

Responses to comments from NRC Regions, Agreement States, and Advisory Committee on Medical use of Isotopes on the NorthStar Medical Radioisotopes, LLC RadioGenix™ Molybdenum-99/Technetium-99m Generator System Licensing Guidance for Medical Use Licensees, Medical Use Permittees, and Commercial Nuclear Pharmacies

Background

The intent of the guidance document is to describe the information a licensee needs to successfully apply for authorization to possess and use a product (in this case the NorthStar RadioGenix™ System) regulated under the provisions of 10 CFR 35.1000. “Other medical uses of byproduct material or radiation from byproduct material.” It is not intended to be an extensive description of the system or its components. Therefore, comments that requested specific and detailed information on shielding, solutions, and how the device works are generally outside the scope of the guidance document and are answered by indicating where the more detailed information can be found, e.g., the Safety Evaluation Report or the NorthStar operator’s manual provided with the system.

The Nuclear Regulatory Commission (NRC) distributed the proposed guidance to the NRC Regions, Agreement States, and the Advisory Committee on the Medical Use of Isotopes (ACMUI) for review and comment. Eight commenters responded. The comments were grouped according to the headings and subheadings located in the final guidance, when possible. This provides an ability to align most of the comments with specific sections in the final guidance. Comments requesting additional information on the materials used to make the NorthStar RadioGenix™ System, how specific components work, and general dimensions are answered in the Safety Evaluation Report, which was not available to the commenters. These comments are found under heading “Safety Evaluation Report.” Further, if more than one commenter had the same or similar comments, the comments were combined and attributed to the specified number of commenters. If a single commenter had more than one closely related comment, the comments were combined and attributed to the single commenter. All regulators may find the responses to the comments provide additional insight in applying the guidance.

Broad Commenter Statements

Comment: One commenter stated that the RadioGenix™ System is a large system that some licensees may not have room for and assumed that the main users would be nuclear pharmacies.

Response: No change was made to the guidance based on this comment. The dimensions and weight of the system are available to licensees from NorthStar and to regulators in the Safety Evaluation Report. Facility specific considerations for accommodation of the size and weight of the device will need to be reviewed and approved in the licensing of this device.

Comment: One commenter stated that they do not see the value in using the RadioGenix™ System and that the positives of the system seem to be outweighed by the negatives. The commenter based this on the increased potential to have workers exposed to higher radiation fields than those normally associated with conventional fission molybdenum/technetium

generators, and the necessity for the licensee to routinely perform additional surveys to identify higher than expected radiation fields and system failures.

Response: No change was made to the guidance based on this comment. Because NRC neither promotes nor endorses products that use radioactive materials and this comment asks for an opinion on the merits of the fission-based generator versus the RadioGenix™ System, this comment is outside the scope of the guidance, which concerns acceptable use of the RadioGenix™ system under 10 CFR 35.1000.

Comment: One commenter stated that the draft Licensing Guidance is overall reasonable and not particularly onerous for prospective users and that given the new and novel features of the NorthStar generator system, licensing under 10 CFR 35.1000 is reasonable.

Response: No change was made to the guidance based on this comment. The comment supports the guidance.

Cover Page

Comment: One commenter pointed out that there was a period on the cover page after LLC in NorthStar Medical Radioisotopes, LLC that needed to be removed.

Response: A change was made to the guidance based on this comment. The period was removed from the cover page.

Comment: One commenter thought that the title was too wordy and did not align with other 10 CFR 35.1000 guidance titles.

Response: No change was made to the guidance based on this comment. The title does not align with other 10 CFR 35.1000 guidance because this document includes guidance for both medical use licensees and commercial nuclear pharmacy licensees. Including this important distinction in the title of the guidance makes the title longer than most 10 CFR 35.1000 guidance documents.

Comment: One commenter wanted to add a revision number to align with other 10 CFR 35.1000 guidance documents.

Response: No change was made to the guidance based on this comment. This is the original guidance document for the Northstar RadioGenix™ System and, as such, no revision number is needed.

Comment: One commenter wanted the guidance incorporated into NUREG-1556 Volumes 9 and 13 for medical use and commercial radiopharmacies, respectively. The commenter believed that with both Volumes 9 and 13 currently undergoing a revision it was an opportune time to include the guidance on the NorthStar RadioGenix™ System. The commenter expressed an additional concern that to date, no 10 CFR 35.1000 regulated use has been moved from that categorization. The commenter acknowledged that the 10 CFR 35.1000 provision is a valuable

and needed path to address types of use that are not otherwise specified in 10 CFR Part 35, but did not believe that this designation should exist into perpetuity.

Response: No change was made to the guidance based on this comment. One of the reasons the RadioGenix™ System has been identified as an emerging technology under 10 CFR 35.1000 is for its unique features, as discussed further in the guidance. As an emerging technology, it is expected to evolve with time as both the users and manufacturer gain experience. For this reason, the guidance document is expected to need future revisions. The revision of the NUREG-1556, Volumes 9 and 13 occur on an infrequent basis and are not designed for changes in emerging technologies.

Introductory information on the The NorthStar RadioGenix™ Molybdenum-99/Technetium-99m Generator system

Figure

Comment: One commenter thought that the color coding used in the figure to identify the components was confusing and recommended arrows to identify each component. A second commenter suggested various changes to the background, colors, and revisions to annotate what was behind the cabinet doors in the graphics. A third commenter pointed out that although the text referred to the red-outlined computer, the drawing of the RadioGenix™ device only used red on the four service doors.

Response: A change was made to the guidance based on these comments. The figure of the RadioGenix™ System was revised to change from color outlines to solid, dashed, dotted and other black and white formats to help differentiate the components. Also, arrows were added with text labelling for clarity. Additional information about the contents of each cabinet is unnecessary for the development of the guidance document, which concerns acceptable use of the RadioGenix™ system under 10 CFR 35.1000, but is included in the Safety Evaluation Report.

Comment: One commenter requested that for a more direct comparison, the rectangle used to designate the common Mo-99/Tc-99m generator in the photo diagram should be compared to a single NorthStar source vessel and the overall RadioGenix™ System compared to a multi generator shielded generator storage cabinet.

Response: A change was made to the guidance based on this comment. The figure now includes labels and markings that make it clearer. The source vessel, which is approximately the same size as a conventional Mo-99/Tc-99m generator, replaces the rectangle and provides a better size reference point.

Comment: Two commenters liked the inclusion of the RadioGenix™ System picture in the guidance. One questioned whether it should be inserted before the body of the narrative without some introductory description of what the figure depicts. The other requested that it be moved to the back of the guidance as a reference/appendix.

Response: A change was made to the guidance based on these comments. A new section labeled “Introductory information for the RadioGenix™ System” was added after the Table of Contents. This image is now at the front of the guidance because it is important to see the differences in size and complexity between a conventional Mo-99/Tc-99m generator and the RadioGenix™ System.

Comment: One commenter noted that the phrase, “...for the...,” is repeated in the text describing the components of the RadioGenix™ System that went with the picture of the RadioGenix™ System.

Response: A change was made to the guidance based on this comment. The original RadioGenix™ System diagram was replaced with a new Figure and the description of RadioGenix™ System was revised. The phrase “for the ...” in the comment is no longer in the guidance.

Comment: One commenter requested that numbers be added to the figure to show the order in which the Mo-99 flows through the system to produce the Tc-99m product, and show how various liquids flow through the system during the complete process into the waste container.

Response: No change was made to the guidance based on this comment. The system is designed to run different protocols, and each protocol has different fluid pathways. Adding numbers to illustrate the flow pathways would therefore be confusing. The written description in the guidance of the Mo-99/Tc-99m movement in this complex process is therefore preferable. Further, the RadioGenix™ System includes videos that show the step-by-step procedures for each protocol. These videos can be displayed on the computer monitor at any time.

Comment: One commenter wanted to know what a source vessel is.

Response: No change was made to the guidance based on this comment. The manufacturer calls the shielded radiation transport vessel that the Mo-99/Tc-99m is shipped in the source vessel. There is a picture of the source vessel in the figure and it is defined the first time the term appears, which is in the section “Molybdenum/Technetium (Mo/Tc) flow through the RadioGenix™ System.” Further, the source vessel is shown in Attachment 4 of the Safety Evaluation Report.

Comment: One commenter stated that the guidance should include a statement that with typical use, the user only has to open the waste cabinets to exchange waste approximately once every few weeks, or provide the expected number of uses before an exchange would be necessary.

Response: No change was made to the guidance based on this comment. The Operation and Maintenance Manual will be available to the licensee and will describe when to open the waste cabinets to exchange waste. This will vary from location to location depending on use. Each waste container holds approximately 3.5 liters, which is approximately 230 elutions.

Safety Evaluation Report

Comment: One commenter pointed out that there was no information on expected dose rates to operators in the guidance document. A second commenter believed that inclusion of expected dose rate information in the Safety Evaluation Report would be helpful for estimating typical doses to radiation workers who will be responsible for changing out the source vessel. The commenter also wanted to know the maximum number of cycles and/or duration of use before the source vessel must be exchanged.

Response: No change was made to the guidance based on this comment. The intent of the guidance document is to describe the information a licensee needs to successfully apply for authorization to possess and use the RadioGenix™ System under 10 CFR 35.1000. It is not intended to be an extensive description of the system or the components. A radiation dose map is included in both the RadioGenix™ System Operator Guide and the Safety Evaluation Report. The dose map can be used to estimate expected worker doses. The source vessel maximum number of cycles of use is dependent on facility usage. An individual source vessel cannot be used for more than 14 days because of its expiration date.

Comment: One commenter pointed out that there was no information regarding the actual size or weight of this system in the guidance document.

Response: A change was made to the guidance based on this comment. The weight and dimensions of the RadioGenix™ System were added to the figure. The RadioGenix™ System, with shielding and excluding the source vessel and discarded waste container cabinet, weighs approximately 3,011 pounds (1360 kg). This information is also available to licensees from NorthStar and to the regulators in Attachment 2 of the Safety Evaluation Report.

Comment: One commenter pointed out that there was no shielding information for the device in the guidance document.

Response: No change was made to the guidance based on this comment. This information is available to licensees from NorthStar and to the regulators in the Description Section of the Safety Evaluation Report, but is not necessary for the guidance, which concerns acceptable use of the RadioGenix™ system under 10 CFR 35.1000.

Comment: One commenter suggested using specific language in the guidance when describing “chemical solutions.”

Response: No change was made to the guidance based on this comment. The specific name for each chemical solution is available to licensees from NorthStar and to regulators in the Description Section of the Safety Evaluation Report. The applicant may use this information to develop their radiation safety program but the applicant does not need to submit this information to get a license under the guidance, which concerns acceptable use of the RadioGenix™ system under 10 CFR 35.1000.

