drug called Methotrexate (NSN 6505009635353) in the plant's Custom Chemical Operation building. Monsanto Plant Manager Dick Hart said one of the chemicals, liquid bromide, reacted with some acetone that had not been cleaned from a tank. The reaction produced a gas that was 'essentially, tear gas' Hart said. Officials said the Montgomery Combined Health District's Regional Air Pollutions Control Agency was notified, but officials do not believe the fumes escaped from the plant. Hart said the Tuesday incident was the first in about 10 years in which workers at the plant, which mixes specialized chemicals for businesses and industries, had suffered injuries that required hospitalization. A committee will be formed to investigate the incident and determine what went wrong, Hart said (8:52).

The CERCLA law establishes that cytotoxic drugs are not subject to the jurisdiction of federal regulation if: (1) the quantity spilled is less than one pound released into the environment per incident or (2) it involves the generation of less than 1000 kg/month solid waste.

Hazardous Materials Transportation Act (HMTA). It is difficult for logistics personnel to readily identify a cytotoxic drug that has been damaged in shipment because the FDA has excluded pharmaceutical

companies and hospitals from the strict labeling requirements required by Title 49, HMTA. The finished drug product shipped to hospitals is excluded; however, the ingredients that are used in the manufacturing process are not.

The HMTA regulates the labeling of and identification of hazardous materials shipped within the country and the provisions of the law are written in Title 49, Code of Federal Regulations. Under Title 49 § 172.401(6), the Department of Transportation requires the labeling of hazardous items that exceed the NIOSH 1% by weight or volume standard. This includes all items manufactured or used by industries in the United States that are commercially shipped and distributed. Instead of being labeled hazardous, cytotoxic drugs are classified as "Poison B" substances in the DOT Hazardous Materials Regulation which defines a Poison B substance as:

(a) ... those substances, liquid or solid, ... which are presumed to be toxic to man because they fall within anyone of the following categories when tested on laboratory animals: (1) oral toxicity ... , (2) toxicity on inhalation ... , (3) toxicity by skin absorption, (b) the foregoing categories shall not apply if the physical characteristics or the probable hazards to humans as shown by experience indicate that the substances will not cause serious sickness or death. Neither the display of danger or warning labels pertaining to use nor the toxicity tests set forth above shall prejudice or prohibit the exemption of any substances from provisions of ... of this chapter(5:596).

The regulation further exempts certain drugs and medicines under section § 173.345, "limited quantities of Poison B liquids." These same liquids are those seven cytotoxic drugs that, once administered, become hazardous wastes. Cytotoxic drugs are further regulated under the Poison B classification as "ORM-D" poison which is defined as:

a material such as a consumer commodity that presents a limited hazard during transportation due to its form, quantity, and packaging ... The gross weight of each package must not exceed 65lbs ... Poison B solids or liquids must be inside containers each having a rated

capacity of 8 ounces or less ... packaged in strong packagings ...
(5:291,658).

It is this federal regulation that specifically allows cytotoxic drugs to be distributed in very innocuous looking shipping containers.

Adding to the identification and labeling issue is the 40% local purchase rate that exists within the medical supply system. It takes the Defense Medical Standardization Board approximately eighteen months to determine that a newly released medical supply item is being used enough within the DOD DLA system to assign a NSN to it and stock it for use. In the interim, MTF's buy these items directly from the manufacturer or a distributor. There are no shipping papers or invoices attached to the outside of the shipping container when these locally procured items arrive at the medical warehouse. If these items have been damaged in shipment medical supply personnel have no way of knowing what is in the container or box without physically opening it up. Likewise, depot shipped medical supplies are packaged in boxes called "multipacks" and also arrive at the medical supply receiving dock with no markings on them indicating that cytotoxic drugs are contained inside.

The Depot readily identifies other hazardous items when it ships them to medical facilities. Flammable items come secured in special metal barrels filled with non-flammable packaging that are labeled "FLAMMABLE," on the outside in unmistakable orange lettering. All other medical supplies that require labeling on the outside of the shipping container by current DOT regulations are labeled by the depot prior to shipment.

Within the above laws and regulations various federal executive departments with direct or oversight responsibilities have been seeking public input concerning the labeling and handling of hazardous substances

including cytotoxic drugs. The major activities are reviewed.

Activities of Federal Agencies Currently Investigating Cytotoxic Drugs

There have been a number of federal and state agencies that have reexamined the "hazardous status" of cytotoxic drugs. These activities and product liability case law are reviewed below:

Occupational Safety and Health Administration (OSHA) Hazard
Communication Ruling
Product Liability Case Law
Worker's Right-to-Know Legislation
OSHA Publication, "Guidelines for Cytotoxic (Antineoplastic) Drugs"

Occupational Safety and Health Administration (OSHA) Hazard
Communication Ruling. In accordance with the provisions of the
Occupational Safety and Health Act, Section 6(b)(7), the Occupational Health
and Safety Administration (OSHA) is mandated to promulgate an
occupational safety and health standard entitled "Hazard
Communication" (29CFR§1910.1200), which

requires manufacturers and importers to assess the hazards of chemicals which they produce or import and all employers having work places in the manufacturing division, Standard Industrial Classification (SIC) codes 20-39, to provide information to their employees concerning hazardous chemicals by means of hazard communication programs including labels, material safety data sheets (MSDS, OSHA SF 20), training and access to written records. In addition, distributors of hazardous chemicals are required to ensure that containers they distribute are properly labeled, and that a material safety data sheet is provided to their customers in the manufacturing division SIC codes (9:53280).

During testimony by the Department of Defense (DOD), pharmaceutical companies, chemical companies, labor officials, and health care professionals

much support was given to the proposed communication standard for hazardous substances that exceed the NIOSH 1% by weight or volume standard. For instance, DOD stated that it "strongly supports the intent of the proposed standard to help ensure that personnel are aware of potential workplace chemical hazards and adequately protected therefrom" (9:53283). The only drawback was that OSHA restricted its rule changes to SIC codes 20-39 for the following reasons:

although hazardous chemicals are used in other industries as well, OSHA determined that the employees in the manufacturing sector are at the greatest risk of experiencing health effects from exposure to hazardous chemicals ... This decision was based upon an Agency analysis of occupational injury and illness statistics compiled annually by the Bureau of Labor Statistics (BLS) ... Since illnesses are more likely to be due to chemical exposure than injuries are, it is in this area that the effects of hazard communication should be most apparent (9:53284).

Concurrently, it should be emphasized that the EPA does not believe that employees in other industries are not exposed to hazardous chemicals, or that they should not be informed of those hazards ... Although not required for those employers outside SIC codes 20-39, the increased availability of material safety data sheets will also benefit them. Thus this standard will increase the general availability of hazard information in all of industry, and will establish the informational framework upon which standards dealing with other industries can be based if necessary (9:53289).

This change excludes cytotoxic drugs. The FDA does require the listing of those quantities of hazardous substances found in cytotoxic drugs in a table of contents. However, the writing on the outside of the drug packaging is almost too small to read and the average warehouse person is probably not familiar with the scientific terminology used to identify the hazardous components. Learning medical terminology and chemical names are only required for the medical technician and pharmacy technician career fields.

During the hazard communication regulation public hearing, there was considerable support from the participants to label, as hazardous, substances currently excluded from this regulation. DoD stated:

We recognize the practical need for limiting the applicability of the standard with regard to hazardous ingredients of a mixture. We believe, however, that there is significant health risk involved when carcinogens, strong sensitizers or other compounds with extremely low permissible exposure limits are present in mixtures in concentrations below 1% ... (9:53291).

One of the companies that testified to raise the 1% NIOSH standard was Merck and Co., a large cytotoxic drug manufacturer which stated: "... a 1% mixture of a flammable, combustible, or reactive chemical in an inert diluent" ("powdered cytotoxic, author's comments) may hardly be 'hazardous' given the properties of the components" (9:53291). Another association that criticized the 1% rule was the Pharmaceutical Manufacturers Association which stated:

While the one percent standard may be appropriate for some types of materials such as a very highly toxic or carcinogenic material, it is not appropriate in most cases ... While a manufacturer may know that a mixture is not hazardous, the regulation would require that it be labeled as hazardous unless tests were conducted to show otherwise (9:53291).

OSHA did not change the standard. If cytotoxic drugs become more concentrated in the near future, they will qualify because of OSHA sticking to the 1% rule. OSHA concluded the hearing with the following rule concerning the safety of items that fall below the 1% by weight or volume hazardous substance standard:

For health hazards the one percent cutoff for mixtures where the health hazard potential of the whole mixture is not known will apply ... If the employer has reasons to believe that an existing permissible

exposure limit for a component present in quantities of less than one percent may be exceeded under normal conditions of use, or that such a component could present a serious health hazard in such quantities, that component will also be required to be listed ... The Assistant Secretary has the authority to issue separate rules for specific substances in any event (9:53292).

Health hazard is defined as "a chemical which upon exposure may result in the occurrence of acute or chronic health effects in employees" (9:53296).

As further evidence of what appears to be the disregard that some cytotoxic drug manufacturers may have for their employees, Monsanto testified that:

Monsanto feels that lists of chemical substances in the work place (a requirement of the hazard communication standard) are unnecessary since the product identification and hazard information are all included on the Material Safety Data Sheet (MSDS, OSHA SF 20) and available to the employee. Lists are difficult to maintain up to date and give casual observers the wrong impression that listing of substances is equated to exposure, which of course it is not. Lists can be made by anyone who wishes to make them from the MSDS's available (9:53300).

The hazard communication rule was implemented in May 1986 in some 300,000 U.S. businesses at an estimated cost of \$600 million or \$43.00 per worker in SIC Code industries 20-39. The law is expected to put "right to know" information about hazardous substances in the hands of half of the estimated 25 million workers who face potential exposure to hazardous substances in their workplace.

OSHA officials believe the impact in the manufacturing industry of the hazard communication rule will be pervasive due to a synergistic effect. This assumption is based on an increased number of expected law suits that will be filed by workers alleging that a hazardous substance caused their injury or disability. OSHA officials also believe that eventually U.S. firms will

have to remove many of the hazardous substances from the work place. Currently there are some 2,300 basic hazardous substances being used to manufacture 575,000 chemical products in the United States.

The hazard communication worker information program was implemented in November 1985 in the chemical industry.

From November 1985 through April 1986, OSHA found 497 violations at 175 of the 762 chemical plants inspected, including one serious and one willful, warranting \$1,000 and \$10,000 fines respectively (10:4A).

To recap, a MSDS is developed for each hazardous chemical produced or imported in the United States. Employers are required to obtain or develop a MSDS for each hazardous chemical used in their work places. Cytotoxic drugs are excluded from such MSDS overview as it applies to the placement of warning labels on the outside of shipping containers or the classification of each drug as hazardous. Cytotoxic drug manufacturers are required to generate MSDS's for personnel directly involved in the manufacture of the drug.

This standard took eleven years to develop since the original standard was proposed in 1974. The standard applies to chemical manufacturers and excludes the distributors of drugs regulated by the FDA. The subsequent development of a cytotoxic drug standard to be used by the distributors cannot be ignored. As a basis for concentrating on the manufacturing codes 20-39, OSHA relied upon the fact that 50% of the total chemically induced worker illnesses occurred in industries in these categories. In 1981, 17% of all service industry illnesses, hospitals and distributors included, were due to chemical origins (9:53285). While the health care industry, SIC codes 8062 and 8069, comprises a fair share of the services industry, no information is available about chemically induced worker illnesses in this sector.

Product Liability Case Law Statutes. The medical literature also contains warnings from attorneys that the lack of labeling on the outside of a cytotoxic drug container and the lack of in-depth explanations of the hazard associated with its use may constitute a breach of the liability case law statutes described below.

Current product liability case law statutes are described as:

The area of negligence that are generally applicable to product liability are as follows: (1) Failure of a manufacturer to inspect his product properly, (2) Failure to warn of known defects or danger, (3) Failure to test, and (4) Failure to design a reasonably safe product ... A warning that is not obvious or that fails to warn of the gravity of the potential injury may be considered lack of due care ... A supplier's or manufacturer's liability associated with the handling and manufacture of cytotoxics is legally limited to 'remedies for occupational illness and injury.' In order to understand the legal cause and effect relationship between one's actions and one's liability for one's acts we must define: negligence -- is legally defined as the failure to exercise the degree of care that would have been exercised by a reasonable person with comparable training and experience acting in the same or similar circumstances. Four elements are required in order for a party to establish a legal cause of action for negligence. They're: (1) duty of reasonable care -- the person injured must be someone to whom is owed a duty of due or reasonable care, (2) breach of the duty of reasonable care -- in deciding whether the defendant's conduct fell below that of a reasonable person, a jury considers all of the circumstances surrounding the act, e.g., what degree of care would be exercised by a reasonable person with comparable training and experience acting in the same or similar circumstances, (3) damage or injury -- there must be injury or damage to someone or something; and (4) proximate cause -- is the proof of proximate cause, e.g., the injured party must show, the defendant's act was the proximate cause of his injury ... With the handling of cytotoxic drugs, it may not be exceedingly difficult to prove damage of some sort, (e.g., testimony of a person's illness who handled cytotoxic agents), but the difficulty will likely arise in establishing a causal relationship between the handling of the drug and the illness ... In a civil case the requirement is only that the plaintiff prove his case by a preponderance of the evidence ... an injured party may be awarded damages (by the jury) at the conclusion of a trial even though there is reasonable doubt as to whether

the defendant should be held liable for the injury to the injured party. In a civil case, all the plaintiff must do is convince a jury that it is more likely than not that the facts are as he alleged (11:1115,1121).

Worker's-Right-to-Know Laws. When OSHA excluded the pharmaceutical manufacturing firms from the requirement of passing through the MSDS information about the potential risk associated with the handling of cytotoxic drugs to hospitals and distribution companies, approximately 20 states passed more restrictive versions of the Hazard Communication Standard in an attempt to ensure that non-manufacturing personnel were properly educated about cytotoxic drugs. As a group, these laws are referred to as "Worker's-Right-to-Know" laws. The New York law includes state official's development of the MSDS's, and the California law includes a "cytotoxic exposure monitoring program" for hospital employees who track "mean exposure time" in the preparation and administration of cytotoxics. The Minnesota state law is similar to the federal standard in that it requires the employer to develop a MSDS or "drug monograph" dealing with the handling of cytotoxic drugs. The Minnesota law requires employers to provide the following:

- (1) generic, trade, chemical and commonly used name of the substance, (2) level at which exposure to the substance has been determined to be safe, if known, (3) known acute and chronic effects of exposure to a substance at hazardous levels, (4) known symptoms of adverse effects, (5) potential for flammability, explosion, or reactivity, (6) known proper conditions for safe use and exposure to the substance, (7) procedures for cleanup of leaks and spills, (8) name, phone number, and address of the manufacturer of the hazardous substance, and (9) a written copy of the above items readily accessible in the areas where the hazardous substance is handled ... The information requirement may be fulfilled by having a properly completed federal OSHA form 20, MSDS, on file (12:1974).

These laws were enacted because the federal government took eleven years to develop the hazard communication ruling which ended up excluding cytotoxic drugs. During the eleven years a typical federal government answer to an inquiry were answered as follows:

a number of organizations are currently addressing the (labeling) issue, however, it would be premature for the committee to make specific recommendations at this time. A suggestion was made that one might say on the package insert for these drugs, is, that they are possibly hazardous (13:1).

