Survey of Sterile Product Compounding Practices in Canadian Hospital Pharmacies

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ABSTRACT

Improper preparation of sterile products by hospital or community pharmacies may have serious consequences. Recent reports of deaths or injury to patients as a result of receiving products that were contaminated during their preparation in a pharmacy have highlighted the importance of maintaining good sterile compounding practices. Efforts are now underway to develop revised guidelines for the compounding of sterile products in order to minimize the potential for future recurrence of similar incidents. This survey study was undertaken to provide background data on current sterile products compounding practices and procedures in Canadian hospital pharmacies. It was also anticipated that these data would be helpful in identifying issues that needed to be addressed in the new guidelines.

Surveys were distributed to 700 Canadian hospitals with 50 or more beds. Responses from returned surveys were entered into and analyzed using the database program RBase®. A total of 306 hospital pharmacies responded, with 200 indicating that sterile products were compounded within their department. The information provided by respondents provides insight into the types of sterile products being prepared in Canadian hospitals, the training background of staff involved in sterile product preparation, the type of facilities and equipment used for compounding these preparations, and the quality control/quality assurance procedures that are in place in hospital pharmacies.

The information arising from this survey underscores the need for comprehensive guidelines or standards with respect to sterile product compounding, and the need for improved training of personnel involved in sterile product compounding. The results should be of interest to hospital pharmacy administrators, pharmacy regulatory bodies, and government agencies responsible for assuring the safety of pharmaceutical products used in patient care.

Key Words: *compounding, hospital pharmacy practice, quality assurance, sterile products.*

RÉSUMÉ

Les mauvaises méthodes de préparation des produits stériles utilisées dans certains hôpitaux et dans certaines pharmacies communautaires peuvent avoir des conséquences graves. Des cas récents de décès ou de blessures causés par des produits contaminés au cours de leur préparation en pharmacie ont montré à quel point il import de suivre à la lettre les méthodes prescrites de préparation des produits stériles. On s'attache actuellement à réviser les lignes directrices en la matière, afin d'éviter la répétition de tels incidents. La présente étude vise à recueillir des informations de base sur les méthodes de préparation actuellement en usage dans les pharmacies hospitalières canadiennes. Elle devrait également permettre de cerner les questions dont il conviendra de tenir compte lors de l'élaboration des nouvelles lignes directrices.

Des questionnaires ont été distribués à 700 hôpitaux canadiens de 50 lits ou plus. Les réponses obtenues ont été compliées et analysées à l'aide du logiciel de base de données RBase®. Sur les 306 pharmacies hospitalières ayant répondu au questionnaire, 200 ont déclaré préparer des produits stériles. Les informations recueillies donnent un aperçu des types de produits préparés dans les hôpitaux canadiens, du niveau de formation des personnes chargées de ce travail, du type d'installations et d'équipments dont elles disposent et des méthodes d'assurance et de contrôle de la qualité mises en place dans les pharmacies hospitalières.

Les résultats de l'enquête soulignent l'importance d'avoir un ensemble complet de lignes directrices ou de normes concernant la préparation des produits stériles, ainsi que la nécessité d'améliorer la formation du personnel chargé de ce travail. Les résultats devraient intéresser les gestionnaires de pharmacies hospitalières, les organismes de réglementation des pharmacies et les organisations gouvernementales chargées d'assurer l'innocuité des produits pharmaceutiques utilisés pour les soins aux patients.

Mots Clés: *assurance de la qualité, pratique en pharmacie d'hôpital, préparation, produits stérile.*

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INTRODUCTION

The preparation of sterile drug products is an important role of many hospital pharmacy departments. Recently, some concern has arisen concerning the safety of sterile compounding practices because of several incidents reported in the United States where improperly prepared sterile products have been linked to patient morbidity and mortality[1-3]. As a result, pharmacy organizations and relevant government departments have been reviewing this area of practice to determine if current sterile product compounding practices are appropriate.

The manufacturing of sterile products falls under Section C.01.065 of the Food and Drugs Regulations. This section is applied to commercial manufacturing of sterile products and imposes strict end product sterility, identity and concentration testing on all products[4,5]. The Health Protection Branch (HPB) has not attempted to apply Section C.01.065 to the extemporaneous compounding of individual patient orders by hospital pharmacists. However, HPB does expect that appropriate procedures, equipment and facilities will be used when sterile products are prepared. The HPB's 1989 *Intravenous Therapy Guidelines* and the Canadian Society of Hospital Pharmacists' *Standards of Practice* appear to be the most widely recognized guidelines for assessing the appropriateness of sterile product compounding practices. The Canadian Society of Hospital Pharmacists (CSHP) is currently developing new, more detailed guidelines for sterile product compounding and HPB is being provided with the opportunity to review and comment on the draft versions of these guidelines. This survey study was undertaken to provide background data on current practices and procedures, to identify areas where improvements might be required.