Comment: One commenter requested inclusion of the software name and version used in the RadioGenix™ system in the guidance.

Response: No change was made to the guidance based on this comment. The software name and version is available to licensees from NorthStar and to regulators in the Safety Evaluation Report.

Comment: One commenter questioned if there will be a Sealed Source and Device Registration Certificate for the RadioGenix™ system.

Response: No change was made to the guidance based on this comment. The RadioGenix™ system is not a sealed source and it will not have a Sealed Source and Device (SSD) Certificate. However, a Safety Evaluation Report was developed and it will be accessible to the U.S. NRC and the Agreement States in the Sealed Source and Device Registry (SSDR). Licensees and potential licensees should obtain information on the RadioGenix™ system directly from the manufacturer.

Comment: One commenter suggested deleting references to the Sealed Source and Device (SSD) Safety Evaluation because the RadioGenix™ system is not a sealed source.

Response: A change was made to the guidance based on this comment. The references to the SSD/Safety Evaluation Report were replaced with Safety Evaluation Report in the guidance. The RadioGenix™ System does not meet the definition of a sealed source.

Comment: One commenter stated that a review that emulates an SS&D review should be performed by qualified individuals to assess radiation safety issues and that the information be available to all involved parties. In the absence of such a review, the licensing reviews will be longer as the licensing agency will have to get specific information directly from the vendor in order to review the application.

Response: No change was made to the guidance based on this comment. The guidance references a Safety Evaluation Report (SER). A copy of the SER will be available to regulators in the SSDR and to applicants from the manufacturer.

Comment: One commenter wanted more information on what the syringe pump and multichannel distribution valve were connected to, when materials move through them, and whether the system was closed.

Response: No change was made to the guidance based on this comment. The system is closed and the protocols listed in the guidance determine when various materials move through the system. The detailed information concerning the syringe pump and multichannel distribution valve functioning is not necessary for submitting an application to possess and use the RadioGenix™ System and is thus beyond the scope of the guidance, which concerns acceptable use of the RadioGenix™ system under 10 CFR 35.1000. This information is contained in the staff's Safety Evaluation Report.

Molybdenum/Technetium (Mo/Tc) flow through the NorthStar RadioGenix™ Molybdenum-99/Technetium-99m Generator System

Comment: One commenter asked to have the cradle to grave approach to the RadioGenix™ System and the purpose for each cabinet.

Response: Changes were made to the Safety Evaluation Report and guidance based on this comment. The Safety Evaluation Report addresses installation, service and repair, removal, and disposal with regard to cradle to grave for the entire device as well as describing the purpose of each cabinet. Furthermore, information was added to the “Molybdenum/Technetium (Mo/Tc) flow through System” section of the guidance to describe the “cradle-to-grave” movement of Mo-99 through the system

Comment: One commenter requested that the title to the section “Molybdenum/Technetium (Mo/Tc) flow through the RadioGenix™ System” be deleted and that the information be added to the figure at the appropriate places.

Response: No change was made to the guidance based on this comment. Having the flow description as a standalone section conveys the complexity of the Mo-99/Tc-99m processor and putting this information into the figure would increase the figure’s complexity.

Comment: One commenter suggested including a statement that “The generator system is only designed to draw liquid from one molybdenum vessel at a time, until it has decayed below its useful activity.”

Response: No change was made to the guidance based on this comment. Although the operator can only draw from one vessel at a time, the operator can choose which one of the four available vessels to draw from.

Comment: One commenter suggested including a statement that “The generator system is not designed to have multiple "active" vessels.” The commenter also stated that the system is only designed to draw liquid from one molybdenum vessel until that vessel has decayed below its useful activity and that the other three cabinets hold molybdenum vessels for decay-in-storage.

Response: No change was made to the guidance based on this comment. All four cabinets of the RadioGenix™ System can hold active vessels. The operator can choose which active vessel to draw from for an elution.

Comment: One commenter questioned how much users are interacting with the RadioGenix™ System and suggested including in the guidance a description of how often the user opens the various doors during normal routine use.

Response: No change was made to the guidance based on this comment, as it is not necessary for the guidance, which concerns acceptable use of the RadioGenix™ system under 10 CFR 35.1000. This information is available to licensees from NorthStar and to regulators in the Safety Evaluation Report. The PSC door is opened to add a new column and Product door is opened to retrieve the final product for each production run; the Source Bay doors and

Discard Material doors are only opened to replace source vessels and waste containers; the Service door and Transfer door will be accessed only during maintenance performed by NorthStar or an individual certified by NorthStar to perform the maintenance; and the Service door and Transfer door also may be opened in the physical presence or in the direct audio or video communication of a NorthStar service representative.

Protocol tasks

Comment: One commenter requested that the heading “Protocol tasks” be deleted and that the information under this section be moved to the figure and attached to the computer or alternatively to define the term “protocol”.

Response: No change was made to the guidance based on this comment. However, the term “protocol” was further clarified based on a different comment.

Comment: One commenter recommended adding the word “the” before door and “and” instead of the comma to the phrase “opening shielded door, handling and disposal of radioactive materials and potentially contaminated components.”

Response: A change was made to the guidance based on this comment. The shielded doors were made plural and the “and” was added to replace the comma.

Comment: One commenter stated that term “protocol” is confusing in the following sentences: “The RadioGenix™ System is fully computer-driven with specific protocols that must be performed in a set sequence and by individuals with specific radiation safety training and experience for each protocol,” and “To use the accounts and roles structure of the RadioGenix™ System’s software to limit what protocol can be initiated by an individual.”

Response: A change was made to the guidance based on this comment. The term “protocol” has been clarified in the introductory section of the guidance to refer to discrete portions of the software program that focus on performing a specific function.

Comment: One commenter wanted to replace the word “protocol” with “task”. The commenter stated that “a protocol usually connotes a series of tasks and not an individual task. The most common meaning of protocol is “a system of rules that explain the correct conduct and procedures to be followed in formal situations.” This was made clear under the subheading of “Protocol tasks” which was placed before the body of the narrative of the Licensing Guidance, where all the individual “tasks” were listed: 1) initialize system, 2) add/change reagent kit, 3) produce (i.e., separate) Tc-99m, 4) remove source vessel, 5) sterilization, and 6) exchange used reagent container.” The commenter further noted inconsistencies with the use of the terms “protocol” and “software,” and recommended using the term, “individual tasks,” throughout the document for consistency and to clarify that there is only one protocol and software program with this system.

Response: A change was made to the guidance based on this comment. The term “protocol” has been clarified in the introductory section of the guidance. The NorthStar protocols refer to discrete portions of the software program containing multiple steps that have to be performed by

the user to complete a certain function. Thus, these protocols include multiple steps and tasks under a single heading, and the term “protocol” is still used to designate these activities.

Comment: One commenter noted that the sequence of tasks and training was felt to be more analogous to chemistry modules for preparing cyclotron-produced radiopharmaceuticals rather than generator-produced radiopharmaceuticals. The commenter also suggested clarifying the entire sequence of training for individual tasks within a “protocol” and then adding the applicant’s name to the “software”.

Response: No change was made to the guidance based on this comment. The guidance addresses the training and authorization sequence per “protocol tasks” in the “Training and Experience – System Administrator and RadioGenix™ System Administrator Designee” section. NorthStar’s name for the software version was added to the Safety Evaluation Report.

10 CFR 35.1000 Use

Comment: One commenter thought that the statement “The built in safety features are designed to ensure that the device fails in a shielded manner,” as written, makes the device appear as if it is expected to fail. The commenter further stated that if there were an SS&D certificate or Safety Evaluation Report to refer to, this might be easier to explain.

Response: A change was made to the guidance based on this comment. Clarification was added to the guidance to indicate that **if** the device failed, the radioactive material would remain shielded. There is a Safety Evaluation Report for this device that will be available in the Sealed Source and Device Registry. As part of the device safety evaluation, consideration was given to what will happen if the device fails. The conclusion of the safety evaluation was that the device design (i.e., the liquid retention feature built into the system) was sufficient to ensure that if a failure were to occur, there was adequate volume for retention of the radioactive fluid to ensure no leakage or high radiation doses with the doors closed.

Comment: One commenter wanted to know who produced the source vessel and for the first bullet to be parallel in structure to the other bullets.

Response: A change was made to the guidance based on this comment. The text was revised to make the structure parallel and clarified that both the source vessel and the liquid molybdenum are produced specifically for NorthStar for the RadioGenix™ System.

Comment: One commenter wanted information on how the material is ordered and delivered to the licensee, and initially installed in the system to be included in the guidance.

Response: No change was made to the guidance based on this comment. The level of detail requested by this commenter is not addressed in this guidance because it is part of the general procedures a licensee develops in the ordering and receipt of any radioactive material and instillation of any device containing radioactive material. The guidance concerns the acceptable use of the RadioGenix™ system under 10 CFR 35.1000.

Comment: One commenter wanted to know when a licensee would add a new source vessel and when it would remove an old source vessel.

Response: No change was made to the guidance based on this comment. The guidance under the section “Molybdenum/Technetium (Mo/Tc) flow through the RadioGenix™ System” addresses when a new source vessel is obtained and when it is taken out of service. In response to another comment, text was added to this section to show the source vessel with the decayed liquid molybdenum solution is returned to the manufacturer. In general, the source vessel is used until all the material is no longer usable (i.e., beyond its expiration date). At that point, the vessel will be replaced with a new one, ensuring that the licensee does not exceed the maximum activity possession limit.

Comment: One commenter wanted to know how much activity is contained in the source vessels.

Response: No change was made to the guidance based on this comment. The maximum activity in each source vessel (7.5 curies of Mo-99/Tc-99m) is given in the guidance document under “Radionuclides, Form, Possession Limits” and “License Authorizations.” This information is also found in the Safety Evaluation Report.

Comment: One commenter wanted to know what other hazards are a concern other than adding new and removing old source vessels.

Response: No change was made to the guidance based on this comment. The guidance document and Safety Evaluation Report address the radiological safety hazards associated with the RadioGenix™ System in general terms and requires the applicant or licensee to have training in the radiation safety precautions and instructions associated with the system.

Comment: One commenter wanted to know if the liquid molybdenum was in solution.

Response: A change was made to the guidance based on this comment. In the examples of new features that differentiate the RadioGenix™ System from other generators, the word “solution” was added after “molybdenum liquid” to clarify that it is a dissolved chemical solution in liquid form. This is to differentiate the liquid Mo/Tc-99m from the Mo adsorbed on the traditional generator column.

