Original Article

The Effect of the Interventions on Basic Knowledge of and Skills of Health Care Workers in the Preparation of Cytotoxic Drugs at Sappasithiprasong Hospital, Ubon Ratchathani Province

ผลการบรรยายความรู้และสาธิตโดยผู้เชี่ยวชาญต่อองค์ความรู้และทักษะในขั้นตอนการเตรียมยาเคมีบำบัดของบุคลากรการแพทย์ ในโรงพยาบาลสรรพสิทธิประสงค์ อุบลราชธานี

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Abstract

The study aimed to evaluate the effects of the interventions including; a lecture on cytotoxic preparation and practice simulation on the basic knowledge of and skills in the preparation of cytotoxic drugs before, immediately after, and one month after the interventions. The study was designed as a one group pre-/post-test type in which eight participants completed a pre-test of a measurement of basic knowledge of cytotoxic drugs as well as an assessment of skills involved in cytotoxic preparations. This assessment was developed based on a standard checklist of preparation skills from a range of different guidelines and was subsequently implemented by a panel of assessors consisting of three clinical pharmacists, 4 technicians, and 1 temporary staff working. The participants were then exposed to the interventions containing of a lecture on cytotoxic preparation, practice simulation on the basic knowledge of and skills in cytotoxic preparation, then the assessments were repeated. Results from these processes were followed by immediate post-test. One month later, similar assessments of basic knowledge and skills were also performed. Attitudes of the participants toward these processes were also evaluated. The results were reported using descriptive & statistical analyses in term of mean $\pm$ SD, frequencies, paired t-tests, and Wilcoxon. The results showed there was no significant differences between basic knowledge scores in pre- compared to immediate post-tests, and in immediate compared to 1 month post-tests ($p = 0.070$ and 0.336 respectively). The overall results of the skills assessment in cytotoxic drugs preparation demonstrated significant differences in scores including basic knowledge, cytotoxic drugs preparation skills between the pre- and immediate post-tests, and between the scores in the immediate posttest and 1

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month post-tests (p = 0.026 and 0.045 respectively). The immediate posttest scores were significantly higher in all aspects preparation skills compared to those of pre-test (p = 0.001, 0.021, and 0.017 respectively). However, there were no significant differences between the immediate posttest and 1 month post-test scores in the 3 skills including; aseptic hand-washing, vertical laminar air flow hood, and hazardous drug vial preparation (p = 0.279, 0.593, and 0.086, respectively). Generally, the attitudes of the participants to the implementation of the intervention were favorable. Conclusively, the intervention improved basic knowledge of and skills in the preparation of cytotoxic drugs and participants' attitudes to the intervention were positively favorable.

Keywords: Cytotoxic drugs preparation, Interventions, Aseptic hand-washing, Vertical laminar air flow hood, Hazardous drug vial preparation
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บทคัดย่อ

