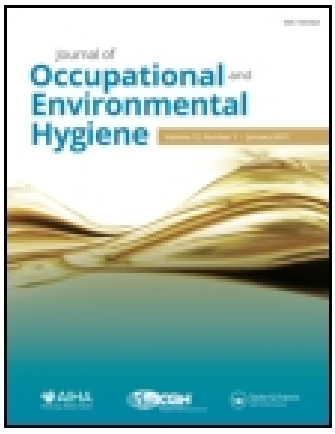

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Adherence to Precautionary Guidelines for Compounding Antineoplastic Drugs: A Survey of Nurses and Pharmacy Practitioners

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Precautionary guidelines detailing standards of practice and equipment to eliminate or minimize exposure to antineoplastic drugs during handling activities have been available for nearly three decades. To evaluate practices for compounding antineoplastic drugs, the NIOSH Health and Safety Practices Survey of Healthcare Workers was conducted among members of professional practice organizations representing primarily oncology nurses, pharmacists, and pharmacy technicians. This national survey is the first in over 20 years to examine self-reported use of engineering, administrative, and work practice controls and PPE by pharmacy practitioners for minimizing exposure to antineoplastic drugs. The survey was completed by 241 nurses and 183 pharmacy practitioners who compounded antineoplastic drugs in the seven days prior to the survey. They reported: not always wearing two pairs of chemotherapy gloves (85%, 47%, respectively) or even a single pair (8%, 10%); not always using closed system drug-transfer devices (75%, 53%); not always wearing recommended gown (38%, 20%); I.V. lines sometimes/always primed with antineoplastic drug (19%, 30%); and not always using either a biological safety cabinet or isolator (9%, 15%). They also reported lack of: hazard awareness training (9%, 13%); safe handling procedures (20%, 11%); and medical surveillance programs (61%, 45%). Both employers and healthcare workers share responsibility for adhering to precautionary guidelines and other best practices. Employers can ensure that: workers are trained regularly; facility safe-handling procedures reflecting national guidelines are in place and support for their implementation is understood; engineering controls and PPE are available and workers know how to use them; and medical surveillance, exposure monitoring, and other administrative controls are in place. Workers can seek out training, understand and follow facility procedures, be role models for junior staff, ask questions, and report any safety concerns.

Keywords chemotherapy, compounding antineoplastic drugs, hazardous drugs, nurses, pharmacists, pharmacy technicians, safe handling practices, web-based survey

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INTRODUCTION

Adverse health effects associated with exposure to antineoplastic drugs are well documented. Pharmacy personnel and nurses who handle these drugs have reported acute health effects including nausea, headache, skin and eye irritation, hair loss, and allergic reactions.[1,2] Occupational exposures have been linked to significantly increased rates of DNA damage, infertility, miscarriage, premature birth, and congenital problems among prenatally exposed children.[3–8] Oncology nurses exposed to antineoplastic drugs have increased risk of leukemia and other cancers.[3] An increased frequency of genotoxicity biomarkers were reported in oncology personnel handling these drugs.[9,10]

Guidelines developed by professional practice organizations and government agencies for the safe handling of hazardous antineoplastic drugs have been available for nearly three decades.[11–14] These precautionary guidelines are applicable to compounding both sterile and non-sterile preparations containing antineoplastic drugs. In 2007, the guidelines were also incorporated into a pharmacy practice standard[15] for healthcare settings where antineoplastic drugs are compounded as sterile preparations, the most common form of handling for pharmacy practitioners. The guidelines are generally consistent with respect to primary prevention measures and application of a hierarchical approach for control technologies to mitigate workplace hazards.[16] This approach specifies that unless the hazard can be eliminated or substituted by a substance less toxic (not feasible with antineoplastic drugs), exposure controls should be systematically implemented in the following decreasing order of efficacy: (1) engineering controls, (2) administrative controls, (3) work practice controls, and (4) personal protective equipment (PPE).

Since the mid-1980s, several surveys of nurses[17-21] and, to a lesser extent, pharmacists and pharmacy technicians[22,23] have been conducted to evaluate use of PPE and other exposure control measures during compounding activities. Each of these studies reported on use of gloves and gowns. Sporadically

reported are: specialized training; awareness of employer hazardous drug programs; use of ventilated safety cabinets or isolators, eye protection, and respirators; medical monitoring practices; reasons for PPE disuse; and comparison of selected practices by work setting. Recent studies[24,25] have reported on full ensemble PPE use among nurses in addition to other practices such as gown re-use, double-gloving, and availability of written procedures and spill kits. The latter study[25] also examined workplace factors including safety climate, staffing, and barriers to use of hazardous drug safe handling precautions.

The primary objective of this study is to describe work practices including use of exposure controls and barriers to using PPE by nurses, pharmacists and pharmacy technicians who compound (i.e., prepare/mix) and handle antineoplastic drugs. This national survey is the first in over 20 years to examine self-reported use of engineering, administrative, and work practice controls and PPE by pharmacy practitioners for minimizing exposure to antineoplastic drugs.

METHODS

Survey Methodology

The NIOSH Health and Safety Practices Survey of Healthcare Workers is an anonymous, multi-module, web-based survey conducted January 28–March 29, 2011. The study population included members of professional practice organizations representing healthcare occupations which routinely use or come in contact with selected chemical agents. Practices around compounding of antineoplastic drugs were addressed by one of seven hazard modules targeted to professional organizations representing oncology nurses, hematology/oncology nurses, infusion nurses, pharmacists, and pharmacy technicians. Practices around administration of antineoplastic drugs were addressed in a separate hazard module and reported elsewhere.[26] Methods used to identify professional practice organizations; develop and perform cognitive testing on questions and instructions; develop and test the functionality of the web survey instrument; and implement the online survey along with strengths and limitations are published elsewhere.[27]

Study Population and Survey Implementation

The survey population for the module on compounding antineoplastic drugs was targeted to members of six professional practice organizations representing oncology nurses, pharmacists, and pharmacy technicians. These organizations invited members via email which included a survey link. Because relatively low numbers of respondents completed this module three weeks post-survey launch, the survey was subsequently opened to others beyond those invited by the 21 partnering organizations (hereafter referred to as non-professional organization respondents). Although these respondents may have been members of the participating professional practice organizations, they were not specifically selected in our preliminary process. A survey announcement and link was posted on publicly accessible websites and selected listservs in an effort to increase the number of participants. The announcement included a unique password which allowed identification of non-professional organization respondents.

