IN THE MATTER OF	*	**BEFORE THE**
CARDINAL HEALTH, INC.	*	**STATE OF MARYLAND**
Pharmacy Permit No. PW0080 **Distributor Permit No. D01333**	*	**BOARD OF PHARMACY**
	*	**DHMH-BPH-113-05-16013 &** **DHMH- BPH-114-05-17212**
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FINAL ORDER

Procedural History

This case arose from allegations that Cardinal Health Inc., Permits No. PW0080 and D01333, ("Cardinal") compounded and distributed 16 doses of a heart imaging solution, called Cardiolite, that was contaminated with the Hepatitis C virus. The contaminated doses of Cardiolite infected 16 patients who had been administered Cardiolite while undergoing cardiac stress tests on October 15, 2004. Based on this information and pursuant to its authority under the Administrative Procedure Act, *Md. Code Ann.*, State Gov't. § 10-201 *et seq.*, the Maryland Board of Pharmacy (the "Board") issued a summary suspension against Cardinal on January 11, 2005, requiring Cardinal to cease its pharmacy and distributing operations at its Timonium facility.[1] The Board held a show cause hearing on January 19, 2005, during which Cardinal was given an opportunity to show cause why the Board should

1 Cardinal owns and operates approximately 162 pharmacies nationwide. The Board's summary suspension and charges were issued solely against Cardinal's Timonium, Maryland, facility.

not continue the summary suspension. The Board subsequently voted to continue the summary suspension of Cardinal.

Subsequently, on March 31, 2005, the Board charged Cardinal with violating the Maryland Pharmacy Act, *Md. Code Ann.*, Health Occ. § 12-409, which provides:

> (a) *In general.* - Subject to the hearing provisions of § 12-411 of this subtitle, the Board may suspend or revoke any pharmacy permit, if the pharmacy:
>
> (1) Is conducted so as to endanger the public health or safety;
>
> (2) Violates any of the standards specified in § 12-403 of this subtitle; or
>
> (3) Otherwise is not conducted in accordance with the law.

The Board also charged Cardinal with violation of the following provisions of § 12-601:

> (a) *In general.* – Subject to the hearing provisions of § 12-315 of this title, for a violation of this subtitle or any regulation adopted under § 12-602 of this subtitle, the Board may:
>
> (1) Deny a permit to any applicant;
>
> (2) Reprimand a permit holder;
>
> (3) Place a permit holder on probation; or
>
> (4) Suspend or revoke a permit.

The Board charged Cardinal with violations of the Board's regulations, specifically Code Md. Regs. tit. 10 §34, which states:

> Chapter 19 Parenteral/Sterile Enteral Compounding

.04 General Requirements

F. The pharmacy shall provide protection for its products, environment, and personnel involved in the handling of antineoplastics and other sterile parenterals by using the proper equipment and having a procedure manual for those agents. The manual shall include, among its other requirements, the following mandatory special requirements:

....

(4) proper aseptic procedures shall be used by the pharmacist at all times to prevent bacterial contamination of the product.

Chapter 32 Licensing of Wholesale Prescription Drug Distributors

.08 Violations and Penalties

B. Commits any of the following acts:

....

(6) Violates any provision of Health Occupations Article, Title 12, Annotated Code of Maryland, or any regulation promulgated under Title 12.

The Board delegated its authority to conduct a hearing to the Office of Administrative Hearings. *Md. Code Ann.*, State Gov't § 10-205. A consolidated evidentiary hearing on the summary suspension and charges was held on May 25, 26 and 27, 2005. Laurie Bennett, Administrative Law Judge (the "ALJ"), presided over the hearing. On September 19, 2005, the ALJ issued a Proposed Decision ("Proposed Decision") wherein she concluded by a preponderance of the evidence that the summary suspension against Cardinal was properly issued and that Cardinal did not follow proper aseptic procedures. The ALJ's proposed disposition was that Cardinal must submit a corrective action plan prior to resuming

operations.

The Proposed Decision contained notice informing the parties of the right to file exceptions to the ALJ's Proposed Decision. The State filed exceptions on October 4, 2005. Cardinal filed exceptions on October 5, 2005. Cardinal filed a Response to State's Exceptions on October 14, 2005, and the State filed a Reply to Cardinal's exceptions on October 19, 2005.

On January 18, 2006, the parties appeared before a quorum of the Board for a hearing on the exceptions. On that same date, January 18, 2006, the Board convened for a final decision in the case.

STATEMENT OF THE CASE

The Board adopts and incorporates by reference the proposed Statement of the Case set forth by the ALJ in the Proposed Decision issued on September 19, 2005, as the Board's final Statement of the Case. The entire Proposed Decision is attached hereto as Appendix A.[2]

ISSUE

The Board adopts and incorporates by reference the proposed Issues set forth by the ALJ in her Proposed Decision issued on September 19, 2005.

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[2] In order to protect confidentiality, the Proposed Decision has been redacted to remove identifying information.

SUMMARY OF THE EVIDENCE

The Board adopts and incorporates by reference the proposed Summary of the Evidence made by the ALJ in the Proposed Decision issued on September 19, 2005, as the Board's final Summary of the Evidence.

FINDINGS OF FACT

The Board adopts and incorporates by reference certain proposed Findings of Fact, modifies certain Findings of Facts, and rejects certain Findings of Fact made by the ALJ in the Proposed Decision issued on September 19, 2005, as set forth below.[3] In addition, the Board adds certain findings of fact based on the evidence in the record.

Finding No. 1: Adopted

Beginning on February 25, 2003, and at all relevant times thereafter, the Respondent-Pharmacy ("Cardinal") has been authorized, in Maryland, to operate a pharmacy, under license number PW0080, and to distribute prescription drugs, under license number D01333.

Finding No. 2: Adopted

At all relevant times, Cardinal has operated as a nuclear pharmacy.

Finding No. 3: Adopted

Cardinal operates 162 nuclear pharmacies, including two in Timonium and Silver, Spring, Maryland.

