MEDICOR CANCER CENTRES

December 29, 2016

Ms. Lisa Mueller
Investigator
Investigations and Resolutions
The College of Physicians and Surgeons of Ontario
80 College Street
Toronto ON M5G 2E2

File #LM/7214399

Dear Ms. Mueller:

Re: **Report of Heather Arnott, Community Practice Advisor, Ontario College of Pharmacists**

I write this letter in response to Ms. Arnott's letter of May 6, 2016. Ms. Arnott's main concerns relate to:

1) "incomplete containment measures" for carboplatin chemo, "without the appropriate 'ante' room"; and
2) aseptic preparation of drugs to avoid bacterial and fungal contamination.

Incomplete Containment: Protection of Staff and others in the Clinic

Ms. Arnott expresses concern around the protection of staff and others in the Clinic arising from the preparation of carboplatin doses in the clinic. She goes on to detail several levels of control which are expected in such environments, all of which we comply with (to the extent the requirement is applicable to Medicor's facility).

Ms. Arnott speculated during the interview at Medicor on February 10, 2016 that our lack of negative pressure in the Biological Safety Cabinet (BCS) room would lead to carboplatin being released through the air outside the room. It was carefully explained to Ms. Arnott that negative pressure is not required since *we do not use volatile chemotherapy drugs*.

The purpose of "negative pressure" is to contain vapours released from volatile hazardous drugs (liquids and aerosols will be contained in the certified BSC, but vapours can escape). To be clear, our primary chemo drug is carboplatin which is known to be non-volatile, with rare use of gemcitabine which is also non-volatile. Please see attached carboplatin and gemcitabine MSDS which show no measurable vapour pressure of either of these drugs.

Nevertheless, we took Ms. Arnott's speculative concern very seriously, as it was implied that carboplatin could be circulating through the air and could cause serious contamination of our entire office, putting staff and patients at risk. This speculation is repeated in Ms. Arnott's report.

In order to confirm that Medicor's system is safe, we promptly retained an independent engineering firm (EH&S Consulting Inc.) with special expertise and experience in hazardous drug monitoring, to confirm the safety of our chemo preparation. Prolonged air sampling inside and outside the BSC room (compounding room) conducted during and after carboplatin chemo preparation on February 24, 2016 shows the concentration of carboplatin in the air to be undetectable, establishing that lack of negative pressure is not a concern at all as we originally stated (copy of EH&S Consulting Inc. report dated March 18, 2016 is enclosed).

Regarding lack of formal ante room at our facility, an ante room is also not required for the same reasons stated above. *BCCA Pharmacy Standards for Hazardous Drugs* (Nov 2008) allows the use of non-negative pressure BSC rooms without ISO certified ante-rooms under certain conditions:

> *"The cleanroom or buffer room housing the BSC must be an ISO Class 7 environment physically separated from an adjacent ISO Class 7 or better ante-area. However,* ***in facilities that prepare a low volume of hazardous drugs****, the use of two tiers of containment (example: closed-system vial-transfer device within a BSC or CACI that is located in a* ***non-negative pressure room****)* ***is acceptable****"*

This is a general standard referring to all chemos (including volatile chemos), and Medicor uses only non-volatile chemos. We prepare a very low volume of chemos (typically averaging less than 10 doses per week in 2016). We always use "closed system transfer devices" or CTSDs, as Mr. Arnott noted. Therefore we are in compliance with this *BCCA* guideline. Furthermore we have proven by independent engineering testing that chemo containment is up to standard, and there is no risk posed to people present in the office. In any event, due to the recent expansion of our office, we now have moved all non-chemo related items and personnel out of the current "ante room" so that there is now a formal ante room in place.

All other comments relating to negative pressure are thus also not relevant to our practice. For example *BCCA Pharmacy Standards for Hazardous Drugs* (Nov 2008) states that:

"Many HDs have sufficient vapour pressures that allow volatilization at room temperature, therefore should be stored within a contained negative pressure room…"

Since we exclusively use non-volatile chemos, hazardous drugs and hazardous waste do not need to be stored in a negative pressure area.

Ms. Arnott's report goes on to state that the BSC we are using "may not be the most appropriate choice", and a comment is made about the BSC venting back into the room. However, the type of BSC that we use (Class II, type A2/B3) falls within the *CCO guidelines* (*Safe Handling of Parenteral Cytotoxics,* Apr 13, 2007), which state that "A Class II Type B2 is preferred but Types A2 and B1 are acceptable under certain conditions". Since we only use non-volatile chemos, our BSC is acceptable and safe.

Aseptic Preparation

Ms. Arnott's report raised a valid concern about preparation of mesna doses in advance of administration, with potential for contamination. Medicor always uses 0.2 micron bacterial filters on every mesna syringe before administration, and syringes are refrigerated, which should address the concern. We have never had an incident of an infection resulting from our current practice. Regardless we have accepted Ms. Arnott's observation and made immediate changes, so that mesna is now prepared daily for immediate use only.