The committee did act on this suggestion and sent a letter in the fall of 1985 to the pharmaceutical companies requesting such a "hazardous" statement. (See Figure 1).

OSHA Publication, "Guidelines for Cytotoxic (Antineoplastic) Drugs."

Without fanfare or advanced notice, the Office of Occupational Medicine, under the Department of Labor, recently issued OSHA Instruction PUB 8-1.1 (29 Jan 86) titled: "Guidelines for Cytotoxic (Antineoplastic) Drugs." While this guideline is substantially a copy of the ASHP guidelines referenced earlier, it does specifically address labeling and transportation issues within the health care facility setting. The guidelines were published by OSHA because:

The volume of requests to OSHA indicates a broader interest among administrators and health care professionals who are not aware of, or who have not had access to these guidelines (ASHP). Moreover, recent surveys reveal that there is little standardization of work practices and that proper practices and adequate protective equipment are not being currently utilized. Therefore, OSHA considers implementation of its work practice guidelines important for protecting workers against these serious occupational hazards (14:1).

FDA

Date: Nov 7, 1985

***Name and Address of the
Specific Drug Company in this Space**

Dear Sirs:

The FDA has been evaluating the labeling of cytotoxic anticancer drugs for safe handling. This subject was addressed by the FDA Oncology Drugs Advisory Committee on March 29, 1985 and on June 28, 1985.

The following statement should be added to the DOSAGE and ADMINISTRATION section of the package insert for all cytotoxic anti-cancer drugs by April 1, 1986. The references should be added either at the end of the DOSAGE and ADMINISTRATION section or at the end of the package insert.

Procedures for proper handling and disposal of anti-cancer drugs should be considered. Several guidelines on this subject have been published. There is no general agreement that all of the procedures recommended in the guidelines are necessary or appropriate' ... The addition of this general statement is not intended to replace or substitute for more specific information in the package insert related to safe handling of the drug.

Our records indicate that the following drug products marketed by your firm would be candidates for inclusion of package insert information concerning cytotoxic anti-cancer drugs. If these records are incomplete please inform us.

John F. Palmer, M.D., Director,
Division of Oncology and
Radiopharmaceutical Drug Products
Office of Drug Research & Review
Center for Drugs and Biologicals

Figure 1. OSHA Letter to Chemical Manufacturer's Requesting Inclusion of Cytotoxic Drug Warning in Drug Package.

The guideline discusses the subjects of isolating cytotoxic drugs from all other drugs in storage areas, applying warning labels to all storage shelving and to the drugs containers themselves, opening damaged cytotoxic drug shipments in hoods or by personnel clothed and trained to do so. The guideline also addresses the issue of training personnel, placing particular emphasis on the training of shipment-receiving personnel who are the first line of defense against environmental contamination that often results from handling cytotoxic drugs with normal procedures. This guideline hopefully will be the basis for a change to the Code of Federal Regulations (CFR) regarding cytotoxic drugs. In order to implement such a change, OSHA would have to propose that the guidelines are in fact going to be incorporated into the CFR and hold hearings for public comment and suggestions. This is a lengthy process and would require a minimum of two years to be enacted. The importance of this publication cannot be overstated.

Current Air Force Practices

Introduction. The prior sections reviewed the existing federal statutes and administrative regulations applicable to the manufacture, transportation, labeling, and disposal of cytotoxic drugs and drug wastes. The following section will review the current Air Force policies and practices. Policy and procedure changes are recommended in Chapter 5.

Review of Existing Policies and Directives. Two cytotoxic drug handling directives have been issued since December 1984 (15,16). The first directive was from HQ AFOMS/SGPC, Pharmacy Services and office of primary responsibility for policies concerning cytotoxic drugs; the second

from the Air Force Medical Logistics Office/DPSC. Both directives reference the following articles: (1) USAFOEHL Report, which included the National Safety Commission on Cytotoxic Exposure Report, and (2) ASHP Technical Assistance Bulletin on Handling Cytotoxic Drugs in Hospitals.

The AFOMS/SGPC directive requires that Pharmacy personnel establish policies and procedures for all hospital personnel by the end of 1989 regarding the handling of cytotoxic drugs. While this directive is quite specific about the mixing of cytotoxic drugs in the Pharmacy setting, it does not address the storage, handling, and distribution of cytotoxic drugs. AFOMS/SGPC does not feel the need for labeling to be important enough to warrant any changes to existing non-pharmacy procedures. Attempts by the AFMLL staff to publish articles suggesting that medical supply officers initiate local policies for labeling cytotoxic drugs have been overruled by AFOMS/SGPC.

The AFOMS/SGPC directive simply references the ASHP guidelines for implementation guidance on non-pharmacy policies, which cannot be implemented until cytotoxic drugs are labeled. HQ AFOMS/SGPC personnel are not aware that cytotoxic drugs are shipped in this country in non-environmentally controlled surface freight trucks and how medical supply items are distributed within medical treatment facilities.

The Air Force Medical Logistics Letter (AFMLL), a bi-monthly publication distributed by the Air Force Medical Logistics Office, recommends that each medical treatment facility (MTF) logistics department establish local policies and procedures, in conjunction with the hospital's bioenvironmental engineering, environmental health, and pharmacy personnel, regarding the handling of cytotoxic drugs within the hospital setting. The AFMLL further recommends that the ASHP guidelines should be followed and in the event of

a spill, the bioenvironmental engineering department be notified to respond to the incident scene. Quite simply, until cytotoxic drugs and cytotoxic drug shipping packages are labeled, the implementation of the guidelines referenced in the directives cannot be accomplished.

Professional Groups Recommendations for Handling Cytotoxics

The material below is a paraphrasing of the ASHP technical bulletin and the OSHA publication 8-1.1 guidelines.

The guidelines recommend that hospital's establish four overall objectives: (1) Protect and secure packages of hazardous drugs, (2) Inform and educate hospital personnel about the specific nature of antineoplastic drugs and train them in the safe handling procedures relevant to their responsibilities, (3) Do not let the drugs escape from their containers when they are manipulated, and (4) Eliminate the possibility of inadvertent ingestion, inhalation, and direct skin contact or eye contact with the drugs.

Each of the four overall objectives can be further divided into the following measureable goals:

1. Maintain Physical Integrity and Security of Packages of Cytotoxic Drugs--
 - a. Limit access to all areas where cytotoxic drugs are stored. Partition or designate specific warehouse shelving and refrigeration, and/or storage areas specifically for cytotoxic drugs.
 - b. Identify all cytotoxic drugs within each storage location by applying appropriate warning labels to all cytotoxic drug containers and shelves and bins where they are permanently stored.
 - c. Establish and maintain written procedures for handling damaged packages of cytotoxic drugs. Shipping cartons of cytotoxic drugs

received in a damaged condition should be cautiously opened in an isolated area, preferably in a fume hood.

d. Establish procedures for the use of protective apparel, such as a closed front gown, double disposable latex or vinyl gloves, a disposable dust and mist respirator and eye protection, when handling cytotoxic drug containers.

e. Establish the use of storage containers, carts, shelving and similar items that are designed to prevent breakage via the use of plexiglass barriers at the front or other designs that reduce the chance of drug containers falling to the floor.

f. Transportation of cytotoxic drugs and/or IV admixtures (intravenous bags with one or more cytotoxic drugs mixed together) should be done by responsible personnel and not conveyed using any mechanical means other than an elevator. The use of dumbwaiters, pneumatic tubes, automatic cart-exchange systems or other material handling systems should be forbidden.

2. Ensure that the hospital environment is not contaminated with cytotoxic drugs or cytotoxic drug waste materials produced in the course of using cytotoxic drugs.

a. Written policies and procedures governing the containment, collection, and disposal of cytotoxic waste materials are established and maintained. Throughout the facility, cytotoxic waste materials are contained and segregated from all other hospital trash.

b. Materials to clean up spills of cytotoxic drugs are readily available and personnel are trained in their proper use. A standard clean up protocol should be established and followed. A "cytotoxic drug spill team" comprised of members from the departments of pharmacy, bioenviron-

mental engineering, environmental medicine and housekeeping should be formed. All spills are documented in the Quality Assurance Incident Reporting System in accordance with AFR 168-13. "Spill kits", whether locally devised or commercially obtained, should be located in each area where cytotoxic drugs are stored, prepared, administered, or disposed of.

c. Cytotoxic drug wastes must be disposed of in accordance with all applicable governmental regulations. State permits or written permission from the appropriate state department should be obtained to incinerate cytotoxic drug wastes at the proper incinerator temperature. Each hospital or base incinerator used to incinerate cytotoxic drug wastes must be checked annually by either the manufacturer or base civil engineering to ensure that the required operating temperature is routinely obtained during the burn cycle.

Manufacturing Company Policies Regarding the Handling of Cytotoxics

Eli Lilly and Company, the manufacturer of cytotoxic drugs, submitted the following "Guidelines for the Safe Handling of Cytotoxic Drug Products," as an attachment to the OSHA 20 Form, Material Safety Data Sheet. A MSDS is required by the Department of Health and Human Services for each drug that contains a hazardous substance as the active ingredient in quantities greater than 1% by weight or volume. The guidelines state:

Generally, the active ingredient in a drug product is so diluted that exposure to the final dosage form does not involve any significant risk ... a few products such as cytotoxic agents warrant special considerations ... the potential exposure possible under normal circumstances is so limited that the usual safeguards followed ... would appear to be adequate, but, ... even under the best planned and implemented conditions, however, accidental contact may occur which may involve

pharmacists, nurses, shipping and receiving personnel and/or individuals responsible for the disposal of broken or damaged containers or empty or partially filled administration devices (syringes, needles, tubing etc.). Shipping and receiving considerations stipulate that all personnel should never attempt to open a damaged shipping container. If a damaged container is received, receiving personnel should notify the appropriate personnel and initiate the proper response (17:1).

Summary

In light of the current product liability statutes and the personnel education and product labeling requirements of existing laws that are applicable to industries using hazardous substances, it appears that the exclusion of the cytotoxic drug pharmaceutical industry from the labeling and pass-through education requirements because of the 1% by weight or volume standard, is a questionable practice from a safety and human welfare perspective.

The laws reviewed above demonstrate that cytotoxics are regulated in a unrealistic manner that does not address the potential hazard that clearly exists for all personnel involved in the distribution, preparation, administration, and disposal of cytotoxic drugs in the health care setting.

In Chapter 3, the questionnaire methodology is discussed. The purpose of the questionnaire was to determine the medical supply officer's level of knowledge regarding the handling of cytotoxic drugs within the hospital or clinic setting.

In Chapter 4, the results and analysis of the survey are presented.

In Chapter 5, a proposal is presented for DLA self-initiation of labeling practices for cytotoxic drugs that would result in a higher level of safety for logistics personnel and not interfere with the current provisions of the HMTA. The changes required in certain Air Force manuals and the Military

Standard Requirements and Issue Procedure (MILSTRIP) are presented in outline form. Expert review and comments about the validity of the MILSTRIP recommendations are discussed. The findings and conclusions from analysis of the survey are presented. Recommendations for corrective action are provided.

III. Survey Instrument

Introduction and Scope

According to Emory "the process of moving from the general management objective or problem to specific measurement questions involves answering four major questions" (18:200) which are (1) the first or management question of this project is: Are cytotoxic drug handling procedures stringent enough to ensure personnel safety? The preponderance of medical literature indicates that current laws and practices are lacking in key areas; (2) the second or research questions of this project are: (a) what laws and federal policies exist that regulate the labeling of and handling of cytotoxic drugs?; and (b) can the labeling of and safer handling of cytotoxic drugs be procedurally defined and implemented within the DLA structure without interfering with or exceeding the existing laws and federal regulations?; (3) the third or investigative questions of this project are : (a) what changes are necessary to solve the perceived problem?; and (b) what level of knowledge exists currently within the medical service corps about the issues surrounding the handling of cytotoxic drugs in the medical treatment facility environment?; and (4) the fourth or measurement questions of this project are found in the questionnaire, Appendix A.

In order to ascertain the "level of knowledge" that exists in the field, a family of investigative questions concerning the issues involved with the handling of cytotoxic drugs in the hospital/clinic setting was developed for the targeted population of medical supply officer corps to test the following hypotheses and to meet the objective:

Hypothesis One: Medical supply officers in 1986 have a higher "level of knowledge" about cytotoxic drugs (CD's) than medical supply officers who vacated similar positions prior to the treatment period, defined as CY 1985.

Hypothesis Two: Current medical supply officers (1986) "level of knowledge" about handling CD's is inadequate, despite publication of AF directives during 1985.

Measurement questions are further divided into three categories by Emory. They are: data, characteristics, and administrative. The majority of questions in the survey instrument are data oriented. These questions attempt to measure the level of knowledge of current issues surrounding the handling of cytotoxic drugs possessed by medical supply officers assigned to medical treatment facilities in the USAF.

The survey results will be analyzed using the Statistical Package for the Social Sciences-X. A classification of answers by population (control vs study) will be performed for all 36 variables and seven construct variables. The t-test analysis will provide the mean, standard deviation, t- test significance levels of each variable and construct. The Pearson Correlation analysis will provide bivariate correlation between pairs of all variables within each construct. The Regression analysis provides multiple linear regression analysis for each construct variable. Factor analysis will be used to find the amount of shared variance between a variable and all other variables in the intercorrelation matrix. Median analysis will be used to look at the distribution of the data.

Questionnaire Objectives

The objective of the questionnaire is to quantify the knowledge base possessed by medical supply officers regarding the current topics of

handling, storage, distribution, labeling, and disposal of cytotoxic drugs within the medical treatment facility environment.

The level of knowledge possessed by the 1984 group were compared to that of the 1986 group. If there is a statistically significant difference, it can be reasoned that hypothesis one will have been verified.

The 1985 AF policy recommendations were compared to actual field practices. If there is a statistically significant difference, it can be reasoned that hypothesis two will have been verified. If no difference exists, then medical logistics officers are informed at that level desired by the Air Force.

Lastly, if the data demonstrates that there are information gaps or areas of uncertainty, recommendations to improve the knowledge base will be proposed.

Questionnaire Design/Sampling Method

A survey instrument was developed comprised of 36 measurement questions and two general information questions. The 36 questions address eight subject areas or constructs. See Table II. The survey instrument was pretested by two medical supply officers and one pharmacist at the Air Force Institute of Technology, School of Logistics, WPAFB, in Dec 1985.

The population to be surveyed is the entire number of AF medical service corps officers (MSC's) currently holding hospital or clinic supply positions. The treatment is the series of HQ and AF articles that were distributed (CY 1985) to the field regarding CD's handling procedures. The control group is the MSC's who occupied similar positions during the CY's 1983-1984. It is therefore reasoned that a baseline level of knowledge about cytotoxics is still intact within the control group. This baseline can

TABLE II

Variable Definitions

<u>Variable</u>	<u>Explanation (See Appendix A, Survey, for each question)</u>
Score	Overall evaluation of Officers Level of Knowledge Questions: 5-8,10-14,16-30,32,33
Trnpck	Transportation and Packaging of cytotoxic drugs Questions: 6,16,17,20
Gknow	General Knowledge about cytotoxic drugs Questions: 5,7,12,13
Handlg	Handling Issues and Facts about cytotoxic drugs Questions: 8,10,15,18,19,21,22,25,26,30
Hospol	Hospital policies, recommended by medical literature and reference documents distributed by the Air Force Questions: 11,23,24,27,28,29,32,33
Lbl drg	Did respondent feel cytotoxic drugs should be labeled Questions: 3,34
AFpol	Did respondent feel that the reference material was beneficial in answering the survey questions Questions: 35,36
Trnhc	Transportation and handling issues related to cytotoxics Questions: 6,7,20

The questions not specifically identified in a variable were demographic or factual questions used to establish the experimental and control groups.

then be subtracted from the 1986 study group and association analysis can be made between the increased level of knowledge (if it exists) and the directives and policies cited in the survey instrument along with other variables. The survey question constructs are shown in Table 2 by question.