Comment: One commenter wanted clarification on the terms “processing” and “isolate” in the bullet “Licensee processing of the molybdenum liquid to isolate the Tc-99m for medical use.”

Response: A change was made to the guidance based on this comment. A revision was made to the bullet which is intended to describe in simple terms how the RadioGenix™ System differs from conventional generators.

Comment: One commenter wanted to know what materials were moved through the system and if the licensee moves the materials referred to in the bullet “Materials move by computer driven syringe pump with a multichannel distribution valve.”

Response: No change was made to the guidance based on this comment. The bullet states that the computer operates the syringe pump and the multichannel distribution valve to move the solutions through the system. The guidance does not specify the particular materials that are moved through the system because the solutions vary depending on the particular processing step. The description of the fluid path is incorporated into the Safety Evaluation Report.

Comment: One commenter wanted more information on what the syringe pump and multichannel distribution valve were connected to, when materials move through them, and whether the system was closed.

Response: No change was made to the guidance based on this comment. The system is closed and the protocols listed in the guidance determine when various materials move through the system. The detailed information concerning the syringe pump and multichannel distribution valve functioning is not necessary for submitting an application to possess and use the RadioGenix™ System, and is therefore beyond the scope of the guidance document, which concerns acceptable use of the RadioGenix™ system under 10 CFR 35.1000. This information is included in the Safety Evaluation Report.

Comment: One commenter wanted to know if there were specifications to replace components after a certain number of elutions and if there were specifications for replacement parts for pumps, valves, and other components.

Response: No change was made to the guidance based on this comment. There are specifications for all components. The consumable components need to be replaced after a set number of elutions. NorthStar has designed the system to keep track of the elutions and inform the user when these components must be changed. The “License Commitments, 1. Routine and non-routine activities” section in the guidance clarifies that the applicant shall commit to both using only manufacturer approved consumable replacement parts and only allowing individuals specifically trained and authorized by the manufacturer to perform any non-routine maintenance activities.

Comment: One commenter wanted to know whether all the tubes are inside the unit and what maintenance is needed for the pumps and valves.

Response: No change was made to the guidance based on this comment. All the tubes are inside the unit behind shielded doors or in shielded channels. The maintenance for the pumps and valves is performed only by NorthStar or individuals specifically trained and authorized by NorthStar to perform such maintenance.

Comment: One commenter expressed concerns about the guidance not addressing the parts of the RadioGenix™ System that licensees will be allowed to replace versus the parts that only the vendor can replace.

Response: A change was made to the guidance based on this comment. The guidance was revised to include commitments to follow the instructions in the manufacturer’s Operators Manual, which includes specific information about replaceable parts that can be used and who

can perform the replacement. Under the guidance, installation, relocation, removal, service, and repair of the device shall only be performed by NorthStar. The end user shall replace the separation column and other components at the interval specified by the device manufacturer. These statements are also in the Limitations and other "Considerations of Use" section of the Safety Evaluation Report.

Comment: One commenter questioned whether there are specifications for certain critical components that require them to be replaced by the vendor.

Response: No change was made to the guidance based on this comment. Under the guidance, only NorthStar is authorized to provide all of the replaceable components. The guidance addresses whether NorthStar or the licensee can perform the replacement.

Comment: One commenter said that a hyphen was needed between fission and produced throughout the guidance.

Response: A change was made to the guidance based on this comment. A hyphen was added between fission and produced when it appeared in the guidance.

Comment: One commenter wanted to know what the first chromatography column was.

Response: A change was made to the guidance based on this comment. The guidance now clarifies that this is the chromatography column that captures the Tc-99m, i.e., when the Mo/Tc-99m solution passes through, the molybdenum continues to flow through but the Tc-99m adheres to the column.

Comment: One commenter wanted to know the replacement frequencies for both the first and second columns and why routine replacement is required.

Response: No change was made to the guidance based on this comment. A new second column is put in the RadioGenix™ System product cabinet before each elution of Tc-99m. The first column in the "PSC" cabinet is changed less frequently and at intervals established by the manufacturer.

Comment: One commenter wanted to know if the first column is replaced when the Tc-99m is inside it after the Tc-99m is eluted, and if the second column is replaced when the Mo-99 is inside it or, after it is washed off. The commenter also wanted to know how much residual Mo-99 activity is on the second column when it is replaced.

Response: No change was made to the guidance based on this comment. The first and second columns are not changed during the production cycle but at different frequencies following production. Both are replaced at a point when the Mo-99 and Tc-99m have been washed off for the first and second columns, respectively. The intent of the second column is to capture any molybdenum captured on the first column but removed in the final wash. The

chromatography columns can still retain some material after they are washed and therefore they may contain small amounts of radioactive material. The residual activity is detectable but expected to be minimal under normal situations.

Comment: One commenter wanted to know more about how the first and second chromatography columns were handled.

Response: No change was made to the guidance based on this comment. The columns are handled with tongs and the manufacturer (or a person certified by the manufacturer) will provide detailed instructions.

Comment: One commenter wanted to know who performs the routine ozone sterilization, how frequently it is performed, and how it is done.

Response: No change was made to the guidance based on this comment. The ozone sterilization is performed by the licensee's individuals that have demonstrated proficiency in the ozone sterilization protocol. Detailed information concerning the frequency is provided by NorthStar in the operator's manual.

Comment: One commenter wanted to know where the radioactive and nonradioactive waste solution is collected and held for decay.

Response: A change was made to the guidance based on this comment. The radioactive and nonradioactive solutions are not only collected, but held for decay in the RadioGenix™ System, and this was clarified in the guidance.

Comment: One commenter wanted to know how the nonradioactive waste is separated from the radioactive waste.

Response: No change was made to the guidance based on this comment. The nonradioactive waste is not separated from the radioactive waste. All solutions, except the molybdenum solution that are run through the RadioGenix™ System are captured in a waste container in one of the two discarded material cabinets. The nonradioactive solutions are combined with the radioactive waste because they may be contaminated with residual radioactive contamination from the tubing.

Comment: One commenter wanted to know how material is added to waste, who handles the waste solutions, and how frequently are they handled.

Response: No change was made to the guidance based on this comment. The RadioGenix™ System protocols handle the solution, and after the solutions are used sends them to the waste container. The licensee does not handle the waste until it has been held for decay. The frequency will depend on how often the RadioGenix™ System is used.

Comment: One commenter wanted to know who does what to the waste solutions to store for decay and disposal.

Response: No change was made to the guidance based on this comment. The RadioGenix™ System is a closed system. The waste solutions are automatically routed to a shielded waste container within the System. The licensee only handles the waste container after the radioactive waste has time to decay.

Comment: One commenter believed that the guidance needed to provide context for the description “computer driven” as it applies to the RadioGenix™ System.

Response: No change was made to the guidance based on this comment. Additional information of how the NorthStar computer driven system works is provided in the operator’s manual and the Safety Evaluation Report. Further explanation of the computer driven processes is not necessary for submitting an application to possess and use the RadioGenix™ System and is beyond the scope of the guidance, which concerns acceptable use of the RadioGenix™ system under 10 CFR 35.1000.

Comment: One commenter believed that “latched” should be replaced with “secured” in the sentence: “The engineering specifications for the materials and components are designed to maintain the device’s integrity as a closed system, withstand high radiation fields for extended periods, and maintain adequate shielding of the radioactive material with all ten cabinet doors closed and latched, as well as supplemental shielding is in place.”

Response: A change was made to the guidance based on this comment. The term “secured” was added to the closed door position description.

Comment: One commenter stated that the unique features of the RadioGenix™ System cited in the guidance align with those addressed in a safety evaluation similar to the SS&D sheet for the Bristol-Meyer Squibb Rubidium-82 generator with infusion system (TN-1004-D-101-S) and a safety evaluation should be performed for the RadioGenix™ System by qualified individuals.

Response: No change was made to the guidance based on this comment. The Bristol-Meyer Squibb Rubidium-82 generator with infusion system (TN-1004-D-101-S) SS&D sheet was retracted based on a letter dated July 15, 2004 from Tennessee because the generator is regulated by the U.S. Food and Drug Administration as a drug under the Federal Food, Drug and Cosmetic Act.

The RadioGenix™ System is not a sealed source or device. NRC developed a Safety Evaluation Report for the RadioGenix™ System that will be located in the Sealed Source and Device Registry and accessible to NRC and the Agreement States.

Comment: One commenter thought that the use of Tc-99m based radiopharmaceuticals is already authorized under the type of medical use in 10 CFR 35.200, as is acknowledged in the proposed guidance for the generator system. The commenter cited multiple parts of the

regulations with specific Tc-99m generator elution and use requirements. The commenter also thought that the licensee in this situation is a 10 CFR 35.200 medical use licensee, not a 10 CFR 35.1000 licensee or a radiopharmacy.

Response: No change was made to the guidance based on this comment. This guidance only addresses the possession and use of the RadioGenix™ System for the production of Tc-99m by a commercial nuclear pharmacy under 10 CFR Part 30 or a medical use licensee under 10 CFR 35.1000. The medical use of the Tc-99m and radiopharmaceuticals containing Tc-99m are regulated under 10 CFR 35.200.

Comment: One commenter believed that the guidance identified issues related to training/radiation safety that are not sufficient reasons to classify use of the RadioGenix™ System as a 10 CFR 35.1000 medical use.

Response: No change was made to the guidance based on this comment. NRC classifies medical uses under 10 CFR 35.1000 if it does not fall under another part of 10 CFR Part 35, i.e., it is missing altogether, an exemption must be granted to the regulations, or there are additional radiation safety considerations that are not included in the regulations if the use was under another section of the regulations. The commenter is correct that the result of the classification of the RadioGenix™ System as a 10 CFR 35.1000 medical use resulted in additional guidance on training and experience and radiation safety.

Comment: One commenter believed that Footnote 1 should be revised to read: ¹ Medical Uses of Byproduct Material Licensed under 10 CFR 35.1000 are designated as Compatibility Category D. Agreement States are not required to adopt guidance promulgated pursuant to these regulations, but are not prohibited from adopting Compatibility Category D regulations, and associated guidance, if they so choose.

Response: A change was made to the guidance based on this comment. A final sentence was added to the footnote to clarify that the Agreement States are not required to adopt guidance promulgated pursuant to 10 CFR 35.1000, but are not prohibited from adopting the guidance.