METHODS

A questionnaire recently used by the American Society of Hospital Pharmacists (ASHP) to survey American hospitals regarding sterile product compounding and quality assurance methods was reviewed. Revisions were made, as deemed appropriate, and additions were made to gather data that were not collected in the ASHP survey. The final survey included questions pertaining to pharmacy department characteristics, types of sterile products prepared, training of staff, clothing requirements, preparation facilities, policies and procedures, quality assurance procedures, and differences between procedures used in centralized sterile product preparation areas and satellite pharmacies where sterile products are prepared. A draft version of the survey was reviewed by Directors of Pharmacy at six hospitals, as well as by the President and Executive Director of CSHP. A revised survey was then distributed by mail to 700 hospitals in Canada through CSHP during the month of March, 1992. A French translation of the survey was not developed and therefore hospitals in Quebec received an English copy. Reminder notices were not sent out to the hospitals who received the survey. Responses from surveys returned by the end of May, 1992 were entered into and analyzed using the database program RBase® (Microrim Inc., Redmond, Washington).

RESULTS

Three hundred and six completed surveys were returned for a response rate of 43.7%. Responses were received from all provinces and the Northwest Territories (Table 1). Despite the distribution of an English version of the survey in Quebec, the response rate from that province was second only to that from Ontario. Two hundred of the respondents (65.4%) indicated that sterile products were prepared in their department. Only 38% of hospitals less than 100 beds in size prepared sterile products while 74% of the hospitals over the 100-bed size did so (Table 2). Pharmacies that prepared sterile products had an average total staff size of 21.8 full time equivalents versus 5.5 in pharmacies that did not prepare sterile products.

Of the 200 survey respondents who indicated that sterile drug

Table 1: Response by Province

Province	Total respondents n=306 # (%)	Those who prepare sterile products n=200 # (%)
Alberta	4 (13.7)	21 (10.5)
British Columbia	40 (13.1)	32 (16.0)
Manitoba	12 (3.9)	7 (3.5)
New Brunswick	12 (3.9)	11 (5.5)
Newfoundland	5 (1.6)	3 (1.5)
Nova Scotia	15 (4.9)	11 (5.5)
Northwest Territories	1 (0.3)	1 (0.5)
Ontario	115 (37.6)	75 (37.5)
Prince Edward Island	1 (0.3)	1 (0.5)
Quebec	51 (16.7)	29 (14.5)
Saskatchewan	12 (3.9)	9 (4.5)
Yukon Territory	0 (0)	0 (0)

products were prepared by their department 74 (37.0%) indicated that sterile drug products were prepared for immediate use only. Nine (4.5%) indicated that sterile products were prepared only in batch lots for storage and later dispensing. The remaining 117 (58.5%) indicated that sterile products were prepared both for immediate dispensing and in batch lots.

The average number of sterile drug doses prepared in the pharmacy on a daily basis was 110. Pharmacists prepared some or all sterile products in 68.5% (137) of hospitals where sterile compounding occurs. Technicians prepared some or all sterile products in 73% (146) of hospitals. In the 146 hospitals where technicians prepared some or all sterile products, technicians were limited in the types of products they prepared in 68 (46.6%), while technicians were not restricted in the type of products they prepared in the remaining 78 (53.4%) hospitals.

The types of sterile drug products which were compounded in hospital pharmacies are shown in Table 3. The product type prepared by the largest percentage of respondents (74%) was intravenous antineoplastics, followed by total parenteral nutrition (68.5%), and intravenous/subcutaneous analgesics (63.0%). Only 10.0% indicated that their department provides a comprehensive sterile products service for their hospital. Forty-two and a half percent of respondents indicated that they prepared products "other" than those listed in Table 3. These "other" products were varied and included local anaesthetic combinations, cardioplegic solutions, papaverine/phentolamine intracavernosal injections, various bladder irrigations, pleurodesis solutions, and various large volume parenteral solutions and infusions such as nitroglycerin, heparin, and hypodermoclysis solutions.

Table 2: Hospital Bed Size

Bed Size	Total respondents n=306 #(%)	Those who prepare sterile products n=200 #(%)
<100	81 (26.4)	31 (15.5)
101-250	102 (33.3)	68 (34.0)
251-500	79 (25.8)	66 (33.0)
501-1000	36 (11.8)	29 (14.5)
>1000	7 (2.3)	5 (2.5)
no response	1 (0.3)	1 (0.5)

Table 3: Types of Sterile Products Prepared.

Type of product	Number (%) of respondents that prepare that product n=200
Intravenous antineoplastics	148 (74.0)
TPN	137 (68.5)
Intravenous/subcutaneous analgesics	126 (63.0)
Ophthalmic products	87 (43.5)
Other*	87 (43.5)
Intravenous antibiotics	82 (41.0)
Sterile nebulizer solutions	38 (19.0)
Otic products	22 (11.0)
Comprehensive sterile products service	20 (10.0)
Insulin pumps	6 (3.0)

*"other" category included local anesthetic combinations, cardioplegic solutions, papaverine/phentolamine intracavernosal injections, bladder irrigations, pleurodesis solutions, various large volume parenteral solutions, and a number of other preparations.