A critical weakness of the survey instrument is that it references the AF and HQ directives, that if reviewed by the respondent prior to or during the completion of the instrument, will invalidate the instrument's purpose of measuring the "level of knowledge" as it exists. In order to minimize this weakness respondents are specifically instructed to answer the survey without doing any research, reading or oral.

Analysis Methodology

Five Statistical Package for the Social Sciences-X computer programs were written to analyze the response data. These programs were tested with a data base generated using a random number generator for each measurement question response. The first analysis, termed t-test, provides all the basic summary statistics for all the survey questions and the combined variables such as Score, Handling, etc. The mean, standard deviation, and number of cases in each group were generated. The variable mean score of each variable per group was tested for statistical significance against the same variable mean score of the other groups. When a t-test was statistically significant at $p < .05$, this indicated that the level of knowledge between the two groups was disparate and that one group knew more about that question or subject (combined variable) area. Most of the survey analysis and conclusions were drawn from the t-test analyses. The second analysis, termed Pearson Corr, provides bivariate correlation between pairs of variables within each construct. This measure indicated the reliability of

the survey instrument in measuring what it was suppose to measure, e.g., the level of knowledge of the responder regarding cytotoxic drugs. The third analysis, termed Regression, provides multiple linear regression analysis for each construct variable as it is entered into the model equation. This methodology requires that each constraint variable to be entered, have the largest F value of the remaining construct variables. If a construct variable falls below the tolerance criteria it is not entered into the model. The objective of regression analysis is to identify which survey questions would most likely predict the level of knowledge of the respondent. The fourth analysis, termed Factor analysis, seeks to determine the commonality, or the amount of shared variance between an item and other items in the intercorrelation matrix. Factor analysis is similar to regression in that the objective is to identify which variables predict the relative level of knowledge of the respondent. The fifth analysis, termed median analysis, shows the distribution of the data. The central limit theorem seeks to demonstrate that when data is randomly drawn from a large sample the resulting mean will be centrally located, e.g., one-half of the data points below the mean and one-half above. The median is the value that divides the data set into two equal halves. The closer the mean and the median value, the greater the likelihood that the data is normally distributed. If the mean and median differ, the distribution of the data may be significant in explaining the relationship between the variables in the survey instrument.

IV. Survey Findings and Analysis

Introduction

The level of knowledge demonstrated by the medical supply officers is used as a measure of the effectiveness of existing cytotoxic laws, policies and directives to provide a safe work place for logistics personnel. The survey findings, a reflection of this measurement, are explained. Each area of knowledge (ref Table II) is examined and defined in conjunction with certain known facts, such as, "had the officer read AFMLL 23-85," etc. The results obtained from each of the five methods of analysis are presented. The hypotheses are validated. Of 178 surveys distributed, 109 were returned. Ninety-nine of the 109 were used in the analysis. There were sixty-five supply officers in Groups 1 & 2 and thirty-four officers in Group 3.

Survey Implications Regarding Existing Laws, Federal and Air Force Policies

The survey findings indicate that the medical supply officers level of knowledge about cytotoxic drugs is not indicative of safety practices. The experimental group of officers did not demonstrate a statistically significant level of higher understanding than the control group of medical supply officers about the variable "Handling" (Handlg, ref Table II), which measured safety practices for handling cytotoxic drugs. There were 10 questions that investigated safety practices in the variable Handlg. The level of understanding was uniform between all sampled officers. The mean of the experimental group of officers was 2.26 with a standard deviation of 2.002 and the mean for control group of officers was 1.51 with a standard deviation of 1.964 out of a possible score of 10. The questions all centered around basic

issues of protection of one's self, the environment, and cleaning up spills. As further evidence of this deficiency, there was no difference between the experimental group of officers when they were divided into the officer's whose facilities handled cytotoxic drugs and those officer's whose facilities did not handle cytotoxic drugs. The mean and standard deviation of the former were: 3.32 and 1.909 versus 1.47 and 1.442 of the latter group.

OSHA indicates in the Cytotoxic Drug Guidelines publication 8-1.1 that despite existing laws, accidents and mishaps are regularly occurring in the hospital environment involving cytotoxic drugs. The frequency of these accidents was one of the reasons that OSHA published the guidelines.

The group of officers whose facilities handled CD's had a higher overall level of knowledge about cytotoxic drugs that was statistically significant from that of medical supply officers whose facilities did not handle cytotoxic drugs. This does not mean that the "knowledgeable" officers level of knowledge was adequate (those who handled cytotoxic drugs). A perfect knowledge score on the survey would have been a score of 26 points, one point per question. "Knowledgeable" officers had a mean score of 9.2 with a standard deviation of 4.4 and officers who didn't handle cytotoxic drugs had a mean score of 3.78 with a standard deviation of 2.35. Median analysis revealed that one-half of the knowledgeable officers who handled cytotoxic drugs scored 13 points on the survey and one-half scored 4.8.

Perfect knowledge of the laws, federal regulations, and Air Force policies regarding cytotoxic drugs does not necessarily result in safe handling, labeling, and distribution practices since the existing laws, regulations, and Air Force policies are inadequate, as shown in the literature review. The specific inadequacy is the failure to label cytotoxic drugs and the lack of specific handling policies that recognize the potential hazard to humans. The

literature review also showed that civilian hospital policies require labeling and the use of specific CD handling practices. Ninety-eight percent of the respondents indicated a need for special labeling of all cytotoxic drug packaging and shipping containers.

Overview of Survey Findings and Analysis

The population surveyed can generally be divided into three distinct and mutually exclusive groups of individuals. Group 1 represents the medical service corps supply officers in hospitals that dispense cytotoxic drugs, Group 2 represents the medical service corps supply officers in hospitals that do not dispense cytotoxic drugs, and Group 3, Control Group, represents medical service corps supply officers who had left the hospital supply officer's position prior to December 1984. It was during calendar year 1985 that a majority of the materials were distributed to the field that first advised personnel of the potential hazards associated with handling cytotoxic drugs.

During the analysis of the data it was useful to combine and sometimes divide groups 1, 2, and 3 into additional larger groups or subgroups. Additional information was obtained in this manner with regard to the impact of certain variables on the population being surveyed.

Each paragraph below briefly describes which groups were compared and which variables were significant. Significance means that the groups were different in their level of knowledge about the subject matter based upon the specific questions asked. The numbers in parentheses after the groups identification refer to the number of respondents in that sample. The number in parentheses after the variable represents the degree of significance, .05 or smaller represents the 95% confidence interval for these t-tests.

Table III contains a tabular summary of these findings, and Table IV contains the variable means and standard deviations of the groups used to evaluate the relative level of knowledge and Table V contains the survey question means and standard deviations of the groups used to evaluate the relative level of knowledge.

t-tests, Findings and Analysis

Criteria No. 1 Groups 1 & 2 (Hosp and Clinic) vs Group 3, (95.34): This analysis compared current hospital supply MSC's against the control group. Statistically significant differences: Trnpck(.026).

Findings and Analysis: Current hospital and clinic medical supply officers, Groups 1 & 2, demonstrated a statistically significant higher level of knowledge about cytotoxic drug properties, policy issues and administrative practices than did the control group (Group 3). Thus Hypothesis One: "Medical supply officers in 1986 have a higher level of knowledge about cytotoxic drugs than medical supply officers who vacated similar positions prior to the treatment period, defined as CY 1985" was statistically validated at the $p < .05$ level of confidence. Specifically, the group of current medical supply officers demonstrated a clear and significant knowledge about how cytotoxic drugs were labeled by the depot, handled, and shipped than did the control group of medical service corps officers. The Pharmacy and Therapeutics Committee (P&T Committee) was functioning in facilities where Group 1 & 2 supply officers worked and had addressed the environmental concerns of cytotoxic drugs whereas the P&T Committee in the control group's (Group 3) facilities had not. The concept of a "response team" was known and in effect at facilities in Groups 1 & 2 whereas, in Group 3, the concept was not known.

TABLE III

t-test Analysis of Statistically Significant Group Variables

Crit No:	1	2	3	4	5	6	7	8
n/n (,)	65,34	49,13	23,25	33,28	41,21	39,22	28,18	35,22
Group	1 vs 3	1 vs 1	1 vs 2	1 vs 2	All	All	All	1 vs 3
Group	HC vs c	H vs C	H vs H	HCvsHC	HCvsHC	HCvsHC	HCvsHC	HC vs c
GrpDiff			Q9	Q9	Q33	Q33/34	Q9+Q33	Q9=No
Score			0.004					
Trnpck	0.026		0.001	0.000	0.000	0.000	0.000	
Gknow			0.004					
Handlg								
Hospol			0.005	0.015	0.001	0.001	0.000	
Lblarg			0.000	0.000	0.000	0.000	0.000	
AFpol								
Trnhc					0.010	0.016	0.048	
Q7		0.032			0.007	0.016		
Q8								
Q11	0.001							0.037
Q12				0.000			0.000	
Q13			0.009	0.025				
Q16			0.023	0.000	0.000	0.000	0.000	
Q17								
Q19					0.016	0.009	0.006	
Q20	0.000			0.004	0.000	0.007	0.004	
Q21	0.047		0.002	0.000	0.005	0.025	0.000	
Q22	0.047		0.002	0.011	0.018	0.006	0.001	
Q23					0.000			
Q24		0.001						
Q25		0.001			0.044		0.022	
Q26				0.017			0.044	
Q27	0.021							
Q29	0.030		0.038	0.002		0.002	0.001	
Q30				0.033				
Q32			0.000	0.000	0.000			
Q33								
Notes:	Group1	Hosp+	Clinic	CytoUse		Q9:Use	Q9:Use	(Y/N)
	Group2	Hosp+	Clinic	Don't	UseCyto	Q33:	Q33:	AFMLL
	Group3	Contr!				Q34:	Q34:	AFOMS
	H:Hosp							
	C:Clinic							
	c:contr		Total	Surveys	178	Return	109	% =61.2

TABLE IV
Mean and Standard Deviation of Variables by Group

Crit No		1		2		3		4	
n/n (,)		65,34		49,13		26,23		29,33	
Group		1 vs 3		1 vs 1		1 vs 2		1 vs 2	
Group		HC vs c		H vs C		H vs H		HCvsHC	
GrpDiff						Q9		Q9	
		MEAN	STDDEV	MEAN	SD	MEAN	STDDEV	MEAN	STDDEV
Score	Group					35.240	4.400		
	Group					29.783	2.354		
Trmpck	Group	4.815	1.130			5.500	1.304	5.483	1.299
	Group	4.500	0.788			4.348	0.647	4.303	0.585
Gknow	Group					5.692	1.087		
	Group					4.391	0.583		
Handlg	Group								
	Group								
Hospol	Group					10.480	1.558	10.500	1.528
	Group					9.522	0.846	9.515	0.972
Lbidrg	Group					3.923	0.272	3.931	0.258
	Group					3.609	0.656	3.667	0.595
AFpol	Group								
	Group								
Trnhc	Group								
	Group								

TABLE IV (cont)

Mean and Standard Deviation of Variables by Group

Crit No.	5		6		7		8	
n/n (,)	21,41		22,39		18,28		35,22	
Group	All		All		All		I vs J	
Group	HCvsHC		HCvsHC		HCvsHC		HC vs c	
GrpDiff	Q33		Q33/34		Q9+Q33		Q9-No	
	MEAN	STDDEV	MEAN	STDDEV	MEAN	STDDEV	MEAN	SD
Score								
Trnpck	5.667	1.461	5.562	1.441	5.888	1.451		
	4.439	0.634	4.436	0.641	4.286	0.600		
Gknow								
Handlg								
Hospol	11.200	1.436	11.136	1.390	11.235	1.480		
	9.3659	0.767	9.308	0.731	9.214	0.568		
Lbidrg	3.952	0.218	3.957	0.209	3.944	0.236		
	3.7073	0.559	3.692	0.569	3.607	0.629		
AFpol								
Trnhc	3.952	1.024	3.913	0.996	4.111	1.023		
	3.439	0.634	3.436	0.641	3.321	0.670		

TABLE V

Mean and Standard Deviation of Survey Questions by Group

Crit No.		1		2		3		4	
n/n (.)		65,34		49,13		26,23		29,33	
Group		1 vs 3		1 vs 1		1 vs 2		1 vs 2	
Group		HC vs c		H vs C		H vs H		HCvsHC	
GrpDiff						Q9		Q9	
		MEAN	STDDEV	MEAN	STDDEV	MEAN	STDDEV	MEAN	STDDEV
Q7	Group			1.061	0.242				
	Group			1.154	0.376				
Q11	Group	1.969	0.175						
	Group	1.912	0.288						
Q12	Group							1.310	0.471
	Group							1.030	0.174
Q13	Group					1.462	0.508	1.414	0.501
	Group					1.087	0.288	1.121	0.331
Q16	Group					1.308	0.471	1.310	0.087
	Group					1.087	0.288	1.061	0.042
Q19	Group								
	Group								
Q20	Group	1.123	0.331					1.207	0.412
	Group	1.029	0.171					1.061	0.242
Q21	Group	1.127	0.336			1.200	0.408	1.250	0.441
	Group	1.061	0.242			1.044	0.209	1.061	0.174
Q22	Group	1.111	0.317			1.200	0.408	1.179	0.390
	Group	1.061	0.242			1.044	0.209	1.061	0.242
Q23	Group								
	Group								
Q25	Group			1.021	0.144				
	Group			1.077	0.277				
Q26	Group							1.276	0.455
	Group							1.091	0.292
Q27	Group	1.234	0.427						
	Group	1.091	0.292						
Q29	Group	1.063	0.244			1.115	0.326	1.103	0.310
	Group	1.029	0.171			1.044	0.209	1.030	0.174
Q30	Group							1.069	0.258
	Group							1.030	0.174
Q32	Group					1.308	0.471	1.310	0.471
	Group					1.044	0.209	1.030	0.174

TABLE V (con't)

Mean and Standard Deviation of Survey Questions by Group

Crit No.	5		6		7		8	
n/n ()	21,41		22,39		18,28		35,22	
Group	All		All		All		1 vs 3	
Group	HCvsHC		HCvsHC		HCvsHC		HC vs c	
GrpDiff	Q33		Q33/34		Q9+Q33		Q9=No	
	MEAN	STDDEV	MEAN	STDDEV	MEAN	STDDEV	MEAN	STDDEV
Q7								
Q11							1.943	0.236
							1.864	0.351
Q12					1.278	0.461		
					1.036	0.189		
Q13								
Q16	1.429	0.507	1.391	0.499	1.444	0.511		
	1.049	0.218	1.051	0.223	1.036	0.189		
Q19	1.905	0.502	1.913	0.288	1.944	0.236		
	1.439	0.301	1.41	0.498	1.286	0.46		
Q20	1.286	0.463	1.261	0.449	1.333	0.485		
	1.049	0.218	1.051	0.223	1.071	0.262		
Q21	1.25	0.444	1.227	0.429	1.294	0.47		
	1.073	0.264	1.077	0.27	1.036	0.189		
Q22	1.2	0.41	1.182	0.395	1.177	0.393		
	1.073	0.264	1.077	0.27	1.036	0.189		
Q23	1.191	0.402	1.175	0.388				
	1.024	0.156	1.026	0.16				
Q25	1.238	0.436			1.222	0.428		
	1.098	0.3			1.071	0.262		
Q26					1.333	0.485		
					1.107	0.315		
Q27								
Q29			1.13	0.344	1.167	0.383		
			1.026	0.16	1.036	0.189		
Q30								
Q32	1.381	0.498						
	1.049	0.218						

Criteria No. 2 Group 1 & 2 (Hosp) vs Group 1 & 2 (Clinic), (49,13): This analysis compared current hospital supply officers against current clinic supply officers. The two significant differences were: Q7(.032) "Currently, DLA supplies:", and Q24(.001) "Stock Records orders all cytotoxics off-line to ensure that the shipped order does not arrive in a multipack."