2. Commercial Nuclear Pharmacy Use under 10 CFR 30.33

Comment: One commenter disagreed that the RadioGenix™ System should be categorized in 10 CFR 35.1000. The commenter based the conclusion on: (1) 10 CFR 35.1000 medical use does not apply to radiopharmacies which are regulated under 10 CFR Part 30 and 10 CFR 32.72; (2) preparation of a radiopharmaceutical by a licensed radiopharmacy is not medical use; (3) the radiopharmacy is authorized to possess and use radioactive materials for the manufacture, preparation, or transfer for commercial distribution of radioactive drugs containing byproduct material for medical use under 10 CFR 35; (4) radiopharmacies are not authorized for medical use and do not have medical use authorized users; and (5) the means of production of the Mo-99 parent isotope is not relevant to the eventual medical use of derivative Tc-99m based radiopharmaceuticals.

Response: No change was made to the guidance based on this comment. The use of the RadioGenix™ System at a commercial nuclear pharmacy is not being regulated under 10 CFR 35.1000. The guidance states that it is regulated under 10 CFR Part 30 and 10 CFR 32.72 and the unique design characteristics and use features that differentiate the RadioGenix™ System from a conventional fission Mo-99/Tc-99m generator results in the need for additional information and commitments that are not required to safely use a conventional fission Mo-99/Tc-99m generator. Therefore, a commercial nuclear pharmacy that is not specifically authorized for the RadioGenix™ System will not meet the requirements in 10 CFR 30.33, “General requirements for issuance of specific licenses” for its use without providing additional training and experience for individuals, and making certain commitments to address specific training and safety provisions.

Comment: One commenter did not believe that the first paragraph of the section under 10 CFR 30.33 provided new information for applicants. The commenter further stated that 10 CFR 30.33, “General requirements for issuance of specific licenses”, contains only general information, in broad statements, and it was the purpose of specific licensing guidance (NUREG-1556 series) is to aid the applicant (and license reviewer) in identifying the specific information needed for the proposed use of licensed material.

Response: No change was made to the guidance based on this comment. The intent of the first paragraph was to provide the reason for concluding that the current licensing guidance for molybdenum generators is not sufficient for licensing the RadioGenix™ System and to inform the commercial nuclear pharmacy of the additional guidance available for the RadioGenix™ System.

3. Licensing Guidance

Comment: Two commenters believed that the guidance should include a statement that eluting Tc-99m from the NorthStar generator is under 10 CFR 35.1000, but medical facilities that use unit doses of NorthStar Tc-99m should be able to administer it under 10 CFR 35.200. Once the drug is in a unit dose, it is handled exactly the same as any other Tc-99m product. At sites that receive unit doses, there should be no need to approve physicians for 10 CFR 35.1000 use.

Response: No change was made to the guidance based on this comment. The guidance clearly states that it applies to medical use applicants and licensees that request or possess the NorthStar RadioGenix™ System and to the commercial nuclear pharmacy licensees and applicants that possess the NorthStar RadioGenix™ System.

4. General

4.1. Sensitive Security- Related Information

Comment: One commenter thought that there should be a hyphen between Security and Related in the Table of Contents heading “Sensitive Security Related Information” and in other locations in the document.

Response: A change was made to the guidance based on this comment. The hyphen was added to the heading in the Table of Contents and in other locations in the guidance.

Comment: Two commenters suggested that the “Sensitive Security Related Information” section was not needed because the RadioGenix™ System does not involve any category 1, 2, (and/or 3) quantities of radionuclides.

Response: No change was made to the guidance based on this comment. This section is included because it is the NRC Sensitive Unclassified Non-Safeguards Information (SUNSI) policy to make licensees aware of security issues associated with locations of radioactive materials at the facility in addition to quantities of certain radionuclides.

Comment: One commenter questioned whether licensees have to follow the SUNSI policy and mark documents in accordance with Regulatory Issues Summary (RIS) 2005-31.

Response: A change was made to the guidance based on this comment. The commenter is correct RIS 2005-31 encourages, but cannot require licensees to mark SUNSI information. The “must” was changed to “should.”

4.2. Radionuclides, Form, Possession Limits, and Purpose of Use

Comment: One commenter suggested adding a subheader “Distribution pursuant to 10 CFR Part 32” under the heading “Radionuclides, Form, Possession Limits, and Purpose of Use” in the Table of Contents and the guidance to align with the NUREG 1556, Vol. 13 “Consolidated Guidance About Materials Licenses Program-Specific Guidance About Commercial Radiopharmacy Licenses.”

Response: No change was made to the guidance based on this comment. This guidance document addresses only the possession and use of the RadioGenix™ System, and not distribution under 10 CFR 32.72.

Comment: One commenter suggested that the guidance separate the Mo-99 and the Tc-99m into separate entries in the tables in “Radionuclides, Form, and Possession Limits” and “License Authorizations” sections. The commenter also suggested removing the text “NorthStar Mo-99/Tc-99m to be used in the RadioGenix™ System” because the chemical physical form is already stated as liquid.

Response: A change was made to the guidance based on this comment. A change was made to explain why the Mo-99 and Tc-99m were not separated. The “License Authorizations” section that lists the “Radionuclides, Form, and Possession Limits” was revised to add additional information on how to license both a conventional generator and the RadioGenix™ System when the licensee possesses both. The guidance does not split the Mo-99/Tc-99m entry into Mo-99 and Tc-99m because the intent is to license the RadioGenix™ System as a single line item and ensure that only the NorthStar source vessels containing the NorthStar

Mo-99/Tc-99m solution are used with the RadioGenix™ System. This is also why the text “NorthStar Mo-99/Tc-99m to be used in the RadioGenix™ System” was not changed in the guidance.

Comment: One commenter wanted to change the chemical/physical form from “Liquid NorthStar Mo-99/Tc-99m to be used in the RadioGenix™ System” to just “liquid”, and thought that it was appropriate to have this information in the Purpose section of the guidance.

Response: A change was made to the guidance based on this comment. The chemical/physical form was revised to read “Liquid Mo-99/Tc-99m produced by NorthStar to be used in the NorthStar RadioGenix™ System” to clarify that the liquid Mo-99/Tc-99m is restricted to the Mo-99/Tc-99m produced by NorthStar. This is restricted because the NorthStar generator is incompatible with fission-produced liquid Mo-99/Tc-99m, and the fission generators are incompatible with the NorthStar liquid Mo-99/Tc-99m.

Comment: One commenter wanted to know why the term “bulk” was used in the tables for “Radionuclides, Form and Possession limits.” The commenter suggested that only the total Mo-99 or Tc-99m should be given.

Response: A change was made to the guidance based on this comment. The term “bulk” was removed. The NorthStar RadioGenix™ System can have up to 4 source vessels and the entry in the tables in the sections “Radionuclides, Form, Possession Limits, and Purpose of Use” and “License Authorizations” now reflect this. The tables continue to provide the total amounts of Mo-99/Tc-99m. Further, there is an asterisk after the Table in the “License Authorizations” that clarifies how to address the total authorization of Tc-99m.

Comment: One commenter stated that the Purpose section of the guidance as written would exclude a medical use licensee, and the issue of commercial or non-commercial aspect is not relevant. The commenter also stated that the license type (medical or commercial radiopharmacy) is apparent from the license document. The commenter requested changing A. to read: “For use in a NorthStar RadioGenix™ System to elute Tc-99m using only NorthStar compatible solutions and components”.

Response: No change was made to the guidance based on this comment. The guidance was developed to include both medical use and commercial nuclear pharmacies. Item A in the Purpose section includes the wording for both types of licensees, and does not exclude the medical use licensee. NRC puts the 10 CFR 35.1000 medical use statement in the Purpose section of the license and does not issue licenses to stand-alone non-commercial pharmacies.

4.3 Facility Address and Description

Comment: One commenter suggested replacing the “or” with an “and” in the sentence “Provide an address of use and submit a facility diagram and description of the location where the RadioGenix™ System will be used, or stored.”

Response: A change was made to the guidance based on this comment. The sentence was revised to clarify that the intent is to address where the radioactive materials associated with the RadioGenix™ System would be stored. The sentence now reads, “Provide an address of use and submit a facility diagram and description of the location where the RadioGenix™ System will be used, and any other areas where the radioactive materials associated with the RadioGenix™ System are stored.”

Comment: One commenter requested that “Facility Address and Description” section also include a description of adjacent areas and rooms both above and below the unit, whether the areas and rooms are unrestricted or restricted, a description of any shielding, and shielding calculations. Another commenter wanted facility shielding information addressed in this section.

Response: A change was made to the guidance based on this comment. The “Facility Address and Description” section was revised to add the sentence “This information should include a description of adjacent areas and rooms both above and below the unit, whether the areas and rooms are unrestricted or restricted, a description of any shielding, and include shielding calculations, if necessary.”

4.4. Posting Requirements

Comment: One commenter wanted the section on “Posting Requirements” moved to the “Specific Information on Radiation Safety Precautions and Instructions” portion of the “Licensee Commitments” section and a corresponding change made to the Table of Contents.

Response: No change was made to the guidance. No change was made to the Table of Contents. The posting requirements is a reminder to the applicant of a regulatory requirement and, as such, is not a commitment.

5. Training and Experience

Comment: One commenter recommended that the “Training and Experience” heading in the Table of Contents and the document should be replaced with “Authorized Individuals” and subheadings of “Authorized Users” and “Authorized Nuclear Pharmacists.” The commenter believed this would align the document with the NUREG-1556 Series and other 10 CFR 35.1000 guidance.

Response: No change was made to the guidance based on this comment. The heading “Training and Experience” clearly describes the focus of the information that follows. Further, the training and experience described under this heading applies to individuals other than the authorized individuals normally listed on a license. It includes specific training needed by “supervised individuals,” the “RadioGenix™ System Administrator,” and the “RadioGenix™ System Administrator Designee.”

Comment: One commenter wanted to delete all the training subheadings in the Table of Contents and just have the heading “Training.” The commenter stated including the specific training subheadings unnecessarily creates confusion.

Response: A change was made to the guidance based on this comment. The suggested change was not made because each of the training subheadings addressed a different aspect of training and it was important to draw attention to each. However, the heading “Training for authorized individuals, Radiation Safety Officer and supervised individuals as a result of changes to the RadioGenix™ System that affect the safety and operation of the generator,” was simplified to read “Updated training resulting from safety and operational changes to the RadioGenix™ System.” Also, the purpose of this training and the program that permits the licensee to use the RadioGenix™ System after changes affecting safety and operations of the system without an amendment was clarified. Additionally, a note was added to inform Agreement State applicants and licensees that some Agreement States may still require an amendment before use after such changes.

Comment: One commenter stated the headings “Supervised Individuals Operating the RadioGenix™ System” and “RadioGenix™ System Administrator” and “RadioGenix™ System Administrator Designee” should be deleted from the “Training and Experience Heading” unless the individuals will be listed on the license.

