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BOARD OF PHARMACY
State of North Dakota

Jack Dalrymple, Governor

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11:10 AM – Wednesday - March 14, 2012
Harvest Room – State Capitol

Chairman Koppelman, members of the Legislative Management's Administrative Rules Committee, I am Howard C. Anderson, Jr, R.Ph., Executive Director of the North Dakota State Board of Pharmacy.

In response to the issues you enumerated in your February 29th, 2012 hearing notification these rules are on pages 135-164 of your printed material:

1. These rules did not result in a statutory change made by the Legislative Assembly.

2. These rules are not related to any federal statue or regulation, although they do address compliance with the United States Pharmacopeia [UPS] Standards on Sterile and Non-sterile Pharmaceutical Compounding. When North Dakota adopts a rule, it becomes the standard of practice, rather than USP 795 and 797 standards, which might be applied by accreditation agencies when reviewing North Dakota hospitals and other compounding facilities.

3. This rule has had a very extensive adoptive process. We began discussing this rule over three years ago and it has been discussed at two pharmacist conventions. The first discussion of changing compounding standards began way back in 2003. We have followed the USP committee process through that period of time. A hearing was scheduled on this rule and advertised for May 2010 and January 2011. Because of the extensive comments we received at that time, the Board decided to hold it and re-advertise for a hearing once the changes were made, which was held November 17, 2011. What you see here is the final adoption as a result of the comments we received before, during and subsequent to the November 2011 Hearing.

4. I have included in this packet, a consideration of comments made relative to this rule. You will see in the final analysis there was some disagreement on what should be in the final rule and the rational for why the final language was adopted. All of the final language was discussed with compounders in North Dakota. The preponderance of those doing this type of work agreed with the version that was finally adopted.

5. The approximate cost of giving public notice and holding the hearings was $3,957.36. This is higher than usual, but we did advertise three times, although two of those were in conjunction with other rule considerations. We did feel that the extensive nature of the rule and the affect that it had on pharmacy practice made this process necessary. Unfortunately, some do not find comments necessary until after decisions have been made.

6. This rule affects both non-sterile and sterile pharmaceutical compounding. Compounding applies to those prescriptions written by a practitioner which ask the pharmacist to make a pharmaceutical preparation that is not available commercially. These compounds are made for a specific patient and tailored to that patient's specific needs. In the case of a non-sterile compound it might consist of mixing one or several ingredients together in an ointment, lotion or oral preparation. In the case of sterile compounding, it might consist of mixing a complicated formula to supply parenteral nutrients to a patient, to prepare eye drops or a specifically tailored injection to be used just prior to surgery. Significant amounts of sterile compounding are done in chemotherapy, where about 50% of the usage is off-label and the specific physician's request for an injectable chemotherapy drug is prepared by a pharmacist, or a registered pharmacy technician supervised by a pharmacist, for administration to the patient. We have developed many techniques about the best way to compound preparations for effectiveness and the safety of the patient. This practice has evolved as the complexity and potency of our medications has evolved and the profession feels it is time to standardize these practices in a rule.

7. We did prepare a regulatory analysis for this rule, as there will be and for the most part have already been, some significant costs associated with pharmacies coming up to speed in both the non-sterile and the sterile compounding requirements. A copy of that regulatory analysis is attached.

8. The Board of Pharmacy is exempt from preparing a small entity regulatory and economic impact analysis. However, we did prepare one when we began the first rule hearing back in May 2010, as we wanted to be sure that the profession knew what those issues might be. A copy of this analysis is also attached.

9. These rules will not have any effect on state revenues and we do not expect any significant effect on Board of Pharmacy expenditures, as compliance with these rules will be ascertained during our regular pharmacy inspections.

10. No takings assessment was prepared as there is no private property being taken for the purpose of this rule.

11. These rules were definitely not adopted as any emergency rule. The process has been a long and involved one, and as the profession has been very involved, there were no exigencies which would have required any emergency rule making.

Compounding Standards-Rule Hearing November 17, 2011- Consideration of comments

Comments from Jesse Rue:

Page 2: 1. Definitions; e); (4); (ii); a.; (1); V.

"V. Must be immediately and completely administered by the person who prepared it, or immediate and complete administration is witnessed by the preparer."
-The concern in the language is that large volume IVs may continue passed the shift of the preparer or if the IV may begin in the ED and the patient may be transferred to the floor while still on the IV to different care.

-In <USP 797> on p 343 it states under the '5. ': "Unless immediately and completely administered by the person who prepared it or immediate and complete administration is witnessed by the preparer, ***the CSP shall bear a label listing patient identification information, the names and amounts of all ingredients, the name or initials of the person who prepared the CSP, and the exact 1-hour BUD and time."***
The Board agrees that it would be appropriate to add the bolded portion into the language as to recognize the 'real world' setting of shift/staff care changes in order to accommodate the proper administration of Immediate-Use CSPs.