Survey Instrument

The web survey included a screening module, core module, and seven hazard modules. The hazard module addressing compounding of antineoplastic drugs contained 51 questions. The format of the questions included multiple choice, multipart, yes/no, and numeric. Most questions sought information for the seven days prior to the survey (hereafter referred to as the past week). Many questions addressed exposure controls included specific engineering controls, administrative controls, and PPE recommended in guidelines available at the time of the survey.[14,28–31] Topic areas and content of key practice questions are presented in Table I.

If the respondent indicated in the screening module that they had compounded antineoplastic drugs in the past week, they were eligible for this module. Respondents were asked to select from a list of 92 antineoplastic drugs and seven monoclonal antibodies (mAbs) those that they had compounded in the past week. Most of the antineoplastic drugs were identified from the publication *NIOSH List of Antineoplastic and Other Hazardous Drugs in Healthcare Settings, 2010*[32] with the remainder identified from literature/internet searches and subject matter experts. For this question and others where the choices were not exhaustive, respondents could mark "Other" and type in a response. These were reviewed and determined if they (a) fit into one of the existing categories, (b) were valid other responses, or (c) were unrelated to the question, i.e., general notes about the survey. Responses were recoded, or left as "other" in the case of (b), to reflect this determination.

The modular survey was programmed to sequentially present, based on screening questions, the most relevant hazard module, the core module, and a second hazard module, if indicated. Respondents were presented with no more than two hazard modules.

Data Analysis

Data were analyzed using SAS 9.3 (SAS Institute, Inc., Cary, NC). Simple frequencies and prevalences are presented. Stratification was used to further describe some aspects of the use of exposure controls. Results include responses to questions in the antineoplastic drug compounding hazard module and selected questions in the core module that describe demographic, employer, and occupation characteristics. Because nearly all respondents (98%) were nurses and pharmacy practitioners the analysis excluded other occupations. Also excluded are the respondents who only handled mAbs ($n = 7$) because mAbs do not meet the definition of a hazardous drug and lack authoritative guidelines. We compared responses to questions addressing training, familiarity with precautionary guidance, availability of employer procedures, and use of exposure controls including and excluding non-professional organization respondents to determine if their exclusion changed prevalence

TABLE I. Survey Instrument Topic Areas and Content of Selected Questions

Topic Area
Training
Frequency (more or less than 12 months ago)
Source (ASHP, ONS, NPTA courses, other)
Awareness of employer safe handling procedures and national safe handling guidelines
Antineoplastic drugs compounded (list of 92 specific drugs)
Compounding practices
Number of days compounding antineoplastic drugs in the past week
Number of doses in the past week
How number of doses compounded compared to usual
Locations antineoplastic drugs were compounded
Frequency of use of selected exposure controls
Physical form (liquid, tablet/capsule) of antineoplastic drug
Frequency of crushing tablets/opening capsules
I.V. tubing priming practices
Frequency of priming
Type of priming solution[A]
Whether or not tubing was primed inside a ventilated cabinet or isolator
Engineering controls
Frequency of use of dedicated work rooms/areas
Frequency of use of engineering controls (i.e., BSCs, isolators) during compounding
Use of engineering controls (i.e., closed system drug-transfer device, needleless system) for transferring antineoplastic drugs from primary packaging to dosing equipment
Spills
Number, quantity, and whether spill was inside or anywhere outside ventilated cabinet or isolator
Availability of spill response kits
Spill cleanup practices
Skin contact/puncture during compounding
Frequency of use of PPE
Chemotherapy gloves[B] (single and double gloves)
Non-absorbent gowns with closed front and tight cuffs
Eye/face protection (e.g., goggles/face shields)
Respirators[C]
Barriers to using PPE
Practices when using PPE
Change gloves or gowns when damaged or contaminated
Reuse same gloves worn while compounding chemo drugs
Wash hands after removing gloves after compounding chemo drugs
Touching work surfaces with gloves that had been used to compound chemo drugs
Took home clothing that came in contact with chemo drugs
Use of surgical masks
Participation in a medical surveillance program[D]
Exposure monitoring practices

Note: ASHP = American Society of Health-System Pharmacists; ONS = Oncology Nursing Association; National Pharmacy Technician Association

[A]Antineoplastic drug or non-drug containing fluid.

[B]Defined in the survey as a medical glove that has been approved by the Food and Drug Administration (FDA) for use when handling antineoplastic drugs.

[C]Includes N95 filtering facepiece respirator, surgical N95 respirator, half-facepiece air-purifying respirator with chemical cartridge(s), and powered air-purifying respirator with chemical cartridge(s).

[D]Defined in the survey to possibly include work history, physical exam, blood and/or urine tests, etc.

substantively. With the exception that a greater proportion of non-professional organization respondents used closed system drug-transfer devices (CSTDs) and protective gowns, no differences were observed and combined data are reported. We also compared responses of pharmacists and pharmacy technicians for these same questions; because no differences were observed, we combined data for these two occupations, hereafter collectively referred to as pharmacy practitioners. This survey was developed to provide descriptive information on practices around compounding antineoplastic drugs. No a priori hypotheses were proposed therefore statistical tests were not done. Unless otherwise noted, the time frame for questions was the past week.

Institutional Review Board

The NIOSH Institutional Review Board determined that the activities in this project were surveillance and did not meet the criteria of research according to 45 CFR 46.1101(b)(2) and CDC Guidelines for Defining Public Health Research and Public Health Nonresearch.[33]

RESULTS

Respondent Characteristics

Four hundred twenty-four respondents, including 241 nurses and 183 pharmacy practitioners, participated in the hazard module addressing compounding of antineoplastic drugs. Most nurses categorized themselves as oncology nurses or hematology/oncology nurses. Pharmacy practitioners primarily included pharmacists and pharmacy technicians. Approximately 2% of nurses and 27% of pharmacy practitioners were non-professional organization respondents.