Response: A change was made to the guidance based on this comment. The guidance clarifies the individuals will be listed on the license (the authorized individuals and the RSO) and to clarify that the NRC will not list the supervised individuals operating the RadioGenix™ System, the “RadioGenix™ System Administrator” and “RadioGenix™ System Administrator Designee” on the license. However, there was no change to the guidance headings because the intent of the “Training and Experience” heading is to alert the applicant or licensee that specific individuals will require additional training and experience to use the “RadioGenix™ System.”

5.1. Authorized Individuals

Comment: One commenter wanted to remove the term “authorized individuals” from the guidance and replace it with “authorized user”. The commenter stated that “authorized individual” is a new term and not defined anywhere. The commenter further stated individuals authorized to use the RadioGenix™ system should be referred to as authorized users.

Response: No change was made to the guidance based on this comment. The term “authorized individual” was already clarified in the document as “physician authorized users (AUs) and authorized nuclear pharmacists (ANPs)”.

Comment: One commenter stated that it was unclear if the guidance was establishing a new category and title of “Authorized Individuals.” The commenter believed that Authorized Nuclear Pharmacists and Authorized Users have extensive training and experience with regard to safe handling of radioactive materials, as is clear from the requirements set forth in 10 CFR 35 for such individuals.

Response: No change was made to the guidance based on this comment. The guidance does not develop a new category. It uses the term “Authorized Individuals” to address the medical authorized user and the authorized nuclear pharmacist at the same time.

Comment: One commenter wanted the “authorized individual” to be bolded and the training and experience for the AU and the ANP separated with a separate section for the Authorized Nuclear Pharmacist so the requirements for each were clear.

Response: No change was made to the guidance based on this comment. No change was made to the term “authorized individual” because it was already bolded in the guidance. In response to a different comment, the terms “authorized user” and “authorized nuclear pharmacist” were bolded in paragraphs A (1) and (2) of this section, respectively.

A separate section was not made for the authorized nuclear pharmacist because the newly bolded text and the regulatory citations in paragraph B (1) and (2) show which requirements apply to the physician and which to the nuclear pharmacist. Also, the requirements in paragraph B (3), C, and D apply to both.

Comment: One commenter questioned using the term “authorized individuals” instead of the more familiar terms of “authorized users” and “authorized nuclear pharmacist.” The commenter stated there was no reason we can’t allow an ANP or AU for 10 CFR 35.1000 (NorthStar etc.) to be an ANP or AU on another license authorizing the same per 10 CFR 35.2 definition of AU. To use alternative language of “authorized individual” will cause complexity and confusion.

Response: No change was made to the guidance based on this comment. The generator can be used by either a medical use licensee or a commercial nuclear pharmacy licensee, and therefore, the guidance uses the generic term “authorized individual.” Depending on which type of licensee requests use of the RadioGenix™ System, the individual responsible for the RadioGenix™ System can be either a medical licensee “authorized user” or a commercial nuclear pharmacy licensee “authorized nuclear pharmacist.” Although the guidance uses the term “authorized individual” in the Training and Experience Section, when a person is authorized to use the RadioGenix™ System, the person will be identified as either an “authorized user” or “authorized nuclear pharmacist”, as indicated in the License Condition Section.

Comment: One commenter stated that the reference to 10 CFR 35.57(b)(2)(i) in Section B. (3) does not exist in the regulations.

Response: A change was made to the guidance based on this comment. 10 CFR 35.57(b)(2)(i) is part of the revisions of 10 CFR Part 35 in the new rule. The new changes to 10 CFR 35.57 will become effective after the publication of this guidance. Therefore, the citation was changed to 10 CFR 35.57 because it will be correct for the current regulations and the new changes once they become effective.

Comment: One commenter stated that Section B. (3) appears to allow individuals who are certified by a recognized specialty board and who also complete the requirements in Section C and D, to be listed as an authorized user to use/elute the RadioGenix generator. The commenter requested clarification because it seems to contradict the rest of the guidance which specifically mentions Authorized Physician User or Authorized Nuclear Pharmacist.

Response: A change was made to the guidance based on this comment. The requirement to be a physician who can be authorized for 10 CFR 35.200 medical uses or nuclear pharmacist who can be an authorized nuclear pharmacist under the provision of 10 CFR 35.57 was added to Section B.(3). Note that a physician who can be authorized for 10 CFR 35.300 medical uses and has training in 10 CFR 35.290(c)(1)(ii)(G) can also be authorized for 10 CFR 35.200 medical uses.

Comment: One commenter stated that there was no proposed path for a qualified ANP or 10 CFR 35.200 AU for NorthStar to act as a preceptor for others to become qualified, and that one should be established.

Response: No change was made to the guidance based on this comment. Under the guidance, an AU or ANP is only authorized to provide the training if NorthStar certifies that individual to provide the training.

Comment: One commenter suggested that there be a provision in the guidance for a consortium, similar to what is permitted by 10 CFR 30.34 for PET production and non-commercial distribution. Such action could effectively increase the availability of Tc-99m to localized medical communities (consortiums).

Response: No change was made to the guidance based on this comment. Distribution of Tc-99m is not permitted under noncommercial distribution to medical use licensees in accordance with 10 CFR 35.200. The provisions for the consortium were because of the expense of procuring a cyclotron that could produce PET radiopharmaceuticals and that some cyclotrons in academic institutions could be included in a nearby consortium with medical facilities to fund the cyclotron. The consortium licensing approach is not permissible for commercial distribution of radioactive drugs.

Comment: One commenter agreed NorthStar should have sole responsibility for the content of the training course and certification because of the unique design and operation of the NorthStar system.

Response: No response is needed because the comment supports the guidance.

Comment: One commenter recommended that NorthStar provide a video clip of how the system operates for the training module.

Response: No change was made to the guidance based on this comment. NorthStar provides video clips showing a person performing the steps in each protocol as part of the computer operating system, and may use these video clips in its training.

Comment: One commenter thought that arranging for the manufacturer to train all users in the protocols would be impractical.

Response: No change was made to the guidance based on this comment. The guidance permits the training to be provided by either NorthStar or an individual certified by NorthStar to provide the training. This should provide an adequate number of trainers.

Comment: Two commenters requested the guidance define “fully loaded” in the criterion that the individual successfully complete the training and experience provided at a facility authorized to have a RadioGenix™ System using a fully loaded and functional generator.

Response: A change was made to the guidance based on this comment. The phrase “fully loaded” is replaced with “fully functional generator connected to a Mo-99/Tc-99m solution and producing Tc-99m” on pages 5 and 6.

Comment: Two commenters noted that current requirements for authorized nuclear pharmacists in 10 CFR 35.55 do not require documentation of any specific “case studies”. The commenters noted that once named an ANP, pharmacists should not need an additional written attestation to use the NorthStar generator. The commenters recommended removing the requirement for written attestation for authorized nuclear pharmacists and removing requirements for authorized nuclear pharmacists to submit documentation of NorthStar training to the licensing authority.

Response: No change was made to the guidance based on the comment. The complexity of the RadioGenix™ system and the potential for radiation exposures justifies the need for a preceptor statement for all authorized individuals to attest to the satisfactory completion of their training and their ability to independently operate and perform the radiation safety related duties of an authorized individual. Because of the critical and extensive training requirements for the safe use of this system, documentation of completion of training must be submitted for review before the authorized use of the RadioGenix™ system is granted to an individual.

Comment: One commenter wanted to know what additional training was needed for an individual. The commenter questioned whether the NorthStar training certificate is the only requirement for an individual that is already an ANP. The commenter indicated that using the model of an AU for 10 CFR 35.600 HDR use requesting another manufacturer’s HDR, the license reviewer for a RadioGenix™ System application with an individual who is already an ANP, could just add the NorthStar generator use by requiring a description of the training and a copy of the training certificate or letter from NorthStar affirming that training.

Response: A change was made to the guidance based on this comment. In section 5.1, Paragraph “C” was revised to read “The individual: Is identified “In A. or B. above, has successfully” The initial bolding of the conjunctions between A, B, and C were retained to make the structure of the guidance easier to follow, and further clarified that an individual coming through the A or B pathways had to meet the criteria in both C and D.

Therefore, if a pharmacist meets the criteria in A(2), i.e., is already recognized as an authorized nuclear pharmacist, the pharmacist also has to successfully complete the training in C and have a written attestation described in D. The licensee, as in other similar requests for adding additional authorizations for an individual, needs to submit documentation that all the requirements are met. In this case, the licensee would submit documentation that the pharmacist was already recognized as an ANP, documentation that the pharmacist successfully

completed the training and experience described in C, and a written preceptor statement meeting the requirements in D.

Comment: Two commenters noted that the NorthStar generator is in many ways similar to PET radiochemistry cells at cyclotrons that do not require the submission of training documentation before authorizing individuals to operate equipment or for the Radiation Safety Officer to perform his/her duties. The commenters recommended removing the written attestation provision for the RSO and to submit documentation of training for AUs and ANPs, and changing the regulator's review to a licensee commitment.

Response: No change was made to the guidance based on this comment. PET radiochemical systems differ from the RadioGenix™ system in a number of critical areas. The PET radiochemical systems are self-contained, located in a single hot cell, not manipulated manually by the licensee, and the radiation fields decay quickly because the half-lives of the PET radionuclides are much shorter than that of Mo-99. The RadioGenix™ system, on the other hand, has a number of shielded compartments that need to be opened to perform different protocols with the potential for exposure to radioactive material. Thus, under the guidance, strictly adhering to engineering and administrative controls set by the manufacturer is necessary for the safe operation of the RadioGenix™ system and effective response to incidents. Further, the training requirements are specific to the RadioGenix™ system and individually assigned roles and responsibilities within the licensee's radiation safety program. The RSO is responsible for the licensee's entire radiation safety program and the RSO's training and experience must be reviewed by the regulator prior to authorizing the use of the RadioGenix™ system by the licensee. Therefore, documentation of completion of training must be submitted for review for the RSO and authorized individuals.

Comment: Several commenters stated that the preceptor attestations for the RadioGenix™ System were unnecessary.

Response: No change was made to the guidance based on this comment. The complexity of the RadioGenix™ System and the potential for radiation exposures justifies a preceptor statement for all individuals to attest to the satisfactory completion of their training and their ability to independently operate and perform the radiation safety related duties of an authorized individual or the independent performance of the radiation safety related duties of a Radiation Safety Officer.

Comment: One commenter questioned the need to delay the written attestation requirements if all the requirements could be completed in a training environment.