Page 11: 4.Compounding Process for Compounded Sterile Preparations; e); (2)

"(2) Don proper garb including shoe covers, head and facial covers, face mask, and non-shedding gown"
-The concern is there may be some leeway in the recommendations of appropriate garb according the what the manufacturer may recommend (i.e. a CAI the manufacturer may not require face mask or shoe covers.)

-In <USP 797>, it does state on page 344, "PPE should include gowns, face masks, eye protection, hair coves, shoe covers or dedicated shoes, double gloving with sterile chemo-type gloves, and compliance with manufacturers' recommendations when using a CACI.

The board agrees and language has been added to allow for evidence from the manufacturer of the primary engineering control that this is not necessary. **If the manufacturer of the primary engineering control has research and documentation demonstrating that some of these things are not necessary, they are not required.**

Page 14: 6. Equipment Specific for Sterile Compounding; b); (3) concerning Environmental Monitoring:
" Where High Risk sterile preparations are being compounded air sampling via sterile nutrient agar plates or suitable electric air samplers must be performed semi-annually at locations judged by compounding personnel to be the most prone to contamination during compounding activities."
-The question is if he is correct in saying the passage applies only to high risk compounding areas?

-Yes. This particular passage labeled (3) pertains to the high-risk CSPs. However, ALL areas that are compounding sterile preparations must have the air quality re-certified every 6 months as indicated elsewhere in the draft and media-fill testing must be performed annually for low and medium risk compounding and every six months for high risk compounding, as indicated in those sections.

Page 15: 11. Hazardous drugs as compounded sterile products (CSPs): e); (1).

(1) When closed-system vial-transfer devices (CSTDs) are used, they shall be used within the ISO class 5 environment of a BSC or CACI. This may be done in a non-negative pressure room when this two tier containment method is used.
-The question asks if that means one may use a CSTD if our BSC is not in a negative pressure room or ISO 7 room and still be compliant.

According the <USP 797> p 348 under "Placement of Primary Engineering Controls" it states "PECs shall be located within a restricted access ISO Class 7 buffer area." Additionally, on pg 343 under "Hazardous Drugs as CSPs" it states, "When CSTDs are used, they shall be used within the ISO Class 5 environment of a BSC or CACI. The use of a CSTD is preferred because of their inherent closed system process. In facilities that prepare a low volume of hazardous drugs, the use of two tiers of containment (e.g., CSTD within a BSC or CACI that is located in a non-negative pressure room) is acceptable.

-Therefore, it is the board's interpretation that you would still be compliant if a CSTD is used in a BSC that is in a non-negative pressure room. However, one would not be compliant using a CSTD in a BSC that is not in an ISO Class 7 environment or better. Remember that some BSCs have the ISO Class 7 chamber built unto them.

Comments from Jocelyn Mohs

Page 15: 11. Hazardous drugs as compounded sterile products (CSPs):

1. Is the term "Hazardous Drugs" defined elsewhere in the rules?

The Board agrees this definition is need and one has been added under definitions.

2. Under 12 (b) Hazardous drugs shall be stored and prepared separately from other ~~(inventory)~~ non-hazardous drugs in a manner to prevent contamination and personnel exposure.

   Maybe this is already addressed in section (e), but I just think it's important to not be making pre-meds and other non-chemo drugs in the same hood as we make chemotherapy because we are likely contaminating those non-chemo drugs. It's been a concern of mine where I currently work. I think it needs to be stressed.

The board agrees and this change has been made.

Comments from Joel Aukes

(2) f) (4) (on page 9) – Pre-packing

Now 2 g); (3); ii

ii. " If a component is transferred from the original container to another, the new container must be identified with the component name, weight or measure, the lot or control number, the expiration or beyond-use date, and the transfer date."

Would splitting tablets, for pre-packaging, be considered "manipulation" ? If so, there should be some wording added to differentiate "splitting" from "manipulation".

Board Comments:

Tablet splitting is not considered compounding and therefore is not addressed here. We have added "tablet splitting" under the "compounding" definition at 1. e) compounding does not include: tablet splitting, prepackaging .....

3) a) through k) (on page 11) Non-sterile compounding.

Should be deleted. This is standard practice not defined in the NDBOP rules for filling other types of prescriptions.

Board Comments

It was moved by Pharmacist Thom and seconded by Pharmacist Ziegler to leave the section intact except to delete ~~the facility and~~ under k)

4) a) through c) (on page 11) – Sterile compounding.

Should be deleted. This is standard practice not defined in the NDBOP rules for filling other types of prescriptions.