Findings and Analysis: These results indicate that hospital supply officers did know more about the shipping and ordering of cytotoxic drugs specific to their facilities than did current clinic supply officers. The level of knowledge difference between the officer's centered around the question of how many types of cytotoxics the depot shipped and whether or not stock records used any specific policies regarding the ordering of cytotoxic drugs.

Criteria No. 3 Group 1 (Hosp only) vs Group 2 (Hosp only), (26,23): This analysis compared hospital supply officers who handle cytotoxic drugs against those who do not. The significant findings were: Score(.004), Trnpck (.001), Gnknow(.004), Hospol(.005), and Lbidrg(.000).

Findings and Analysis: The validity of the survey instrument as a measure of the level of knowledge was established. The variable Score, which is a cumulative summary of all the survey questions, showed a significant difference between the hospital supply officers whose facilities handle cytotoxic drugs (high score) and supply officers whose facilities do not handle cytotoxic drugs (low score). Secondly, the hospital supply officers handling cytotoxic drugs expressed a desire for those drugs to be labeled throughout the distribution channel, whereas the supply officers whose facilities did not handle cytotoxic drugs did not have such a concern.

Criteria No. 4 Group 1 (Hosp & Clinic) vs Group 2 (Hosp & Clinic), (28,33): This analysis compared hospital and clinic supply officers that handle cytotoxics versus those hospital and clinic supply officers that do not.

The significant findings were: Trnpck(.000), Hospol(.015) and Lbl drg(.000).

Findings and Analysis: Clinic supply officers whose facilities handle cytotoxic drugs know more about handling, shipping, hospital policies, spill kits, labeling of cytotoxic drugs and desire labeling of cytotoxic drugs than do clinic supply officers whose facilities do not handle cytotoxic drugs. The difference between these two groups was not as pervasive as the difference between the hospital supply medical supply officers.

Criteria No. 5 Group 1 (Hosp,Clinic & read AFMLL) vs Group2 (Hosp, Clinic and did not read AFMLL), (21,41): The purpose of this analysis was to compare the level of knowledge between supply officers that read AFMLL 23-85 and those that had not. The use or non-use of cytotoxic drugs was not considered. The significant findings were: Trnpck(.000), Hospol(.001), Lbl drg(.000) and Trnhc(.010).

Findings and Analysis: Medical supply officers that had read the 23-85 issue of the AFMLL were more knowledgeable than supply officers that had not, regardless of whether or not the facility handled cytotoxic drugs. The significant level of knowledge differences concerned transportation, handling, shipping, storage, ordering, and the existence of the AFOMS/SGPC memo which had been distributed to pharmacists throughout the Air Force.

Criteria No. 6 Group1 (Hosp,Clinic & read either AFMLL or HQ AFOMS/SGPC memo) vs Group 2 (Hosp, Clinic & did not read either reference),(22,39): This analysis compared supply officers that read either reference distributed (the AFMLL distributed to the medical supply corps or the memo sent to facility pharmacists sent by HQ AFOMS/SGPC) against the level of knowledge possessed by the group of supply officers who had read neither reference. The significant findings were: Trnpck(.000), Hospol(.001), Lbl drg(.000), and Trnhc(.016).

Findings and Analysis: Medical supply officers who had read the AFOMS/SGPC field memorandum but not the AFMLL did demonstrate a level of knowledge greater than those who had not read either reference. This level of difference was far less pervasive than that of the supply officers who had read the AFMLL versus those who had not.

Criteria No. 7 Group 1 (hosp, clinic, handle cytotoxics, & read AFMLL) vs Group 2 (hosp, clinic, do not handle cytotoxics, & did not read the AFMLL), (18,28): This analysis compared supply officers who had read the AFMLL and whose facility distributed cytotoxic drugs against supply officers who had not read the AFMLL and whose facility did not distribute cytotoxic drugs. The significant findings were: Trnpck(.000), Hospol(.000), Lbidrg (.000), and Trnhc(.048).

Findings and Analysis: This is a similar comparison between Group 1 and Group 2 that links handling cytotoxic drugs and reading the AFMLL as a condition of the analysis. The areas of difference between the two groups concerned handling, ordering, storage, shipping, and spill kits. Criteria No. 4, handling cytotoxic drugs, and No. 6, having read the reference, also demonstrated a difference between the groups in 13 variables as does this measure. While the 13 variables do change between criteria numbers 4, 6, and 7, there is a consistent finding throughout the three analyses.

Additional Findings and Analysis

In order to determine the relative significance of the Group 1 level of knowledge compared to the level of Group 2 knowledge, the following analysis was performed.

Criteria No. 8 Group 2 (Hosp, Clinic & do not use cytotoxics) versus Group 3 (Control & do not use cytotoxics),(35,22): This analysis compared

the level of knowledge between the medical supply officers whose facilities do not use cytotoxic drugs against the level of knowledge of the control group of medical supply officers that had not heard of or read anything about cytotoxic drugs. The significant finding was: Q11(.037), The Medical Logistics Management office is represented at the Pharmacy and Therapeutics Committee Meeting."

Findings and Analysis: This result demonstrates that there is no statistically significant difference between the control group and the hospital/clinic group when the facility does not handle cytotoxic drugs. It appears that there has been no environmental learning association occurring in facilities that do not handle cytotoxic drugs, e.g. the AFMLL was not read. Group 1 does demonstrate a significant level of knowledge when compared to that of Group 2, because Group 2 and Group 3 have an equivalent level of knowledge. Group 3, the control groups has not received any CD education.

Pearson Correlation Analysis

The pearson correlation analysis compared 1,369 pairs of variables in a matrix to determine relative correlation between each pair of questions or variable. This analysis determines that like questions were answered in like manner, meaning that the survey measured the level of knowlege of the respondents with consistency. Sixty-two point one percent (62.1%) of the 1,369 paris of variables were statistically significant at $p < .05$. This percentage is a good measure of the survey instruments reliability. Of the statistically significant pairs of variables, 399, or twenty-nine percent of the entire matrix, was statistically significant at $p = .000$. These findings indicate that there were very strong consistent findings throughout the survey instrument between respondents and the survey questions.

Factor Analysis

The factor analysis was inclusive in determining which variables demonstrated commonality. In order for factor analysis to be statistically significant and reliable the number of cases analyzed should be five times the number of variables. With twenty-six questions and seven combination variables, one hundred and sixty-five cases were needed. The usable number of responses for this analysis was ninety-nine. Therefore, factor analysis was not used.

Regression Analysis

The stepwise regression analysis (ref Table VI), using Score as the dependent variable, yielded regression equations with adjusted R Square terms from .7 to 1.0. Adjusted R Square measures the relative fit of the model to the data, adjusted for the number of variables in the equation. The model is the set of independent variables (questions) that are reasonable predictors of the variable Score. Reasonable predictors are defined as those survey questions that indicate the level of knowledge of the survey respondent. If two questions are similar, multiple regression uses only the "better" reasonable predictor of the two. Score is a measure of overall knowledge about cytotoxic drugs. Stepwise regression is used when there are highly correlated independent variables present in a regression model as there was in this case. The model or equation picked, as the reasonable predictor of the variable "Score," the first model that achieved an Adjusted R Square value greater than .95. This equation, called NewScore, is made up of eleven (11) survey questions and a constant value. The Adjusted R Square value was .95717. The ANOVA table and other regression data is presented

TABLE VI

Regression Analysis ANOVA Table and Findings

Multiple R	.98088
R Square	.96213
Adjusted R Square	.95717
Standard Error	.93677

Analysis of Variance

	<u>DF</u>	<u>Sum of Squares</u>	<u>Mean Square</u>
Regression	11	1872.52589	170.22963
Residual	84	73.71370	.87754

F - 193.98415 Signif F - .0000

Variables in the Equation

<u>Variable</u>	<u>Beta</u>	<u>T</u>	<u>Sig T</u>	<u>Variable</u>
Q18	2.393973	9.142	.0000	Handlg
Q33	1.741362	6.627	.0000	Hospol
Q12	2.163268	6.734	.0000	Gnknow
Q21	3.345080	9.589	.0000	Handlg
Q13	1.630357	5.566	.0000	Gnknow
Q28	2.721110	7.570	.0000	Hospol
Q14	1.480230	6.502	.0000	Score
Q32	2.015218	6.280	.0000	Hospol
Q20	2.133290	5.777	.0000	Trnpck
Q5	1.341515	5.735	.0000	Gnknow
Q10	.914211	4.124	.0001	Handlg
Constant	5.110022	7.093	.0000	

in Table VI. The original Score equation used twenty-six (26) survey questions. NewScore accomplishes the same purpose (predicting level of knowledge) with only eleven survey questions. Within NewScore the four strongest indicators of "level of knowledge" (Score) were the questions that dealt with the functions of the P&T Committee (Q21), patient consumables (Q18), the opening of damaged multipacks (Q28), and the AFMLL article (Q32). The higher the "T" score on table 6, the more meaningful the question in predicting the "level of knowledge."

Median Analysis

The first median analysis (See Table VII) compared the hospital and clinic experimental group (1&2) versus the control group (3). The Score variable had a median value of 4.5. The mean (t-test analysis) of groups 1 & 2 was 6.15 and the mean of group 3, was 4.58. The median analysis found no statistically significant difference between the groups. This means that the data was normally distributed.

The second median analysis compared only hospital medical supply officers that handled cytotoxic drugs versus those that did not (Criteria #3). The median value was 5.5 and the difference in the level of knowledge between the two groups was statistically significant at $p=0.0001$. Basically, 80% of the officers who handled cytotoxic drugs demonstrated a level of knowledge above the median. Of the officers who did not handle cytotoxic drugs, 82.6% had a level of knowledge below the median. This means that if the officer handled cytotoxic drugs there was only a 20% probability the officer would know less than the median level of knowledge and that if the officer did not handle cytotoxic drugs there was only a 17.4% probability that the officer would have a level of knowledge above the median.

TABLE VII

Median Analysis

Median Analysis No. 1

	GT/LT Median	Group One	Group Two
n=94 Significance - None	GT	74.4%	25.6%
Score median value 4.5	LT	59.5%	40.5%

Group One - Hospital and Clinic Medical Supply Officers (Groups 1 & 2)

Group Two - Control Group (Group #3)

Median Analysis No. 2

	GT/LT Median	Group One	Group Two
n=48 Significance - .0001	GT	16.6%	83.3%
Score median value 5.5	LT	79.2%	20.8%

Group One - Hospital medical supply officers who do not handle CD's

Group Two - Hospital medical supply officers who handle CD's

Median Analysis No. 3

	GT/LT Median	Group One	Group Two
n=61 Significance - .0001	GT	41.4%	58.6%
Score median value 5.0	LT	90.6%	09.4%

Group One - Hospital & clinic medical supply officers who did not read the AFMLL 23-85

Group Two - Hospital & clinic medical supply officers who did read the AFMLL 23-85

Median Analysis No. 4

	GT/LT Median	Group One	Group Two
n=61 Significance - .0000	GT	15.4%	84.6%
Score median value 4.0	LT	91.5%	08.5%

Group One - Hospital & clinic medical supply officers who did not read the AFMLL 23-85 nor handle cytotoxic drugs

Group Two - Hospital & clinic medical supply officers who did read the AFMLL 23-85 and handle cytotoxic drugs

The third median analysis compared the hospital and clinic supply officers that read AFMLL 23-85 versus those that had not (Criteria #5). The median value was 5.0 and the difference in the level of knowledge between the two groups was statistically significant at $p=0.0001$. Basically, 85% of the officers who had read the AFMLL 23-85 demonstrated a level of knowledge above the median. Of the officers who had not read the AFMLL, 70.7% had a level of knowledge below the median value. This means that if the officer read the AFMLL there was only a 15% probability that the officer would know less than the median level of knowledge and that if the officer had not read the AFMLL, there was a 29.3% probability that the officer would have a level of knowledge above the median.

The fourth median analysis compared the hospital and clinic supply officers who had read the AFMLL 23-85 and handled cytotoxic drugs versus those officers that had not read the AFMLL and did not handle cytotoxic drugs. The median value was 4.0 and the difference in the level of knowledge between the two groups was statistically significant at $p=0.0000$. Basically, 84.6% of the officers who had read the AFMLL and handled cytotoxic drugs demonstrated a level of knowledge greater than the median. Of the officers who did not handle cytotoxic drugs and who had not read the AFMLL, 91.5% demonstrated a level of knowledge below the median. This means that if the officer read the AFMLL and handled cytotoxic drugs there was only a 15.4% probability that the officers' level of knowledge would be below the median. Whereas, if an officer had not read the AFMLL and had not handled cytotoxic drugs, there was only a 8.5% probability that this officers' level of knowledge would be above the median.

Summarized Findings

1. Hypothesis One was statistically validated. Current hospital and clinic medical supply officers demonstrated a statistically significant higher level of knowledge about cytotoxic drug properties, policy issues and administrative practices than did the control group. Throughout the sample the level of knowledge about handling/safety issues was equally low.

2. The Pharmacy and Therapeutics Committee (P&T Committee) in facilities where Group 1 supply officers worked had addressed the environmental concerns of cytotoxic drugs whereas the P&T Committee in the control group (Group 3) and non-drug use group (Group 2) facilities had not.

3. The concept of a cytotoxic drug spill "response team" was known and in effect at facilities in Group 1 whereas in Groups 2 & 3 the concept was not known.

4. Hospital supply officers whose facilities handle cytotoxic drugs demonstrated a statistically significant higher level of knowledge about cytotoxic drug properties, policy issues and administrative practices than did hospital supply officers whose facilities did not handle cytotoxic drugs. A parallel finding was established between clinic medical supply officers as well. However, the handling and safety level of knowledge between all the groups was the same.

5. The hospital supply officers handling cytotoxic drugs expressed a desire for those drugs to be labeled throughout the distribution channel whereas the supply officers whose facilities did not handle cytotoxic drugs did not have such a concern.

6. The level of knowledge about cytotoxic drugs was hierarchical depending upon use/non-use and whether or not the 23-85 AFMLL had been read. The median analysis could not determine which was more

important in contributing to the level of knowledge if the other was present. However, in the absence of one, the other was significant in its own right.