Response: A change was made to the guidance based on this comment. A change was made to clarify that after 5 years, NorthStar personnel certified by NorthStar, or other authorized individuals, will provide the training and proctor the task or emergency procedure and provide the attestations. The initial attestations are made by NorthStar or individuals certified by NorthStar to provide the training and proctor the emergency procedure tasks available to sign attestations. There is no prohibition of the attestation being given at the conclusion of the training and proctored tasks. Typically attestations are from other authorized individuals (AUs or ANPs) or RSOs. The guidance clarifies that the delay refers to obtaining attestations from other authorized individuals because it is recognized that initially, only NorthStar will be

able to provide attestations. The NRC will continue to review the availability of preceptors and may revise this guidance if it determines that sufficient preceptors have become available.

Comment: One commenter agreed with the three proctored case component of the training and experience requirements. However, the commenter questioned the practicality of performing each protocol task at least three times in the presence of a NorthStar representative or individual certified to provide the training because of the lifespan of the generator. Specifically, due to the life span of the Mo-99/Tc-99m source vessel, the trainer would have to return to or otherwise be present at the applicant facility on three separate occasions that are days apart in order to satisfy the “add-source-vessel” training requirement. The commenter wanted further clarification of the requirements and suggested the use of a “dummy” (non-radioactive) source vessel or multiple RadioGenix™ Systems at the NorthStar training site.

Response: A change was made to the guidance based on this comment. All of the proctored training (except these four protocols: “add source vessel,” “remove source vessel,” “sterilization” and “add/change reagent kit”) needs to be performed with an active generator to assure familiarity with taking radiation measurements, handling radioactive material and the replaceable generator components, monitoring for contamination, and dealing with potential emergencies.

Therefore under the guidance, except for these four protocols -- “add source vessel,” “remove source vessel,” “sterilization,” and “add/change reagent kit” – the training cannot be performed on “dummy” source vessels. The generator can be eluted at any time for training purposes, i.e., training does not have to be provided only at full production run times. Further, during training, the generator component handling for specific protocols can be performed without running a complete production cycle and multiple protocols or repetition of protocols can be tested each day.

The “add source vessel” and “remove source vessel” protocols may be proctored using “dummy” source vessels (i.e., vessels that do not contain radioactive material) provided the vessel contains material that can be detected in the event of loss of control of the liquid, e.g., contamination, leaks or spills. This should provide ample opportunities for training. The “sterilization” and “add/change reagent kit” protocols do not involve the movement of technetium/molybdenum from the source vessels so they may be performed without an active source vessel.

Comment: One commenter requested that the guidance clarify the differences between the terms “individual certified by NorthStar to provide the training” and “qualified NorthStar service representative.”

Response: A change was made to the guidance based on this comment. The “qualified NorthStar service representative” was revised to read “NorthStar service representative”. The guidance is consistent in using the term “individual certified by NorthStar” for training. And a “NorthStar service representative” is an individual listed on the NorthStar service provider license and authorized for service activities at temporary job sites.

Comment: One commenter wanted clarification on whether the “individual certified by NorthStar to provide the training” and the “NorthStar service representatives” will be designated on a license.

Response: No change was made to the guidance based on this comment. The “individual certified by NorthStar to provide the training” will not be listed on a license. NorthStar will provide a written statement that the individual is certified to perform the training and proctoring. NorthStar will have a service license and the NorthStar service representatives will be listed on the license.

Comment: One commenter wanted to know the training standards that the NorthStar staff had to meet before they could provide training on the RadioGenix™ System; the standards needed to be recognized as “an individual certified by NorthStar;” and whether the NorthStar training staff met the qualifications for an ANP.

Response: No change was made to the guidance based on this comment. The guidance does not provide standards for the NorthStar training staff. The NorthStar staff is expected to have expertise in the design, development, and operation of the device, and do not have to meet to qualifications of an ANP. The individuals that will be authorized to provide the training will work for NorthStar and be identified on the NorthStar service license issued by the State of Wisconsin.

Comment: One commenter wanted to know if NorthStar will “certify” an individual(s) ANP or 10 CFR 35.200 user at a client licensee’s facility in order for that person to train subsequent ANPs or AUs (as applicable). The commenter suggested that the qualifications for a NorthStar staff or NorthStar certified individual be under a service provider license for NorthStar, whereby there would be regulatory oversight of the training program. The commenter noted that the ACMUI, during its October 2016 meeting, proposed establishment of qualifications for vendor trainers/preceptors for 10 CFR 35.1000 use of microsphere brachytherapy.

Response: No change was made to the guidance based on this comment. Under the guidance, trained AUs or ANPs are not permitted to train other AUs and ANPs at their facilities unless NorthStar certifies them to provide the training. The individuals that will be authorized to provide the training will work for NorthStar and be identified on the NorthStar service license issued by the State of Wisconsin. The provision for NorthStar to certify individuals to provide the training was included in the guidance to provide NorthStar with flexibility if it decided to certify other individuals to provide the AU, ANP, and RSO training. As indicated in the guidance, individuals may work under the supervision of an authorized individual and the applicant must commit to provide training to all supervised individuals working under an authorized individual in the operation of any component or handling of licensed material associated with the RadioGenix™ System commensurate with the individual’s duties to be performed.

5.2. Radiation Safety Officer

Comment: A commenter recommended that the abbreviation “RSO” be added to the Radiation Safety Officer heading in the Table of Contents. The commenter believed the heading should read “Radiation Safety Officer (RSO)”

Response: No change was made to the guidance based on this comment. Adding the abbreviation for the RSO is not needed in the title of the heading. The term and its abbreviation appear in the first sentence of this section.

Comment: One commenter recommended changing “have” in the phrase “have a RadioGenix™ System” in the Radiation Safety Officer training and experience section to “posses.”

Response: The guidance was changed based on this comment. The “have” was changed to “possess” in the Radiation Safety Officer training and experience section.

Comment: One commenter wanted the guidance to be more specific in describing the RSO’s training in regulatory issues associated with the RadioGenix™ System.

Response: No change was made to the guidance based on this comment. The criteria are performance based and cover regulatory issues associated with use of the RadioGenix™ System. These include issues resulting in compliance with the regulations, this guidance, and the manufacturer’s instructions.

Comment: One commenter questioned whether practicing the emergency procedures applicable to the RSO at least once in the physical presence of a NorthStar representative (or an individual certified by NorthStar to proctor the emergency procedures appropriate for an RSO) was adequate for an RSO.

Response: No change was made to the guidance based on this comment. The criterion is that the RSO successfully practice the emergency procedures at least once and that the RSO have a written preceptor statement that the individual satisfactorily completed the training and can independently perform the duties of an RSO for the RadioGenix™ System. This recognizes that RSO’s may need to perform the tasks more than once to satisfactorily complete the training and function independently.

Comment: One commenter questioned why an additional attestation for the RadioGenix™ System was needed for an RSO.

Response: No change was made to the guidance based on this comment. The radiation safety issues associated with the RadioGenix™ System are sufficiently different from the use and preparation of radiopharmaceuticals with fission-based Mo-99/Tc-99m generators that, under the guidance, the additional attestation for the RadioGenix™ System is necessary.

5.3. Supervised Individuals Operating the RadioGenix™ System [10 CFR 30.33(a)(3)]

Comment: One commenter questioned why the supervised individuals needed to receive the training and hands-on experience listed in the “Authorized Individuals” training and experience paragraphs C(1) and (2).

Response: No change was made to the guidance based on this comment. The RadioGenix™ System has unique design and use features that differentiate the RadioGenix™ System from a

conventional fission-based Mo-99/Tc-99m generator, which, under the guidance, results in the need for additional hands on training and demonstration of proficiency before the supervised individual can operate the unit.

Comment: One commenter questioned why the commitment that the records of the successful completion of this training and experience shall be maintained for 3 years after the individual is no longer working under the supervision of an authorized individual is under the “Training and Experience” section and not the “License Commitment” section.

Response: A change was made to the guidance based on this comment. The word “this” was ambiguous in the phrase “this training and experience.” The word “this” was changed to “protocol.” The intent was to keep records of the successful training and experience associated with the protocol tasks for each individual performing the protocols. This commitment needs to stay in the “Training and Experience” Section to alert the applicant or licensee that specific individuals will require additional training and experience to use the “RadioGenix™ System. The “Licensee Commitment” Section addresses licensee commitments to provide certain program elements.

5.4. RadioGenix™ System Administrator and RadioGenix™ System Administrator Designee [10 CFR 30.33(a)(3)]

Comment: One commenter thought that although one could infer from the description of the System Administrator designee that there can be only one designee (as the term, “designee,” is used exclusively in the singular), there can and should be multiple System Administrator designees and this should be stated in the guidance.

Response: No change was made to the guidance based on this comment. The intent is to have as few individuals as possible responsible for the key to access the service door and transfer door, and assigning user roles in the RadioGenix™ Application. Therefore, the guidance includes only one System Administrator designee.

Comment: One commenter thought the System Administrator or the System Administrator designee, who has successfully fulfilled the requisite NorthStar training and experience, will subsequently train other individuals responsible for performing the specific tasks within the protocol.

Response: No change was made to the guidance based on this comment. The System Administrator’s duties and responsibilities do not include training other individuals. As it relates to training, the System Administrator only assigns user roles to other individuals if the person is qualified.

Comment: One commenter thought it was important to clarify that a System Administrator can be any individual assigned by the AU without a specifically defined educational or training background.

Response: No change was made to the guidance based on this comment. Under the guidance, the System Administrator cannot be any individual assigned by the AU without a specifically defined educational or training background. The guidance states that the applicant’s

RadioGenix™ System Administrator has to, among other things, successfully complete the training and experience of an authorized individual, i.e., AU or AMP.

Comment: One commenter questioned whether the System Administrator will be named on the license given the individual's unique role.

Response: A change was made to the guidance based on another comment. The guidance clarifies that to provide the licensee flexibility in training and appointing a replacement System Administrator and System Administrator designee, the individual will not be listed on the license for either of these positions.

Comment: One commenter questioned why the "RadioGenix™ System Administrator and RadioGenix™ System Administrator Designee" section and the commitments listed in this section are not included in the "Licensee Commitment" section.

Response: No change was made to the guidance based on this comment. The RadioGenix™ System Administrator and RadioGenix™ System Administrator Designee information remains under the "Training and Experience" section. The intent of the "Training and Experience" heading is to alert the applicant or licensee that specific individuals will require additional training and experience to use the "RadioGenix™ System. The "Licensee Commitment" section addresses licensee commitments to provide certain program elements.

Comment: One commenter suggested that the bullets in this section be revised to change the verb tense to active voice.

