December 21, 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: Dr. Akbar Khan

I write this letter in response to Ms Arnott's letter of May 16, 2016.

By way of background, I would first like to point out to the Committee that the standards for chemo preparation and administration do vary across North America, and are based on opinions and recommendations from various experts, dealing with administration of a multitude of chemo agents (both volatile and non-volatile).

Most standards regarding policies and procedures, personal protective equipment, ventilated cabinets, syringes and intravenous sets, transport and labeling, and education and training are **not requirements but guidelines**, and **often are NOT evidence-based**. In fact:

"…no studies have been carried out examining the effectiveness of these precautions in reducing rates of cancer, adverse reproductive outcomes, or acute adverse effects associated with exposure to cytotoxic drugs among health care workers…"

Safe Handling of Parenteral Cytotoxics: Recommendations for Ontario, http://ascopubs.org/doi/full/10.1200/jop.091014

Therefore, there has to be flexibility in judging my practice against various standards. It is important to keep in mind that Medicor's standards may be different due to our unique practice e.g. we only use non-volatile chemo drugs (mainly carboplatin and occasional gemcitabine) which require fewer handling precautions. This should not be interpreted as a deficiency of any kind. Deviation from a guideline or standard does not necessarily indicate a deficiency, if it is reasonable and there is no evidence that harm would result from this deviation.

MEDICOR CANCER CENTRES

The main concerns in Ms. Arnott's report are:

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

Ms. Arnott speculated during the interview that our lack of negative pressure in the BSC 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 chemo 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). 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 this speculative concern very seriously, as Ms. Arnott was implying that carboplatin would be circulating through the air and could cause serious contamination of our entire office, putting staff and patients at risk.

In order to prove that our system was 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 report dated March 18, 2016 is enclosed).

Regarding lack of proper 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****"*

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This is a general standard referring to all chemos (including volatile chemos), and we only use 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".

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 states 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 raises a valid concern about preparation of mesna doses days in advance of administration, with potential for contamination. We always use 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 her finding and made immediate changes, so that mesna is prepared daily for immediate use only.

Recommendations accepted:

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 daily for immediate use, 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) The 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) The 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) The 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) The 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 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 our policies /procedures revised to ensure compliance.

I am thankful for Ms. Arnott’s detailed report.

Sincerely,

Akbar Khan, M.D.

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