Of the respondents who indicated that sterile products are prepared in their department, 168 (84.0%) indicated that they have written policies and procedures for sterile product preparation. The frequency with which these policies are updated varies. The most common frequency for updating policies and procedures is every year (45.8%), followed by every two years (33.3%). A variety of guidelines or reference sources are used by hospitals for developing departmental policies and procedures for sterile production preparation. The most frequently used reference source is the Canadian Society of Hospital Pharmacists' *Standards of Practice* (131 responses, 78.0%) followed by the Canadian Council on Health Facilities *Accreditation Standards* (94 responses, 55.9%), and Health and Welfare Canada's *Intravenous Therapy Guidelines* (88 responses, 52.3%).

On the job training was the most common type of training for pharmacists (75.5%), followed by the use of IV admixture policies (69.0%), the use of labelling and record keeping policies (67.5%), and formal training (60.5%). The most common training method for technicians involved with sterile product preparation was on the job (67.5%), followed by the use of labelling and record keeping policies (63.0%). Only 44.0% of the respondents indicated that technicians involved with sterile compounding had any formal training. Written tests were used to evaluate the knowledge of pharmacists after orientation and at regular intervals thereafter by only

7.5% and 2.5%, respectively, of respondents. Written tests for technicians after orientation and at regular intervals thereafter were used by 15.5% and 4.5%, respectively, of respondents. Observation of a new employee's technique in the time period immediately after orientation was commonly carried out for both pharmacists (57.0% of respondents) and technicians (67.0% of respondents). However, observations of technique at regular intervals thereafter was carried out by fewer respondents, with only 24.5% indicating that this is done for pharmacists and 36.5% doing so for technicians.

Only 31.5% of respondents indicated that any of the pharmacists had received formal training or refresher courses related to sterile product compounding in the last year. Slightly more (34.0%) indicated that technicians had received formal training or refresher courses in sterile compounding techniques in the last year.

One hundred and thirty-seven respondents listed one or more types of training programs that they felt would be desirable for training their staff in sterile product compounding. Formal instruction at university or community college, practical training under a qualified instructor, and videotapes on sterile product compounding techniques were listed as the most needed types of training by 19.5%, 18%, and 15% of respondents, respectively.

Clothing requirements/restrictions at the hospitals that prepare sterile products are listed in Table 4. The most common requirement is for gloves (95.5%), either for all compounding (80.0%), or for compounding by staff who have skin lesions, abrasions, or sensitivities (15.5%). Gowning is required by 86.5% of respondents. Masks are required by 79.5% of respondents, either for all compounding (54.0%), or for compounding by staff with upper respiratory tract infection (25.5%).

Table 4: Clothing and Related Requirements/Restrictions.

	All respondents n=200 # (%)	Those who have written policies and procedures n=168 # (%)	Those who do not have written policies and procedures n=32 # (%)
Gown/outer garment	173 (86.5)	149 (88.7)	24 (75.0)
Mask (all sterile products)	108 (54.0)	93 (55.4)	15 (46.9)
Mask (staff with upper respiratory tract infections)	51 (25.5)	47 (28.0)	4 (12.5)
Glove (all sterile products)	160 (80.0)	137 (81.5)	23 (71.9)
Glove (staff with skin lesions,etc.)	31 (15.5)	28 (16.7)	3 (9.4)
Jewellery restrictions	139 (69.5)	128 (76.2)	11 (34.4)
Makeup restrictions	22 (11.0)	20 (11.9)	2 (6.3)
Hair covers	95 (47.5)	90 (53.6)	5 (15.6)
Shoe covers	14 (7.0)	13 (7.7)	1 (3.1)
Eye protection	52 (26.0)	44 (26.6)	8 (25.0)

Table 5: Preparation Areas/Facilities

	Central pharmacy n=200 # (%)	Satellite pharmacy n=200 # (%)
Counter or other clean surface	21 (10.5)	3 (1.5)
Horizontal LAH in general dispensing area	24 (12.0)	3 (1.5)
Horizontal LAH in room dedicated to sterile compounding	81 (40.5)	8 (4.0)
Vertical air flow with biohazard hood, in general dispensing area	20 (10.0)	8 (4.0)
Vertical LAH (not classed as biohazard cabinet) in general dispensing area	1 (0.5)	3 (1.5)
Vertical air flow biohazard hood, in room dedicated to sterile compounding	116 (58.0)	32 (16.0)
Vertical LAH (not classed as a biohazard cabinet) in room dedicated to sterile compounding	30 (15.0)	4 (2.0)

Preparation facilities and equipment used at the responding hospitals are shown in Table 5. The most common type of laminar air flow hood (LAH) in use was a vertical air flow biohazard hood, located in a separate compounding room (116 responses, 58.8%). In total, 190 respondents (95.0%) indicated that they have at least

one type of LAH. Of those who indicated that they have at least one hood located in a limited access area dedicated to sterile compounding, 54.4% indicated that their sterile compounding area had positive air pressure relative to adjacent areas. Five respondents who compound sterile products without a hood indicated that they had a sterile compounding room with positive air pressure relative to adjacent areas. The low response rates in the column for satellite pharmacy areas is likely a result of the fact that many hospitals in the responding group did not have satellites in their hospital. Unfortunately, the questionnaire design did not permit us to determine with certainty how many hospitals actually had satellite pharmacies.