Respondent demographic and employer characteristics are presented in Table II. Nurses were predominantly female, white, 41–55 years of age, had bachelor's degrees, worked in their profession and for their current employer more than 10 years, and spent more than 75% of their time in patient care. Only 2% were members of labor unions. Nurses' employers were best characterized as: ambulatory healthcare services, 10–99 employees, for profit, located in large cities, and equally distributed across four U.S. Census regions.

Two-thirds (68%) of pharmacy practitioners were female. Nine of every 10 (92%) were white, and three-quarters (76%) were 26–55 years of age. While over 40% had doctoral degrees or higher education (i.e., pharmacists), 30% had Associate's degrees or less. Most (>70%) worked in their profession and for the same employer for more than 10 years (40%), with a third (32%) having no direct patient care. Seven percent belonged to labor unions. Employers were best characterized as: hospitals, >1,000 employees, non-profit, and located in large cities, and fairly equally distributed across four U.S. Census regions. In general, gender, age distribution, education, time providing care to patients, labor union membership, employer industry category, employer size, and ownership type were markedly different between these nurses and pharmacy practitioners.

Compounding characteristics of nurses and pharmacy practitioners are presented in Table III. Nurses' compounding practices were best characterized as follows: 55% compounded for ≥11 years; approximately 25% each compounded either on one day or on 5 days of the past 7, with the remaining compounding on 2–4 days; 60% compounded ≤20 total doses; 87% reported that all of the doses they had compounded were solely liquids (as opposed to tablets/capsules) and 90% reported that they had compounded in ambulatory care settings. Compounding experience among pharmacy practitioners was equally distributed in 4 categories ranging from 1 to >20 years with few having <1 year of experience. Almost 40% compounded >40 doses and 36% compounded/handled both liquids and tablets/capsules. More than a third (37%) of pharmacy practitioners compounded antineoplastic drugs 5 days a week. Most (>70%) respondents in both groups reported that the number of doses compounded during the past week was about the same as usual. Pharmacy practitioners reported compounding in both inpatient and outpatient work settings, with over half (59%) in main and satellite inpatient (hospital) pharmacies, and others in oncologist's office/clinic/centers and outpatient pharmacies.

The top 20 antineoplastic drugs compounded by nurses and pharmacy practitioners during the past week are presented in Table IV. Nineteen of the top 20 drugs were the same for both groups. Dacarbazine and cytarabine were unique to nurses and pharmacy practitioners, respectively; the former was the 21st most compounded drug by pharmacy practitioners (29%), but the latter was compounded by only 5% of nurses. The top three antineoplastic drugs compounded by nurses were paclitaxel, carboplatin, and fluorouracil and for pharmacy practitioners they included cyclophosphamide, fluorouracil, and cisplatin. Pharmacy practitioners reported compounding a greater variety of antineoplastic drugs (max = 68, median = 13) than nurses (max = 40, median = 11). About one of every ten respondents (nurses and pharmacy practitioners combined) reported that they had compounded "other" antineoplastic drugs and "investigational compounds (not yet named)" during the past week.

Training, Availability of Employer Procedures, and Familiarity with Guidelines for Safe Handling of Antineoplastic Drugs

Training on the safe handling of antineoplastic drugs was not universal among respondents. Thirteen percent of pharmacy practitioners and 9% of nurses reported that they had never received such training (Table V). Of those who had received training, about half of each group reported that it had been more than 12 months ago. With respect to continuing education courses addressing safe handling of antineoplastic drugs, most pharmacy practitioners and nurses had received training via courses developed by the American Society of Health-System Pharmacists (ASHP) and the Oncology Nursing Society (ONS), respectively. On-the-job-training was the most common "other training" reported by both respondent groups.

TABLE II. Respondent Characteristics

Characteristic	Nurse (n[A]) %	Pharmacy Practitioners (n[A]) %
Gender	(n = 240)	(n = 182)
Male	3	32
Female	97	68
Race[B]	(n = 237)	(n = 178)
White	95	92
Black	3	3
Asian	3	4
Native Hawaiian, other Pacific Islander, American Indian or Alaskan Native	<1	2
Ethnicity	(n = 240)	(n = 182)
Hispanic	3	4
Age	(n = 240)	(n = 179)
18–25 years	0	0
26–40 years	13	30
41–55 years	54	46
56–70 years	33	23
>70 years	1	1
Education	(n = 239)	(n = 180)
Grade 12 or less	2	15
Vocational certificate	2	10
Associate's degree	34	5
Bachelor's degree	51	24
Master's degree	10	5
Doctoral degree/Professional Degree+	1	41
Time in Current Occupation[C]	(n = 241)	(n = 183)
< 1 year	0	1
1–5 years	14	13
6–10 years	16	16
11–20 years	33	29
20–30 years	32	24
>30 years	6	18
Percent of Time Spent in Direct Patient Care[C]	(n = 241)	(n = 182)
76–100%	73	9
51–75%	17	16
26–50%	7	14
1–25%	4	28
No direct patient care	0	32
Time with Current Employer	(n = 241)	(n = 183)
< 1 year	4	5
1–5 years	32	34
6–10 years	21	21
11–20 years	32	21
>20 years	11	19
Member of a Labor Union	(n = 241)	(n = 182)
Yes	2	7
Employer Industry Category[C,D]	(n = 240)	(n = 183)
Ambulatory healthcare services	84	26
Hospital	16	70
Nursing and residential care	<1	1
Social assistance/services	0	3

(*Continued on next page*)

TABLE II. Respondent Characteristics (*Continued*)

Characteristic	Nurse (n[A]) %	Pharmacy Practitioners (n[A]) %
Size of Employer (number of employees)	(n = 240)	(n = 183)
1 (i.e., only myself)	0	0
2–9	20	6
10–99	54	19
100–249	9	8
250–1,000	9	22
>1,000	8	45
Employer Ownership Type[C]	(n = 238)	(n = 182)
For profit	81	22
Non-profit	15	58
City, county, district, state government	4	13
Federal government (VHA, military, IHS)	1	7
Employer Regional Location[C,E]	(n = 235)	(n = 181)
Northeast	24	15
Midwest	24	32
South	32	28
West	19	25
Employer Location by Population Density	(n = 241)	(n = 183)
Large city (≥ 50,000 people)	51	62
Small city (< 50,000 people)	25	17
Suburbs (developed areas adjacent to cities)	16	13
Rural (areas outside cities generally characterized by farms, ranches, small towns, and unpopulated regions)	8	8

Note: VHA = Veterans Health Administration; IHS = Indian Health Service

[A]Number of respondents varied for individual items (i.e., number of eligible respondents less number who elected not to answer).