Board Comments

It was moved by Pharmacist Thom and seconded by Pharmacist Ziegler to leave this section intact as the Board feels the reinforcement is valuable.

4) d) (on page 11) – Sterile compounding.

The number and type of Primary Engineering Controls are already specified in the rules. If a facility installs operates and maintains these controls according to the manufacturer's standards this wording is not necessary. The manufacturers should set these standards of practice for their products as the NDBOP can not possible be familiar with or keep up-to-date on all the available products and their associate specifications.

Board Comments

Pharmacist Ziegler stated that she feels the language is reasonable and makes the rule clearer. The Board concurred.

4) e) (2) (garbing) and 4) e) (3) (donning gloves) (on page 11) – sterile compounding.

It is my professional opinion that the gloving and garbing wording be deleted from the rules. I have not seen any studies showing that taking these steps increases public safety or decreases morbidity / mortality over using "standard aseptic technique" when compounding low / medium risk parenterals with the appropriate primary engineering controls. My professional opinion is that the improvement to public safety is negligible, if at all. Therefore, this requirement would add unneeded cost and time burden on pharmacies with little, if any, benefits to public safety.

Gloving and gowning should be dependent on each specific facility's configuration risk level, configuration and type(s) of Primary Engineering Controls used. Therefore, should be developed and set by each facility in their Policies and Procedures.

Board Comments

Pharmacist Ziegler stated that this procedure is intended to reduce particles and microbial counts and studies are why USP adopted this procedure. A change has been made to accommodate BSCs if the manufacturer of the primary engineering control has research and documentation demonstrating that some of these things are not necessary, they are not required.

4) f) (1) through (2) (sterile isopropyl alcohol) (on page 11) – Sterile compounding.

It is my professional opinion that the use of sterile isopropyl alcohol **not** be required for the cleaning of compounding surfaces. There is no evidence, scientific or anecdotal, that contamination has been caused by the use of standard non-sterile, 70% isopropyl alcohol. The mandate of utilizing sterile isopropyl alcohol would again, unnecessarily, increase the costs and barriers to sterile compounding without any beneficial effect on public safety.

Board Comments

Although there is some disagreement, the majority of North Dakota Compounding Pharmacists have come to accept sterile isopropyl alcohol as evidence has shown, that spores can survive in non-sterile isopropyl alcohol.

5) a) (2) (on page 12) Facilities for Sterile Compounding.

The number and type of Primary Engineering Controls are already specified in the rules. If a facility installs operates and maintains these controls according to the manufacturer's

standards this wording is not necessary. The manufacturers should set these standards of practice for their products as the NDBOP can not possible be familiar with or keep up-to-date on all the available products and their associate specifications.

Board Comments:

Pharmacist Ziegler stated that she feels the language is reasonable and makes the rule clearer. The Board concurred.

5) a) (3) i. (on page 12)) Facilities for Sterile Compounding.

Should be deleted. This is standard of practice and not defied in NDBOP rules for filling other types of prescriptions.

Board Comments:

The Board feels the language is reasonable and each facility must be familiar with the equipment they have purchased.

5) a) (3) i. a. through d. (on page 12)) Facilities for Sterile Compounding.

Should be deleted. This is standard of practice and not defied in NDBOP rules for filling other types of prescriptions.

Board Comments:

The Board feels this is a reasonable standard and probably will not be done unless specifically required here.

(6) a) (on page 13) – Equipment specific for sterile compounding.

> "Primary Engineering Controls such as: Laminar Airflow Workbenches, Biological Safety Cabinets, Compounding Aseptic Isolators, and Compounding Aseptic Containment Isolators; must be used to prepare all sterile preparations except those compounded for immediate-use and must be capable of maintaining ISO Class 5 or superior air quality during normal compounding activity."

Should be changed to just "Primary Engineering Controls" all the rest of the wording is covered in other parts of the rule.

Board Comments:

The Board agrees that the rule will be best served by a single definition and the specific language has been removed here and is available in the definition at 1. p).

(7) (on page 14)

This should be deleted as it has already been stated in the rules for both sterile and non-sterile compounding.

Board Comments:

The Board agrees and this, which is actually section 6. has been deleted.

Additional Points

1. I would request that wording be added indicating that pharmacies have at least 3-years, from the time of final rule adoption, to comply with any of these new rules.

Board Comments:

The Board agrees and although this has already been a three year process, giving pharmacies an opportunity to begin their planning process, a provision has been added to require compliance by January 1, 2015.

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NDCC 28-32-08.1 – Regulatory Analysis relative to amendment of rules in NDAC 61 Specifically Chapter 61-02-01-03 – Pharmaceutical Compounding Standards.

Neither the Governor, nor any member of the Legislative Assembly has filed a written request for a Regulatory Analysis.