Finding No. 4: Adopted

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3 Footnotes from the Proposed Findings in the Proposed Decision, although adopted unless otherwise specified, have not been replicated in this Order.

A nuclear pharmacy does not dispense pharmaceutical products in the manner of a traditional pharmacy. That is, a patient does not present Cardinal with a prescription and leave the pharmacy with medication. Rather, a nuclear pharmacy is akin to a laboratory, where radioactive materials are compounded and dispensed for use in nuclear medicine procedures.

Finding No. 5: Adopted

To qualify as a nuclear pharmacist, an individual must complete 700 hours of training and experience, in addition to the training and experience all pharmacists must receive.

Finding No. 6: Adopted

The work pace at a nuclear pharmacy can be very hurried because of a large number of doses to be prepared and their short expiration periods, together with the need to transport those doses expeditiously to clinics and hospitals.

Finding No. 7: Modified

Cardinal compounds both blood and sterile drug products, which require strict adherence to aseptic procedures to avoid environmental contamination and cross-contamination between products, and for the protection of pharmacy personnel.

The Board relies on its expertise in aseptic procedures to modify the above finding to differentiate between blood products and sterile drug products. Blood products, by their very nature, are not sterile products. The Board also clarifies that aseptic procedures must be followed in the compounding of blood products to avoid contamination of the blood, cross-contamination of the blood products with other sterile drug products, and for the protection of pharmacy personnel.

Finding No. 8: Rejected

Hospital scrubs, face masks and bonnets, the hallmarks of a clean room, are not necessary in nuclear pharmacies.

The Board relies on its expertise in sterile compounding to reject the above finding. Nuclear pharmacies may or may not require clean rooms, or clean room alternatives, depending upon the particular drug product that is compounded. Some nuclear pharmaceuticals may require adherence to USP 797 sterile compounding standards, which require a clean room. Nuclear pharmacies are not exempted from compliance with USP 797 standards merely by virtue of being a nuclear pharmacy.

Finding No. 9: Modified in part/Rejected in part

Cardinal purchases individually wrapped syringes in bulk. [Vol. 3, T. 500] The syringes are then unwrapped and kept in large boxes. [Vol. 2, T. 276 ; State's Ex. 14WW] Unlabeled, unwrapped syringes were scattered throughout the pharmacy area in boxes, in Styrofoam cups and laying on countertops. [Vol. 2, T. 262; State's Ex. 14NN] Syringes, if unwrapped prior to the compounding process, may be unwrapped away from the hood and stored safely in hard plastic containers in the hood in amounts necessary for the "run", or in cupboards, drawers or plastic bins. Syringes to be used in the blood labeling process and stored in the blood room should remain individually wrapped in the blood room, and unwrapped when needed away from the blood hood. [Cardinal's Ex. 44, pp.6-29, 6-35]

The Board relies on the evidence admitted to modify the above finding. Furthermore, the Board relies upon its expertise in sterile compounding to reject the ALJ's finding that individually wrapped syringes cannot be unwrapped in the blood room. Indeed, Cardinal's own policies and procedures manual requires that syringes remain wrapped in the blood room until utilized for a procedure.

Finding No. 10: Modified

A safety syringe can be used only once by design. Health facilities typically use safety syringes to protect healthcare workers against needlesticks. [Vol. 2, T. 263] A nuclear pharmacy cannot use safety syringes for all purposes because, for some procedures, the syringe acts as the container for the final product which is delivered to the facility where the product will be administered directly to the patient. [Vol. 3, T. 525]

The Board relies on the evidence in the record to clarify that only the final step in the drug compounding process requires that Cardinal recap syringes.

Finding No. 11: Modified

Cardinal's policy permitted in-process syringes that were used during the compounding process and not for the administration of the final drug products to be recapped. The standard of practice, even in nuclear pharmacies, requires that in-process syringes should be disposed of without being recapped. [Vol. 3, T. 524-25, 547]

The Board relies upon Cardinal's expert and its own expertise to modify the above finding to emphasize that recapping of syringes, unless required as set forth in Finding No. 10, is against the standard of practice.

Finding No. 12: Modified

A nuclear pharmacist must use techniques to minimize his/her exposure to radiation. To that end, Cardinal developed a *Pharmacy Practice Policy & Procedure Manual* (the "Manual") which has been in effect since October 2003. (Cardinal's Ex. 44) The manual includes a chapter titled Pharmacy Practice, Quality Assurance Procedures,

which tests a worker's competence to use aseptic techniques.

The Board deletes a portion of the above finding which states that Cardinal's policies and procedures manual establishes its commitment to using aseptic procedures. As set forth in this Order, the record reflects that notwithstanding the existence of Cardinal's manual, Cardinal failed to implement many of the aseptic procedures required in its manual.

Finding No. 13: Adopted

The manual includes a process for disposing of waste. The process is consistent with industry standards.

Finding No. 14: Adopted

It is common in the industry to work on two blood labeling procedures for two different patients at the same time. A trained nuclear pharmacist should have no problem performing multiple procedures.

While the Board adopts this finding based on the evidence presented, it seriously questions utilizing this practice particularly when engaging in high risk compounding such as blood labeling procedures. The Board relies on its own expertise to find that this is not the standard in compounding IV (intravenous) products and cannot imagine that the standard would be any lower when compounding blood products.

Finding No. 15: Adopted

Cardinal has two main rooms: the so-called main pharmacy and the blood room.

Finding No. 16: Adopted

A "blood room" is not the best place in a pharmacy to house a hand washing station. A hand washing station attracts foot traffic, and traffic is contraindicated in a blood room.

Finding No. 17: Adopted

Cardinal does not have a door between the blood room and the pharm hood.

Finding No. 18: Adopted

Only individuals trained in the safe handling of radioactive materials are permitted into restricted areas.