[B]Percents may add to more than 100% because respondents could select more than one answer.

[C]Percents may not add up to exactly 100% due to rounding.

[D]Industry categories based on North American Industry Classification System (NAICS)

[E]Northeast (CT, ME, MA, NJ, NH, NY, PA, RI, VT); Midwest (IL, IN, IA, KS, MI, NE, ND, OH, SD, WI); South (AL, DE, DC, FL, GA, KY, LA, MD, MS, NC, OK, SC, TN, TX, VA, WV); West (AK, AZ, CA, CO, HI, ID, MO, NE, NM, OR, UT, WA, WY).

One of every 5 (20%) nurses and one of every 10 (11%) pharmacy practitioners reported that their employer either did not have, or they themselves were not aware if their employer had, procedures addressing safe compounding. When asked to choose their level of familiarity with national safe handling guidelines, both occupational groups were most familiar with guidelines developed by professional practice organizations representing their occupations. A greater proportion of pharmacy practitioners were more familiar with NIOSH than OSHA guidelines with the reverse being reported by nurses.

Adherence to Safe Handling Guidelines

Use of Engineering and Facility Controls

Respondents were asked whether they always, sometimes, or never used engineering controls such as a biological safety cabinet (BSC), isolator or both, and a room or area dedicated to handling and compounding antineoplastic drugs (Table VI). Fifteen percent of pharmacy practitioners and 9% of nurses did not always use either a BSC or an isolator. Pharmacy practitioners (14%) and nurses (9%) reported that they did not always compound in a dedicated room or area.

When transferring liquid antineoplastic drugs from primary packaging (i.e., vials) to dosing equipment (i.e., infusion bags), respondents were asked to select engineering controls they had used during the past week from the following choices: CSTDs, needleless system, glove box, and none of these. Nearly half of the nurses and a third of pharmacy practitioners chose none of these. Three-quarters (75%) of nurses and more than half (53%) of pharmacy practitioners did not use CSTDs. For needleless systems, 75% of pharmacy practitioners and almost 60% of nurses did not use them. Few reported using a glove box in either group.

I.V. Tubing Priming Practices

When respondents were asked about I.V. tubing priming practices, 94% of nurses and 77% of pharmacy practitioners

TABLE III. Antineoplastic Drug Compounding Characteristics of Respondents

Characteristic	Nurse (n[A]) %	Pharmacy Practitioners (n[A]) %
No. of years (in career) compounding antineoplastic drugs	(n = 240)	(n = 183)
< 1 year	5	5
1–5 years	23	29
6–10 years	18	19
11–20 years	37	21
> 20 years	18	26
No. of days compounding antineoplastic drugs in past week[B]	(n = 233)	(n = 183)
1 day	26	20
2 days	17	17
3 days	14	10
4 days	17	9
5 days	24	37
6–7 days	2	6
Total doses compounded in the past week[B]	(n = 233)	(n = 183)
1–5 doses	23	20
6–10 doses	16	13
11–20 doses	21	11
21–40 doses	27	16
>40 doses	13	39
Total doses compared to usual	(n = 232)	(n = 183)
More doses than usual	8	11
Fewer doses than usual	20	13
About the same number of doses as usual	72	77
Antineoplastic drugs compounded as a liquid	(n = 232)	(n = 183)
100% of doses	87	64
90–99% of doses	10	20
1–89% of doses	1	14
None of the doses	2	2
Location(s) where antineoplastic drugs were compounded[C]	(n = 228)	(n = 183)
Oncologist's office/clinic/center	90	27
Main inpatient pharmacy	4	39
Outpatient pharmacy	3	20
Satellite inpatient pharmacy	1	16
Other location	4	10

[A]Number of respondents varied for individual items (i.e., number of eligible respondents less number who elected not to answer).
[B]Percents may not add up to exactly 100% due to rounding.
[C]Percents may add to more than 100% because respondents could select more than one answer.

reported that they had primed I.V. tubing during the past week (Table VI). Of those who primed, 66% of nurses and 24% of pharmacy practitioners reported that they did not always prime I.V. tubing inside a ventilated cabinet or isolator. Also, of those who primed, nearly one-fifth of nurses (19%) and 30% of pharmacy practitioners reported that they did not always prime with a non-drug containing fluid such as saline. Although we did not specifically ask respondents whether they primed with antineoplastic drugs outside of a ventilated cabinet or isolator, we calculated the percent who did not always prime with non-drug containing fluid while also reporting not always using a ventilated cabinet or isolator. Eleven percent of nurses and 9% of pharmacy practitioners reported both of these practices from which we conclude that they are at least sometimes priming I.V. tubing with antineoplastic drugs outside a containment device.