การศึกษาครั้งนี้ วัตถุประสงค์เพื่อประเมินความรู้และทักษะการเตรียมยาเคมีบำบัดหลังจากให้การบรรยายความรู้และสาธิตโดยผู้เชี่ยวชาญกับกลุ่มตัวอย่างในช่วงเวลาก่อนให้ความรู้-หลังให้ความรู้-หนึ่งเดือนหลังให้ความรู้ มีการใช้แบบประเมินทักษะการเตรียมยาเคมีบำบัดซึ่งถูกพัฒนาโดยใช้เกณฑ์มาตรฐานสากล การศึกษาครั้งนี้มีรูปแบบ one group pre-posttest กลุ่มตัวอย่างที่เข้าร่วมการศึกษามีทั้งสิ้น 8 คน ซึ่งประกอบด้วยเภสัชกร 3 คน เจ้าหน้าที่เภสัช 4 คน และลูกจ้างชั่วคราวที่ทำงานในหน่วยเคมีบำบัด 1 คน ผู้วิจัยทำการประเมินความรู้และทักษะการเตรียมยาเคมีบำบัดหลังจากให้การบรรยายความรู้และสาธิตโดยผู้เชี่ยวชาญเกี่ยวกับการเตรียมยาเคมีบำบัดกับกลุ่มตัวอย่างในช่วงเวลาที่ต่างกัน โดยทำการทดสอบความรู้และทักษะการเตรียมยาเคมีบำบัดก่อนให้ความรู้ (pre-test) ต่อจากนั้นทำการบรรยาย สาธิตทักษะการเตรียมยาเคมีบำบัดอย่างถูกวิธี จากนั้นทำการประเมินความรู้และทักษะทันที (immediate posttest) จากนั้น 1 เดือนต่อมาทำการประเมินความรู้และทักษะอีกครั้ง (one month posttest) เพื่อดูความคงอยู่ขององค์ความรู้และทักษะการเตรียมยาเคมีบำบัด ในการประเมินทักษะการเตรียมยาเคมีบำบัด จะอาศัยแบบประเมินที่พัฒนาขึ้นมา (standard checklist) จากเกณฑ์มาตรฐานสากล นอกจากนั้นกลุ่มตัวอย่างจะได้รับแบบประเมินความพึงพอใจในการนำเอา intervention มาใช้ครั้งนี้ ข้อมูลที่ได้ทั้งหมดจะถูกนำไปวิเคราะห์ทางสถิติแบบพรรณนาต่อไป (เช่น Mean $\pm$ SD, frequency, Paired t-test, Wilcoxon) ผลการศึกษาพบว่ากลุ่มตัวอย่างส่วนใหญ่เป็นเพศชาย (6) มีอายุในช่วง 25-45 ปี ส่วนใหญ่มีประสบการณ์การทำงานในช่วง 1-5 ปี เมื่อพิจารณาค่าคะแนนภายในกลุ่ม พบว่าไม่มีความแตกต่างของค่าคะแนนความรู้ในช่วงเวลาต่างๆ เช่น ระหว่างก่อน-หลังให้การบรรยายความรู้และสาธิตโดยผู้เชี่ยวชาญเกี่ยวกับการเตรียมยาเคมีบำบัดทันที และระหว่างหลังให้การบรรยาย

คำสำคัญ: การเตรียมยาเคมีบำบัด การเข้าแทรกแซง การล้างมือแบบปลอดเชื้อ เครื่องไหลเวียนอากาศภายในแบบแนวตั้ง การเตรียมยาฉีดชนิดอันตราย
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Introduction

Hospital staff including clinical pharmacists, pharmacy technicians, temporary workers working in cytotoxic drugs preparation units may be exposed to hazardous substances at many steps during manufacture, transport, distribution, receipt, storage, preparation, and/or administration processes (ASHP, 2004). Early concerns regarding the safety of hospital staff arose when reports of secondary cancers in patients treated with some cytotoxic agents were linked to the discovery of mutagenic substances in nurses and staffs who prepared and handled the drugs and/or cared for cancer patients (Harris 1976; Falck et al, 1979). Exposure to cytotoxic agents in the workplace has been associated with acute and short-term adverse reactions as well as long-term effects. Anecdotal and case reports in the literature ranging from skin-related and ocular effects to flu-like symptoms and headaches were frequently published (NIOSH, 2006; Harrison, 2001; Ladik et al, 1980; Crudi, 1989; Reynolds et al, 1982; Knowles and Virden, 1980; McFarlane, 1986; Curran and Lure, 1989; McLendon and Bron, 1978). Two controlled surveys reported significant increase in a number of symptoms including sore throat, chronic cough, and infection among nurses, pharmacists, and pharmacy technicians routinely exposed to these hazardous drugs in the workplace (Valanis et al, 1987; Valanis et al, 1993). Also there was a report of the high risk assessment of occupationally-exposed pharmacy workers that estimated that cyclophosphamide caused an additional 1.4 to 10 cases of cancer per million workers each year (Sessink et al, 1995; Ensslin et al, 1994). The risk to health care personnel from handling these hazardous drugs is the result of a combination of the inherent toxicity of the drugs and the extent to which workers are exposed to the drugs in the course of their daily jobs (ASHP, 2000). Thus there are standard guidelines for the safe handling of cytotoxic drugs in many countries, including a process validation checklist that contains measurements of staff performances in steps of preparation, such as aseptic hand-washing, vertical laminar air flow hood, and hazardous drug vial preparation.The standard guideline used is referredto this web address; http://www.asia4safehandling.org

In Thailand, cytotoxic preparation services have been conducted in local and central hospitals around the country. However, there is currently no standard process validation checklist to measure hospital workers involvement in the preparation process. This situation exists despite the large use of cytotoxic drugs in many hospitals. For example, it was estimated that there were 1,200 items of cytotoxic drugs distributed to patients monthly by eight staff at Sappasithiprasong Hospital (Sappasithiprasong Hospital, 2005). This distribution of a large quantity of drugs by a small number of staff may lead to inappropriate practice and difficulties in enhancing their knowledge and skills due to heavy routine workloads. Additionally, as basic knowledge and skills in cytotoxic drug preparation among those staff are different. As a result, there is a gap of knowledge that lead to misconducting in practice. Nevertheless, this situation may also involve high risk exposure to cytotoxic drugs during the preparation and distribution processes and the possibility of resultant illnesses. This study aimed to evaluate the performance of routine skills and measure the effectiveness of the interventions on the knowledge

and skills of hospital staff of cytotoxic drugs preparation. Also a survey of attitudes of staffs toward the implementation of the interventions was conducted.

