DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 202158

NDA APPROVAL

NorthStar Medical Radioisotopes, LLC
Attention: James W. Brodack, Ph.D.
Vice President of Regulatory Affairs and Quality Assurance
1800 Gateway Blvd.
Beloit, WI 53511

Dear Dr. Brodack:

Please refer to your New Drug Application (NDA) dated January 4, 2013, received January 4, 2013, and your amendments, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for RadioGenix System (Sodium Pertechnetate Tc99m Injection USP) injection 6 Ci.

We acknowledge receipt of your amendment dated May 7, 2017, which constituted a complete response to our November 4, 2013, action letter.

We acknowledge receipt of your major amendment dated October 13, 2017, which extended the goal date by three months.

This new drug application provides for the use of RadioGenix™ System (technetium Tc 99m generator) used to produce sodium pertechnetate Tc 99m injection. Sodium pertechnetate Tc 99m injection is a radioactive diagnostic agent and can be used in the preparation of FDA-approved diagnostic radiopharmaceuticals. Sodium pertechnetate Tc 99m injection is also indicated in:

- Adults for: salivary gland imaging and nasolacrimal drainage system imaging (dacryoscintigraphy).
- Adults and pediatric patients for: thyroid imaging and vesicoureteral imaging (direct isotopic cystography) for detection of vesicoureteral reflux.

We have completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling text.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at

http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. Content of labeling must be identical to the enclosed labeling (text for the prescribing information). Information on submitting SPL files using eLIST may be found in the guidance for industry *SPL Standard for Content of Labeling Technical Qs and As*, available at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf

The SPL will be accessible via publicly available labeling repositories.

CARTON AND IMMEDIATE CONTAINER LABELS

Submit final printed carton and immediate container labels that are identical to the carton and immediate container labels submitted on January 19, 2018, as soon as they are available, but no more than 30 days after they are printed. Please submit these labels electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (May 2015, Revision 3)*. For administrative purposes, designate this submission "**Final Printed Carton and Container Labels for approved NDA 202158**." Approval of this submission by FDA is not required before the labeling is used.

Submit the final user manual that is identical to the user manual submitted on January 31, 2018 as soon as it is available, but no more than 30 days after they are printed.

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

Because none of these criteria apply to your application, you are exempt from this requirement.

POSTMARKETING REQUIREMENTS UNDER 505(o)

Section 505(o)(3) of the FDCA authorizes FDA to require holders of approved drug and biological product applications to conduct postmarketing studies and clinical trials for certain purposes, if FDA makes certain findings required by the statute.

We have determined that an analysis of spontaneous postmarketing adverse events reported under subsection 505(k)(1) of the FDCA will not be sufficient to assess a signal of a serious risk of excess microbiological contamination of the RadioGenix™ System that causes sterility failures or pyrogenicity in patients.

Furthermore, the new pharmacovigilance system that FDA is required to establish under section 505(k)(3) of the FDCA will not be sufficient to assess this serious risk.

Therefore, based on appropriate scientific data, FDA has determined that you are required to conduct the following study:

3336-1 Evaluate the fluid path bioburden and final product endotoxins and sterility in the RadioGenix™ System at interim timepoints and the System expiry from diverse clinical sites.

The timetable you submitted on January 19, 2018, states that you will conduct this study according to the following schedule:

Draft Protocol Submission:	03/2018
Final Protocol Submission:	04/2018
1st Interim Report, including data tables :	03/2019
2nd Interim Report, including data tables:	06/2019
3rd Interim Report, including data tables:	09/2019
Study Completion:	12/2019
Final Report Submission:	03/2020

We also request that you submit data tables for all 10 sites within 30 days of each time point.