Crushing Tablets and Opening Capsules of Antineoplastic Drugs

Nearly four of every 10 pharmacy practitioners (39%, n = 66) and two of every 10 nurses (20%, n = 30) who handled solid (i.e., tablets/capsules) antineoplastic drugs reported

TABLE IV. Top 20 Antineoplastic Drugs Compounded by Nurses and Pharmacy Practitioners

Nurse (n = 241)		Pharmacy Practitioners (n = 183)	
Antineoplastic Drug	**%**	**Antineoplastic Drug**	**%**
Paclitaxel	68	Cyclophosphamide	64
Carboplatin	64	Fluorouracil	64
Fluorouracil	64	Cisplatin	63
Cyclophosphamide	61	Carboplatin	61
Gemcitabine	61	Paclitaxel	59
Docetaxel	59	Doxorubicin	58
Cisplatin	59	Vincristine	56
Oxaliplatin	57	Etoposide	55
Doxorubicin	52	Gemcitabine	54
Vincristine	51	Oxaliplatin	51
Etoposide	50	Docetaxel	51
Irinotecan	47	Methotrexate	48
Bortezomib	37	Bortezomib	44
Pemetrexed	37	Irinotecan	43
Vinorelbine	32	Cytarabine	39
Vinblastine	29	Vinblastine	36
Topotecan	28	Vinorelbine	35
Bleomycin	27	Bleomycin	34
Methotrexate	23	Pemetrexed	34
Dacarbazine	22	Topotecan	33

that they always or sometimes crushed tablets and/or opened capsules during the past week.

Personal Protective Equipment

Frequency of Use and Reasons for Disuse

Use of chemotherapy gloves and non-absorbent gowns with closed front and tight cuffs was not universal. Most (85%) nurses and 47% of pharmacy practitioners reported they did not always wear two pairs of chemotherapy gloves while compounding and 10% of pharmacy practitioners and 8% of nurses reported that they did not wear even a single pair (Table VII). Most nurses (n = 34, 87%) and pharmacy practitioners (n = 38, 95%) who used an isolator reported that they always wore chemotherapy gloves, presumably the interchangeable chemotherapy gloves attached to the isolator. Non-absorbent gowns with closed front and tight cuffs were not always worn by 38% of nurses and 20% of pharmacy practitioners. Other types of PPE including respirators and eye and face protection were much less commonly used by each group.

Respondents who reported that they did not always wear PPE during compounding were asked to select from a list of 10 reasons (including "other, please specify") all applicable reasons for not always wearing the aforementioned PPE (Table VIII). Although the numbers of nurse and pharmacy practitioners not always wearing chemotherapy gloves was small (i.e., most respondents wore at least one pair), the primary reason for not wearing chemotherapy gloves for nurses was "skin exposure was minimal." For pharmacy practitioners there were several reasons with equivalent frequencies including "skin exposure was minimal," "not provided by employer," and "too uncomfortable or difficult to use."

Pharmacy practitioners reported that the use of engineering controls was the primary reason for not wearing non-absorbent gowns, eye/face protection and respirators. The primary reason reported by nurses for not wearing nonabsorbent gowns and respirators was "not part of our protocol" and for eye/face protection it was "engineering control was being used." The most commonly reported "other" reason for not wearing chemotherapy gloves by both groups was "use other type of glove" and for protective gowns it was "use non-disposable gown or lab coat."

Lack of Adherence to Recommended Safe Practices Associated with Glove and Gown Use

Respondents were queried about specific practices relative to the use of chemotherapy gloves and protective gowns which could result in exposure and/or contamination of the work area (Table IX). Nine percent of pharmacy practitioners and 4% of nurses reported that they had removed and later reused the same gloves that had been worn while compounding antineoplastic drugs. Twenty-two percent of pharmacy practitioners and 16% of nurses reported that they did not always wash their hands after removing gloves. Three percent of both groups did not always change gloves when they became damaged or contaminated. Respondents were also asked whether they engaged in specific activities which could potentially result in cross-contamination of work surfaces while wearing gloves that had been used to handle antineoplastic drugs. Activities most frequently reported by nurses and pharmacy practitioners included: "use pens/pencils outside of lab hoods" (34%, 43%, respectively) and "touch door knobs, cabinets or drawers" (32%, 37%). Regarding gowns, 7% of nurses and 5% of pharmacy practitioners who suspected that their gowns had become damaged or contaminated did not always replace them. In addition, 61% of pharmacy practitioners and 48% of nurses reported they did not always replace gowns after using them for more than 3 hr.

Took Home Clothing

When respondents were asked if they took home any clothing that came into contact with antineoplastic drugs, 24% of nurses (n = 216) and 9% of pharmacy practitioners (n = 183) responded "yes," not including 10% and 16%, respectively, who did not know.

Skin Contact and Sharps Injury

More than 11% of nurses (n = 221) and nearly 4% of pharmacy practitioners (n = 183) reported that their skin came in direct contact with antineoplastic drugs during compounding activities. Nearly 6% of nurses (n = 221) and over 8%

TABLE V. Training and Awareness of Employer Procedures and National Guidelines for Safe Handling of Antineoplastic Drugs

	Nurse				Pharmacy Practitioners			
	n[A]	% Yes			n[A]	% Yes		
Never received training in safe handling of antineoplastic drugs	239	9			183	13		
Training >12 months ago	218	48			160	51		
Specific training courses ever taken[B,C]								
ONS Chemotherapy and Biotherapy Course	224	80			163	3		
ONS Safe Handling Hazardous Drugs Course	224	59			163	5		
ASHP Oncology Pharmacy Development Course	224	4			163	45		
ChemoTEQ Safe Handling of Hazardous Drugs Training	239	4			183	13		
NPTA Best Practices for Safe Handling Hazardous Medications in the Pharmacy	224	<1			163	13		
Other	239	23			183	44		
Employer has procedures for safe compounding	240	80			183	89		
Familiarity with national safe handling guidelines	n[A]	% familiar with guideline			n[A]	% familiar with guideline		
		Very	Somewhat	Not at all		Very	Somewhat	Not at all
ONS safe handling of hazardous drugs	240	76	21	3	182	17	42	41
OSHA guidelines for the management of antineoplastic drugs	240	52	40	8	183	39	46	15
ASHP guidelines for handling hazardous drugs	239	18	33	49	183	63	30	7
NIOSH Alert on preventing occupational exposures to antineoplastic and other hazardous drugs in healthcare settings	238	30	36	34	183	48	34	18

Note: ONS = Oncology Nursing Society; ASHP = Association of Health-System Pharmacists; NPTA = National Pharmacy Technician Association
[A]Number of respondents varied for individual items (i.e., number of eligible respondents less number who elected not to answer).
[B]Percents add to more than 100% because respondents could select more than one answer.