Methods

Step I Development of a Process Validation Evaluation Checklist

The standard validation checklist for cytotoxic drugs preparation skills was developed based on well-acceptable guideline manuals (ASHP, 2004; ASHP, 2000; Luci et al, 2006; Pharmacy Group of Cancer Disease, 2005). There are totally 53 checklist items divided into 3 aspects including; aseptic hand washing, vertical laminar air flow hood, hazardous drug vial preparation. Content validity was assessed by 2 oncologists and 3 clinical pharmacists. Modifications were made prior to the implementation. The checklist was piloted in volunteers consisting outpatient pharmacists (10), Warinchumrab Hospital, Ubon Ratchathani province for the purpose of a reliability, resulting in an acceptable overall average Cronbach-alpha (α) of 0.78.

Step II Development of study materials

Study Materials

The materials used in the study were

1. A standard validation checklist of cytotoxic drugs preparation skills
2. A multiple choice examination of basic knowledge of cytotoxic agents (15 points)
3. An assessment form regarding cytotoxic drugs preparation skills including:
   a. aseptic hand-washing (11 points)
   b. vertical laminar air flow hood (17 points)
   c. hazardous drug vial preparation (25 points)

Step III Measurement of the Effectiveness on Knowledge and Skills of Hospital Staff including; clinical pharmacists, pharmacy technicians, and temporary staff of the Interventions in Cytotoxic Drugs Preparation

Study design

The design of the study was a one group pre-/post-test type from October 2007 to January 2008. The assessment of the knowledge and skills of hospital staff of the preparation of cytotoxic drugs was carried out by 2 hospital pharmacists and 1 clinical pharmacy lecturer who had completed training and certified skills in the oncology prior to the study.

Participants

Three clinical pharmacists, 4 technicians, and 1 temporary staff working in the Cytotoxic Drugs Preparation Unit at Sappasithiprasong Hospital volunteered to participate in the study. They were required to have at least 1 year's work experience and willing to complete the interventions including; a lecture on cytotoxic preparation and practice simulation on the basic knowledge of and skills in the preparation of cytotoxic drugs.

Method

The participants' basic knowledge of cytotoxic drugs was assessed via a pre-test consisting of fifteen multiple choice questions. Subsequently, the baseline cytotoxic drug preparation skills of the 8 participants were assessed individually by assessors who observed the participants as they performed their routine tasks and evaluated them using the pre-developed checklist according to step I. This assessment involved the evaluation of 3 major skills, including aseptic hand-washing, vertical laminar air flow hood, and hazardous drug preparation. Volunteers were not informed beforehand when the assessment would be

conducted. Any interruption to the assessment were resulted in re-assessment. One week after assessment, the participants had to complete a 3-day intervention involving attending presentation by a guest lecturer from the Oncology Department at Siriraj Hospital and attending cytotoxic drugs preparation demonstration. Upon completion of the interventions, an assessment of basic knowledge and skills in cytotoxic drugs preparation was performed (immediate post-test). One month later, the participants completed the same assessment (one-month post-test). All results were statistically analyzed using method of analysis

3. Assessment of Attitudes to the Intervention Program

The participants expressed their opinions about the implementation of the intervention program by the completion of responses using a Likert scale (strongly agree [5] >>> strongly disagree [1]).

Step IV Data Analysis

Descriptive analysis

Frequencies, means, Standard deviation (SD), and percentages were calculated for the results of the assessment of demographic data, scores of basic knowledge and cytotoxic drugs preparation skills.

Analytical analysis

A paired t-test was implemented to analyze the pre-and immediate post-test scores, and immediate post-test and 1 month post-test scores. The confidence interval was 95% and type I error (α) equaled to 0.05.