Finding No. 19: Adopted

At all relevant times, Cardinal has produced a radionuclide-tagged cardiac scanning solution ("Cardiolite") and has performed white blood cell radiolabeling (a.k.a. leukocyte labeling) at the Timonium and Silver Spring pharmacies.

Finding No. 20: Adopted

Cardinal dispenses approximately 60,000 doses of Cardiolite each year at its Timonium facility.

Finding No. 21: Modified

Cardiolite is a tool for diagnosing coronary artery disease. Cardinal receives Cardiolite in the form of a kit, marked "sterile", for the preparation of technetium tc99m sestamibi for injection. A Cardiolite compounding kit consists of a protein named sestamibi that is marked with a radiopharmaceutical, technetium tc99m. sestamibi. It is injected into a patient and travels through the bloodstream to the heart.

The Board relies upon the evidence in the record to add the fact that the Cardiolite kit is marked "sterile". (State's Ex. 14KK)

Finding No. 22: Modified

In the preparation of radiopharmaceuticals, such as Cardiolite, a quality assessment procedure is done to verify the radiochemical purity of the product, not the sterility of the product. Quality assessment is part of the compounding procedure. At the end of the procedure, the pharmacist draws a dose and it is assayed in the dose calibrator. [Vol. 3, T. 525-26] Quality assessment for radioactivity is performed by pharmacy technicians. [Vol. 3, T. 497]

The Board modifies the above finding to clarify that the purpose of Cardinal's quality assessment process is to measure the radioactivity of the product, not its sterility. In addition, this process is performed by pharmacy technicians, not pharmacists.

Finding No. 23: Adopted

In the case of Cardiolite, the pharmacist draws .1 ml of the product for quality control testing, and the remainder is placed on the counter that is labeled "Tech 1" or "Tech 2", for the technicians to draw up the individual doses.

Finding No. 24: Adopted

Cardiolite is heated during the compounding procedure to 100 degrees centigrade for 10 minutes.

Finding No. 25: Adopted

After the Cardiolite is prepared, a small vial of the drug is placed in the top part of a tungsten allusion shield, commonly referred to as a "PIG". The PIG is transported to a

medical facility, so that the Cardiolite can be injected into a patient. After the Cardiolite is injected, the used syringe in capped and placed in the bottom part of the PIG and returned to pharmacy for disposal.

Finding No. 26: Modified

Cardinal cleans only the outside of its PIGS with alcohol before they are reused. Current standards do not require that Cardinal clean the inside of the PIGS before every use. [Vol. 2, T. 446-448]

A pharmacist needs to leave the pharmacist's hood (also known as a "pharm hood") during Cardiolite compounding. For instance, the pharmacist must obtain technetium from the generator room, and boil the Cardiolite compound in the hot plate room. [Vol. 3, T. 493-496]

The Board modifies the above finding to state that PIGS are not required to be cleaned before every use provided that the PIGS contain a protective insert. In addition, the Board relies on the record to add that the pharmacist must also leave the pharm hood during Cardiolite compounding to boil the compound in the hot plate room.

Finding No. 27: Adopted

A pharmacist completes all aspects of Cardiolite production, except for the last step of the quality check and the volume adjustment, which are completed by a pharmacy technician.

Finding No. 28: Adopted

Between October 16, 2004, and December 6, 2004, Cardinal produced 6,000 stress doses of Cardiolite, meaning that 6,000 patients were injected with the drug during that

period.

Finding No. 29: Adopted

Cardinal had two "runs" of Cardiolite each day. The first left the building at approximately 4:30 a.m. and second at 8:30 a.m. A pharmacist would arrive at the pharmacy from 12:30-1:00 a.m. to produce the first run. Pharmacist A prepared the first lot of Cardiolite, Lot 140, at 1:05 a.m. on October 15, 2004.

Finding No. 30: Modified

At all relevant times, Cardinal has employed the following process in leukocyte labeling: Cardinal receives a patient's blood sample from a medical facility. The blood is washed and treated chemically, so that the cells will take up radioactive material. The patient's blood is placed in a centrifuge, which separates the plasma, white blood cells and red blood cells. After the plasma is separated, the compacted mass is agitated with saline solution to separate out the white blood cells. The white blood cells are then tagged with a radioisotope and the blood is remixed. The radioactivity is assayed to ensure that the appropriate amount of radioactivity has actually attached to the blood cells. [Vol. 1, T. 49] The blood is placed in a syringe and transported to a medical facility to be reinjected into the patient.

The pharmacist must leave the blood room two times to complete the blood labeling process. The pharmacist must retrieve the indium 111, the radioactive ingredient, from barrels located outside the blood room. The pharmacist must also assay the blood in the

calibrator located under the pharmacy hood located in the main pharmacy area. [Vol. 1, T. 49; State's Ex. 15]

The Board modifies the above finding based on the evidence in the record which indicates that the blood labeling process was not confined to the blood room and required the pharmacist to leave the blood room no less than two times in order to complete the procedure.

Finding No. 31: Adopted

Syringes and saline are used in the production of Cardiolite and during leukocyte labeling. Saline can become contaminated with blood or a blood product, and a syringe can transmit infected blood or blood product.

Finding No. 32: Modified

Syringes that will not be used are recapped and disposed of in a leaded waste container located under the pharmacy hood. [Vol. 1, T. 53] It may be impossible to determine whether a syringe has been used previously if it is recapped.

The Board modifies the above finding to include the determination that a used syringe is virtually indistinguishable from an unused syringe if it is recapped.

Finding No. 33: Adopted

Industry standards do not require that the dose calibrator, used to assay the amount of radioactivity of a substance, be cleaned after each use. Doing so is not practical because it would significantly slow the process and is unnecessary to avoid contamination.

Finding No. 34: Adopted

Approximately once per day a blood product is produced in Cardinal's pharmacy.

Finding No. 35: Adopted

Prior to December 6, 2004, the Board's inspections of Cardinal had not revealed any deficiencies.