(n = 183) of pharmacy practitioners reported that they accidentally punctured their skin by a sharp in the past 12 months while compounding antineoplastic drugs.

Spills of Liquid Antineoplastic Drugs and Availability of Spill Response Kits

Respondents were asked whether or not spills or leaks occurred during the past week while handling liquid antineoplastic drugs and, if so, whether the spills were inside a containment device (e.g., ventilated cabinet or isolator) or anywhere outside containment in the work area. Respondents who reported spills during the past week were also asked whether or not they experienced spills/leaks of "less than 5 mL" or "5 mL or more." For each category of spill, respondents were asked to select the number of spills from one of the following choices: "no spills," "1–2 spills," "3–5 spills," or "more than 5 spills" (Table X).

Overall, spills of "5 mL or more" were less common and because of the relatively low number of respondents further discussion focuses on spills of "less than 5 mL." A greater proportion of nurses compared to pharmacy practitioners reported spills both inside and outside containment devices. When spills occurred inside containment, 8% of nurses and 6% of pharmacy practitioners reported that they were not always cleaned up. More importantly, when spills occurred anywhere outside of a ventilated cabinet or isolator 11% of nurses reported that they were not always cleaned-up. Of the relatively few pharmacy practitioners who reported spills outside containment, all of them reported that the spills were always cleaned up. Four percent of nurses and 6% of pharmacy

TABLE VI. Use of Facility, Engineering, and Administrative Controls When Compounding and Priming Antineoplastic Drugs

Facility, Engineering and Administrative Controls	Nurse % of Frequency of Activity[B]				Pharmacy Practitioners % of Frequency of Activity[B]			
How often did you compound antineoplastic drugs in a. . .	n[A]	Always	Sometimes	Never	n[A]	Always	Sometimes	Never
Biological safety cabinet	228	89	2	9	179	77	1	22
Isolator	221	17	2	81	175	25	1	74
Biological safety cabinet and isolator	221	91	2	7%	172	85	1	14
Dedicated room or area	229	91	<1	9	183	86	1	13
	n[A]	% Who Checked This Item[B]			n[A]	% Who Checked This Item[B]		
Devices used when transferring liquid antineoplastic drugs from primary packaging (e.g., vials) to dosing equipment (e.g., infusion bags) (select all that apply)								
Closed system drug-transfer device	224		25		179		47	
Needleless system	224		41		179		25	
Glove box	224		10		179		12	
None of the above	224		45[C]		179		32[C]	
Priming practices								
	n[A]	Percent Yes			n[A]	Percent Yes		
Primed I.V. tubing in past week	225		94		179		77	
		Percent of Frequency of Activity				Percent of Frequency of Activity		
	n[A]	Always	Sometimes	Never	n[A]	Always	Sometimes	Never
Primed I.V. tubing inside ventilated cabinet or isolator	211	34	26	40	138	76	12	12
Primed I.V. tubing with liquid other than antineoplastic drug (e.g., saline)	211	81	11	8	138	70	21	9

[A]Number of respondents may vary for individual items (i.e., number of eligible respondents less number who elected not to answer and excluded respondents where the activity was not applicable to them).
[B]Percents add to more than 100% because respondents could select more than one answer.
[C]Percent of respondents who selected this response.

TABLE VII. Use of PPE When Compounding Antineoplastic Drugs

Type of PPE	Nurse %				Pharmacy Practitioners %			
	n[A]	Always	Sometimes	Never	n[A]	Always	Sometimes	Never
Chemotherapy gloves[B]	213	92	5	3	175	90	4	6
Double chemotherapy gloves[B]	205	15	23	62	165	53	21	26
Non-absorbent gown with closed front and tight cuffs	219	62	9	29	183	80	7	13
Eye or face protection[C]	210	11	3	85	179	18	6	77
Respirator (N95 filtering facepiece respirator,[D] half-facepiece air purifying respirator, or powered air-purifying respirator)	214	7	2	91	183	5	5	90

[A]Number of respondents varied for individual items (i.e., number of eligible respondents less number who elected not to answer and excluded respondents where the activity was not applicable to them).
[B]Defined in the survey as a medical glove that has been approved by the Food and Drug Administration (FDA) for use when handling antineoplastic drugs.
[C]This response option was only offered to respondents whose treatments included liquid antineoplastic drugs.
[D]Surgical N95 respirators were included in this category.

TABLE VIII. Reasons for Not Always Wearing PPE When Compounding Antineoplastic Drugs

Reason[E]	Chemotherapy Gloves[A]		Non-absorbant Gown[B]		Eye/Face Protection[C]		Respirator[D]	
	Nurse (n = 17) %	Pharmacy Practitioners (n = 17) %	Nurse (n = 81) %	Pharmacy Practitioners (n = 36) %	Nurse (n = 184) %	Pharmacy Practitioners (n = 147) %	Nurse (n = 194) %	Pharmacy Practitioners (n = 172) %
An engineering control was being used	—[F]	—	27	47	42	78	42	71
(Skin[G]) exposure was minimal	35	29	31	17	26	11	22	12
Not part of our protocol	29	12	36	39	39	28	45	42
Not provided by employer	12	29	21	8	17	15	18	23
No one else who does this work uses them	12	6	17	11	10	12	6	10
Too uncomfortable or difficult to use	18	29	25	8	7	7	5	3
Not readily available in work area	24	12	12	22	7	10	7	9
Cross contamination to other areas is not a concern	12	0	4	3	—	—	—	—
Concerned about raising the patient's anxiety	6	0	10	0	4	1	4	1
Other	24	29	9	11	5	2	2	2

[A]Defined in the survey as a medical glove that has been approved by the Food and Drug Administration (FDA) for use when handling antineoplastic drugs.
[B]With closed front and tight cuffs.
[C]Examples included goggles and face shields
[D]Choices included N95 respirator, surgical N95 respirator, half-facepiece air-purifying respirator with chemical cartridge(s), and powered air-purifying respirator with chemical cartridge(s).
[E]Column percents add to more than 100% because respondents were instructed to mark all that apply.
[F]Dash (—) indicates this reason was not included in question response options.
[G]Response for eye/face protection and respirator was "Exposure was minimal."

practitioners reported that hazardous drug spill kits were not available or they did not know if they were (Table X).