Results

A process validation evaluation checklist was initially developed via implementing standard guidelines such as American Society of Health-System Pharmacists (ASHP) Guideline on Handling Hazardous drug, ASHP Guideline on Quality Assurance for Pharmacy-Prepared Sterile Products, ASHP Self-Assessment Tool for Compounding Sterile Preparations, Implementation Initiation Workload and Conceptualization of Cycotoxic Pharmacy Practice, Process Validation Evaluation Checklist and Group of Thai Oncology Pharmacy Practitioners. The checklist was evaluated both content validity and reliability via experts. Eight hospital personnel including; three pharmacists, 4 pharmacy technicians, and a temporary member of staff participated in the study participated in the study. All working in the Cytotoxic Drugs Preparation Unit at Sapasithiprasong Hospital. There were 6 males and 2 females with ages between 25 and 45 years. Their education levels were bachelor degree (6), vocational college degree (1), and high school (1), their work experience in cytotoxic drug preparation ranged from 1 to 5 years. Most participants informed had approximately one time of short training in cytotoxic preparation per year. Table 1, there was no statistical significance between pre-and immediate post-test scores nor between immediate post- and 1 month post-test scores ($p = 0.07$ and 0.336 respectively).

Table 1 Results of assessment of basic knowledge of cytotoxic agents (n=8)

Number of participants	Basic Knowledge Scores (/15)		
	Pre-test	Immediate	post-test
1	13.00	14.00	15.00
2	15.00	15.00	15.00
3	15.00	14.00	13.00
4	10.00	15.00	14.00
5	6.00	11.00	10.00
6	13.00	14.00	15.00
7	13.00	13.00	15.00
8	6.00	9.00	14.00
Means ± SD	11.37 ± 3.66	13.12 ± 2.10	13.87 ± 1.72

Comparisons	t	df	p-value
Pre-and immediate post-test	-2.139	7	0.070
Immediate post-test and 1 month post-test	-1.033	7	0.336

Before and after the implementation of the interventions, the 3 specific skills involved in the preparation of cytotoxic drugs, aseptic hand-washing, vertical laminar air flow hood, and hazardous drug vial preparation were measured at the pre-, immediate post-, and 1 month post-test stages. Noticeably, Mean scores of aseptic hand-washing skills were increasingly significantly high in immediate post-scores compared to pre-scores (p=0.001). Nevertheless, there is no statistically significant difference between immediate post- and 1 month post-scores (p=0.279) (Table 2). It may imply most volunteers realized the importance of how to clean hands prior to a cytotoxic drug preparation.

Table 2 Results of assessment of skills of aseptic hand-washing (n=8)

Scores (/11)	Pre-test	Immediate post-test	1 month post-test
Means ± SD	5.50 ± 1.93	8.63 ± 1.41	8.00 ± 1.77
Comparisons			
	t	df	p-value
Pre-and immediate post-tests	-6.063	7	0.001
Immediate and 1 month post-tests	1.174	7	0.279

Table 3 Results of assessment of skills of vertical laminar air flow hood (n=8)

Scores (/17)	Pre-test	Immediate post-test	1 month post-test
Means ± SD	12.23 ± 1.28	14.63 ± 2.50	15.00 ± 1.93
Comparisons			
	t	df	p-value
Pre-and immediate post-tests	-2.967	7	0.021
	Z (Wilcoxon)		p-value
Immediate and 1 month post-tests	-0.535		0.593

Table 4 Results of assessment of skills of hazardous drug vial preparation (n=8)

Scores (=25)	Pre-test	Immediate post-test	1 month post-test
Means ± SD	18.88 ± 2.36	21.25 ± 1.04	22.25 ± 1.15
Comparisons			
	Z (Wilcoxon)		p-value
Pre-and immediate post-tests	-2.388		0.017
	t	df	p-value
Immediate and 1 month post-tests	-2.00	7	0.086

There were significant differences between pre- and immediate post-test scores of vertical laminar air flow hood and hazardous drug vial preparation skills (p = 0.021 and 0.017 respectively). There were no significant differences between immediate and 1 month post-test scores in any of the 3 assessed skills (p = 0.279, 0.593, 0.086). Nevertheless, the total scores showed some statistically significant differences between pre- and immediate post-test scores and between immediate post- and 1 month post-test scores (p = 0.026 and 0.045 respectively). The participants improved their overall performances in all aspects of cytyotoxic drugs preparation skills after the implementation of the interventions (see Tables 2, 3, 4, and 5). Similarly, volunteers had a better significant performances in cytotoxic drug preparation skills regarding vertical laminar air flow hood, and hazardous drug vial preparation immediately after implementing a lecture on cytotoxic preparation and practice simulation on the basic knowledge of and skills in the preparation of cytotoxic drugs. However, their performances tended not to be different over the period of time (1 month).