Recommendations accepted:

While certain of Ms. Arnott's observations are either not relevant to Medicor's current practice, certain of her other observations have been reviewed and implemented as follows:

1. Gloving procedure for chemo preparation changed to from inner ASTM certified gloves to 2 layer ASTM certified gloves. Current black outer gloves (that meet the safety standards but are not certified) are being phased out.
2. Monthly cleaning procedure for the compounding room will be implemented, with logging.
3. BSC cleaning procedure has been revised to include commercial 2 stage chemo cleaner (sodium hypochlorite followed by sodium thiosulfate), then distilled water, then sterile alcohol.
4. Compounding pick list will be computer generated each week according to the chemo doses that are to be administered.
5. Internal hazardous drug compounding audit will be performed (using a commercial ChemoTEQ kit containing vials of fluorescein and ultraviolet light) to ensure no spillage is occurring during routine compounding, and compounding technique will be adjusted if needed. The College is welcome to have a video recording of this internal audit.
6. Mesna syringes will only be prepared <u>daily for immediate use</u>, and will no longer be stored before administration. We will continue to use the 0.2 micron bacterial filters regardless, as a second layer of safety.
7. Regarding a compounding course, a review of Medica.ca website shows that "MEDISCA is a leading Health Canada and FDA-registered supplier of quality pharmacy compounding products." I am not able to find any Canadian courses offered by this company to physicians for

hazardous drug handling. For medical doctors, the principle of lifelong self-education is well-established and one I adhere to zealously. In the absence of an available formal hazardous drug handling course that will accept a physician student, I believe this principle of self-education should continue to be respected by the College in the case of my chemo-immunotherapy practice. We also we consider Ms. Arnott's suggestion to hire a pharmacy technician to take over the chemo compounding at such time that patient volume increases significantly.

There are a few inaccuracies or possibly typos in the report:

1) Ms. Arnott's report states that the chemo compounding room has "**suspended ceiling tiles**". The BSC compounding / BSC room actually has a closed/sealed painted ceiling, not tiles. Standard ceiling tiles would shed a large number of particles into the compounding room, and are unacceptable. Ms. Arnott had taken photos of the room during her inspection, which if reviewed again, should confirm my statement.
2) Ms. Arnott's report states that **"there was no measuring or monitoring of differential air pressure for** the office, compounding room, or **BSC**…" While we do not need pressure monitoring for the office or compounding room for the reasons explained above regarding negative pressure (we do not use volatile chemo), the BSC does indeed have a pressure differential monitor gauge. This should be evident in the photos Ms. Arnott took of our compounding room. It is also noted on the BSC certification reports which we presented to Ms. Arnott (see "magnehelic" pressure reading on the report).
3) Ms. Arnott's report states that our chemo gowns should be replaced with impervious gowns for handling hazardous drugs. In fact we do use impervious Covidien brand gowns specifically designed for chemotherapy.
4) Ms. Arnott's report states that I opened the chemo compounding room door with a gloved hand. This is correct however, I was wearing double gloves, and I removed the outer glove before opening the door in order to prevent potential contamination of the door handle.

In summary, we are pleased that Medicor that did not have any deficiencies which were serious, or placed patients / staff at risk of harm. All reasonable critiques or those supported by the relevant standards have been accepted and implemented, and our policies /procedures revised to ensure compliance.

I sincerely appreciate Ms. Arnott's detailed report.

Sincerely,

Akbar Khan, M.D.

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Ontario College of Pharmacists

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Memo

TO:	**Lisa Mueller, Investigator, CPSO**
DATE:	**6 May, 2016**
CC:	
FROM:	**Heather Arnott, Community Practice Advisor, Ontario College of Pharmacists**
RE:	**Medicor Cancer Centre – site visit February 10, 2016.**

I have been employed as an Inspector (now titled Community Practice Advisor) with the Ontario College of Pharmacists since 1988. I visit community pharmacy sites to assess the operational standards of the pharmacy and to assess and provide mentoring to the pharmacists on duty in order to ensure appropriate patient care is being delivered.
In addition, I perform the site visits/assessment of community pharmacies that provide sterile compounding prescription services to patients. I also inspect the Drug Preparation Premises facilities – which provide non-patient specific sterile and non-sterile compounding services to hospitals (when adequate compounding facilities are not available within the hospital site).
I have completed a certificate program (2014) and continuing education with respect to aseptic technique and sterile compounding practices.

I certify that I have been informed and I understand that although the College of Physicians and Surgeons of Ontario (CPSO) has retained me to provide an independent opinion, my duty in doing so is not to the CPSO, nor is it to the member under investigation. My duty is to assist the Inquiries, Complaints and Reports Committee and the Discipline Committee on matters within my expertise.