Medical Surveillance and Exposure Monitoring

A medical surveillance program, as defined in the survey, may include work history, physical exam, and blood and/or urine tests. Most nurses (80%, n = 221) and 70% of pharmacy practitioners (n = 183) reported that their employer does not provide a medical surveillance program or that they did not know whether their employer offered such a program or not. Twenty-seven percent of pharmacy practitioners and 15% of nurses reported participating in a medical surveillance program. A small proportion of nurses (5%) and pharmacy practitioners (3%) reported that their employer offered such a program but they elected not to participate.

Respondents were asked whether or not exposure monitoring (e.g., air and or wipe sampling) had been conducted in the past 12 months to assess personal or co-worker exposure to antineoplastic drugs. Sixty-six percent of nurses (n = 220) reported that exposure monitoring had not been conducted, not including 19% who reported that they did not know whether it had been done. Of pharmacy practitioners, 52% (n = 183) reported that exposure monitoring had not been conducted; another 17% reported they did not know.

DISCUSSION

The purpose of this study was to describe self-reported use of safe handling precautions during compounding of antineoplastic drugs, and to better understand barriers to PPE use which were marginally assessed in previous studies. Many past studies[17-25] assessed safe handling practices among oncology nurses and only a few,[22,23] in the early 1990s, examined these practices among pharmacists and pharmacy technicians. Studies[17–20,22–24] assessing precautionary practices during compounding primarily focused on use of PPE and, to a lesser extent, engineering controls (i.e., BSCs or isolators). Some of these studies[18,20,22–24] compared safe compounding practices by occupation (nurses vs pharmacy practitioners), type of work setting (outpatient vs inpatient), and also reported on trends in adherence practices over time. This study adds to our understanding of safe handling practices by nurses in outpatient settings since 93% of the nurses worked in oncologist's offices/clinics/centers and outpatient pharmacies.

TABLE IX. Non-recommended Practices Associated With the Use of Protective Gloves and Gowns

	Nurse		Pharmacy Practitioners	
	n[A]	%	n[A]	%
Gloves				
Did not always change gloves when damaged/contaminated	220	3	178	3
Reused gloves previously worn while compounding chemo drugs	214	4	183	9
Did not always wash hands after removing gloves	223	16	183	22
Activity performed while wearing gloves used to compound antineoplastic drugs[B]	215		183	
Use pens/pencils outside of lab hoods		34		43
Touch door knobs, cabinets or drawers		32		37
Touch waste basket/garbage bags		30		31
Use of computer/calculator		22		29
Handle files or charts		16		21
Use of phone/cell phone or pager		3		11
Eat, drink, chew gum or smoke		3		3
Use restroom		1		2
Apply cosmetics		1		1
Gowns				
Did not always change gowns when damaged/contaminated	171[C]	7	164[C]	5
Did not always change gowns after using more than 3 hr	169[C]	48	157[C]	61

[A]Number of respondents varied for individual items (i.e., number of eligible respondents less number who elected not to answer and excluded respondents where the activity was not applicable to them).
[B]Percents add to more than 100% because respondents responded "yes" or "no" to each activity.
[C]Excludes respondents who reported that question was not applicable (e.g., gowns were not damaged/contaminated).

This study reveals a lack of universal adherence to recommended national safe handling guidelines. Deficiencies were observed across all exposure control categories. With respect to facility and engineering controls, both pharmacy practitioners and nurses reported that they did not always use a dedicated room/area or either a BSC or isolator while compounding antineoplastic drugs. Also, neither CSTDs nor needleless systems including luer-lock fittings were routinely used. CSTDs were more commonly used by pharmacy practitioners while nurses used needleless systems more. In a 2011 survey, 38% of hospital pharmacy directors reported that CSTDs were used to prepare hazardous drugs.[34] Although we did not collect information on barriers to using these devices/systems including availability, CSTDs may not have been used because they are relatively costly and require user training. Studies show that they are effective in containing liquid antineoplastic drugs and reducing surface contamination when compared to standard drug preparation techniques.[35–37] Furthermore, availability maybe more of an issue in non-hospital settings where most (93%) of the nurses worked. It is also unclear why needleless systems were not used to a greater extent when transferring antineoplastic drugs from primary packaging to dosing equipment. In addition to reducing the risk of exposure to antineoplastic drugs, needleless systems have also been shown to reduce the risk of skin punctures and cuts. Our study found skin contact with antineoplastic drugs and skin punctures from sharps continue to occur; they could be prevented using these technologies.

Training and education is a fundamental administrative control which is recommended upon initial job assignment, annually thereafter for those who handle hazardous drugs[29] or whenever a new chemical or process is introduced.[29,38] Not all nurses and pharmacy practitioners had received training addressing safe handling of antineoplastic drugs and, of those who had received training, half of both groups reported that it was more than a year ago. Relative to specific training courses taken, most nurses reported receiving training via courses developed by ONS. By comparison, most pharmacy practitioners reported receiving training from either ASHP or on-the-job training. Priming I.V. tubing with a non-drug containing fluid is another example of a recommended administrative control which can minimize exposure to antineoplastic drugs. In this

TABLE X. Spills of Liquid Antineoplastic Drugs During Compounding: Percent of Respondents Reporting Number of Spills by Location and Quantity, How Often Cleaned-up, and Availability of Spill Response Kits