7. The level of knowledge of the hospital medical supply officers in facilities that distribute cytotoxic drugs was vast (9.2 mean vs 3.7 mean) compared to the level of knowledge of any other group or combinations of groups, with the exception being the handling and safety "level of knowledge." However, "vast" is relative only to the sample. "Knowledgeable" officers, on the average, only knew 1/3 of the information that had been contained in the AFMLL article. Hypothesis Two states: "Current medical supply officers (1986) level of knowledge about handling CD's is inadequate, despite AF directives issued in CY 1985." The definition of inadequate is central to the validity of the statistical determination of the level of knowledge difference between the means of the two groups. At the 70% level of knowledge, the mean score of the respondents would have been 18.2 compared to the actual 9.2. At the p.05 level of confidence the difference is statistically significant with a Z score of 1.99. If a 50% level of knowledge (mean of 13) is presumed to be adequate, then with a standard deviation of 4.527, a mean of 9.2 is not statistically significant. This means that this sample of officers could represent a group that did know 50% of the material. It is the author's belief that a 70% level of knowledge is not unreasonable since all the survey questions came from the CY 1985 distributed materials. This belief is the basis for stating that Hypothesis Two has been statistically validated.

8. Ninety-eight percent of the respondents indicated: (1) that a "brochure or quick reference guide" that explains what cytotoxic drugs are and how they are to be handled would be a beneficial education tool for medical logistics personnel and (2) that "all cytotoxic drug packaging and

shipping containers should be identified as such using some sort of labeling scheme." It is this level of support for CD labeling that is the basis of the inference on page 2, Investigative Question, that labeling and only labeling is the mechanism available for increasing the level of knowledge about CD's. The median analysis demonstrated that officers had either a "high" or "low" level of knowledge relative to the sample. Yet all the officers supported the labeling idea.

9. Current Air Force and Defense Logistics Agency procedures comply with existing federal laws and regulations regarding the shipping, handling, and distribution of cytotoxic drugs. The Veterans Administration has initiated its own labeling and shipping identification procedures to ensure that VA personnel are aware of cytotoxic drugs within the VA distribution system. The Defense Materials Standardization Board and DLA are reviewing the VA initiatives as well as the author's proposals.

V. Research Conclusions and Implications

Introduction

This chapter will use the level of knowledge areas of weakness, as determined by the survey findings, to propose recommendations to the existing laws, policies and directives. A review of the latest activity at the federal agency level is also provided. Within the Air Force structure, specific changes are proposed for: (1) the depot and supply manuals, (2) improved monitoring of the cytotoxic drug handling procedures in military treatment facilities, and (3) better coordination between the Air Force directorates involved with cytotoxic drugs. The suggested changes to the depot and supply manuals were reviewed at the directorate level and the feedback is provided. Lastly, the overall research conclusions and implications of the research effort are listed.

Courses of Possible Action at the Federal Level

The literature review and survey results have shown that additional action is required to resolve the issues of: (1) cytotoxic drug shipping containers not being identified or labeled as hazardous, (2) individual cytotoxic drug packaging containers not being identified or labeled as hazardous, and (3) the classification of cytotoxic drug product wastes as hazardous within the hospital setting, and (4) the inadequate "level of knowledge" about the safe handling of cytotoxic drugs in the hospital setting. There are at least five possible alternative courses of action available at the federal level.

The first possible action is having the Assistant Secretary of the EPA

determine that a specific cytotoxic drug is not to be excluded from being classified as a hazardous substance under CERCLA or NIOSH standards. This would change its classification to something other than a ORM-D, Class B Poison. The second possible action is to have the Assistant Secretary of the EPA determine that a specific cytotoxic drug is to be reclassified out of the ORM-D Poison B class irrespective of the drug's classification, thus making it a hazardous substance. The third possible action is having Congress pass a law specifically including all SIC code industries to be included in the CERCLA and Hazard Communication standard, to include abolishing the 1% rule thereby forcing all substances containing hazardous substances to be labeled as such. The fourth possible action is to have the Defense Logistics Service Center (DLSC), Battle Creek, MI., decide that DoD won't purchase any cytotoxic drugs that are not marked as hazardous on the shipping containers and on the individual unit dose vials etc., using DoD's purchasing power as leverage on the pharmaceutical companies. The last possible action is to have the Defense Logistics Service Center and its subsidiary agency, the Defense Logistics Agency (DLA) unilaterally implement MILSTRIP policy and procedural changes which specify how cytotoxic drugs are to be specifically identified and safely distributed to MTF's.

The first two alternatives involve raising the level of awareness of the NIOSH and EPA staffs. The Department of Labor, via the publication of the "Guidelines for Cytotoxic (Antineoplastic) Drugs" appears to be very conscious of the potential hazards associated with cytotoxic drugs. Since cytotoxic drugs are classified as ORM-D Poison Class B items, no specific statistics exist concerning hospital worker contamination incidents. It appears that lack of evidence of illness associated with the logistical handling of cytotoxic drugs is interpreted by the NIOSH and EPA to mean that cyto-

toxic drug contamination of logistics personnel is not occurring. The RCRA or EPA Superfund legislation required a "Love Canal" to prod Congress into dealing with the problem of environmental contamination due to hazardous wastes (Love Canal was a significant environmental waste dumping incident involving a community of 10,000 people). The problem of cytotoxics pale in comparison to this national situation. Using DoD's contractual purchasing power as a means of forcing manufacturers to print warnings on the exterior of cytotoxic shipping containers is theoretically feasible. There is a long history of using acquisition practices to achieve socio-economic policy initiatives. The Small Business Set-Aside Act is one example. The initiation of such an action by the Defense Materials Standardization Board without concurrent NIOSH approval, however, is unlikely. The last alternative, which is a self determination by the Defense Logistics Service Center to protect its personnel from a perceived health risk, based upon a review of the medical literature, is fraught with difficulties also. The Defense Materials Standardization Board would have to decide to label cytotoxic drugs on it's own without support from other federal agencies.

Within the Air Force, HQ USAF/SGPC, (Pharmacy Services), has been appointed by the USAF Surgeon General as the Office of Primary Responsibility (OPR) for Air Force policy involving cytotoxics. It appears that while the HQ USAF/SGPC staff has been conscientious in establishing the necessary policy guidance to pharmacy personnel in the field, they have failed to grasp the logistical safety concerns due to a unfamiliarity with supply procedures and warehouse practices. Basically, supply personnel cannot be aware of a medical supply item's potential health risk if that risk isn't clearly established on the outside of the shipping container and on the individual drug package in unmistakable fashion.

This research is directed toward two distinct but complementary goals: increased awareness of problems in handling cytotoxic drugs and changing the procedures for labeling cytotoxic drug shipping containers. It can be seen that to do so would involve both changing congressional laws as well as the cooperation and coordination of agencies within and outside of the USAF. Without a basic change in the incidence reporting methodology involving cytotoxic drugs and/or the abolishment of the 1% rule, the exact magnitude of the problem cannot be fully identified. If the proposed changes are made, the required database of incidents and related health problems may determine that further action is necessary.

This current state of affairs is not a static situation though. Many federal agencies are involved in rethinking this issue. Because no one agency is primarily responsible for changing the procedures that implement the CERCLA act, it appears that additional extensive deliberations will have to precede any proposed change at the federal level.

Summary of Federal Level Activities

The most promising action by any one federal agency is the recent distribution of the OSHA publication regarding cytotoxic drugs. From a logistics perspective, all the major areas of concern are adequately addressed. Of particular import were the guidelines recommending segregation of cytotoxic drugs from other medical supply items, the labeling of cytotoxic drug shipping containers and hospital storage locations, and lastly, the documentation that health care personnel have received a briefing on what and how to handle cytotoxic drugs as it relates to their work environment. While possibly redundant for nurses and pharmacists, such training and documentation is of fundamental importance to the

safeguarding of logistics and other non-medical hospital personnel.

The continuing efforts of OSHA to monitor the implementation of the hazard communication information program in SIC Code industries 20 - 39 is also an indication that the government is vigorously enforcing the "workers right to know" perspective of the law as it was intended.

Purpose of Proposed Changes to AF Policies

The goal of these proposed changes is to improve the cytotoxic drug handling methods used by logistics personnel within DOD, DLSC and DLA. If Air Force practices were more closely aligned to the recommendations of the ASHP technical bulletin and OSHA Publication 8.1-1, higher levels of personnel safety could be achieved. The recommendations below, if adopted, would achieve this higher level of personnel safety without necessitating the changing of any federal laws. Changes to the existing Military Standard Requisitioning and Issue Procedure guidance (MILSTRIP) would be required.

Recommended Changes to the Directives

1. Supply-Depot Procedures-- USAF Supply Manual, AFM 67-1, Vol V, Chapter 8, "Requirements, Requisitions, and Due-Ins," establishes the policies and procedures utilized by the medical logistics personnel to procure medical supplies for use within MTF's. These procedures are quite extensive and it is not the intent of this project to suggest changes line by line. The following suggestions would result in changes to all the supporting documentation. Briefly, all medical supply items are requisitioned from the depot or commercial vendors using an 80 column punch card format or a "local purchase" request form (DD Form 1348-6). Each column or block on the respective card/form has a specific purpose. Various combinations of numbers

and letters on the card or information on the DD Form 1348-6 result in the requisitioning of different items. The cards are also used for a number of communication actions between the MTF, the depot and base contracting agency.

The first recommended change is to the Document Identifier Code field on the punch card. "The document identifier code identifies each document by type, that is, requisition, receipt, etc ... , and further identifies data as to its intended purpose and use ... (it), is a mandatory entry on all requisitions ... and lastly, each product necessary to perform various inventory functions will be identified by an appropriate code."(3:8-36) In order to identify and track cytotoxic drugs, a cytotoxic drug document identifier code needs to be established. The following codes are suggested:

Columns(1,2,3)	Document Title	Explanation
A06	Requisition	Cytotoxic Drug, overseas, NSN
A07	Requisition	Cytotoxic Drug, overseas, other
A08	Requisition	Cytotoxic Drug, domestic, NSN
A09	Requisition	Cytotoxic Drug, domestic, other

These changes would provide the computerized medical material management system with the necessary data base information to track and process cytotoxic drug requisitions, follow-ups, shipping and inventory management actions.

The second recommendation is to include a cytotoxic drug identifier code in the "advice code" column. This would achieve the following: (a) require all cytotoxic drugs requisitioned by the MTF to be shipped together and excluded from shipment with other non-cytotoxic drug medical supply items being shipped to that MTF by the depot, and (b) allow the defense logistics agency to place a label on the outside of the cytotoxic drug shipping

container with the advice code on it. This would result in supply personnel at the receiving hospital to be instantly aware that this box or package contained cytotoxic drugs. A code such as 2X (columns 65/66) with the following explanation is recommended: "ship by self or with other 2X items only, place 2X label on outside of package, immediately below mailing label."

The third recommendation is to create a "cytotoxic drug" mode shipment code and assign it the code of "J." These codes are defined within the hazardous materials transportation act and the letter "J" is available. The mode shipment code change would enable the depot to identify which boxes or shipping containers required the special "cytotoxic drug" identification label to be pasted adjacent to the destination label prior to shipment to a medical treatment facility. If not feasible because it deals with the HMTA, the "2X" identifier would be sufficient.

The fourth suggestion pertains to use of the DD Form 1348-6 local purchase request form. Block G, which can be used for such shipping information as, Poison, Class B, cannot be used in this instance because the HMTA excludes the labeling of cytotoxic drugs as ORM-D Poison Class B items. To get around this stipulation, logistics personnel could, in block G of this form; (1) request that the supplier mark the outside of the shipping container, under the mailing label with the 2X advice code nomenclature, and (2) that the commercial shipper only send cytotoxic drugs in containers by themselves.

The fifth recommendation concerns the Defense Logistics Agency Manual 1455.5, "Quality Control, Depot Serviceability Standards, Appendix M, Medical Supplies." The purpose of this manual is to: "determine the condition of medical materiel stored within the DLA supply system, establish the responsibility of each defense supply center (DSC) to develop service-

ability standards for their assigned commodities ... and to control the quality of supplies during receipt, storage, and shipment."(19:M-I-1)

Section III of the Depot manual, "Monographs, contains specific inspection/extension information on NSN medical supply items ... and/or information about NSN items that require special instructions not included elsewhere."(19:M-III-1). Current items listed include x-ray film, developer, fixer etc. Each monograph contains the following information: item description, signs of deterioration, special inspection and testing requirements, special notes and the like. Appendix B, is the suggested monographs of the leading 22 cytotoxic drugs now in use for inclusion in the DLAM, 1455.5 Appendix M manual. This exhaustive work was compiled by Mr. Wallace B. Wadd, Director of Pharmacology Services, Midway Hospital, St Paul, MN., and was edited to conform to DLA format. Each pharmaceutical company was contacted for their MSDS OSHA 20 forms and any other supplemental information. These monographs were published in part by the American Journal of Hospital Pharmacy in 1985. It is suggested that DLA adopt these monographs as written and distribute them to all MTF's. The information contained in them is not readily available in such a concise format anywhere. Their use in educating logistics personnel about the potential hazards associated with the cytotoxics drugs they handle daily in the warehouse is immeasurable.

To recap, it is recommended that a new advice code, identifier code, shipment mode code, Block G DDForm 1348-6 policy, and DLAM Appendix M manual cytotoxic drug monographs be adopted and implemented. The result of these actions would be the labeling of shipping containers at the depot with the advice code 2X, which in turn would result in logistics personnel being able to identify such containers upon receipt, and the initiation of

handling procedures that result in maximum safety of personnel. Secondly, these procedures would further identify cytotoxic drugs within the medical materiel management system database for easier tracking and reporting purposes.

2. Improved monitoring of the cytotoxic drug handling procedures in military treatment facilities.

The Health Services Management Inspection team conducts biennial management and medical practice inspections of AF medical treatment facilities. Prior to each inspection, an inspection guide is distributed to each facility. This 1400 page guide is a master checklist that is divided into functional areas and is used by each team inspector to evaluate the management practices and compliance to existing Air Force regulations, policies, practices and directives. The medical logistics management department is one such functional area, as is housekeeping and facility management. A well coordinated and comprehensive policy regarding the safe handling of cytotoxic drugs throughout the facility, the roles of each department, and minimum criteria required to achieve an effective policy that increases the safety of personnel could be implemented and enforced using the HSMI team inspection checklist.

Within the medical logistics management functional area, the adoption of the ASHP and OSHA publication 8-1.1 guidelines reviewed in Chapter 2 would achieve an increase in the level of safety associated with the handling of cytotoxic drugs and waste products within the medical treatment facility setting.

3. Better coordination between the Air Force directorates involved with cytotoxic drugs.

Interviews with Pharmacists who have called HQ AFOMS/SGPC

Inquiring as to why the labeling suggestions of the logistics staff have not been accepted, have determined that the pharmacy HQ staff does not feel that labeling is a "reasonably feasible action." The directive states:

The following guidelines are essential and all reasonably feasible action should be initiated now or completed as soon as possible, but in no case later than the end of 1989 where multiple patients are routinely treated with cytotoxic, antineoplastic agents: a. The pharmacy maintains overall responsibility for mixing and preparation of cytotoxic, antineoplastic agents as well as training medical treatment facility staff in safe handling of these drugs ... (16:1).

On paper, this directive sounds like it will provide an adequate program to educate the nursing and physician staffs. The professional staff handles these items after the pharmacy staff has mixed them and labeled the IV bag with bright orange stickers. The logistics staff deserves to be provided the same warning on the outside of the shipping containers and in the warehouse.