Based on my observations of Dr. Khan's practice and procedures within the Medicor Cancer Centre premises, 4576 Yonge St., Toronto on February 10, 2016, I would state that the practice does not entirely meet the standards of practice expected for the preparation of chemotherapy.

The pharmaceutical ingredient being used in Dr. Khan's practice is CARBOPLATIN, which is recognized internationally as a hazardous drug (HD), in that inadvertent exposure to the drug poses a health risk. I have included a reference to the National Institute for Occupational Safety and Health document which categorizes HD and provides guidance for safe handling practices. Carboplatin is an antineoplastic agent and also has teratogenic risks.
http://www.cdc.gov/niosh/docs/2014-138/pdfs/2014-138_v3.pdf
With the preparation of the carboplatin doses, the primary concern is the protection of staff and people in the clinic from exposure to the HD. The secondary concern is that the injection is prepared in an aseptic manner so that the patient is not exposed to any bacterial or fungal contamination.

When handling/compounding hazardous drugs, there are several levels of control which must be implemented to safeguard the compounder and everyone else in the facility:
1) Engineering Controls - equipment and room design to isolate the compounder and other personnel from the hazard (Biological Safety Cabinet or Containment Aseptic Compounding Isolator, negative room pressure, using Closed System Transfer Devices – CSTD)
2) Administrative and workplace practices (handwashing, cleaning routine, safe work practices)
3) Personnel Protective Equipment (Chemotherapy tested gown, chemotherapy tested gloves, respirator, eye and face protection, shoe covers)

OBSERVATIONS AND DISCUSSION:

1) Engineering Controls - Compounding room, Biological Safety Cabinet, CSTD:

The compounding room was a small 'closet' size room within an office. The office had carpeted floors, a desk, infusion pump apparatus, side table and chairs and a shelving unit which was used for general storage, storage of some compounding supplies and garb.

The compounding room had suspended ceiling tiles, painted walls, ceramic tiled/grouted floors. It had a window and windowsill and shelf units on the wall. An open waste container (for gowns/gloves etc) and a closed cytotoxic waste container was also contained in this area. There was a compounding space (protected workstation – Nuaire Biological Safety Cabinet (BSC) – Type II / A/B3) however the unit was only turned on for about 30min prior to compounding. The unit was not exhausted to the exterior of the building; rather, the air was passed through a HEPA filter then introduced back into the compounding room. The room was supplied with air via a regular ceiling air vent.

The carboplatin was stored in a protected box inside the compounding room. The room did not have negative air pressure relative to other areas of the office. There was no measuring or monitoring of differential air pressure for the office, compounding room or BSC, although the BSC did have a pressure gauge to indicate it was operating properly. Dr. Khan indicated that he regularly cleaned the BSC unit using a 2 step process, but that the room itself (floor, walls, shelves etc.) was not regularly cleaned.

The BSC was last inspected in October 2015 and was being inspected every 6 months. This was a mechanical check to ensure the unit was operating appropriately. This was not a validation that the workspace was in compliance with ISO Class 5 standards (would include airborne particle counts and surface sampling to 'prove' it was clean)

Dr. Khan did use a CSTD (vented filter) when preparing the carboplatin doses.

The compounding room was a very small space – without the appropriate 'ante' room which would allow for appropriate storage of supplies, and would have a defined 'clean' and 'contaminated' side with respect to the HD.

The compounding environment for HD should be a containment environment (negative air pressure relative to surrounding areas at **all** times) This area will be used to store the supply of medication (carboplatin) prior to compounding. The room surfaces shall be cleaned monthly (using a 2 step process to deactivate and decontaminate all surfaces)

There should be a designated area for removal of HD contaminated garb, and storage of waste within the 'contaminated' area.

Air introduced into the compounding room is to be HEPA filtered.

Surfaces (walls, floors, ceilings) are to be caulked (sealed), smooth and impervious in order to be thoroughly cleaned and to prevent backflow of any contamination into other areas of the clinic.

HD waste containers are to be within a consistently negative pressure area and should only be removed from the room once they are properly sealed.

- The design of the compounding room needs to be reviewed as it does not provide adequate protection from HD exposure.
- The BSC being used by Dr. Khan may not be the most appropriate choice, given the space constraints of the clinic/office/compounding room. Using the following questionnaire, a more appropriate Primary Engineering Control could be determined:
  http://www.labconco.com/scout-ventilation-equipment-selector?utm_source=scout-ventilation-selector&utm_medium=tool&utm_campaign=Scout
  http://www.labconco.com/category/class-ii-type-b2-total-exhaust
  OR: CACI – compounding aseptic containment isolator
  https://www.cleanroomworld.com/articles/Web%20site%20Definitions%20Pharmacy%20Equip.pdf

2) Administrative and Workplace Practices
   - Safe Work Practices - Dr. Khan has done research and has been self taught in the handling practices for sterile compounding and for handling HD. I would recommend that if Dr. Khan is to continue to compound the intravenous medications himself, that it would be prudent to attend a practical training session (eg. Medisca.ca) or to employ a staff member who has current/validated sterile HD compounding experience.