Finding No. 36: Adopted

Anne Arundel County Health Department first became aware of a possible Hepatitis C outbreak when one infected person had a chance encounter with an acquaintance who was also infected, and they both had taken cardiac stress tests in the same facility in Glen Burnie, Maryland. Those patients had no other possible mode of transmission in common. The Anne Arundel County Health Department reported the possible outbreak to the Department.

Finding No. 37: Adopted

On or about December 6, 2004, the Board received a complaint from the Department's Epidemiology Program regarding a suspected outbreak of Hepatitis C among patients receiving Cardiolite from a batch that had been produced by Cardinal.

Finding No. 38: Adopted

In collaboration with the Centers for Disease Control and Prevention ("CDC"), on or about December 6, 2004, the Department commenced an investigation (the "Investigation") into the reported cluster of Hepatitis C cases.

Finding No. 39: Adopted

Cardinal halted operations at the close of business on December 6, 2004, and

voluntarily suspended its preparation and distribution of all radiolabeled parenteral compounds.

Finding No. 40: Adopted

Hepatitis C is a viral infection that lives in the blood and causes inflammation of the liver. It is a chronic, sometimes life-threatening disease. It is unrelated to the other common Hepatitis viruses (A, B, D, and E). Hepatitis C virus is a member of the Flaviviridae family of viruses. Other members of this family of viruses include those that cause yellow fever and dengue. Viruses belonging to this family all have ribonucleic acid ("RNA") as their genetic material.

Finding No. 41: Adopted

Hepatitis C has numerous modes of transmission. Hepatitis C may be transmitted through contaminated blood or blood products from an infected individual to an uninfected individual during illegal intravenous drug use, surgery, needle sticks, transfusions, tattooing and body piercing. Hepatitis C can also be transmitted through a contaminated pharmaceutical product. Hepatitis C is rarely transmitted from person to person.

Finding No. 42: Adopted

The genes that make up the Hepatitis C virus can vary. As such, Hepatitis C virus is categorized into six major genetic types ("genotypes") and as many as 40 subgenotypes, based on the sequence (order) of nucleotides in the virus. The most common genotype in the U.S. is genotype 1, which accounts for 80% of Hepatitis C virus cases in the United States.

Approximately 55 % of Hepatitis C infected patients have genotype 1a.

Finding No. 43: Adopted

Initially, the case definition for this matter included patients who had either clinical or laboratory evidence of having developed Hepatitis C, especially acute Hepatitis C, and a history of having had a cardiac stress test, with Cardiolite, at a particular medical facility in Glen Burnie on October 15, 2004. As Hepatitis C appeared in patients who had had stress tests at other facilities surfaced, the Glen Burnie facility was removed from the case definition.

Finding No. 44: Adopted

The case definition eventually included Cardinal when the Department identified 16 Hepatitis C infected patients, whose only link, other than having a cardiac stress test on October 15, 2004, was that they received a Cardiolite preparation from the same lot of Cardiolite, prepared in Cardinal on October 15, 2004.

Finding No. 45: Adopted

Of the 16 individuals in the case definition, 14 were male. They ranged in age from 45 to 80 years old. They resided in various places, such as Anne Arundel, Baltimore, Cecil and Harford counties in Maryland and one person from Pennsylvania. All 16 patients received Cardiolite from the same batch produced by Cardinal.

Finding No. 46: Adopted

The Department examined 19 blood samples, including 3 from the source patient and

16 from the outbreak patients. Fifteen samples had C genotype 1a. One had genotype 1 but could not be subtyped and did not have sufficient RNA for complete genotyping. One patient, who received Cardiolite from Cardinal on October 14, 2004, had previously been diagnosed with acute Hepatitis C, subgenotype 1b.

Finding No. 47: Adopted

The Department sequenced the quasispecies from the hypervariable 1 regions of the Hepatitis C virus genome isolated from 13 specimens, including 3 from the source patient. The samples showed a high degree of relatedness.

Finding No. 48: Adopted

Hepatitis C can be transmitted by using contaminated Cardiolite but because Cardiolite does not contain a blood component, it is not reasonable to expect that, in the ordinary course of compounding, Cardiolite could become infected with the Hepatitis C virus.

Finding No. 49: Adopted

During the course of the Department's outbreak investigation, Cardinal's employees tested negative for Hepatitis C RNA and one tested positive for Hepatitis C antibodies. The pharmacy employees were not, at the time of testing, capable of transmitting the virus because only the RNA is transmissible through blood. Transmission is not possible from a person who is positive for Hepatitis C antibodies.

Finding No. 50: Modified

During the outbreak investigation, the Department asked Cardinal for records of patients who had radioactive related white blood cells procured there from October 1 - 14, 2004. The Department took particular notice of a Patient X, whose blood was sent to Cardinal on October 14, 2004 for leukocyte labeling. The Department sought additional medical records for Patient X from various medical facilities in Maryland. Those records revealed that Patient X, now deceased, had the antibodies for the Hepatitis C virus and the RNA from Hepatitis C.[4] Thus, Patient X was the source patient for the Hepatitis C outbreak.

The Board modifies the above finding to omit the ALJ's references to the specific name of Patient X.

Finding No. 51: Adopted

Lot 140 of Cardiolite was prepared at Cardinal on October 15, 2004 at 1:05 a.m.

Finding No. 52: Adopted

The Department initiated an environmental investigation to determine whether environmental factors caused the outbreak. Officials from Maryland Occupational Safety and Health ("MOSH") investigated and, although notified, the Maryland Department of the Environment did not.

Finding No. 53: Adopted

On or about December 10, 2004, the Board's investigator along with officials from the Food and Drug Administration, the Department's Division of Drug Control and the

4 Patient X had also been previously diagnosed with the hepatitis B virus and the human immunodeficiency virus. (State's Ex. 31)

Epidemiology Program met with Cardinal's employees, who explained the various steps involved in the preparation of Cardiolite and blood for Tropolone Leukocyte labeling and demonstrated both preparation processes.