Response: A change was made to the guidance based on this comment. The verb tense was changed to active voice.

Comment: One commenter requested clarification between a NorthStar representative or an individual certified by NorthStar in the second bullet within item 3 under the "RadioGenix™ System Administrator and RadioGenix™ System Administrator Designee" section.

Response: No change was made to the guidance based on this comment. The "NorthStar representative" is an individual working for NorthStar that NorthStar authorizes to provide the evaluation. The "individual certified by NorthStar" is not a NorthStar employee, but an individual for whom NorthStar has provided a written statement saying the individual is certified to perform the training, proctoring, and evaluation.

Comment: One commenter suggested that another bullet be added under item 5 of the "RadioGenix™ System Administrator and RadioGenix™ System Administrator Designee" section. The commenter wanted to add "Review user roles and accounts annually."

Response: No change was made to the guidance based on this comment. The licensee is already required under 10 CFR 20.1101 to periodically (at least annually) review the radiation safety program content and implementation. The user roles and accounts are a part of that radiation safety program.

6. License Commitments

6.1. Routine and non-routine activities.

Comment: One commenter asked whether there are daily QA or other routine maintenance not mentioned in the guidance that need to be tied-down. For example, how the tubing or other components get checked.

Response: A change was made to the guidance based on this comment. The guidance was revised to include a provision requesting a commitment from the applicant/licensee to follow the manufacturers QA procedures. The QA procedures do not have to be submitted in the license application. The daily QA and other routine maintenance performed by the end user are programmed into the pre-operational check of the device. These checks are performed prior to allowing the user to operate the device for Tc-99m production.

To assure the sterility of the final product, many of the components that the licensee handles on a routine basis have been sterilized and packaged in containers to maintain their sterility. They may not be handled or checked in a manner that will compromise that sterility. Other components are by design inaccessible to the licensee and are to be checked only by NorthStar (or a NorthStar representative) during its routine maintenance or repair service. These components include the tubing, valves, and pump behind the service door and transfer door.

6.2. Molybdenum-99 concentrations at time of elution

Comment: One commenter wanted to know if the licensee needed to keep records of the molybdenum-99 concentration test results.

Response: A change was made to the guidance based on this comment. A commitment was added to the guidance for the applicant/licensee to maintain a record of each elution test for 3 years and describes the information that must be maintained.

6.4. Updated training for individuals resulting from safety and operational changes to the RadioGenix™ System.

Comment: One commenter questioned the responsibility of the vendor/manufacturer to inform and train the applicants on changes in a timely manner when the manufacture makes software, hardware, or procedure changes to the RadioGenix™ System. The commenter also wanted to know the appropriate time period allotted for training on the “changes”.

Response: No change was made to the guidance based on this comment. NorthStar is responsible for making software, hardware, or procedural changes to the licensee’s RadioGenix™ System. If these changes affect the safety and operation of the NorthStar RadioGenix™ System, NorthStar has to provide the training before the system can be used.

After these changes are made and before use at the licensee’s facility, training must be provided to key individuals (i.e., at least one authorized individual, the Radiation Safety Officer, supervised individuals initially using the updated system, RadioGenix™ System Administrator and RadioGenix™ System Administrator designee). No time period was provided in the guidance because the time needed will depend on the number of individuals needing training and the complexity of the training.

Comment: One commenter asked whether the generator will be “nonoperational” until all individuals (including the AU, RSO, System Administrator, etc.) handling the generator are trained in the changes as a result of software, hardware, or procedural changes to the RadioGenix™ System that affect the safety and operation of the generator. The commenter also wanted to know if only the AU needed the training and questioned if the AU is then solely responsible for training all others on these changes.

Response: A change was made to the guidance based on this comment. Under the guidance, the unit cannot be used until there are key individuals (at least one authorized individual, the Radiation Safety Officer, individuals initially using the updated system, the RadioGenix™ System Administrator and RadioGenix™ System Administrator designee) who have completed the training in the changes. All other individuals need to complete the training before they can use or supervise the use of the RadioGenix™ System. The licensee can have the remaining individuals trained by NorthStar or individuals certified by NorthStar to provide the training. The AU cannot provide the training if the AU is not certified by NorthStar to provide the training.

6.5. Annual Emergency Procedures Refresher Training

Comment: One commenter stated that the Draft Licensing Guidance is largely silent on emergency response other than to defer to the procedures of the manufacturer. The commenter recognized that while the NRC tries to be non-prescriptive, given the potential severity of a spill with such large quantities of radioactivity in liquid form, the commenter proposed that the manufacturer’s procedures should be reviewed and incorporated into the Licensing Guidance itself.

Response: No change was made to the guidance based on this comment. The NRC believes that the performance based criteria for the applicant to develop, implement, and maintain written procedures based on information specific to the RadioGenix™ System’s likely failure modes is adequate. Further, the manufacturer designed the liquids to move through the system at low pressure and added physical barriers within the cabinets to keep spills and leaking fluids contained.

Comment: Two commenters questioned why an annual emergency training is needed for the NorthStar generator when the only other modalities that require this are in 10 CFR 35.600.

Response: No change was made to the guidance based on this comment. Because the system is both automated as it runs complex processes and requires staff change out of key components, two effects were considered in making the emergency training annual in the guidance. First, there is frequent handling of potentially radioactive components and more points in the processes that can potentially expose individuals to higher levels of radiation. This means individuals need be very familiar with emergency procedures at all times. Also, the automation of the system may lead the user/operator to become complacent and not

immediately identify and appropriately respond to an emergency condition without annual training. If an incident should happen, the operators need to be familiar with the types of failures that may occur and how to manually respond to these incidents. For these reasons, annual instructions in emergency procedures are needed.

6.6. Revision to NRC’s Training and Experience Criteria Guidance

Comment: One Agreement State regulator and the Organization of Agreement States believed that licensees who commit to a particular version of the guidance should not use updated T&E guidance until they apply for and receive a license amendment. They believed "gap training" for existing authorized individuals should not happen until the changes and training are reviewed by license reviewers and an amendment is issued. Their position was that licensees cannot and should not commit to this in advance.

Response: A change was made to the guidance based on this comment. The guidance was clarified to indicate that while authorized NRC licensees could use the described program without requiring an amendment, this may not be permitted by some Agreement States. The Agreement State applicants were reminded to check with the Agreement State to see if the provisions applied to licensees in that state, because the guidance can be used by both NRC and Agreement State applicants.

6.7. Specific Information on Radiation Safety Precautions and Instructions

6.7.1. Surveys/Survey meters/monitors:

Comment: One commenter requested that the guidance provide a range of activities that can be in the RadioGenix™ System because the generator can hold up to four molybdenum sources.

Response: No change was made to the guidance based on this comment. The guidance already provides the expected activity ranges to be licensed in “Radionuclides, form, possession limits.” At this time, each of the source vials may at the time of shipping, contain up to 7.5 curies. The RadioGenix™ System may contain up to four source vials plus two waste containers for decaying waste, with an anticipated maximum activity of 30 curies of Mo-99 and an equal amount of Tc-99m when in secular equilibrium for a total of 60 curies of radioactive material. Additionally, the guidance was not changed because the manufacturer may increase source vessel capacity or usage in subsequent iterations or updates to the device.

Comment: One commenter requested that the guidance provide a distance instead of “within arm’s reach” because “within arm’s reach” is too subjective for a safety margin.

Response: No change was made to the guidance based on this comment. The phrase “within arm’s reach” is performance based and was used in place of a specific distance because there is no specific distance that is close enough to the system for the person in all situations using the system to be able to read a monitor/meter reliably. In a large facility, this ensures that the person does not have to rely on an area monitor at some distance. “Within arm’s reach” also permits the survey of hands and monitoring of immediate radiation levels without having to walk to a survey meter for performing the surveys.

Comment: One commenter stated that if there is a need in the guidance for a radiation survey instrument to be within arm's reach, then there should be a requirement to use a personal electronic alarming dosimeter for worker protection.

Response: No change was made to the guidance based on this comment. A survey meter is sufficient to determine the radiation field for worker protection and also permits the worker to perform contamination surveys. The regulations in 10 CFR Part 20, Subpart F, do not require monitoring with personal electronic alarming dosimeters.

Comment: One commenter stated that the guidance says that a stationary monitor adequately covering the radiation area that is on and operational may be used, provided its readout is visible and readable before entering a potential radiation field. The commenter questioned if there will be a warning that would alert an individual that the radiation level had changed or increased due to some unforeseen event.

Response: A change was made to the guidance based on this comment. The guidance was revised to include a new criterion that a radiation monitor/survey meter has an audio indicator that is on and used when the monitor/meter readout is not in the line of sight of the operator, after the surveys in 6.7.1(4) are performed. The audio indicator that will warn the individual of changes due to unforeseen events is required, rather than an alarm, because it will be difficult to determine an alarm set point due to expected fluctuations in a pharmacy.

Comment: One commenter noted that the guidance says that a stationary monitor adequately covering the radiation area that is on and operational may be used, provided its readout is visible and readable before entering a potential radiation field. The commenter requested guidance on whether an individual is expected to be able to see and read the monitor at all times while in the radiation area or only upon entering.

Response: A change was made to the guidance based on this comment. The guidance was revised to include a new criterion clarifying that if only one stationary radiation monitor/survey meter is used, it must meet all five criteria in the surveys/survey meters/monitors section and the readout must be visible and readable before entering a potential radiation field. With the addition of the audible function in the fifth criterion, the individual is able to monitor the radiation fields without having to read the monitor/meter at all times.

Comment: One commenter stated that the term "higher than expected" should be defined in the "Specific Information on Radiation Safety Precautions and Instructions" section. The commenter believes it should be defined in terms of maximum specific exposure or exposure-rate limit which a survey meter is capable of measuring.

Response: No change was made to the guidance based on this comment. The criterion "higher than expected" is performance based. Depending on the source vial activity within the device and changes with the radioactive materials transfers during processing, the licensee would be familiar with the typical radiation levels of the device. Hence, "higher than expected" is a relative term that would be recognized by the licensee. A related example would be monitoring of radioactive materials packages. A licensee would be familiar with the radiation levels

associated with typical shipments, but would be alerted by a “higher than expected” radiation level that the contents of a package might no longer be contained as it should and additional precautions may need to be implemented.

Comment: One commenter believed that the guidance about the radiation monitors/meters with the ability to detect expected transient radiation levels is ambiguous and should include the maximum exposure or dose rate value measurable for a compliant radiation monitor.