Table 5 Overall results of assessment of cytotoxic drugs preparation skills (n=8)

Scores (=53)	Pre-test	Immediate post-test	1 month post-test
Means ± SD	36.63 ± 4.66	44.50 ± 3.55	45.25 ± 3.49
	Comparisons		
	t	df	p-value
Pre-and immediate post-tests	-2.827	7	0.026
Immediate and 1 month post-tests	-2.443	7	0.045

In term of attitudes evaluation, most (n=7(85%)) of the participants indicated their positive attitude to the usefulness of the three day interventions. The majority (n=6(76.59%)) expressed a desire to have a further workshop to enhance their skills. However, 67.54% (n=5) stated the lecture topics could be more interesting and needed to be more up-to-date. Sixty percent needed the duration of the intervention to be extended. Seventy-three percent of volunteers (n=6) stated the importance of the standard checklist evaluation in the preparation of cytotoxic agents. Generally, the majority (n=7(85%)) felt more confident to prepare cytotoxic drugs after the implementation of the intervention.

Discussion

The results showed a general improvement in the participants' basic knowledge of cytotoxic agents but no statistically significant differences at the 3 stages of the study (see Table 1). Noticeably, due to a small number of volunteers and a short duration of study, they might cause the interference of study outcomes and lead to non-significant values. This lack of differences may be explained by the fact that most of the participants may have already had some basic knowledge due to their regular work routines involving the preparation of cytotoxic drugs. Also, participants may have discussed and shared items of knowledge during the study period. Knowledge retention was encouragingly maintained over a period of one month. However, there was no correlation between high levels of knowledge and good work skills as other factors in the development of good skills may have been involved, such as self-motivation, frequency of practice, workload, and adequate facilities (Sessink et al, 1995; Vanderbroucke and Robays, 2001). After exposure to a lecture and demonstration, the participants' performances in all skills in cytotoxic drugs preparation improved. These skills included hand soaping, rinsing, and drying in aseptic hand-washing techniques, a standard uniform, self-protection equipment, contamination avoidance, and laminar air flow preparation in vertical laminar air flow hood, and dosage calculation, needle insertion techniques, mixing techniques, labeling, and traced hazardous vial elimination in hazardous drug vial preparation. This improvement could be due to participants previously performing routine cytotoxic drugs preparation based on inaccurate and/or inappropriate basic knowledge and understanding. The implementation of the standard checklist brought about a correction of this situation and a resultant improvement in skills.

Generally, the skills were maintained over the duration of the study except in the case of the 1 month post-test of aseptic hand-washing (see Table 2). This may have been due to the lack of recognition by the participants of the importance of this skill and the difficulties experienced in learning and maintaining the cytotoxic drug preparation techniques. If this is so, then it emphasizes the necessity for hospitals and other health institutions to adopt and maintain strict adherence to basic principles in the preparation of cytotoxic drugs. Such adherence is a significant factor in the efficient preparation for the benefit of patients and carers (Sorsa et al, 1988; Sessink et al, 1992; Sessink et al, 1992, and Ensslin et al, 1994).

The attitudes of the participants to the intervention illustrated that they regarded the implementation of a standard checklist of the preparation of cytotoxic drugs as an essential tool for hospital staff. They considered it was important to improve the quality of preparation and to produce a safe work environment without hazardous contamination. However, they believed that the frequency of the intervention should be increased, evaluations needed to be made regularly to maintain standards, and the content required modification.

There are a number of limitations of the study. Firstly, the number of participants in the study was relatively small and may not reflect the larger picture of cytotoxic drugs preparation. Secondly, the judgments of the assessors require standardization because of their different professional backgrounds and work experiences. Thirdly, more study sites are needed to make the results more reliable. Finally, there needs to be consideration of a range of external factors that may impact on the implementation of a standard checklist of cytotoxic drugs preparation, such as busy workloads, quality control of facilities and equipments, and hospital policy.

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References

American Society of Hospital Pharmacists: ASHP guideline on quality assurance for pharmacy-prepared sterile products. *Am J Hosp Pharm* 2000; 47: 54-72.

American Society of Hospital Pharmacists: ASHP technical assistance bulletin on handling cytotoxic and hazardous drugs. *Am J Hosp Pharm* 2004; 47: 1033-49.

Crudi CB. A compounding dilemma: I've kept the drug sterile but have I contaminated myself? *NITA* 1989; 3: 77-8.