Finding No. 54: Adopted

None of the individuals who investigated Cardinal on behalf of the State had ever been inside a nuclear pharmacy.

Finding No. 55: Modified

Because Cardinal had already ceased operations, the investigators did not see the actual compounding of pharmaceuticals. Rather, they observed simulations. The simulations were not performed in real time or using blood products. The investigators were interested in seeing the general work flow and use of aseptic techniques. (State's Ex. 15)

The Board modifies the above finding to clarify that Cardinal had voluntarily ceased operations, on December 10, 2004, when the investigators conducted a site visit, and had not been "shut down" by the Board at that time. Furthermore, the Board modifies the finding to emphasize that the purpose of the simulations was to demonstrate the aseptic procedures employed by Cardinal. In addition, the Board rejects the ALJ's finding that the investigators did not instruct Cardinal pharmacists to perform simulations "as if they were working with actual pharmaceuticals". A pharmacist performing a simulation, even if it is not in real time, should follow procedures as if he/she were compounding the actual product. To do otherwise obviates the purpose of a simulation. The reason for the simulation was to determine how the Cardiolite at issue became contaminated with Hepatitis C. One hypothesis was that the Cardiolite was cross-contaminated by the blood product that was compounded in the adjacent area. It is illogical to say that the pharmacist performing the simulation of the blood labeling process should not have adhered to the same aseptic procedures he would have used had he been compounding with actual blood when the sole purpose of the simulation was to observe the process for possible theories as to how the cross-contamination occurred.

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Finding No. 54: Adopted

None of the individuals who investigated Cardinal on behalf of the State had ever been inside a nuclear pharmacy.

Finding No. 55: Modified

Because Cardinal had already ceased operations, the investigators did not see the actual compounding of pharmaceuticals. Rather, they observed simulations. The simulations were not performed in real time or using blood products. The investigators were interested in seeing the general work flow and use of aseptic techniques. (State's Ex. 15)

The Board modifies the above finding to clarify that Cardinal had voluntarily ceased operations, on December 10, 2004, when the investigators conducted a site visit, and had not been "shut down" by the Board at that time. Furthermore, the Board modifies the finding to emphasize that the purpose of the simulations was to demonstrate the aseptic procedures employed by Cardinal. In addition, the Board rejects the ALJ's finding that the investigators did not instruct Cardinal pharmacists to perform simulations "as if they were working with actual pharmaceuticals". A pharmacist performing a simulation, even if it is not in real time, should follow procedures as if he/she were compounding the actual product. To do otherwise obviates the purpose of a simulation. The reason for the simulation was to determine how the Cardiolite at issue became contaminated with Hepatitis C. One hypothesis was that the Cardiolite was cross-contaminated by the blood product that was compounded in the adjacent area. It is illogical to say that the pharmacist performing the simulation of the blood labeling process should not have adhered to the same aseptic procedures he would have used had he been compounding with actual blood when the sole purpose of the simulation was to observe the process for possible theories as to how the cross-contamination occurred.

Finding No. 56: Adopted

On or about December 13, 2004, the Board received a written complaint from the Maryland State Epidemiologist regarding the possibility that certain Cardiolite produced by Cardinal was contaminated.

Finding No. 57: Modified

On December 15, 2004, the Board voted to summarily suspend the pharmacy and distributor permits issued to Cardinal. On January 11, 2005, the Board issued its Order of Summary Suspension.

The Board modifies the above finding to reflect the date of the Board's vote as well as the date of the issuance of the summary suspension order. (State's Exs. 15 and 18)

Finding No. 58: Adopted

On or about December 21, 2004, the investigative team visited the Silver Spring pharmacy, with Cardinal's employees present on site. The purpose of the visit was to see a working pharmacy. They observed Cardiolite compounding but not leukocyte labeling. A sign on the blood room door indicated that "hazardous materials" were being used. The blood room was strictly dedicated to blood products. The breakdown of PIGs was the same as Cardinal's Timonium pharmacy. Radioactive waste was stored in a separate room and was organized by radioactive material.

Finding No. 59: Modified

The Respondent uses a Typenex labeling system to track the patient's blood. Cardinal

requires that two pharmacists sign off that utensils or pieces of equipment were labeled with the correct patient's name. [Vol. 3, T. 503-504]

The Board modifies the above finding to clarify that the labeling system was used for the blood products only. The Cardiolite process did not use the Typenex labeling system. In addition, the system did not address in-process syringes that did not handle blood.

Finding No. 60: Adopted

Cardinal used Typenex to verify that a syringe contained Patient X's blood.

Finding No. 61: Rejected

A clean room refers to an area that is used for the preparation of sterile materials. A nuclear pharmacy does not contain a clean room because its workers practice aseptic techniques and essentially work in an aseptic environment.

The Board rejects this finding based upon its expertise in sterile compounding. Aseptic techniques are an integral part of sterile compounding standards. However, the use of aseptic techniques does not obviate the need to comply with USP 797 sterile compounding requirements if a pharmacy, including a nuclear pharmacy, is compounding sterile drug products. A nuclear pharmacy is not exempt from such requirements by virtue of being a nuclear pharmacy.

Finding No. 62: Adopted

Time, distance and shielding refer to the effort to limit one's exposure to radiation. It is fundamental in a nuclear pharmacy. Time refers to the fact that radiopharmaceuticals have a short half-life and, as a result, decay fairly quickly. As a result, it is important for pharmacists and technicians to work quickly. Distance means increasing one's physical distance from the radioactive materials. Shielding refers to various items such as lead

syringe shields, vial shields, a pharm hood, which has a glass barrier between the pharmacist and the radioactive material with which [s]he's working.

Finding No. 63: Adopted

On or about March 24, 2005, the Board received a copy of the Epidemiology Program's summary report reporting the Hepatitis C Outbreak (also known as Outbreak # 04-272) contamination of one lot of radiolabeled product occurred during its preparation by Cardinal.