The percentage of sterile drug doses which were not prepared by pharmacy staff are shown in Table 6. For hospital areas serviced from central pharmacies, 91 respondents (45.5%) indicated that over 75% of sterile doses are prepared by non-pharmacy staff. This response is not surprising, given that the data in Table 3 indicated that only 10% of responding pharmacies provided a comprehensive service covering all or most of the sterile products used in their facility. For areas served by a satellite pharmacy, the most common response was that less than 25% of doses are prepared by non-pharmacy staff. This suggests that where satellite pharmacies do exist they provide a fairly comprehensive sterile compounding service.

The frequency with which respondents had their LAH recertified and had the LAH prefilter cleaned or changed is shown in Table 7. Laminar air flow hoods are most commonly recertified every 12 months (72.6%) but the range of responses varied from every month to every 36 months. LAH prefilters are also most commonly cleaned or changed every 12 months (31.6%), but again there was a wide range reported, from every month to every 48 months.

The frequency with which the floors and other surfaces in the sterile products preparation area were disinfected is shown in Table 8. Floors were disinfected on a daily basis by 41.0% of all respondents and by 44.4% of respondents who prepare sterile products in batch lots. Other surfaces such as counters, shelves, and

Table 6: Percentage of Sterile Products Prepared by Disciplines Other Than Pharmacy

Percentage of sterile products not prepared by pharmacy staff	Areas served by central pharmacy n=200 # (%)	Areas served by satellite pharmacy n=200 # (%)
0-25%	54 (27.0)	21 (10.5)
25-50%	18 (9.0)	4 (2.0)
50-75%	27 (13.5)	3 (1.5)
75-100%	91 (45.5)	2 (1.0)
no response	10 (5.0)	170 (85.0)

Table 7: Laminar Airflow Hood Maintenance

Frequency	Number (%) of respondents who recertify LAH on a regular basis n=190	Number (%) of respondents who clean/ change LAH prefilters on a regular basis n=190
Every month	1 (0.5)	16 (8.4)
Every 2 months	0	8 (4.2)
Every 3 months	1 (0.5)	29 (15.3)
Every 4 months	0	8 (4.2)
Every 6 months	34 (17.9)	33 (17.4)
Every 12 months	138 (72.6)	60 (31.6)
Every 18 months	1 (0.5)	0
Every 24 months	5 (2.6)	0
Every 36 months	1 (0.5)	1 (0.5)
Every 48 months	0	1 (0.5)
No response	9 (4.7)	34 (17.9)

Table 8: Frequency of Floor and Surface Disinfection

Frequency of Disinfection	Floors		Other surfaces	
	Number (%) of respondents n=190	Number (%) of those who prepare batch lots n=126	Number (%) of respondents n=190	Number (%) of those who prepare batch lots n=126
Daily	78 (41.0)	56 (44.4)	36 (18.9)	24 (19.0)
Weekly	51 (26.8)	31 (24.6)	22 (11.6)	18 (14.3)
Monthly	8 (4.2)	3 (2.4)	27 (14.2)	19 (15.1)
> Monthly	7 (3.7)	5 (4.0)	36 (18.9)	27 (21.4)
Not done	34 (17.9)	23 (18.3)	41 (21.6)	25 (19.8)
No response	22 (11.6)	8 (6.3)	38 (20.0)	13 (10.3)

stools were disinfected less frequently. Only 18.9% indicated that they disinfect these surfaces on a daily basis, another 18.9% indicated that they disinfect these surfaces at intervals greater than monthly, and 21.6% indicated that they do not disinfect these surfaces. Of those respondents who prepare sterile products in batch lots, 21.4% disinfect these surfaces at intervals greater than one month, 19.8% do not disinfect these surfaces, and only 19.8% disinfect these surfaces on a daily basis.

The majority of respondents who had at least one LAH (62.1%) did not perform microbial or particulate sampling of the air and/or surfaces inside and around the LAH. This was true for respondents who had written policies and procedures for sterile compounding (55.4%) as well as for those who did not, although the percentage who do not perform microbial or particulate sampling was higher (78.1%) for those who did not have written policies and procedures.

The quality control procedures performed on sterile products are shown in Table 9. The most frequently performed procedure was to spray or wipe containers with alcohol before items entered and when items were removed from the hood (68.3% for batch lots; 67.0% for immediate use products). Other frequently performed procedures included filtration sterilization for both immediate use products and batch lots, and microbial testing for immediate use products and batch lots.