Crudi CB, Stephens BL, Maier P. Possible occupational hazards associated with the preparation/administration of antineoplastic agents. *NITA* 1982; 5: 264-6.

Curran CF, Lure JK. Ocular adverse reactions associated with adriamycin (doxorubicin). Am J Ophthalmol 1989; 108: 709-11.

Ensslin AS, Stoll Y, Pethran A, et.al. Biological monitoring of cyclophosphamide and ifosfamide in urine of hospital personnel occupationally exposed to cytotoxic drugs. *Occup Environ Med* 1994; 51: 229-33.

Falck K, Grohn P, Sorsa M, et.al. Mutagenicity in urine of nurses handling cytotoxic drugs. *Lancet* 1979; 1: 1250-1.

Harris CC. The carcinogenicity of anticancer drugs: a hazard in man. *Cancer* 1976; 37: 1014-23.

Harrison BR. Risks of handling cytotoxic drugs. In: Perry MC, ed. *The chemotherapy source book*. 3rd ed. Philadelphia: Lippincott, Williams and Wilkins; 2001: 566-82.

Knowles RS, Virden JE. Handling of injectable antineoplastic agents. *Br Med J* 1980; 281: 589-91.

Ladik CF, Stoehr GP, Maurer MA. Precautionary measures in the preparation of antineoplastics. *Am J Hosp Pharm* 1980; 37: 1184-86.

Luci A, Thomas H, Joseph H. ASHP reports Handling hazardous drug. ASHP guidelines on handling hazardous drugs. *The united states of America* 2006: 1172-1191.

McFarlane A. Ophthalmic problems in staff handling cytotoxic drugs. *Aust J Hosp Pharm* 1986; 16: 145. Letter.

McLendon BF, Bron AJ. Corneal toxicity from vinblastine solution. *Br J Ophthalmol* 1978; 62: 97-9.

National Institute for Occupational Safety and Health. NIOSH alert: preventing occupational exposure to antineoplastic and other hazardous drugs in health care settings. www.cdc.gov/niosh/docs/2004-165/ (accessed 2006 Mar 14).

Pharmacy Group of Cancer Diseases, Hospital Pharmacy Organization, Thailand. Group of Thai Oncology Pharmacy Practitioners. *Cytotoxic preparation techniques*, 2005.

Pharmacy Unit, Sappasithiprasong Hospital. *An annual report of cytotoxic drug utilization. Sappasithiprasong Hospital Committee. Sappasithiprasong Hospital*, Thailand: 1-18.

Reynolds RD, Ignoffo R, Lawrence J, et.al. Adverse reactions to AMSA in medical personnel. *Cancer Treat Rep* 1982; 66: 1885.

Sessink PJ, Anzion RBM, vanden Broek PHH, et al. Detection of contamination with antineoplastic agents in a hospital pharmacy department. *Pharm Weekbl Sci* 1992; 14: 16–22.

Sessink PJ, Boer KA, Scheefhals APH et al. Occupational exposure to antineoplastic agents at several departments in a hospital. Environmental contamination and excretion of cyclophosphamide and iphosfamide in urine of exposed workers. *Int Arch Occup Environ Health* 1992; 64:105–12.

Sessink PJ, Kroese ED, Kraren HJ, et al. Cancer risk assessment for health care workers occupationally exposed to cyclophosphamide. *Int Arch Occup Environ Health* 1995; 67: 317-23.

Sessink PJ, Kroese ED, Van Kranen HJ, et.al. Cancer risk assessment for health care workers occupationally exposed to cyclophosphamide. *Int Arch Occup Environ* Health 1995; 67: 317-23.

SorsaM, Pyy L, Salomaa S, et al. Biological and environmental monitoring of occupational exposure to cyclophosphamide in industry

and hospitals. *Mut Res* 1988; 204: 465–79.

Valanis BG, Hertzberg V, Shortridge L. Antineoplastic drugs: handle with care. *AAOHN J* 1987; 35: 487-92.

Valanis BG, Vollmer WM, Labuhn KT, et.al. Association of antineoplastic drugs handling with acute adverse effects in pharmacy personnel. *Am J Hosp Pharm* 1993; 50: 455-62.

Vandenbroucke J, Robays H. How to protect environment and employees agonist cytotoxic agents. *J Oncol Phar Practice* 2001; 6: 146-52. Http://www.asia4safehandling.org/preparation.html: Access on October 19th 2009.