Finding No. 64: Adopted

A review of Cardinal's records of prepared products identified a possible source of HCV-contaminated blood or blood products from a leukocyte donor. Genetic testing showed that a specimen from this person, Patient X, contained HCV RNA of the same genotype and with similar genetic findings as the predominant outbreak HCV RNA strain.

Finding No. 65: Adopted

At all relevant times, Cardinal's work areas have been poorly defined, without discernible delineation between the areas where blood or blood components are prepared or processed and areas where other products were prepared or processed.

Cardinal's Timonium facility did not have a door separating the blood room from the main pharmacy area, unlike the Silver Spring facility. In addition, the two areas shared supplies and equipment, such as unwrapped syringes and a calibrator. Furthermore, ingredients needed for the blood labeling procedure were kept outside of the blood room. [Vol. 1, T. 49-50]

Finding No. 66: Adopted

At all relevant times, while Cardinal employed multiple safeguards to prevent employee exposure to radioactivity, it failed to employ adequate safeguards to prevent their exposure to blood.

Cardinal failed to employ adequate safeguards to prevent its employees' exposure to blood by permitting employees to recap syringes that were disposed.

Finding No. 67: Adopted

The safe handling of human blood and preparation of a human blood product requires strict adherence to aseptic sterile techniques.

Finding No. 68: Adopted

At all relevant times, Cardinal has employed inadequate procedures to avoid cross-contamination between screened and unscreened blood, blood components prepared or processed and other injectable products prepared, processed, and stored on site.

Finding No. 69: Modified

After Cardinal voluntarily halted production, the Department granted it permission to re-open to produce a single dose of Bexxar. Bexxar is a therapy used in the treatment of non-Hodgkins lymphoma. The Department granted the exception because the production of Bexxar would not involve the use of blood products and, therefore, the risk of cross-contamination was zero and Cardinal was the only nuclear pharmacy that had the necessary equipment.

The Board modifies the above finding to state that the Department found the risk of cross-contamination, not contamination, to be zero for the production of the single dose of Bexxar. (Cardinal's Ex. 14)

Finding No. 70: Adopted

Cloth rags should not be used to clean up radioactive material.

Finding No. 71: Adopted

Cardinal houses a refrigerator in the cell labeling area.

Finding No. 72: Adopted

At the time of the December 7th visit by investigators, a refrigerator was housed in the blood room. Timonium officials later moved it into the main lab area.

DISCUSSION

The Board modifies the ALJ's proposed Discussion in the Proposed Decision, dated September 19, 2005, as set forth below.

The issue in this case is whether the Board's summary suspension of Cardinal was appropriate given that Cardinal had dispensed 16 doses of Cardiolite, a sterile drug product, contaminated with the Hepatitis C virus. A secondary issue is to determine whether the charges issued against Cardinal should be affirmed and whether the sanction proposed by the ALJ in this matter is sufficient to protect the public's safety and welfare against a reoccurrence of a similar incident.

Cardiolite is a heart imaging agent that is injected into patients for cardiac stress tests, and therefore, it must obviously be compounded and distributed in a manner that

maintains the sterility and integrity of the product. In addition to compounding mass volumes of Cardiolite, Cardinal also compounds blood products, which entails tagging white blood cells with a radioisotope. If Cardinal compounded either its sterile products or blood products using deficient aseptic procedures, it could have disastrous ramifications for many patients since, as Cardinal states, it dispenses approximately 300 doses of Cardiolite per day just at the Timonium facility. [Vol. 2, T. 442] Indeed, that is exactly what occurred in this case. Although neither the Board nor Cardinal was able to pinpoint the exact cause of the cross-contamination between Cardinal's blood product and its Cardiolite products, it occurred nonetheless, and 16 patients were infected with the Hepatitis C virus.

The Board's Summary Suspension was properly issued.

Cardinal argues that its transmission of a deadly disease through a high volume pharmacy did not warrant emergency action. However, the ALJ opined that "if an outbreak of Hepatitis C that has spread to 16 people does not establish a substantial likelihood that a licensee posed a risk of harm to the public health, safety or welfare, [I] cannot imagine what would." Proposed Decision at p. 25. Cardinal argues that it had voluntarily ceased operations and therefore the summary suspension was not necessary. However, since Cardinal had voluntarily ceased operations, it could reopen at any time. It was imperative that the Board fulfill its obligation to protect the public and suspended Cardinal's licenses, rather than rely on the voluntary actions by the very licensee being

investigated.

On or about December 14, 2004, the Board consented to Cardinal's request that it dispense a single dose of Bexxar[5], a specialized drug used to treat lymphoma, for a single patient. Cardinal argues that since the Board consented to Cardinal dispensing a single dose of Bexxar during the investigatory period, Cardinal's operation could not have posed a risk to the public. On the contrary, the Board consented to the dispensing of the single dose of Bexxar because, it that particular case, the Bexxar was produced for one patient who would not have been able to obtain it anywhere else. Furthermore, the patient required Bexxar as part of the second phase of the patient's treatment for lymphoma. [Vol. 2, T. 374] The Board balanced one patient's dire need for a single dose of a product that could not be produced anywhere else, with the danger of causing further harm to the public, and made the decision to acquiesce to Cardinal's request for this particular patient. The Board's rationale in this scenario is simply not applicable to Cardinal's production of Cardiolite. Cardinal's Timonium pharmacy dispenses 300 doses of Cardiolite per day. Because the cause of the contamination was unknown at that time, the Board would have risked the health of thousands of cardiac patients while the investigation was pending if it permitted Cardinal to continue dispensing Cardiolite. The Board declined to do so.