When non-sterile chemical ingredients were used for compounding sterile products, five respondents tested the ingredients for concentration, seven tested for chemical purity, and nine tested for pyrogenicity. However, the survey did not identify the total number of respondents who prepared sterile products from non-sterile chemical ingredients. Hence, the percentage who tested for concentration, purity, and pyrogenicity could not be determined.

Table 9: Quality Control Procedures Routinely Performed on Products

Type of testing / Type of product	Number (%) of those who prepare that type of product n=200	Number (%) of those with written policies and procedures n=168	Number (%) of those without written policies and procedures n=32
MICROBIAL TESTING			
Immediate use	44(23.0)	42(25.0)	2(6.25)
Batch lots	48(38.1)	44(26.2)	4(12.5)
PYROGEN/ENDOTOXIN TESTING			
Immediate use	2(1.0)	2(1.2)	0(0)
Batch lots	10(7.9)	10(6.0)	0(0)
PRODUCTS QUARANTINED WHILE AWAITING TEST RESULTS			
Immediate use	3(1.6)	3(1.8)	0(0)
Batch lots	21(16.7)	21(12.5)	0(0)
AUTOCLAVING			
Immediate use	31(16.2)	27(8.4)	4(12.5)
Batch lots	39(31.0)	36(21.4)	3(9.4)
MICROBIAL FILTRATION (Sterilization)			
Immediate use	84(44.0)	78(46.4)	6(18.0)
Batch lots	55(43.7)	50(29.8)	5(15.6)
DRY HEAT STERILIZATION			
Immediate use	23(12.0)	22(13.1)	1(3.1)
Batch lots	20(15.9)	19(11.3)	1(3.1)
ETHYLENE OXIDE STERILZATION			
Immediate use	14(7.3)	14(8.3)	0(0)
Batch lots	14(11.1)	14(8.3)	0(0)
ALCOHOL SPRAY/WIPE OF ITEMS ENTERING AND LEAVING LAH			
Immediate use	128(67.0)	116(69.0)	12(37.5)
Batch lots	86(68.3)	81(48.2)	5(15.6)
NONE OF THE ABOVE			
	46(23.0)	31(18.5)	15(46.9)
Other: All batched products tested by clinical chemistry = 1			

The temperature of refrigerators and freezers used to store sterile products was monitored by 51.0% of those who prepare sterile products. Temperature was monitored daily by 45.1%, weekly by 11.8%, monthly by 26.5%, and less frequently than monthly by 15.7% of the respondents who perform this checking procedure.

The most common reference sources used in the determination of expiry dating were published reference books and articles (86.0%) and manufacturers' recommendations (78.0%). Comparison with similar products was used by 26.5% of respondents. Relatively few respondents based expiry dating on in-house chemical (8.5%) or microbiological testing (15.5%). Arbitrary expiry dates were relatively rare.

The expiry dates for lipid emulsion and amino acid/dextrose solutions used for total parenteral nutrition are shown in Table 10. The most common expiry date for

lipid emulsion was 12 to 24 hours (62.5%) from the time the bottle was opened, and the most common expiry for TPN basis solution was 24-48 hours from time of manufacturing (29.5%).

The length of time that unused portions of single use vials or ampoules and multiple use vials were kept before being discarded is shown in Table 11. The most common discard time for unused portions of single use products was immediately after the ampoule/vial was first used (41.5%). However, unused portions were retained by many respondents for varying lengths of time. Some respondents indicated that unused portions of single use products are retained for the full length of the manufacturer's original expiry dating. The most common discard time for unused portions of multiple use vials was 30 days (27.0%), followed closely by discarding after the manufacturer's expiry date is reached (26.0%). The survey did not include questions that would have identified if unused portions of ampoules or vials are stored in a LAH, in a refrigerator, or in some other location.

Data were collected on the expiry dating, storage conditions, and product testing performed on 54 specific sterile drug products that were identified as commonly prepared products, either through the personal experience of the authors, informal discussion with other hospital pharmacists or the previously conducted ASHP survey. These included 21 products that are usually prepared in batch lots, 15 ophthalmic products, and 18 antineoplastic products. The response to these questions were quite varied, although some generalizations can be made. Most pharmacy departments assign expiry dates of one month or less, few products are stored frozen, and product testing, other than visual testing, is seldom done. The data collected are presented in Tables 12-14.

Table 10: Expiry Dating of TPN Solutions

Expiry dating of lipid emulsion	Number (%) of those who prepare sterile products n=200*
12 hr	8 (4.0)
12 - 24 hr	125 (62.5)
>24hr	10 (5.0)
N/A	46 (23.0)
No response	11 (5.5)
Expiry dating of amino acid/dextrose solutions	
24 hr from manufacture	31 (15.5)
24hr from leaving pharmacy	15 (7.5)
24 - 48 hr from manufacture	59 (29.5)
> 48 hr from manufacture	50 (25.0)
N/A	34 (17.0)
No response	11 (5.5)

* More than the 137 respondents who indicated that they prepare TPN (see Table 3) provided expiry dating information for lipid and amino acid/dextrose solutions. This suggests that although some respondents do not prepare TPN solutions they probably obtain such products from outside sources such as Baxter's sterile compounding facilities and assign expiry dating to these products.