Response: A change was made to the guidance based on this comment. The guidance was revised to clarify that the expected transient was in radiation levels and that the radiation monitor/meter should be able to measure greater than the expected transient levels. The guidance now includes an example of an expected transient radiation level. Surveys meters with the detection capabilities normally required for medical and pharmaceutical preparation should be adequate for most locations.

Comment: One commenter stated that there was insufficient information on the transient and/or static exposure rates, from the various components of the system to either confirm or dispute the statement that a radiation and high radiation posting may be required. The commenter further stated that license reviewers will need this information to evaluate a facility diagram for radiation safety/as low as reasonably achievable (ALARA) considerations. The commenter also stated that the vendor must have actual or calculated exposure rate measurements for each component section of the system, including the variation due to the specific location (flow) of the Mo-99 and Tc-99m solutions, at the various times/steps in the automated process/protocols, etc., and this information should be made available to licensing agencies.

Response: No change was made to the guidance based on this comment. Information on the transient and/or static exposure rates from the various components of the system is important and will be available to regulators in the Safety Evaluation Report and to applicants and licensees from the manufacturer.

Comment: Two commenters wanted clarification on what was meant by “action levels” and wanted more specific regulatory reporting requirements since high radiation levels alone are typically not reported.

Response: A change was made to the guidance based on this comment. The guidance was revised to remove action levels and clarify that specific examples need to be given in the emergency procedures addressing when the licensee has to report under 10 CFR Parts 20, 30.50, and 21.

Comment: Two commenters stated that the commitment “To confirm that individuals will not stand near the system during the protocol due to elevated dose rates that will occur during portions of the protocol” is ambiguous. A third commenter had similar concerns. They wanted a minimum specific distance away from the generator to be given in the guidance instead and it was suggested that if specific guidance is provided then the commitment should be removed.

Response: No change was made to the guidance based on this comment. The confirmation of not standing near the device when in operation is a performance based criterion and is for maintaining doses ALARA without imposing unnecessary operational constraints on the licensee. Further, it is difficult to define a specific distance because radiation levels around the device will vary during its operation and in each case the licensee should determine an appropriate distance to prevent unnecessary radiation exposures.

Comment: One commenter questioned why personnel exposure is controlled by administrative procedures (such as don't stand near the unit during the protocol) when the exposure could be reduced to safe levels with increased shielding or improved engineering.

Response: No change was made to the guidance based on this comment. The manufacturer has provided significant shielding and engineering controls, but there will be transient radiation levels, as well as increases in radiation levels during incidents, unusual events, or abnormal operating conditions. Therefore, the licensee's administrative controls are used in addition to these shielding and engineering controls to keep worker doses within NRC limits and ALARA.

Comment: One commenter asked if the system operator visually monitors the system during the elution procedures and if that would require the operator being near the system.

Response: No change was made to the guidance based on this comment. An elution procedure takes about 45 minutes. During this time, the operator may perform other duties while in the vicinity of the system. The operator can periodically check the progress of the system without visually monitoring or having to stand near the device because the audible system is on and the RadioGenix™ System displays warnings and halts the operation if there are issues with the elution procedure.

6.7.2. Emergency Procedures

Comment: One commenter suggested deleting the phrase "selecting and" from the 5th bullet of the Emergency Procedures Commitment section.

Response: A change was made to the guidance based on this comment. This phrase appears in the 4th and not the 5th bullet. The guidance was revised to remove the phrase "selecting and" from the 4th bullet.

Comment: Two commenters questioned whether the licensee should be required to have specific safety equipment such as tongs, to remove vials from the shielded cabinet, and whether a spill kit will be provided by NorthStar.

Response: No change was made to the guidance based on this comment. The licensee is expected to have appropriate radiation safety equipment at the facility, but does not have to provide a description of all safety equipment during the licensing process. NorthStar does not provide a spill kit because this is the responsibility of the licensee. The licensee is required to develop, implement, and maintain written emergency procedures that list all available emergency response equipment (e.g., spill kits).

Comment: One commenter suggested replacing the phrase “needed responses” with “actions required” in the sentence “To reflect the unique components and operation of the RadioGenix™ System, the applicants must commit to develop, implement, and maintain written emergency procedures that are based on information specific to the RadioGenix™ System’s likely failure modes (this includes but is not limited to spills and loss of shielding) and needed responses to reduce exposure to higher than normal radiation fields”.

Response: A change was made to the guidance based on this comment. The phrase “needed responses” and the rest of the sentence was deleted.

Comment: One commenter suggested revising the bullets in this section to change the verb tense to active voice.

Response: A change was made to the guidance based on this comment. The verb tense was changed to active voice.

Comment: One commenter questioned what was meant by the word “instrument” in the bullet “To perform an assessment to determine if a NorthStar representative is needed to assist in returning the instrument to a serviceable state in cases when the Stop button has been used.”

Response: A change was made to the guidance based on this comment. The word “instrument” was changed to “RadioGenix™ system.” This clarifies that based on the nature of the fault that caused the system to stop operating, the device may or may not require a NorthStar representative to review the system state to determine the appropriate course of action. If there was a system error with the Mo-99 in the transfer tubes during production, specific manufacturer overrides could be required to analyze and ensure that the Mo-99 is safely returned to the source vial.

Comment: One commenter suggested using “and” instead of “or” in the following sentences in the section under Specific Information on Radiation Safety Precautions and Instructions – Emergency Procedures: “Written emergency procedures must provide instructions for responding to major and minor spills (or leaks) of radioactive materials ... Close all cabinet doors (if possible) to ensure that any possible leaks or spills of radioactive materials are retained within the recessed cabinets and to reduce elevated radiation levels by maximizing use of available shielding in the cabinet doors”.

Response: A change was made to the guidance based on this comment. The “or” in the sentences referenced were not changed to “and.” However, the parenthesis around “(or leaks)” was removed, and the order of “leaks or spills” was reversed to “spills or leaks” for consistency.

Comment: One commenter suggested using the phrase “leakage or spillage” instead of “loss of containment.”

Response: A change was made to the guidance based on this comment. The phrase “loss of containment” was changed to “leakage or spillage” for clarity.

Comment: One commenter suggested changing the term “frisking” to “monitoring” in the sentence: “Address frisking personnel for contamination and the means for personnel decontamination, if necessary”

Response: A change was made to the guidance based on this comment. The term “frisking” was replaced with “surveying” to clarify the action required.

Comment: One commenter questioned why other requirements were not added to the guidance, for example: “key control, routine operation (i.e. – using manufacturer operating and safe-handling procedures, ordering and receiving procedures, occupational dose w/in 10% of Part 20 limits, daily/weekly etc. wipe tests and surveys, continuous monitoring, routine maintenance procedures, non-routine maintenance procedures (and any individuals specially authorized to do those), and waste management were not specifically in the guidance).”

Response: No change was made to the guidance based on this comment. The licensee is required to have a radiation safety program and the general radiation safety components of the program are addressed in the routine licensing of the facility. This guidance addresses only those aspects of the radiation safety program that are unique to using the RadioGenix™ System.

7. Notes to Licensees-

7.1. Alterations to RadioGenix™ System

Comment: One commenter wanted to know if customers and regulators will have a copy of the Safety Evaluation Report and if the Safety Evaluation Report will be added to the guidance as an appendix.

Response: No change was made to the guidance based on this comment. If an applicant or licensee needs information or a copy of the Safety Evaluation Report, they can obtain a copy from the manufacturer. Regulators will be able to access the Safety Evaluation Report in the Sealed Source and Device Registry. The Safety Evaluation Report is not publically available and will not be added to the guidance document as an appendix.

8. Notes to Regulators –

8.1. Inspection Frequency

Comment: One commenter pointed out that the authorized use of the device “bumps the licensee up to a 2-year inspection frequency.”

Response: No change was made to the guidance based on this comment. The commenter correctly points out that the medical use licensee’s authorization of the NorthStar RadioGenix™ System under 10 CFR 35.1000 requires the program code be 02240, which has an inspection priority of 2. The radiation safety differences between other generators and the NorthStar RadioGenix™ System is the basis for the increased inspection frequency to 2 years for limited

specific medical licensees. The inspection frequency for both a broad scope medical institution and a commercial nuclear pharmacy licensee is already 2 years.

8.3.1. Radionuclides, Form, Possession Limits

Comment: One commenter suggested updating the tables in the “Radionuclides, Form, and Possession Limits” and “License Authorizations” sections to clarify how the commercial nuclear pharmacy will request and be authorized to use the RadioGenix™ System.

Response: No change was made to the guidance based on this comment. The guidance highlights the only difference between how to request possession of the RadioGenix™ System and how to write the authorization for the RadioGenix™ System on a medical use license and a commercial nuclear pharmacy license. Specifically, the “Purpose” and “Authorized Use,” under “Radionuclide, Form, Possession Limits” sections states “elution of Tc-99m in a NorthStar RadioGenix™ System” for the commercial nuclear pharmacy.

8.3.2. License Conditions

Comment: Two commenters suggested removing the license condition, “[Authorized Nuclear Pharmacist’s name] for the elution of Tc-99m from the RadioGenix™ System”.

Response: No change was made to the guidance based on this comment. An Authorized Nuclear Pharmacist will be required for a commercial nuclear pharmacy because they do not have a medical Authorized User, and the individual has to be specifically authorized to elute the RadioGenix™ System.

Comment: One commenter suggested changing the sequence number of the license condition section to reflect how the condition would appear on a license.

Response: A change was made to the guidance based on this comment. The guidance was changed to reflect that license condition 12 is usually used to list the authorized individuals on a medical use and commercial nuclear pharmacy license. The other condition does not have a specific number and was marked with XX because it may appear as a later license condition.

Comment: One commenter wanted to know how to determine which replacement parts are defined as consumable.

Response: No change was made to the guidance based on this comment. The manufacturer determines the user replaceable items, e.g. sterile solutions, source vessels, and separation columns, which are verified by integrated barcodes and Radiofrequency Identification systems. The compatible kit part numbers are listed in the RadioGenix™ System Operator Guide.

Comment: One commenter suggested adding additional license conditions regarding routine monitoring, training record, maintenance, and emergency procedure commitments.

Response: No change was made to the guidance based on this comment. The need for these and other commitments in the guidance document are already addressed in the guidance and the actual commitments will be incorporated in the license as a “tie down” condition.

Comment: One commenter suggested adding additional license conditions to allow an authorized user/authorized nuclear pharmacist to be authorized on the license before becoming fully qualified to use the RadioGenix™ System.

Response: No change was made to the guidance based on this comment. Only fully qualified individuals (physician authorized users, authorized nuclear pharmacists and Radiation Safety Officer) will be listed on the license as authorized for the RadioGenix™ System.