Submit nonclinical and chemistry, manufacturing, and controls protocols and all final report(s) to your NDA. Prominently identify the submission with the following wording in bold capital letters at the top of the first page of the submission, as appropriate: **Required Postmarketing Protocol Under 505(o), Required Postmarketing Final Report Under 505(o), Required Postmarketing Correspondence Under 505(o).**

Section 505(o)(3)(E)(ii) of the FDCA requires you to report periodically on the status of any study or clinical trial required under this section. This section also requires you to periodically report to FDA on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. Section 506B of the FDCA, as well as 21 CFR 314.81(b)(2)(vii) requires you to report annually on the status of any postmarketing commitments or required studies or clinical trials.

FDA will consider the submission of your annual report under section 506B and 21 CFR 314.81(b)(2)(vii) to satisfy the periodic reporting requirement under section 505(o)(3)(E)(ii) provided that you include the elements listed in 505(o) and 21 CFR 314.81(b)(2)(vii). We remind you that to comply with 505(o), your annual report must also include a report on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. Failure to submit an annual report for studies or clinical trials required under 505(o) on the date required will be considered a violation of FDCA section 505(o)(3)(E)(ii) and could result in enforcement action.

POSTMARKETING COMMITMENTS NOT SUBJECT TO THE REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitments:

3336-2 NorthStar will perform studies to evaluate effectiveness of radiolabeling all commercially available technetium Tc 99m drug product kits in the US (except the ones already evaluated in NDA 202158), as per kit manufacturer's directions using representative sodium pertechnetate Tc 99m injection solutions obtained from three different RadioGenix™ Systems. The studies for each kit will cover different volumes (from low to high end range) of sodium pertechnetate Tc 99m injection solutions obtained throughout the 14-day shelf life of the potassium molybdate Mo 99 source. The effectiveness study must verify that the radiolabeled kits meet the quality requirement listed in the kit manufacturer's package insert.

The timetable you submitted on January 25, 2018, states that you will conduct this study according to the following schedule:

Final Protocol Submission:	04/15/2018
Interim report:	11/15/2018
Study Completion:	04/15/2019
Final Report Submission:	06/15/2019

NorthStar agrees to amend the RadioGenix™ System labeling based on the result of the study (PMC 3336-2), as appropriate.

3336-3 During the annual maintenance check of each of 10 systems:

1. Identify and report all locations of occlusion, clog or deposit buildup in the fluid lines including the valves.
2. Identify and report all locations of leaks in the system.
3. Report any elution radioactivity yields which are out of tolerance from the estimate provided by the software.
4. Report any elution volumes which are out of tolerance.

The timetable you submitted on January 22, 2018, states that you will conduct this study according to the following schedule:

Draft Protocol Submission:	03/2018
Final Protocol Submission:	08/2018
Interim Report Submission:	10/2019
Study Completion:	02/2020
Final Report Submission:	04/2020

Submit nonclinical and chemistry, manufacturing, and controls protocols and all postmarketing final reports to this NDA. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii), you should include a status summary of each commitment in your annual report to this NDA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies/trials, number of patients entered into each study/trial. All submissions, including supplements, relating to these postmarketing commitments should be prominently labeled **"Postmarketing Commitment Protocol," "Postmarketing Commitment Final Report," or "Postmarketing Commitment Correspondence."**

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the prescribing information, Medication Guide, and patient PI (as applicable) to:

OPDP Regulatory Project Manager
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion
5901-B Ammendale Road
Beltsville, MD 20705-1266

Alternatively, you may submit a request for advisory comments electronically in eCTD format. For more information about submitting promotional materials in eCTD format, see the draft Guidance for Industry (available at: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM443702.pdf).

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the prescribing information, at the time of initial dissemination or publication, accompanied by a Form FDA 2253. Form FDA 2253 is available at http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf. Information and Instructions for completing the form can be found at http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf. For more information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), see http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm.

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Alberta Davis-Warren, Regulatory Project Manager, at (301) 796-3908.

Sincerely,

{See appended electronic signature page}

Libero Marzella, M.D., Ph.D.
Director
Division of Medical Imaging Products
Office of Drug Evaluation IV
Center for Drug Evaluation and Research

Enclosure(s):
Content of Labeling

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

LIBERO L MARZELLA
02/08/2018