Table 11: Expiry Dating For Unused Portions of Ampoules and Vials

	Single use ampoules and vials n=200	Multiple use vials n=200
Discard after single use	83 (41.5)	4 (2.0)
Discard after 6 hr	5 (2.5)	2 (1.0)
Discard after 6-12 hr	8 (4.0)	2 (1.0)
Discard after 12-24 hr	37 (18.5)	7 (3.5)
Discard after 24-48 hr	18 (9.0)	20 (10.0)
Manufacturer's expiry date	8 (4.0)	52 (26.0)

DISCUSSION

This survey demonstrated that approximately two-thirds of the responding hospital pharmacy departments in Canada prepare sterile drug products. This is lower than might be expected, which may be due to several factors. Many of the respondents who did not prepare sterile products indicated that they are extended care hospitals, or long term care psychiatric hospitals, and do not have a need for these products. Surveys were also returned by a number of small hospitals (<100 beds, 81 responses, 26.4% of total responses) and the majority of these do not prepare sterile products. It is possible that many small hospitals do not treat patients who have a need for special sterile products. Even if sterile products are used in these small hospitals, many employ small numbers of pharmacy staff or contract services from a retail pharmacy and therefore would probably rely on nursing staff for the preparation of sterile products.

Written policies and procedures relating to preparation of sterile products are in place at 168 of the 200 departments which prepare sterile products (84.0%). Most respondents indicated that their policies and procedures were updated on a regular basis with a variety of references used as guidelines for the policies and proce-

Table 12: Products Prepared in Batch Lots (Numbers = Respondents Who Checked Off the Response Represented by Each Cell)

	Expiration Dating (days) n=200				Storage Conditions n=200				Product Testing n=200				
Product	<7	7-30	31-90	>90	Frozen	Refrig-erated	Room Temp.	Light Protect	Visual	Microbial	Pyro/ Endo	Drug Concen-tration	Chemical
Albumin 5% in NaCl			1	1		1			1				
Alum bladder irrigation	5	3		1		6	3		8	2			
Amino acid/ dextrose sol'n for inpatient TPN	29	25	14	2		70		16	56	28	3	3	3
Amino acid/ dextrose sol'n for home TPN		8	3			10		2	8	8	1	1	1
Ampicillin	26					23	1	1	18	3	1	1	1
Other Beta Lactam antibiotics	9	21	2		5	27			24	4	1	2	1
Bacitracin irrigation	4	4	2			10			8	2			
Cardioplegic solution		10	7			16		3	14	10	1	4	3
Cefazolin	9	33	1	6	11	36		1	35	7	1	2	1
Other cephalosporin antibiotics	12	20	4	6	15	25			30	3	1	2	1
Heparin subcutaneous injection		4	4			6	2	1	7	2			
Heparin intravenous injection	9	7		2		14	4		15	3			
Histamine dilutions		2	13	1	1	14	1	2	15	4		1	
H2 receptor antagonists		27	5	1	4	28		1	26	7	1	2	1
Leuprolide injection			1			1			1				
Lidocaine infusions	1	1				2		1	2				
McCoy's sol'n with albumin and/or tobramycin	1	1	5			6			5				
Morphine injections	18	28	5			30	19	4	36	9		1	
Neomycin irrigation	2	1	1	1		4	1		4	1	1	1	1
Polymyxin B inhalation solution				1		1			1				
Thiopental injections	15	17	1			28	5	1		2	1		

Table 13: Ophthalmic Products (Numbers = Respondents Who Checked Off the Response Represented by Each Cell)

	Expiration Dating (days) n=200				Storage Conditions n=200				Product Testing n=200				
Product	<7	7-30	31-90	>90	Frozen	Refrig-erated	Room Temp.	Light Protect	Visual	Microbial	Pyro/ Endo	Drug Concen-tration	Chemical
Acetylcysteine drops	13	4			1	13	2	1	12	1			
Amikacin introocular injection	6	1				3	3		4				
Amphotericin B drops	10	7				16		3	9	1			
Ascorbic acid drops	4	2				2	4	1	4	1			
Atropine drops		2	2	1		1	4		3	1			
Bacitracin drops	8	8				13	3	1	10	1			
Cefazolin drops	49	14				54	8	6	39	3			
Clindamycin drops		4	3			4	2		4				
Cocaine drops	7	8	10	10		13	21	7	22	7			
EDTA drops	8	2	13			8	5	20	10	2			
Gentamicin drops	33	16	66	2		39	17	5	35	3			
Hyaluronate drops		2	1			2	1	1	3				
Pilocarpine drops	3	2	5	1		4	6	1	9				
Tobramycin drops	18	14	3	2		27	9	4	22	2			
Vancomycin drops	15	8				17	5	1	13	1			

dures. Written policies and procedures for sterile compounding should be available in all departments which regularly compound sterile products, regardless of whether they are required by provincial legislation or not. Policies and procedures are useful in many ways. They help ensure consistency in sterile product preparation, provide a written standard for training of new staff, ensure proper maintenance of preparation facilities, and can serve as evidence of standards of care. Evidence of compliance with, and regular review of, written policies and procedures can serve as verification that the pharmacy has taken due care to ensure patient safety.