	Inside Cabinet or Isolator		Outside Cabinet or Isolator	
	Nurses %[A]	Pharmacy Practitioners %[A]	Nurses %[A]	Pharmacy Practitioners %[A]
Spill[B] quantity and frequency				
Spills or leaks less than 5 ml	(n = 216[C])	(n = 179[C])	(n = 217[C])	(n = 179[C])
No spills <5 mL	50	63	80	96
1–2 spills	32	29	17	3
3–5 spills	14	6	3	1
>5 spills	4	3	<1	1
Spills or leaks 5 mL or more	(n = 212[C])	(n = 178[C])	(n = 213[C])	(n = 179[C])
No spills ≥5 mL	97	99	99	96
1–2 spills	3	1	1	3
3–5 spills	<1	0	<1	1
>5 spills	0	0	0	1
Spills of any quantity	(n = 109[C])	(n = 67[C])	(n = 45[C])	(n = 11[C])
Spills not always cleaned up	8	6	11	0
Spill control	**Nurses** %	**Pharmacy Practitioners** %		
Spill response kits not available/ do not know	(n = 221[C]) (4)	(n = 183[C]) (6)		

[A]Percents may not add up to exactly 100% due to rounding.
[B]Reported in the past week
[C]Number of respondents varied for individual items (i.e., number of eligible respondents less number who elected not to answer).

study, nearly one of every 5 nurses and three of every 10 pharmacy practitioners reported that they had primed I.V. tubing with antineoplastic drugs. This practice may cause the drug to drip from the end of the tubing, potentially contaminating the work area and increasing exposure risk. Barriers to implementing engineering and administrative controls should be examined further.

The safe handling guidelines are very prescriptive regarding the types of PPE to use when compounding antineoplastic drugs. These guidelines stipulate use of double chemotherapy gloves, non-absorbent gowns with closed front and tight cuffs, and eye/face protection and respiratory protection when splashes, aerosols, or vaporization of antineoplastic drugs are likely. We found that wearing two pairs of chemotherapy gloves was not a common practice; some respondents reported not wearing even a single pair of chemotherapy gloves. Our findings are consistent with recent studies of nurses reporting 92–100% use of single gloves and up to 25% use of double-gloves when compounding.[24,25] Our findings are also consistent with previous studies of pharmacy practitioners reporting 90–100% use of single gloves;[22,23] however, other studies lacked information on double-gloving. A greater proportion of pharmacy practitioners than nurses re-used their gloves, touched various high contact work surfaces with gloves after handling antineoplastic drugs, and did not always wash their hands after removing their gloves. The same proportion of both groups reported not always changing gloves that were damaged or contaminated. The practice of touching various office-related items (e.g., phones, files) with gloves that had been used to handle or compound antineoplastic drugs was widespread and may contaminate work surfaces and the hands of unprotected co-workers who are not involved in antineoplastic drug compounding.[39,40]

Non-absorbent gowns with closed front and tight cuffs were not always used by nearly 40% of nurses (i.e., 60% always used them) and 20% of pharmacists (i.e., 80% always used them). These findings are consistent with recent studies[24,25] of nurses who reported gown use as high as 62%, and previous studies of pharmacists who reported gown use as high as 79%.[22,23] A greater proportion of nurses than pharmacy practitioners took home clothing that had come into contact with antineoplastic drugs and did not always replace gowns after they had become damaged or contaminated. Of the other PPE included in this survey, respirators and eye/face protection were least used by both groups.

Barriers to using chemotherapy gloves most reported by nurses and pharmacy practitioners ("not part of our protocol," "exposure was minimal") suggests that employers either do not provide appropriate protections or have necessary protocols, or that respondents misjudge the risk of any exposure to antineoplastic drugs, respectively. The same holds true for nurses with respect to protective gowns. However, for

pharmacy practitioners, use of engineering controls (i.e., ventilated safety cabinet or isolator) was the most commonly reported reason for not wearing protective gowns, and may suggest that respondents believe gowns are unnecessary when using this equipment. The importance of using chemotherapy gloves and non-absorbent gowns is underscored by the reports of skin contact and punctures which may expose workers to antineoplastic drugs.

NIOSH and OSHA recommend medical surveillance of workers potentially exposed to antineoplastic drugs and NIOSH recommends environmental sampling and biological monitoring when exposure is suspected or symptoms have been observed.[14,29,41] Of particular concern was the relatively large proportion of respondents who reported that their employer did not provide a medical surveillance program (nurses 61%; pharmacy practitioners 45%). Participation in such a program was very low (nurses 15%; pharmacy practitioners 27%) and markedly lower than reported in previous studies of nurses (46%, 47%).[20,24] Studies of pharmacy practitioners lacked this information. Exposure monitoring, not reported in previous studies, was uncommon for each group. The lack of these programs suggests that employers are not aware of, or do not fully appreciate the hazards associated with handling antineoplastic drugs.

Small spills (<5 mL) of liquid antineoplastic drugs were not uncommon. Of particular concern are the spills that occurred in the work area (outside of containment devices) where a small percentage of nurses reported that the spills were not always cleaned up. Respondents were not queried on the reasons for not cleaning up spills. ASHP recommends that hazardous drug spill kits be available in all areas where antineoplastic drugs are handled. A small percentage of nurses and pharmacy practitioners reported that spill kits were either unavailable or they did not know if they were, a finding consistent with another survey.[24]

Additional studies are needed to evaluate barriers to using engineering and administrative controls and the contribution of work organization factors on the use of precautionary measures. For example, a recent study suggested that factors including improved positive safety climate, reduced patient work load, and fewer barriers to using PPE may play an important role relative to the use of precautionary measures.[25] In another study, the likelihood of antineoplastic drug exposure decreased when nurses reported adequate staffing, resources and favorable working conditions.[42]

CONCLUSION

Pharmacists and pharmacy technicians who compound antineoplastic drugs have been understudied when compared to nurses; this national survey is the first in over 20 years to examine self-reported use of engineering, administrative and work practice controls and PPE by pharmacy practitioners. Findings from this survey show that recommended safe handling guidelines have not been universally adopted, placing nurses and pharmacy practitioners, co-workers, and even family members of these healthcare workers at risk of exposure. Shared responsibility is essential to ensure safe-handling guidance is followed. Employers can ensure that: workers are trained regularly; facility safe-handling procedures reflecting national guidelines are in place and support for their implementation is understood; engineering controls and PPE are available and workers know how to use them; and medical surveillance, exposure monitoring, and other administrative controls are in place. Workers can seek out training, understand and follow facility procedures, be role models for junior staff, ask questions, and report any safety concerns.

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