This proposed rule is expected to have an impact on the regulatory community as a whole in excess of $50,000. The regulated community consists of hospital pharmacies, retail pharmacies and any others who anticipate preparing sterile and non-sterile compounded prescription products.

Many of our larger hospitals have already begun compliance with this rule and will be required by their accreditation agency to be in compliance with United States Pharmacopeia [USP] 795 and 797 standards. The modification and installation of primary engineering controls can amount to substantial amounts of money. This amount can vary significantly from facility to facility, based on their current level of readiness and their plans for the future. Some of our medium size to smaller facilities will have to begin preparations for compliance with this rule. They do have a period of three years to come into compliance or to alter their procedures to reduce the modifications necessary in their operations to come into compliance.

The cost directly to the North Dakota Board of Pharmacy will be minimal. We will spend some time and energy in consulting with facilities and our inspectors will spend some additional time when visiting facilities during the annual inspection visit to asses the level of compliance and help with anticipated needs to bring each facility into compliance with the rule.

There should be no effect on state revenues with this rule.

The North Dakota State Board of Pharmacy has already deferred for approximately three years, in working to develop this rule. We have consulted at two state conventions and with numerous preliminary meetings involving stakeholders, primarily hospital pharmacists. We have attempted to write these rules to be the least onerous for our facilities. We feel that federal agencies, accreditation bodies and payers will require some kind of compliance with United States Pharmacopeia [USP] 795 and 797 standards. The accreditation agencies will usually defer to the state's requirements, if they are adopted in rule or statute. For protection of the public health it is necessary that the Board of Pharmacy move forward with these rules to establish standards for compounding pharmaceuticals and sterile pharmaceutical products.

More information on the affect on small entities is available in the Small Entities Analysis which is included with this packet, or is available from the Board of Pharmacy Office.

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NDCC 28-32-08.1 – Small Entity Regulatory Analysis Pertaining to adoption of NDAC 61-02-01-03 – Pharmaceutical Compounding Standards.

Although the Board of Pharmacy is exempt from this analysis as an occupational professional licensing authority, I do want to point out the following:

There is a range of compliance standards available in the rule. Facilities adopting Level 1 compounding procedures and immediate use procedures will reduce their compliance costs significantly.

There is a schedule for coming into compliance which will allow small entities flexibility to plan their remodeling and changes in their policies & procedures.

Small entities who have lower levels of compounding will have a smaller work load in keeping logs and will need to conduct testing less frequently as their number of compounds will be lower.

We do not wish to exempt any entities, as every patient is as important as the next. We want every patient to receive quality pharmaceuticals from those compounding medications for them.

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NDCC 28-32-08.1 – Small Entity Economic Impact Statement Pertaining to adoption of NDAC 61-02-01-03 – Pharmaceutical Compounding Standards.

Although the Board of Pharmacy, as the Board of Pharmacy is a professional or regulatory Licensing Board authority is exempt from the sections on Small Entity Regulatory Analysis, I believe it is prudent to describe some potential impacts, so the regulated parties will understand the rules implications.

All those who prepare compounded pharmaceutical products will potentially be affected by this rule. These may include pharmacies, hospitals, an occasional nursing home and some practitioner offices. Those benefiting from these rules are the patients who will receive these compounded preparations or will have them administered, or injected as in the case of sterile products.

Depending on the current progress of modification or remodeling of the pharmacy or compounding area, the impact may vary considerably. The Joint Commission and the Center for Medicaid and Medicare Services are gradually moving towards requiring compliance with United States Pharmacopeia [USP] 795 and 797. These rules will help entities establish a state accepted standard, along with a transitional period for adoption of the new standards in their practice and give them guidance for planning, which might not otherwise be in place. For some pharmacies there will be almost no costs, for others who are just beginning the transition to USP compliant operations and need major remodeling, the costs could be quite high. Most of the larger hospitals in North Dakota have already begun, and many have completed the transition, which will comply with these standards. There may be a few hospitals that either need remodeling or are building new facilities, which will need to spend $20,000 to $30,000 if they intend to comply with the higher level sterile compounding standards.

The North Dakota State Board of Pharmacy routinely conducts annual inspections and we do not expect the additional costs to monitor compliance with this rule to be substantial. Obviously, if a for profit facility spends money complying with the rule, that money will reduce their profits and the subsequent taxes on revenue may be diminished.

Alternative methods are available within the rule to reduce the costs of compliance to entities. An entity may chose to change their operations so they adopt the lowest level of use and immediate administration of compounded products. Many facilities have already done this. We will place in the rule a transitional period of perhaps three years, which will allow planning and transition for facilities to come into full compliance. Specific facilities may ask for variances if they are planning remodeling or new construction in the near future and have specific plans to come into compliance.