Summary of Recommendations to AF Policies

Current Air Force policies, procedures, and directives do not adequately address the potential risk to logistics personnel and housekeeping personnel who handle cytotoxic drugs and drug products. The medical literature conveys an explicit and severe view of the potential risk to all personnel involved in the preparation, administration, distribution, and disposal of cytotoxic drugs, drug products, and drug wastes. The literature stresses these points: (a) maximum precautions should become a matter of routine, and (b):

that since no method currently exists for routinely monitoring personnel for evidence of cytotoxic drug exposure, all institutions should have a strong quality assurance program that periodically

evaluates and verifies staff adherence to and performance of the established safe handling policies and procedures (2:137).

Without HQ AFOMS/SGPC and DLA action to label cytotoxic drug containers with the suggested advice code 2X, procedures by receiving personnel to ensure their own safety cannot be reasonably implemented. Typically, in a 35 bed hospital, receiving personnel check in 25 to 50 boxes daily. Wilford Hall Medical Center, Lackland AFB, has 1,000 beds and specialized chemotherapy programs. It would appear that the large volume of cytotoxic drugs shipped to such a facility should be a cause of concern for the safety of the warehouse personnel.

Lastly, the monographs (Appendix B) for the sampled 22 drugs indicate the following: (a) 41% are soluble in water, (b) 50% are a fire explosion hazard, (c) 68% require firefighters to be wearing a breathing apparatus to prevent inhalation of toxic fumes, (d) 95% require that handlers wear protective clothing, and (e) 95% require that special precautions be taken to avoid any type of contact. Based upon the recommendations of Eli Lilly Co., it is clear beyond a reasonable doubt that extreme caution should be exercised by any personnel who handle these cytotoxic drugs.

Expert Review of AF Policy Change Recommendations

Emory states that "research is a systematic inquiry aimed at providing information to solve problems" (18:10). This research project has two major components: (1) a series of recommendations for changing Air Force policy and (2) a survey of medical supply medical service corps officers to measure their level of knowledge concerning the issues surrounding the handling of cytotoxic drugs within the medical treatment facility environment.

Scientific research conducted in accordance with accepted operations

research industry wide practices leads to "conclusions confined to those justified by the data of the research and limited for which the data provide an adequate basis" (18:11). Proposing recommendations to change existing Air Force policies and procedures without subjecting those recommendations to expert review, is analogous in many ways to experimental research results being applied to areas beyond the scope of the research. "The benefits of research mean different things to different people" (20:58). The benefits associated with the adoption of the recommended procedural changes lies within the "avoidance of litigation" arena in concert with the doctrine of "duty of reasonable care." If the Air Force does not adopt policies and procedures that a reasonable person would when informed of the dangers associated with cytotoxic drugs, the Air Force might be found guilty by a jury in a court of law of violating the legal tenet of "duty of reasonable care." If the divergence between military practices and the civilian community widens (1985 AF directives versus OSHA publication 8-1.1) and the focus of civilian hospitals on safety at any cost continues, the easier it may be for plaintiffs' counsel to allege that the Air Force's current practices were the proximate cause of the party's injury. This is the veiled threat that surrounds the current practices of handling cytotoxic drugs. What ill effects will be evident 10 to 20 years down the road in personnel who handled the items cannot be approximated. Being at the forefront in procedures designed to keep personnel contamination-free would fulfill the requirements of "duty of reasonable care."

Three letters (an example, Appendix C) containing the proposed procedural changes were sent to the offices of primary responsibility for each HQ functional area; DLA, Logistics and Pharmacy. The questions asked of the reviewers were: (1) do the proposed recommendations accomplish their

objectives, (2) are the proposed recommendations adoptable, both in principal and content, and (3) if the answer to either question is "no", why not?

Reviewer's Responses

AFOMS/SGSLP, Directorate of Health Care Support, Medical Logistics Division, Office of the Surgeon General responded favorably to the recommendations. It is estimated that the changes to the MILSTRIP would take "at least two years due to the many automated systems involved" (21:1). The Office of Primary responsibility for coordinating a MILSTRIP change package is AFMLO/FOR-O. The recommendations, similar to those in Appendix C, were forwarded to the Air Force Medical Logistics Office/FOR-O for their review and action.

The response from the Defense Logistics Agency, Defense Personnel Support Center, Office of Medical Material/DPSC-A agreed "that cytotoxic drugs present a special hazard." As stated in the response, Appendix D, the Defense Logistics Agency and the Defense Logistics Service Center cannot unilaterally adopt any of the author's suggested proposals because: (1) the Defense Medical Standardization Board is the approval agency for policy changes, and (2) the "Veterans Administration has implemented special marking requirements of cytotoxic drugs which could impact DOD because of the DOD/VA Shared Procurement Program" (22:1). The notes code and identifier concept has been endorsed by DLA in principle and changed to "Note D" and "T6 Antineoplastic (chemotherapy)." The proposed changes, monographs, and DLA comments.

will be forwarded to the Defense Medical Standardization Board, Fort Dietrick, MD for coordination with and approval by the Military Medical Services. If concurrence is obtained, appropriate recom-

mendations will be made to Headquarters, DLA for changes in the handling of cytotoxic drugs (22:1).

Summary of Expert Review

Essentially, DPSC-A has accepted the concept of the recommendations, which was to track cytotoxics through the computer based acquisition and management system and to label the shipping containers with some type of label. It would appear, that without the self initiated action undertaken by the Veterans Administration to label cytotoxic drugs in the VA Medical Centers and to track cytotoxics through their own computer based acquisition system; that while technically correct, the recommendations may not have been forwarded to the Defense Medical Standardization Board so quickly. The outcome of the Board meeting is unknown at this time.

Research Conclusions

The purpose of this research effort was to determine the level of knowledge about handling cytotoxic drugs that exists within the medical supply officer corps and to test that knowledge against a predetermined measurement of adequacy. Likewise, the current laws, policies and directives for handling cytotoxic drugs were measured against the more conservative and safety oriented self-imposed civilian hospital policies and practices. The existing laws, Air Force policies and directives along with the supply officers level of knowledge were found to be inadequate when compared to the policies and practices of the civilian sector. The secondary goals of the research effort were to increase the level of awareness of supply MSC's throughout the Air Force about the problems associated with the handling of cytotoxic drugs and to submit "labeling policies" to the Defense Materials Standardization Board for review. These objectives have been

achieved.

1. Medical supply officers can be classified into two groups, those whose facilities do treat patients with cytotoxic drugs and those whose do not. Medical supply officers in facilities that treat patients with cytotoxic drugs do possess a rudimentary level of knowledge about the range of current issues surrounding the handling and distribution of cytotoxic drugs.

2. Medical supply officers working in facilities that do not treat patients with cytotoxic drugs do not have a level of knowledge about cytotoxic drugs that is any different from that of supply officers who left the field prior to the calendar year 1985 education efforts by higher headquarters. It would appear that a need-to-know/don't need-to-know orientation exists regarding the contents of the AFMLL as read by medical logistics officers.

3. The preponderance of medical literature suggests that cytotoxic drugs do present a clear and verifiable danger to logistics personnel. The United States Air Force and the Defense Logistics Service Center should follow the lead of the Veterans Administration and establish specific shipping identifier codes and labeling procedures for CD's. The guidelines outlined in the OSHA publication 8-1.1 for labeling and handling cytotoxic drugs within the hospital and clinic environment should be adopted immediately.

Research Implications

1. Medical supply officers selectively retain information from the AFMLL that is pertinent to the discharge of their duties at that point in time. In this specific situation it would appear that a learning for learning's sake outlook about reference articles distributed in the AFMLL did not occur. The

AFMLL reference was highlighted with a specific article lead-in that a person had been injured in the line of duty while handling a cytotoxic drug. This approach apparently did not have the desired effect of gaining interest and passing knowledge at facilities which did not handle cytotoxic drugs.

2. One of the most important implications of this study concerns the high probability that the handling of cytotoxic drugs will increase to all DoD MTF's in the near future. The current practice of vertical military patient referral from smaller bases to larger bases is soon to be changed within DoD. A new horizontal health care finder concept will be initiated whereby patients are referred to civilian facilities within the same geographic location as the DoD facility. Retirees once treated with cytotoxics at referral military facilities will be cared for at local civilian facilities and transferred back to local DoD facilities for follow-on outpatient maintenance therapy with cytotoxic drugs. Currently only 50% of the hospitals and 15% of the clinics report handling cytotoxic drugs (ref. Table III). The likelihood that all DoD medical treatment facilities would be stocking cytotoxic drugs is real. Similar hazardous substances could also find their way into small hospital inventories under the horizontal health care concept. Medical supply officers must adopt a more expansive attitude regarding the applicability of the reference material provided in the AFMLL.

3. The effectiveness of the AFMLL was demonstrated as an education tool for some medical supply officers. The significance of the information provided was determined. The question of whether the article prompted medical supply officers to determine if their facilities were handling cytotoxic drugs or whether a supply officer's knowledge that the facility did handle cytotoxic drugs prompted an interest in the AFMLL article could not be determined. The importance of retaining AFMLL information even when

there is no direct applicability to the officers present position should be reinforced by the AFMLL office in the heading of each publication.

4. In light of the recent U.S. Department of Labor, Occupational Safety and Health, Office of Occupational Medicine Publication 8-1.1, "Guidelines for Cytotoxic (Antineoplastic) Drugs" and the gradual shift to a horizontal health care referral system within DoD, an additional, more effective, cytotoxic drug education program needs to be established within the Office of the Surgeon General, United States Air Force and distributed to the medical logistics field, irrespective of or coordinated with the program mandated by AFOMS/SGPC. A reply by written endorsement that the medical supply officer has read, briefed his staff and his Commander about the contents of the cytotoxic drug education program should ensure this important and valuable information is comprehended in the medical logistics field at the lowest level. This program should be initiated concurrently with the development of a specific identifier code for ordering, shipping, and labeling cytotoxic drugs.

Recommended Areas for Future Study

1. The purpose of labeling is to lower the risk associated with handling hazardous items. To conclusively determine that labeling results in an increased "level of knowledge" and lower risk, a labeling study should be performed that would test supply officers' knowledge of current items that are labeled by the depot prior to shipment. For example, the labels "explosive, corrosive, flammable and biological hazard" all convey specific meanings and policies to support MSC's. If the level of knowledge is different between depot labeled items and cytotoxic drugs, labeling could be inferred to be the key missing ingredient contributing to the lower level of knowledge about cytotoxic drugs.

2. The Air Force should determine the actual number of cytotoxic drug mishaps that are occurring in its medical treatment and depot settings. Within the medical environment, AFR 168-13, "Quality Assurance," requires incident reports to be completed by hospital personnel whenever non-routine medical situations occur. In each facility a risk manager is charged with the responsibility of ensuring completion of incident reports and the reporting of summary statistics to higher headquarters. Incidents involving cytotoxic drugs could be broken out as a specific tracking interest item for a specified time period. The major commands could collate the reports and forward them to a central coordinator within the Surgeon General's office. The number and nature of the incidents would provide conclusive evidence regarding the effectiveness of current Air Force directives. Within existing Air Force regulations, the Safety Officer of each the depots would be charged with the same responsibility as the MTF risk manager.

3. A policy evaluation could be pursued using cost benefit analysis, comparing centralized cytotoxic drug therapy at specific Air Force MTF's versus the existing decentralized approach. Along with this evaluation, a similar cost benefit analysis could occur proposing the "exclusive use of civilian facilities" for the treatment of DOD patients requiring cytotoxic drug therapy.

Appendix A: Survey



DEPARTMENT OF THE AIR FORCE
AIR UNIVERSITY
AIR FORCE INSTITUTE OF TECHNOLOGY
WRIGHT-PATTERSON AIR FORCE BASE OH 45433-6663

REPLY TO: LSM(Capt Rennie)
ATTN OF:
SUBJECT: Survey about Cytotoxic Drugs

TO

1. In fulfillment of the thesis requirement I am investigating the current policies and practices that exist in AF medical treatment facilities regarding the receipt, storage, and handling of cytotoxic drugs.
2. Your completion of this survey is important so the results will be truly representative of the field. An analysis of the results will be forwarded to DPSC.
3. No individual names or other references (i.e., base) will be used with any analysis of the surveys, which are being distributed to all MSC's in SGL positions Air Force wide.
4. Please answer the survey without doing any research (reading or oral). If the survey is not completed individually, without use of references, the results will not be a help to anyone in understanding this important issue.
5. If you have any questions I can be reached at autovon 785-6569. Please leave a message and I will get back to you.
6. If you would like a copy of the tabulated survey results you may provide your name and address under item #38, additional information.
7. Please complete the survey and return it in the envelope provided no later than 10-15 days after receipt. Thank you.

Robert J. Rennie

Robert J. Rennie, Capt, USAF, MSC
Graduate Student, Logistics Management

CYTOTOXIC DRUG INFORMATION SURVEY

INSTRUCTIONS:

Please circle one answer per question in order that represents your knowledge level at this point in time without any outside help.

Please do not guess; if the subject area asked in the question is unfamiliar to you, please just circle the "?" to indicate you are unsure.

SURVEY QUESTIONS:

1. What do you think is the overall level of knowledge about cytotoxic drugs in the medical logistics management field.
 - a) Excellent
 - b) Good
 - c) Fair
 - d) Poor
 - e) ?

2. How would you rate your level of knowledge about cytotoxic drugs.
 - a) Better than most
 - b) Average
 - c) Lower than most
 - d) ?

3. You feel that a brochure, "a quick reference," that explains what cytotoxic drugs are would be helpful as an education tool for medical logistics personnel.
 - a) Agree
 - b) Disagree
 - c) ?

CYTOTOXIC DRUG INFORMATION SURVEY

4. The medical material warehouse (primary receiving and storage area) is located within the main medical treatment facility.
 - a) Yes
 - b) No

5. A cytotoxic drug is:
 - a) antihistamine
 - b) antineoplastic
 - c) analgesic
 - d) ?

6. Cytotoxic drugs are shipped as:
 - a) tabs or caps
 - b) powders
 - c) liquids
 - d) all of the above
 - e) ?

7. Currently, DLA supplies:
 - a) 0 - 5 different cytotoxic drugs
 - b) 6 - 10 different cytotoxic drugs
 - c) 11 - 20 different cytotoxic drugs
 - d) 21+ different cytotoxic drugs
 - e) ?

CYTOTOXIC DRUG INFORMATION SURVEY

- 8 The minimum accepted temperature for satisfactorily incinerating cytotoxically contaminated patient consumables (IV bags, needles, tubing) is:
- a) 2400°F
 - b) 1800°F
 - c) 1050°F
 - d) 500°F
 - e) 0°F (They do not require incineration)
 - f) ?

(T=True, F=False, ?=Unsure)

9. Your facility does treat patients with cytotoxic drugs. T F ?
10. In general, when cleaning up spills due to breakage in the warehouse, contamination of the personnel involved does not occur if the contents do not touch their skin. T F ?
11. The Medical Logistics Management office is represented at the Pharmacy and Therapeutics Committee Meeting. T F ?
12. Cytotoxic drugs are flammable. T F ?
13. Cytotoxic drugs do not require any specific temperature controlled environment. T F ?
14. Your state (or host nation) has a "Worker's Right-to-Know" law. T F ?
15. You have heard of and/or completed OSHA Form #20, Material Safety Data Sheet (MSDS) for each logistics person who might handle a cytotoxic drug during the routine discharge of their duties. T F ?