Staff should be assessed regularly for their HD compounding technique using a verification test kit (eg. ChemoTEQ - http://www.valiteq.com/cart/100C)

- Dr. Khan should have a 'pick list' of all items that will be used for preparation, so that there is no need to exit the room once compounding has started. He initially forgot the chemo prep pad and had to exit the compounding room to retrieve one.
- Spill protocol
  While we were observing Dr. Khan preparing the carboplatin doses, he had an accidental spill. He did have a chemo (plastic backed) prep pad to cover the compounding area, however now it was contaminated. He removed the contaminated pad and placed it into the HD disposal bag, and sprayed the area with sterile 70% isopropyl alcohol (IPA). He then opened the compounding room door (with gloved hands) and called out to us (in the office) to retrieve another prep pad from the shelving. Had we not been there, he would have exited the room and walked to the shelving unit.
  This incident was particularly unnerving – since the room is not a proper containment environment (negative pressure) and there was no ante room separating us from the compounding, we would have been inadvertently exposed to carboplatin, due to the air washing out of the room when the door was opened. The door handle would likely be contaminated as well.
  Cleaning after a spill should be a 2 step process...1) Deactivate - done by wiping with pre-moistened wipes (preferable a detergent or bleach solution, then 2) Decontaminate/disinfect with sterile 70% IPA. Wiping is preferred over spraying, as it is less likely to spread the contamination.
  Contaminated prep pad, cleaning materials and gloves should be discarded and the waste container stored within a negative pressure area, the waste bag properly sealed before being removed from the negative pressure area.
  There was no emergency eye or handwash station in the immediate area.
- Decontamination and cleaning of BSC and containment of all HD materials (gloves, gown, mask, used vials, sharps, prep pad etc.) should be done immediately.
  The patient medication iv bags were wiped down then labelled and placed into yellow plastic bags, sealed and placed into a transport bin. On the day I observed Dr. Khan, he indicated that he would do the compounding area clean-up later, as the patients needed their medication to be infused right away. He removed his gown, gloves, mask etc and placed them in the yellow disposal bag in the compounding room.
- A regular cleaning routine should be implemented. A monthly, weekly and daily routine should be developed for floors, walls, shelves, equipment etc.

3) Personnel Protective Equipment
   Dr. Khan did wear the following Personnel Protective Equipment (PPE) – hair bonnet, shoe covers, disposable gown (tied at the back), 2 pairs of gloves (blue nitrile gloves and black 'grease monkey' gloves) and a fitted N-95 mask.
   However, the gown should be replaced with an impervious (special for handling HD) and the black 'grease monkey' gloves should be replaced with ASTM tested (impervious to HD) chemo gloves. Dr. Khan may be inadvertently exposing himself to carboplatin.

ADDITIONAL REFERENCES FOR CONSIDERATION:

Standards for Pharmacy Compounding of Hazardous Sterile Preparations (NEW)
http://www.ocpinfo.com/library/practice-related/download/NAPRA%20Hazardous.pdf

Best Practices for the Safe Handling of Hazardous Drugs (2015)
http://www.worksafebc.com/publications/health_and_safety/by_topic/assets/pdf/bk153.pdf

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Model Standards for Pharmacy Compounding of Non-Hazardous Sterile Preparations
http://napra.ca/Content_Files/Files/Mdl_Stnds_for_Pharmacy_Compounding_NonHazardous_Sterile_Preparations_Dec2015_FINAL.pdf

Current OCP Community Pharmacy Operations Assessment Criteria:
http://www.ocpinfo.com/library/practice-related/download/OperationalCriteria.pdf (pgs 36-41)

It would be my opinion that in light of the incomplete containment measures being put into place in the Medicor Cancer Centre, Dr. Khan, staff and patients (and visitors) may have been inadvertently exposed to carboplatin.

(Dr. Khan also prepared doses of MESNA in his facility. I did not observe Dr. Khan compounding this as he prepared the doses the day prior to our visit. Of concern is that this medication was prepared in multiple syringes for each patient, to be administered on subsequent days. Dr. Khan indicated that he used the same compounding room and BSC for these doses. I would be concerned that the technique used, the ambient air and the room itself would be a source of contamination of these syringes. Dr. Khan has not validated that he has appropriate aseptic technique (fingertip testing, media fill testing) and that the room has minimal particle burden (surface sampling, viable air particle sampling) to minimize the risk of these injections being contaminated.
With this type of compounding, maintaining sterility and protection of the product is the primary concern.)