In deliberating as to whether Cardinal should be able to dispense the single dose of

5 Bexxar is a relatively new drug used to treat patients with lymphoma. The treatment is a two-step process. "After the patient is dosed the first week, they calculate then what the dose should be for the patient. And that dose is administered the second week. These products have to be prepared and administered within about a two-hour period. The Timonium pharmacy was the only one that had the calibrated equipment calibrated according to the NIST traceable protocol to be able to dispense that particular product." [Vol. 2, T. 373-74]

Bexxar on December 14, 2004, Dr. Roche, the Chief of the Department's Epidemiology Division, stated that he would "judge the benefit from preparing this one dose of Bexxar for the lymphoma patient to outweigh the risk of HCV transmission, especially since the potential for cross-contamination with a human blood product [was] zero". (Cardinal's Ex. 14) Cardinal misplaces reliance on this statement to argue that the Board could have utilized less "draconian" measures by limiting its summary suspension to Cardinal's blood labeling processes. The Board issued its Order for Summary Suspension on January 11, 2005. As stated in *Mullan,* the appropriateness of a summary suspension is determined "at the time the decision to suspend summarily is made." *Board of Physician QualityAssurance v. Mullan*, 381 Md. 157, 163 (2004). On January 11, 2005, the Board did not have a final report from the Department's Epidemiology Division as to its outbreak investigation. Therefore, without the Department's final report stating that cross-contamination caused the Cardiolite to be contaminated with the Hepatitis C virus, the Board could not rule out other causes such as environmental contamination. In fact, Cardinal itself could not offer an explanation as to how the Cardiolite became contaminated. Without any explanations from Cardinal as to how the contamination occurred and without a final report of the Department's outbreak investigation, the Board could not permit Cardinal's Timonium facility to operate, at any level. Because of the mass volume of Cardiolite produced by Cardinal, to permit Cardinal to resume operations without knowledge of the cause of the contamination would pose a serious health risk to

countless individuals.

Cardinal further argues that the press release issued by the Department on December 9, 2004, indicates that the Board was not required to take emergency action. The Department's press release, in relevant part, states "The investigation currently points to a unique event and not an ongoing public health risk". (Cardinal's Ex. 8) Dr. David Blythe, State Epidemiologist, drafted the press release without any input from the Board. In addition, at the time of the press release, Cardinal had ceased operations. Therefore, the Department's intent was "to inform, but not to alarm, the public." Proposed Decision, p. 26. Furthermore, while the Board is a unit of the Department, its disciplinary matters are wholly autonomous from the Department. Thus, any conduct on behalf of the Department is not binding upon the Board in its determination of disciplinary matters. *Md. Code Ann.*, Health Occ. § 1-203.

Cardinal further argues that between October 15 and December 6, 2004, it dispensed approximately 6,000 doses of Cardiolite without incident and therefore, emergency action was not warranted by the Board. [Vol. 3, T. 489] The Board examined all factors involved in this matter in determining whether a summary suspension was an appropriate course of action. First, as the cause of the contamination was unknown, the Board could not be reasonably assured that contamination of Cardinal's sterile products would not reoccur. Second, again, since Cardinal is a high volume distributor of Cardiolite, the reoccurrence of such contamination could have life-threatening

consequences for thousands of patients. Third, the nature of the error was extremely serious. Contamination of a sterile drug product with the hepatitis C virus is not a minor medication error, and should not be treated as such. Finally, since Cardiolite is a sterile drug product that does not contain blood, and should not be contaminated with Hepatitis C, the Board finds it difficult to give credit to Cardinal for doing what it was supposed to do. Based upon the assessment of the above factors, the Board decided to take action commensurate with the threat posed to the public and summarily suspended Cardinal's permits.

Cardinal Employed Deficient Aseptic Procedures in violation of the Maryland Pharmacy Act

Cardinal not only compounds sterile drug injectables such as Cardiolite, it also compounds blood products. It goes without saying that any process in which blood is handled must follow strict adherence to aseptic procedures. The Board relies on its extensive expertise in sterile compounding as well as the factual evidence in the record in reviewing Cardinal's aseptic procedures as set forth in its policies and procedures manual, and as implemented at its Timonium facility. [6]

The purpose of utilizing aseptic procedures during blood compounding is three-fold: to protect the health professionals from contamination; to protect other products from cross-contamination; and to protect the integrity of the blood product itself.

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6 The ALJ was given very little evidence regarding proper aseptic procedures. In fact Cardinal did not offer any expertise on the issue and the State's expert's testimony was wholly lacking in substance. (See Proposed Decision, footnote, p. 8) Therefore, it is not surprising that the ALJ was not able to fully appreciate the applicability of aseptic

Although Cardinal maintained a policies and procedures manual that sufficiently addressed aseptic procedures, Cardinal failed to implement certain procedures at its Timonium facility.

For example, Cardinal's policies state that a refrigerator should not be located in the blood room. The reason for this is that refrigerators, as well as other appliances and furniture, attract particles and are very difficult to keep clean in an aseptic environment. Cardinal housed a refrigerator in its blood room, in violation of its own policies. Cardinal later removed the refrigerator after the Department and Board's investigators conducted their inspection. [Vol. 1, T. 46; Cardinal's Ex. 44 p. 6-34]

With respect to Cardinal's procedures in the use and handling of syringes, Mr. Coffey testified that it bought syringes in bulk that were individually wrapped. The purposed of the wrapping is to maintain the sterility of the instruments. However, Cardinal's process was to unwrap mass quantities of the syringes in preparation for the compounding of products. Since Cardinal is engaged in nuclear compounding, the syringes were unwrapped beforehand to expedite the compounding process and lessen the amount of time pharmacists were exposed to radioactive elements. While the Board understands the need to unwrap a certain quantity, it is counterintuitive to unwrap mass quantities of syringes when the very reason the syringes are wrapped is to maintain their sterility. Indeed, Cardinal's procedures manual states that syringes should remain

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procedures in the compounding of sterile drug products.

wrapped in the blood room for the blood procedures.[7] Cardinal's expert, Dr. Hinkle, stated that unwrapping syringes in front of the blood hood would compromise the aseptic quality of the product. The Board believes that syringes should be unwrapped in the blood room, away from the hood, in accordance with Cardinal's policies. It is preferable to keep stored syringes in the blood room with the individual wrapping in tact, and unwrap the amount of syringes needed to compound the particular blood product away from the blood hood. Not only would this maintain the sterility of the syringes, it would help to differentiate between unused syringes and used syringes.