CYTOTOXIC DRUG INFORMATION SURVEY

16. Cytotoxic drug packages are clearly marked with a skull and crossbones on the outside. T F ?
17. Cytotoxic drugs are routinely shipped in multipacks. T F ?
18. Cytotoxically contaminated patient consumables (IV bags, needles, tubing) do not require special disposal handling techniques, e.g., double bagging. T F ?
19. No special cleanup procedures are required for cytotoxic drug spills or when open breakage of the drug container occurs. T F ?
20. Cytotoxic drugs are shipped in containers that have a label on the outside adjacent to the address label that says: "Cytotoxic Drug." T F ?
21. The Pharmacy and Therapeutics Committee has established guidelines for handling cytotoxic drugs for all the departments in the hospital/clinic including the medical warehouse(s) and storage area(s). T F ?
22. The Pharmacy and Therapeutics Committee has not established guidelines for handling cytotoxic drugs. T F ?
23. Medical Logistics Management has established specific (Operating Instruction or Hospital Regulation) Stock Records and Warehouse policies for handling and ordering cytotoxic drugs. T F ?
24. Stock Records orders all cytotoxics off-line to ensure that the shipped order does not arrive in a multipack. T F ?

CYTOTOXIC DRUG INFORMATION SURVEY

25. All cytotoxic drugs are segregated in the warehouse(s) or storage area(s) (all locations) from all other items. T F ?
26. A "chemical substances" spill kit has been purchased and/or assembled in each warehouse or storage location where cytotoxic drugs are stored. T F ?
27. If a spill occurs in the medical material warehouse or storage location, a "response team" comprised of Housekeeping, Bioenvironmental Engineering, Environmental Medicine, and Plant Management personnel are called to the scene. T F ?
28. A policy exists that requires all damaged medical supply shipments or containers (including local purchase) to be opened by medical logistics personnel that have donned protective garments, e.g., gloves, gown, goggles, breathing mask. T F ?
29. The State Department of Health (or host nation) has granted written permission to the hospital or base to incinerate patient consumables (IV bags, needles, tubing) that have been used in conjunction with a cytotoxic drug. T F ?
30. If patient consumables used in conjunction with a cytotoxic drug are not incinerated are they segregated and collected for disposal by a licensed "low-level hazardous waste" refuse company? T F ?
31. During the last three years at your facility you are aware of a medical material specialist being exposed to or contaminated by a cytotoxic drug that required medical attention(MD or PA). T F ?

Survey No. _____
MPC Auth No. 86-010

CYTOTOXIC DRUG INFORMATION SURVEY

32. You are aware of the field memorandum and its contents distributed to the MAJCOM's in Dec 84 by AFMSC/SGPC regarding the handling of cytotoxic drugs in AF MTF's. T F?
33. You read the AFMILL 23-85 (8NOV85) issue and Atch#3 "American Journal of Hospital Pharmacists" article on the safe handling of cytotoxic drugs. T F?

For questions 34-36 please circle the answer that describes your opinion.

34. You feel that all cytotoxic drug packaging and shipping containers should be identified as such using some sort of labeling scheme.

Strongly Agree Agree Don't Care Disagree Strongly Disagree

35. If you read the 23-85 AFMILL/Atch#3 (if not, skip the question and please do not read it now and reanswer the survey) approximately, about how much information did it provide in addition to what you already knew?

Significantly Moderately Some Little None at All

37. If you read the 23-85 AFMILL/Atch#3 (if not skip the question and please do not read it now and reanswer the survey) approximately, about how much of the survey were you able to answer with a definite "yes" or "no" versus "I" unsure?

100% 75% 50% 25% 0%

Survey No. _____
MPC Auth No. 86-010

CYTOTOXIC DRUG INFORMATION SURVEY

37. Suggestions and/or Comments:

38. Please provide the following information under provisions of the Privacy Act:

Name(Optional): _____

Yrs in Service(Total): _____

Yrs in Medical Logistics: _____

Current Position Title: _____

Length of Time in Current Position(Yrs/Months): _____

THANK YOU.

Appendix B: Cytotoxic Drug Monographs

Monographs

Cytotoxic Drugs

Description. Individual containers within U/I size shall have same lot number.

Signs of Deterioration. Physical deterioration is evidenced by:

- a. solution becomes cloudy
- b. water droplets are present in vial with powder

Inspection and Test Requirements. When the expiration date is reached, all supplies of the items shall be disposed of IAW Host nation, state and/or local environmental protection rules and policies. Normally written permission is required for incineration, sewage line disposal and surface (landfill) disposal.

Special Notes by Drug Name/Generic Name:

Asparaginase (synonym: L-Asparaginase, brand: Elspar)-

Acute Overexposure:

Skin: Rashes, urticaria have been reported.

Systematically toxic by inhalation or ingestion. Inhalation may cause dizziness, nausea, diarrhea, and slight respiratory distress.

Allergic reactions have occurred including anaphylactoid reactions.

Chronic Overexposure: May exacerbate pre-existing liver disease.

Potentially teratogenic.

Emergency First Aid:

Skin: Wash with soap and water.

Eyes: Wash with water for 15 minutes.

Inhalation: Remove from exposure and get medical attention.

Flammable Potential: None

Reactivity Potential: Unstable, stored below 8°C.

Fire Fighting: Self-contained breathing apparatus.

Manufacturer: Merck & Co., Inc., Rahway, New Jersey

Emergency Phone No.: (201)574-5555

Azathioprine (Sodium Salt)(Imuran):

Acute Overexposure:

Skin and Eyes: Solution is alkaline and very irritant to skin and or eyes.

Chronic Overexposure: Teratogenic and mutagenic. Suspected to be carcinogenic. Leukopenia and/or thrombocytopenia may occur with exposure at therapeutic levels. Nausea and/or vomiting.

Emergency First Aid:

Skin: Wash with soap and water immediately, if prolonged contact, see physician.

Eyes: Wash thoroughly with water, seek medical attention.

Flammable Potential: N/A, Heating may give rise to toxic fumes.

Reactivity Potential:

Alkaline admixtures will metabolize drug to mercaptopurine.

Fire Fighting: Self-contained breathing apparatus.

Manufacturer: Burroughs Wellcome Co., Research Triang. Park, N.C.

Emergency Phone No. : (919)248-3000

Bleomycin (Blenoxane):

Acute Overexposure:

Skin: Potential skin contact rash or allergic reaction.

Eyes: Potential conjunctivitis.

Chronic Overexposure:

Potential cytotoxic agent. Possibly teratogenic. Skin hyperpigmentation; alopecia.

Emergency First Aid:

Skin: Wash thoroughly with soap and water.

Eyes: Wash with copious amounts of water for 15 minutes and seek medical attention.

Flammable Potential: Unknown.

Reactivity Potential: Unknown.

Fire Fighting: Self-contained breathing apparatus.

Manufacturer: Bristol-Myers Co., Syracuse, N.Y. 13321

Emergency Telephone No. : (315) 432-2714, Evenings (315)-432-2000

Carmustine (synonyms: BCNU, Brand Name: BiCNU):

Acute Overexposure:

Skin: Potential skin contact rash and brown hyperpigmentation and burning sensation.

Eyes: Potential conjunctivitis.

Chronic Overexposure: May be carcinogenic, mutagenic, and teratogenic.

Emergency First Aid:

Skin: Wash thoroughly with soap and water.

Eyes: Wash with copious amounts of water for 15 minutes. Seek medical attention.

Flammable Potential: Unknown.

Reactivity Potential: Unknown.

Fire Fighting: Self-contained breathing apparatus.

Manufacturer: Bristol-Myers Co., Syracuse, N.Y. 13221

Emergency Telephone No. : (315)432-2714, Evenings (315)432-2000

Cisplatin (synonyms: DDP, cis-DDP, cis-Diamminedichloroplatinum, cis-PlatinumII, Brand: Platinol).

Acute Overexposure: Lightheadedness, dizziness, facial flushing.

Skin: Potential contact skin rash, allergic reactions to platinum may occur with accidental injection. Cellulitis may also occur.

Eyes: Potential contact eye conjunctivitis.

Chronic Overexposure: Mutagenic, carcinogenic and possibly teratogenic.

Emergency First Aid:

Skin: Wash thoroughly with soap and water.

Eyes: Wash with copious amounts of water for 15 minutes. Seek medical attention.

Flammable Potential: Unknown.

Reactivity Potential: Unknown.

Fire Fighting: Self-contained breathing apparatus.

Manufacturer: Bristol-Myers Co., Syracuse, N.Y. 13221

Emergency Telephone No. : (315)432-2714, Evenings (315)432-2000

Cyclophosphamide Monohydrate (Cytosan):

Cyclophosphamide U.S.P. (Neosar):

Acute Overexposure: (Liver metabolism required before becoming cytotoxic.)

Skin: Wash to prevent accidental hand to mouth ingestion.

Ingestion/Inhalation: Nausea, vomiting, hair loss, leukopenia.

Chronic Overexposure:

After accidental ingestion; leukopenia, hair loss, urinary bladder inflammation.

Emergency First Aid:

Irrigate affected area with copious amounts of water. Skin

should be washed with with soap and water.

Flammable: Non-flammable.

Reactivity Potential: Stable Compound.

Fire Fighting: Self-contained breathing appartus.

Manufacturer:

Cytoran: Mead Johnson & Co., Evansville, Indiana 44721

Neosar: Adria Labs (distributor), Columbus OH 43216

Emergency Telephone No. :

Cytoran: (812)428-5123, Evenings (812)426-6064

Neosar: (614)764-8100

Cytarabine (synonyms: Cytosine arabinoside, Ara C, Cytosar-U, Brand-Cytosar):

Acute Overexposure:

Skin: Not absorbed through intact skin, slight irritation on broken skin.

Eyes: Possibly some slight irritation.

Chronic Overexposure:

Teratogenic, potentially mutagenic or carcinogenic.

Skin: Slight irritation with repeated or continuous contact.

Eyes: Corneal speckling if applied to eyes for several days.

Emergency First Aid:

Skin: Wash with soap and water.

Eyes: Wash with copious amounts of water for 15 minutes.

Flammable Potential: None known.

Reactivity Potential: None known.

Fire Fighting: Self-contained breathing appartus.

Manufacturer: The Upjohn Co., Kalamazoo, Michigan 49001

Emergency Telephone No. : (616)323-6722

Dacarbazine (DTIC):

Acute Overexposure: Lightedness, dizziness, facial flushing.

Skin: Irritant to skin and mucous membranes. Phlebitis upon accidental injection.

Eyes: Irritant effects.

Chronic Overexposure: Carcinogenic and teratogenic, photosensitivity.

Emergency First Aid:

Skin: Wash with soap and water.

Eyes: Wash with copious amounts of water.

Flammable Potential: Stable at proper storage temperature.

Reactivity Potential: Stable.

Fire Fighting: Self-contained breathing apparatus.
Manufacturer: Miles Pharmaceuticals, West Haven, CT 06516
Emergency Telephone No. : (203)934-9221

Dactinomycin (synonym Actinomycin-D, Brand: Cosmegen):

Acute Overexposure:

Skin: Extremely corrosive to soft tissues. Cellulitis and necrosis at site of accidental injection.

Eyes: Extremely corrosive to soft tissue.

Inhalation: Anaphylactoid reactions, nausea, vomiting, hematopoietic depression, esophagitis, ulcerative stomatitis.

Chronic Overexposure:

Teratogenic, mutagenic, and potentially carcinogenic.

Emergency First Aid:

Skin: Wash thoroughly with soap and water.

Eyes: Flush with water for 15 minutes.

Inhalation: Remove from exposure and contact a physician.

Monitor for anaphylactoid reaction.

Toxic effects may not be apparent until 2-4 days after exposure and may not be maximal before 1-2 weeks have elapsed.

Flammable Potential: None.

Reactivity Potential: Unstable -air and light sensitive.

Fire Fighting: Self-contained breathing apparatus.

Manufacturer: Merck and Co., Inc., Rahway, N.J. 07065

Emergency Telephone No. : (201)574-5555

Daunorubicin Hydrochloride (synonym: Daunomycin hydrochloride,
Rubidomycin hydrochloride, Brand: Cerubidine):

Chronic Overexposure:

Local skin and mucous membrane irritant. Chemical cellulitis upon accidental injection. Hypersensitivity reactions.

Chronic Overexposure:

Pigmentation of skin and nails. Potentially mutagenic and carcinogenic. Potentially teratogenic. Potentially cardiotoxic.

Emergency First Aid:

Skin: Wash immediately with soap and water. Seek medical attention if skin is broken (e.g., cuts, scratches) or ulceration occurs.

Eyes: Irrigate immediately with copious amounts of water or normal saline. Seek medical attention.

Flammable Potential: Non-flammable.

Reactivity Potential: Stable.
Fire Fighting: Self-contained breathing apparatus.
Manufacturer: Ives Laboratory, N.Y., N.Y. 10017
Emergency Telephone No. : (212)878-5166, Evenings (212)878-6200

Doxorubicin Hydrochloride (Adriamycin):

Acute Overexposure:
Local skin and mucous membrane irritant, chemical cellulitis upon accidental injection, hypersensitivity reaction.

Chronic Overexposure:
Pigmentation of skin and nails; inhibition of cell production; cell destruction; teratogenicity and carcinogenicity is suspected but not established. Potential cardiotoxic.

Emergency First Aid:
Skin: Wash immediately with soap and water, seek medical attention if skin is broken (e.g. cuts or scratches) or ulceration occurs.
Eyes: Irrigate immediately with copious amounts of water or normal saline, seek medical attention.

Flammable Potential: Non-flammable.
Reactivity Potential: Stable compound.
Fire Fighting: Non-toxic.
Manufacturer: Adria Labs, Columbus, OH 43216
Emergency Telephone No. : (614) 764-8178

Etoposide (synonym VP-16, Brand Vepesid):

Acute Overexposure:
Skin: Potential contact skin rash.
Eyes: Potential contact eye conjunctivitis.

Chronic Overexposure: Unknown. Product is too new to know long term overexposure effects. Potential cytotoxic agent.

Emergency First Aid:
Skin: Wash thoroughly with soap and water.
Eyes: Wash with copious amounts of water for 15 minutes. Seek medical attention.

Flammable Potential: Unknown.
Reactivity Potential: Stable.
Fire Fighting: Self-contained breathing apparatus.
Manufacturer: Bristol-Myers Co., Syracuse, N.Y. 13221
Emergency Telephone No. : (315)432-2714, Evenings (315)432-2000

Floxuridine (F.U.D.R.):

Acute Overexposure: Slight skin inflammation if skin is broken.

Chronic Overexposure:

Possible mutagenic, however not well established. Therapeutic doses can lead to leukopenia and severe G.I. adverse effects. Hyperpigmentation.

Emergency First Aid:

Skin: Flush with water for 10 minutes.

Eyes: Irrigate with copious amounts of water for 15 minutes.

Flammable Potential: None known.

Reactivity Potential: Stable at normal storage conditions.

Fire Fighting: Self-contained breathing apparatus.

Manufacturer: Hoffman-LaRoche, Inc., Nutley, N.J. 07110

Emergency Telephone No.: (201)235-2193

5-Fluorouracil (synonyms: 5-FU, Brand: Fluorouracil (Roche), Adrucil (Adria):

Acute Overexposure:

Skin: Minor local inflammation if skin is broken.

Chronic Overexposure:

Hyperpigmentation of skin/nails. Photosensitivity. Possibly mutagenic and teratogenic.

Emergency First Aid:

Flush affected area(s) with copious amounts of water for 10 - 15 minutes.

Flammable Potential: None known.

Reactivity Potential: Strongly basic solutions (pH>9) causes hydrolysis (especially at increased temperatures).

Fire Fighting: Self-contained breathing apparatus.