Almost all of the pharmacy departments that prepare sterile products do so for products that will be dispensed immediately and used within a short time frame. However, 126 (63%) also prepare batch lots of sterile products that are stored and used over a period of time, and a further 9 (4.5%) exclusively prepare sterile products in batch lots. At the present time, the HPB has indicated that the exemption of hospital pharmacies from Section C.01.065 of the Food and Drug Regulations applies only to sterile products prepared in response to an individual prescription (i.e., for immediate dispensing). Sterile products compounded in batch lots are expected to comply with the end product identity and sterility testing required by Section C.01.065. However, only 38.1% of the pharmacies that prepared batch lots in this survey routinely performed microbial testing on their products. Relatively few respondents indicated that products were quarantined until results were available, and less than half of respondents used any type of sterilization technique (i.e., autoclaving, filtration, dry heat, or ethylene oxide) for sterile products. Since sterility testing is widely available and is relatively inexpensive to perform, it appears that increased usage of sterility testing for batch lots of prepared sterile products should be encouraged. Quality control procedures, such as microbiological or pyrogen/endotoxin testing are useful even for products that are prepared for immediate use. They are useful in validating the compounding technique of the personnel preparing the sterile products, even if test results are not available until after the product is dispensed. Consistent negative growth results indicate that proper technique is being used, while positive growth indicates the need to review facilities, equipment and the compounding technique of the operator.

With respect to end product identity and concentration testing, the situation is somewhat differ-

Table 14: Anti-Neoplastic Products (Numbers = Respondents Who Checked Off the Response Indicated by Each Cell)

	Expiration Dating (days) n=200				Storage Conditions n=200				Product Testing n=200				
Product	<7	7-30	31-90	>90	Frozen	Refrig-erated	Room Temp.	Light Protect	Visual	Microbial	Pyro/ Endo	Drug Concen-tration	Chemical
Bleomycin injection	51	31				67	13	6	58				
Carboplatin injection	50	17				19	43	11	49	1			
Cisplatin injection	59	19				21	56	20	58				
Cyclophosphamide injection	71	17	1			67	19	7	64				
Cytarabine injection	46	25				31	36	3	49				
Dactinomycin injection	46	8	1			33	18	8	38				
Dauorubicin injection	49	10				41	16	10	42				
Doxorubicin injection	53	30		1		63	19	19	62				
Epirubicin injection	49	17		2		50	15	11	47				
Etoposide injection	58	17	1			17	57	9	57				
5-Fluorouracil injection	60	29				27	62	25	66	1			
Ifosamide injection	23	15	6			31	11	2	30				
L-Asparaginase injection	29	24				41	9	2	36				
Methotrexate injection	54	36	1	1		32	58	24	67				
Methotrexate intrathecal injection	44	2				13	23	8	35				
Mitoxantrone injection	44	16	2			23	37	7	42				
Vinblastine injection	35	35				58	11	18	48				
Vincristine injection	48	27	1	1		67	11	15	53	1			

ent. Few hospitals could comply with rigid requirements for end product identity and concentration testing, and patients might; therefore, be denied access to needed products that are not commercially available. It seems reasonable to argue that strict adherence to proper preparation procedures will insure that the products prepared contain the proper amount/concentration of the active ingredient, irrespective of whether the product is prepared for immediate use or in batch lots for use over a period of time. This assumes that the raw materials used meet chemical or pharmaceutical standards. There should not be a major difficulty in assuming this when the raw material comes from the vials or ampoules of a product prepared for human use by a pharmaceutical manufacturer. In the rare situations where non-sterile chemicals, not specifically intended for human use, are utilized to prepare a sterile product the situation is more complex. Very few respondents in this survey indicated that testing for ingredient concentration, purity, or pyrogenicity was performed on non-sterile chemicals that are used to prepare sterile products. This may be a reflection of the fact that most pharmacies do not prepare products from raw chemical ingredients. The survey questions

unfortunately did not identify the total number of pharmacies which compound sterile products using non-sterile chemical ingredients. However, because of the cost and difficulty in carrying out concentration, purity and pyrogenicity testing, it is unlikely that most hospitals could comply with the requirement for this type of testing. Presumably a decision would have to be reached on the need for the patient to be treated with the product in question, versus the risks involved in not being able to test for identity, purity and pyrogenicity.

Only 60.5% of pharmacists and 44.0% of technicians had received formal training in sterile product preparation. The available guidelines recommend that all personnel involved in sterile compounding should receive both theoretical and practical training, as part of a formalized training program. Training programs should include theoretical and practical aspects of product preparation, clean room and LAH design and operation, and quality assurance methods and programs[6,7]. Continuing education programs dealing with these topics should be available to pharmacists and technicians involved with sterile compounding on a regular basis. Continuous monitoring of preparation technique, by methods such as periodic observations of technique, should also be encouraged.