Cardinal further asserts that it must recap syringes in order to compound its specialized drug products. However, Cardinal's own expert, Dr. Hinkle, testified that he does not recap in-process syringes that are disposed. Specifically, Dr. Hinkle stated, "...when you are compounding radiopharmaceuticals and preparing radiopharmaceuticals, oftentimes we draw up materials that are added to the vial. That syringe is not going to be used again. So typically we're trained, and I train people to not recap that syringe and dispose of it right away, because you don't need it any longer." [Vol. 3, T. 524-525] Procedures which require pharmacists and technicians to recap all syringes subjects both healthcare professionals and patients to unnecessary risk of infection.

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7 Cardinal's manual, under the section entitled "Quality Assurance Standards for Cell Labeling Areas", states that "All supplies should be wiped with 70% isopropyl alcohol before entering the labeling room or area. *Pouched supplies (syringes, IV bags) need not be wiped since the pouches can be removed in the labeling room."* (emphasis added) The manual further states to, "Move only one week's supply at a time into the cell labeling room. *Syringes should remain pre-wrapped."* (emphasis added) (Cardinal's Ex. 44, p. 6-35)

In addition, Cardinal's policies and procedures manual states that Styrofoam cups are prohibited in the blood cell labeling area because they shed particles. [Cardinal's Ex. 44, p. 6-34] However, Dr. Roup testified that during her visit to Cardinal on December 6, 2004, while the pharmacy was still in operation, there were Styrofoam cups filled with unlabeled syringes everywhere, including under the hood. [Vol. 2, T. 262] Standard aseptic practice prohibits maintaining Styrofoam cups, which are made of porous material susceptible to shedding particles, directly under the hood. Cardinal did so in violation of standard aseptic practices and in violation of its own aseptic procedures.

Lastly, the Board charged Cardinal with violating its regulatory requirement to maintain a procedure manual outlining proper aseptic procedures. (State's Ex. 33) Cardinal argues against this charge by stating that it did, in fact, have a procedures manual and therefore it was in compliance with the Board's regulation. It is disingenuous, at best, to argue that Cardinal was compliant with the requirement to have an aseptic procedures manual, when it failed to actually implement the procedures contained in the manual. The Board's regulatory requirement would be meaningless unless a pharmacy is required to actually follow its own aseptic procedures. Notwithstanding the technicality relied upon by Cardinal, Cardinal's failure to implement its own procedures caused it to operate in a manner that endangered the public health or safety, in violation of § 12-409.

CONCLUSIONS OF LAW

Based on the foregoing Findings of Fact and Discussion, and after consideration of the hearing record, Respondent's exceptions, the State's exceptions and responses thereto, the Board affirms the ALJ's Conclusions of Law that the summary suspension was properly issued. The Board further concludes that Cardinal violated *Md. Code Ann.,* Health Occ. § 12-409 and § 12-601, and Code Md. Regs. tit. 10 § 34.22.08B(6). However, the Board does not affirm the ALJ's conclusion that Respondent violated Md. Code Regs. tit. 10 § 34.19.04F(4).

SANCTIONS

Cardinal dispensed 16 doses of a sterile drug product that were contaminated with the Hepatitis C virus and administered to 16 cardiac patients. This was obviously a tragic event that caused, and will continue to cause, both physical and mental harm to countless individuals. The Board believes that Cardinal has learned a very sobering lesson as a result of this event. The ALJ recommended that Cardinal be permitted to apply to the Board for reinstatement of its permits provided that it submit a corrective action plan. The Board believes that the ALJ's recommendation is reasonable and therefore will require that Cardinal submit a corrective action plan that addresses the deficiencies outlined in this Final Order as part of any reinstatement. In the event that Cardinal petitions for and is granted reinstatement, the Board will conduct random inspections of its Timonium facility to insure

that it is implementing the provisions of its corrective action plan. The Board believes that this sanction is appropriate in order to address deficiencies revealed in this matter, as well as to educate other pharmacies and distributors of sterile drug products as to the importance of strict adherence to aseptic and sterile compounding procedures.

ORDER

Based on the foregoing Findings of Fact and Conclusions of Law, it is this 18th day of April, 2006, by a majority of the Board considering this case, that under the authority of Health Occupations Article, § 12-313, it is

ORDERED that the Order of Summary Suspension of Cardinal Permits No. PW0080 and D01333 was properly issued; and be it further,

ORDERED that Cardinal may petition the Board for reinstatement, provided that Cardinal submit to the Board a corrective action plan that is approved by the Board; and be it further,

ORDERED that the Board shall conduct a random inspection of Cardinal's Timonium facility no later than six (6) months after the date of this Order to insure compliance with the corrective action plan; and be it further,

ORDERED that Cardinal shall comply with all laws governing the operation of a pharmacy and the distribution of prescription drugs; and be it further,

ORDERED that this is a Final Order of the Maryland Board of Pharmacy and as such

is a PUBLIC DOCUMENT pursuant to *Md. Code Ann.*, State Gov't §§ 10-611 *et seq.*

April 18, 2006
Date

Jeanne Furman, P.D.
Board Secretary

NOTICE OF RIGHT TO APPEAL

Pursuant to *Md. Code Ann.*, Health Occ. § 12-316, you have a right to take a direct judicial appeal. A petition for appeal shall be filed within thirty (30) days of your receipt of this Final Order and shall provide for judicial review of a final decision in accordance with the Maryland Administrative Procedure Act, *Md. Code Ann.*, State Gov't §§ 10-201 *et seq.*, and Title 7, Chapter 200 of the Maryland Rules.