Manufacturer: Hoffman-LaRoche Inc., Nutley, N.J. 07110

Emergency Telephone No.: (201)235-2193

Mechlorethamine Hydrochloride (synonym: Nitrogen Mustard, Mustine, HN2
Brand: Mustargen):

Acute Overexposure:

Skin: extremely vesicant resulting in cellulitis; hyperpigmentation; hypersensitivity reactions.

Eyes: Extremely irritating.

Inhalation: Nasal irritant, nausea, vomiting, vertigo, tinnitus.

Chronic Overexposure:

Hematopoietic depression, jaundice, potentially teratogenic, mutagenic, and carcinogenic.

Emergency First Aid:

Skin: Absorption can occur via the skin. Wash with water for 15 minutes, followed by 2.98% sodium thiosulfate or 3% sodium carbonate solution.

Eyes: Copious irrigation for 15 minutes with water, normal saline, or balanced salt ophthalmic solution. Seek immediate medical (ophthalmic) examination.

Inhalation: Absorption may occur via mucous membranes. Remove from exposure and contact physician immediately.

Flammable Potential: None.

Reactivity Potential: Rapid chemical transformation in neutral or alkaline solutions. Do NOT use if water droplets present in vial or if reconstituted solution is not colorless.

Fire Fighting: Self-contained breathing apparatus.

Manufacturer: Merck & Co., Inc., Rahway, N.J. 07065

Emergency Telephone No.: (201)574-5555

Methotrexate (synonyms: Amethopterin, MTX, Brand: Folex(adria), Mexate (Bristol), Methotrexate(Lederle))

Acute Overexposure: May be irritating to the skin, but is poorly absorbed. Manufacturer states that methotrexate is not irritating to the eyes.

Chronic Overexposure: Can produce marked bone marrow depression, reduction in white blood cells, thrombocytopenia, bleeding, and liver damage. Early symptoms of over exposure may include stomatitis and alter hemogram.

Emergency First Aid:

Skin: Wash thoroughly with soap and water to avoid accidental hand to mouth contact. Oral absorption is rapid.

Eyes: Flush with water thoroughly.

Note: Ca. Leuovorin is a potent antagonist to effects of methotrexate to be used in cases of overexposure where hematopoietic effects are severe. It should be given as soon after exposure as possible.

Flammable Potential: None.

Reactivity Potential: Stable compound.

Fire Fighting: Self contained breathing apparatus.

Manufacturer:

American Cyanamid Co. (Lederle Brand only)
Wayne, N.J. 07470

Emergency Phone Numbers:

American Cyanamid Co.: (201) 835-3100
Adria Labs: (614) 764-8178
Bristol Labs: (315) 432-2714 days
(315) 432-2000 evenings

Mitomycin (synonym: Mitomycin C, Brand: Mutamycin)

Acute Overexposure:

Skin: Extremely irritant. Accidental injection may result in cellulitis, tissue sloughing, and paresthesia. Mucocutaneous toxicity may include mouth ulcerations.

Eyes: Extremely irritant.

Chronic Overexposure: Teratogenic and mutagenic. Potential carcinogenic properties. Photosensitivity.

Emergency First Aid:

Skin: Wash thoroughly and immediately with soap and water. Seek medical attention.

Eyes: Wash immediately with copious amounts of water. Seek medical attention.

Flammable Potential: None.

Reactivity Potential: Stable

Fire Fighting: Self contained breathing apparatus.

Manufacturer:

Kyowa Hakko Kogyo Co., Ltd., 1-6-1 Ontemachi, Chiyoda
Tokyo, Japan

Distributed by: Bristol Labs

(315) 432-2714 or (315) 432-2000 (evenings)

Plicamycin (synonym: Mithramycin, Brand: Mithracin)

Acute Overexposure:

Skin: Irritation is minimal when skin is unbroken. Accidental injection may lead to cellulitis since the drug is a vesicant, stomatitis.

Eyes: May be irritating to the eye tissue.

Chronic Overexposure: Hepatotoxic, nephrotoxic, bleeding episodes, skin hyperpigmentation, stomatitis.

Emergency First Aid:

Skin: Wash with soap and water for 15 minutes.

Eyes: Flush with copious amounts of water for 15 minutes.

Flammable Potential: None

Reactivity Potential: Stable

Fire Fighting: Self contained breathing apparatus.

Manufacturer:

Miles Pharmaceuticals, 400 Morgan Lane, West Haven, CT 06516
Emergency Telephone No.: (203) 934-9221

Streptozocin (Zanosar)

Acute Overexposure: Potential for benign tumor development upon accidental injection (seen in experimental animals).

Chronic Overexposure: Mutagenic, potential carcinogenic, teratogenic.

Emergency First Aid: Wash exposed areas with soap and water.

Flammable Potential: A strong exotherm beginning at 108°C (226°F). Hence store under refrigeration, since first trace of decomposition would quickly raise the temperature of the material, resulting in "runaway" decomposition.

Reactivity Potential: See flammable potential.

Fire Fighting: Self contained breathing apparatus.

Manufacturer:

The Upjohn Co., 7171 Portage Road, Kalamazoo, MI 49001
Emergency Telephone No.: (616) 323-6722

Thiotepa

Acute Overexposure:

Skin: Not irritating, but is well absorbed through the skin.

Eyes: Contact with the powder can cause severe eye irritation.

Manufacturer states the solution is nonirritating to the eye.

Chronic Overexposure: Considered highly toxic. Overexposure can lead to bone marrow depression, nausea, vomiting, loss of appetite, dizziness, headache, and anemia. Fetal malformations and death may occur. Thiopeta is well absorbed by inhalation and/or skin contact.

Emergency First Aid:

Skin: Wash affected areas with cold water and soap to reduce extent of dermal absorption.

Eyes: Wash eyes thoroughly for 15 minutes with cold water and seek medical attention.

Inhalation Exposure: Remove the person to fresh air, keep them warm and observe for signs of respiratory difficulties.

Note: If intoxication exists, hemograms and WBC counts are recommended to assess the level of intoxication on the hemopoietic system.

Flammable Potential: None

Reactivity Potential: Contact with acidic substances and/or temperatures above 40°C may result in explosive decomposition.

Fire Fighting: Self contained breathing apparatus.

Manufacturer:

Lederle Laboratories, Pearl River, N.Y. 10965

Emergency Telephone No.: (914) 735-5000

Vinblastin Sulfate (velban) :

Acute Overexposure:

Skin: May be irritating to the skin, particularly if skin barrier is broken. Accidental injection may lead to cellulitis and phlebitis.

Eyes: A delayed burning and subsequent scarring due to interference with reproduction of epithelium. Corneal ulceration may result.

Chronic Overexposure: May be teratogenic or mutagenic. May cause nausea, vomiting, hair loss, leukopenia and neurologic side effects. Effects depend on the amount and length of overexposure.

Emergency First Aid:

Skin: Wash thoroughly with soap and water.

Eyes: Flush thoroughly with water. See a physician or ophthalmologist immediately and again one week thereafter.

Treatment to include steroid ophthalmic drop or ointment to minimize the associated inflammatory process.

Flammable Potential: None

Reactivity Potential: None at normal storage conditions.

Fire Fighting: No specific mention of need for self contained breathing apparatus.

Manufacturer:

Eli Lilly and Co., 307 East McCarthy Street

Indianapolis, Indiana 46285

Emergency Telephone No.: (317) 261-2000

Appendix C: Letter of Recommendations Sent to DPSC-A

AFIT/LS-GLM/86-S
WPAFB, OH 45433

February 18, 1986

Col Julius C. Archie, Director of Medical Material
Technical Assurance Branch/DPSC-A
Defense Personnel Support Center
2800 South 20th Street
Philadelphia, PA 19101

Dear Col Archie,

Enclosed, please find 22 monographs for possible inclusion in DLAM 1455.5, Appendix M, Medical Supplies. The information was compiled by the pharmacy staff of Midway Hospital, (St. Paul, MN, Mr Wallace B. Wadd, Director) and reformatted by myself. The information was contained in an article published in the American Journal of Hospital Pharmacists, Vol 42, Sept 85 issue). Mr. Wadd's written permission to use the information was obtained by myself.

The information was obtained from published sources obtained by Mr. Wadd directly from the manufacturing companies which included the OSHA MSDS form 20, reports, and the PDR.

As part of my thesis project titled, "Handling Cytotoxic Drugs in the Air Force Medical Treatment Facility Warehouse," at the Air Force Institute of Technology, School of Systems and Logistics, I have included these monographs as an attachment. The monographs are part of a series of policy recommendations that are proposed.

The recommendations include provisions to segregate cytotoxic drugs as a separate classification within the medical material management system. This could be accomplished by using a new advice code("2X"), mode of shipment code("J"), and document identifier code("A06-A09"). The inclusion of the mode of shipment code ("j") would enable the depot system to attach a

small sticker label (either a J or a 2X) to the "cytotoxic drug shipping container" adjacent to the address label. This supplemental labeling system would accomplish the following: (1) it would identify to shipping and receiving personnel those containers that had cytotoxic drugs inside; (2) it would enable the depot to segregate and ship to the accounts containers restricted to cytotoxic drugs only, (3) it would not exceed or interfere with the provisions of the Hazardous Materials Transportation Act, and (4) it would enable logistics personnel to readily identify what handling procedures should be implemented for handling damaged shipping containers. In the presence of the "cytotoxic drug identifier label," the most stringent pre-cautions would be implemented (gowning, gloving, respirator, etc).

The need to identify cytotoxic drugs throughout the distribution system was recently addressed by OSHA. The U.S. Department of Labor, Office of Occupational Medicine released publication 8-1.1, dated 29 Jan 86, titled: "Guidelines for Cytotoxic (Antineoplastic) Drugs." The purpose of this guideline is: "To provide a description of the hazard during the use of antineoplastic drugs in the health care delivery system and recommends controls and work practice technique to reduce the risks of that hazard." Section G.2. Storage and Transport reads: "Damaged cartons should be opened in an isolated area by an employee wearing the same protective equipment as is used in preparation (including a PARR) without a hood." Section G.3. Transport reads: "All drugs should be labeled with a warning label and clearly identified as cytotoxics. Transport methods that produce stress on contents, such as pneumatic tubes, should not be used to transport CD's."

Would you please review the above suggestions and (1) indicate whether or not the suggestions would result in the actions I propose, and (2) indicate whether or not the suggestions are adoptable, (3) if the suggestions are deficient, could you please suggest recommendations that would accomplish the objective of labeling cytotoxics in the manner desired, and (4) comment upon the adequacy of the monographs.

Thank you.

Sincerely,

ROBERT J. RENNIE, Capt, USAF, MSC

Appendix D: DPSC-A Response and Endorsement of Recommendations



DEFENSE LOGISTICS AGENCY
DEFENSE PERSONNEL SUPPORT CENTER
2500 SOUTH 20TH STREET
PO BOX 8418
PHILADELPHIA, PENNSYLVANIA 19101-8418

IN REPLY
REFER TO

DPSC-A

APR 14 1986

AFIT/IS-GLM/86-S
WPAFB, OH 45433
ATTN: Capt Robert J. Rennie, USAF, MSC

Dear Capt Rennie:

Your letter of 18 February 1986, suggesting monographs for possible inclusion in DLAM 4155.51/TB740-10, "Quality Assurance Depot Storage Standards", has been reviewed along with your recommendations to segregate cytotoxic drugs as a separate classification within the Medical Materiel Management System. Although the identification, storage, handling, transportation, and disposal of hazardous materials is fully recognized and covered by various DoD Instructions and regulations, we agree that cytotoxic drugs present a special hazard. However, unilateral implementation of your proposals cannot be done by this Directorate.

Currently the DLAM 4155.5/TB740-10 covers storage standards data (with a hazard code). DoDI 6050.5 prescribes a DoD system to acquire, review, store, and disseminate selected data on hazardous materials. DLAR 6050.1 is the implementing regulation in DLA and designates the Defense General Supply Center as the DLA Technical Focal Point for DLA managed items and to develop and operate the DoD Hazardous Materiel Data Bank. The US Army Environmental Hygiene Agency has developed approved methods of destruction and disposal for small quantities of medical materiel (including hazardous material). This information is published in the Army Medical Department Supply Information Bulletin SB 8-75-9. The Veterans' Administration has implemented special marking requirements of cytotoxic drugs which could impact on DoD because of the DoD/VA Shared Procurement Program.

As part of Shared Procurement, the Directorate of Medical Materiel has requested the Defense Logistic Services Center, Battle Creek, MI, to approve a new "Note D" in the medical catalog. The Note D is defined as "Antineoplastic (chemotherapy drug)". The Note D is currently in use by the VA. The DLAM 4155.5/TB 740-10 does include hazardous storage compatibility codes. No codes currently in use would adequately cover all cytotoxic drugs. A new code "T6 Antineoplastic (chemotherapy drug)" equivalent to Note D" would be appropriate.

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APR 14 1986

In view of the above, your recommendations will be forwarded to the Defense Medical Standardization Board, Fort Detrick, for coordination with and approval by the Military Medical Services. If concurrence is obtained, appropriate recommendations will be made to Headquarters, DIA for changes in the handling of cytotoxic drugs. In addition, at that time coordination with the VA will be instituted to assure uniformity in handling by medical personnel.

Your interest in this matter is appreciated.

Sincerely,



JULIUS C. ARCHIE
Colonel, USAF, MSC
Director, Medical Materiel

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Vita

Captain Robert J. Rennie was born 18 November 1953 in Queens, New York. He graduated from Commack High School North in Commack, New York, in 1971. He attended State University of New York at Stony Brook, graduating with a degree of Bachelor of Science in Biology in 1975 and with a degree of Master of Science in Health Services Administration in 1977. He received a direct commission in the USAF Medical Service Corps in 1982. He served as the Director of Patient Affairs, and then as the Director of Medical Logistics Management at the USAF Hospital, Ellsworth AFB, prior to entering the School of Systems and Logistics, Air Force Institute of Technology, in May 1985.

Permanent Address: 713 Blue Ridge Drive
Medford, NY 11763

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Cytotoxic drugs which are used throughout the health care system to treat cancer, have not been classified in a manner that requires special Department of Transportation labeling even though there is clinical evidence that the drugs are potentially dangerous to humans if the drug material (liquid, powder) accidentally touches the skin, is inhaled, or is ingested.

A field (AF hospital medical supply officer) "level of knowledge" determination was conducted in order to show that the lack of a labeling requirement contributes significantly to the medical supply health care worker's lack of knowledge about the potential hazard to humans associated with these drugs. The findings indicate that medical supply officer's whose facility handled cytotoxic drugs failed to demonstrate a basic knowledge about cytotoxic drugs, particularly in key areas such as environmental protection, spill response, and internal control of the drugs. Those officer's whose facility did not handle cytotoxic drugs demonstrated a level of knowledge equal to the control group. This is significant because during CY 1985 an education effort had been undertaken by the Air Force Office of Medical Support to inform all supply officers about cytotoxic drugs.

The Department of Labor, Office of Occupational Safety and Health, in January 1986, issued a comprehensive guideline for handling cytotoxic drugs which exceeds all existing regulations regarding the labeling, storing, issuing, and handling of cytotoxic drugs. The Veterans Administration has initiated its own labeling and handling procedures that ensure a higher degree of safety for logistics personnel. The Air Force is re-considering its own policies and practices in light of these actions and has submitted a labeling policy program to the Defense Medical Standardization Board for concurrence.