Survey respondents were asked to describe training programs which they felt would be most useful. The most common response was a desire for standardized, formal training programs at universities or community colleges, followed by a desire for practical training and instructional videotapes. Training with respect to quality assurance programs was also identified as an area where more training is needed.

The clothing requirements of the departments which prepare sterile products are varied. The most common requirements are for gloves, gowns (or other outer garments), and masks. The currently available guidelines provide some recommendations concerning clothing requirements and related procedures[6,7]. Prior to compounding, hands should be thoroughly washed with an antimicrobial detergent. Rings and watches should be removed. While gloving and gowning may not be necessary in all situations, gloves and gowns should be worn during extensive manipulations of products, complex compounding procedures, or compounding which requires a prolonged time to complete. Gloves should be changed or rinsed with 70% isopropyl alcohol hourly, or changed if torn or punctured. Masks should be worn when using a horizontal LAH, and hair covers should be used for all compounding. Other clothing restrictions may be indicated in specific situations.

It appears that a number of the respondents do not have facilities and/or equipment that conform to the recommendations contained in currently available guidelines[6,7,9]. These guidelines recommend that sterile compounding should occur in a limited access area that is separated from other pharmacy operations and storage areas[6]. All sterile products should be compounded in a Class 100 horizontal or vertical laminar air flow hood.[7,9] Cytoxic products should be prepared in a vertical laminar air flow hood that is certified as a Class 2, Type B2 biohazard safety cabinet[6,7,9]. For products prepared in batch lots, the hood should be located in a Class 100,000 or better clean room, and positive pressure relative to adjoining room is recommended[6]. In this survey, only 31 (24.6%) of those who prepare batch lots have a sterile room with positive air pressure. These results suggest that some sterile products are not prepared in accordance with the existing guidelines.

While the majority of respondents indicated that their LAH were recertified on a regular basis and that LAH prefilters are cleaned or changed on a regular basis, 10% do not recertify their LAH and 23.2% do not clean/change their LAH prefilter on a regular basis. This suggests that in some cases, even where hoods are used to compound sterile products, the hoods may not be properly maintained.

The majority of respondents do not sample the air or surfaces inside and around the LAH for microbial or particulate contamination. If hoods are maintained on a regular basis, and the department follows an ongoing infection control and quality assurance monitoring program, this sampling is not necessary, although the new ASHP guidelines recommend this sampling if batch lots are prepared[6,8]. In this survey, 71 (56.3% of the respondents who prepared batch lots did not perform any testing of the air or surfaces inside or around the LAH for mocrobial or particulate contamination.

Current guidelines recommend that the floors of the sterile products preparation area be disinfected on a regular basis, and on a daily basis if batch lots are compounded[6]. Other surfaces, such as walls, ceiling, counters, stools, etc should be disinfected weekly if batch lots are compounded. Of the 126 respondents who prepare sterile products in batch lots, only 44.4% indicated that floors are disinfected daily, and likewise only 33.3% indicate that other surfaces are disinfected daily or weekly.

All refrigerators or freezers used to store sterile products or ingre-

dients used in the preparation of sterile products should be monitored to ensure that temperatures are maintained at compendial standards[6]. There are no recommendations for how frequently these temperatures should be monitored. Approximately half (51.0%) of the respondents to this survey indicated that temperatures are monitored, but the monitoring intervals vary substantially.

All sterile drug products should be assigned an expiry date, which should be based upon appropriate stability information or testing[6,7]. Even products which are intended for immediate dispensing or use, such as a PCA syringe or antibiotic eye drops should be assigned expiry dates to ensure that the product is discarded before significant product degradation or contamination occurs. Reliable reference sources, or in-house testing procedures should be used as the basis for expiry dates. Use of arbitrary expiry dates should be avoided. If no literature is available for a particular product, then stability testing should be undertaken.

Survey respondents indicated a variety of expiry dating for unused portions of single and multiple use ampoules or vials. The majority of respondents keep unused portions of single use products for 24 hours or less, and keep multiple use products for 30 days or until the manufacturer's expiry date is reached. Some respondents indicated specific expiry dating for some products, such as insulin, or based expiry dating on the number of times the vial is entered. No attempt was made to determine if the unused portions of ampoules or vials were stored inside the LAH, at room temperature, or under refrigeration. The sterile compounding guidelines that are available indicate that unused portions of vials should only be stored under conditions which limit the risk of microbial contamination or chemical instability, but more specific recommendations are not included.

In conclusion, the majority of hospital pharmacies prepare sterile drug products, but there is great variation between facilities, equipment, and procedures used by different departments. Training of the personnel involved in sterile product preparation needs to be standardized and improved, and more continuing education is required. The variety of responses to the survey underscore the need for official guidelines or standards with respect to sterile drug product preparation.

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