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General Comment

See attached file(s)

Attachments

NRC Patient Release Guide Comments NVS_final

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VIA ELECTRONIC FILING

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Office of Administration
ATTN: Program Management, Announcements and Editing Staff
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U.S. Nuclear Regulatory Commission
Washington, DC 20555-0001

RE: DRAFT REGULATORY GUIDE (DG), DG-8061, RELEASE OF PATIENTS ADMINISTERED RADIOACTIVE MATERIAL

At Novartis, we are united by the purpose to reimagine medicine to improve and extend lives. We are a focused medicines company working in the therapeutic areas of cardiology, immunology, neuroscience, solid tumors, and hematology. We address some of society's most challenging health care issues through innovative science and technology, and work to discover and develop breakthrough treatments and find new ways to deliver them to as many people as possible.

One such innovative breakthrough in oncology is radioligand therapy (RLT) for patients with certain advanced cancers. By harnessing the power of radioactive atoms, RLTs can deliver radiation to target cells anywhere in the body. The goal of the targeted approach is to limit the damage to surrounding tissues. RLT has the potential to combine different kinds of radioactive atoms into different combinations unique for a particular type of tumor. At Novartis, we are experimenting with these interchangeable building blocks with the aim of developing new RLTs to potentially treat a broad range of cancers.

Comments on Draft Regulatory Guide (DG), DG-8061

While we applaud the efforts of the Nuclear Regulatory Commission (NRC) to consider updated patient release protocols, the proposal to update DG-8061 contains problematic provisions that could create the unintended consequence of limiting patient access to critical RLT treatments. Assumptions made in the updated guidance will be difficult to operationalize in a healthcare setting and will have a specifically detrimental impact on community hospitals and other facilities who may not have the expert staffing necessary to comply with the overly burdensome process in DG-8061.

First Tier Approach - Impractical Occupancy Factor Adjustment

The NRC has confirmed that the current 5 millisievert (mSv) total effective dose equivalent (TEDE) remains the standard for a licensee to authorize the release of a patient who has received treatment. However, the proposed revisions to calculate the TEDE in DG-8061 unrealistically assume a default occupancy factor of 1, which assumes that a person would

remain at a distance of 1 meter from the patient 100% of the time. This flawed assumption causes a quadruplicate increase from the previously applied occupancy factor of 0.25. The previously applied occupancy factor of 0.25 corresponds to approximately six hours of contact per day with a patient, which is sufficient to account for contact a patient may have with any one individual.

The Advisory Committee on the Medical Use of Isotopes (ACMUI) was established to advise the NRC on policy and technical issues that arise in the regulation of the medical uses of radioactive material in diagnosis and therapy.[i] The ACMUI membership includes health care professionals from various disciplines who have an operational understanding of the use of radiopharmaceuticals, and patient representatives who work to ensure the best possible outcome and experience for patients who are treated with them. In recommendations to the NRC related to the proposed revisions of DG-8061, the ACMUI stated:

"An occupancy factor of 1.0 is unrealistic and cannot be justified for routine application, even for radionuclides with a physical half-life less than one day. The corresponding activity and dose rate values are extremely conservative, and a factor of four lower than what is currently in RG 8.39 Revision 1. This will result in an increased need for licensees to perform patient specific dose calculations and provide patient instructions at activity levels much lower than previously required. This guidance is also not consistent with the record keeping requirement in 10 CFR 35.2075(a), which only requires a record of the release if using an occupancy factor less than 0.25 at 1 meter. <u>It is recommended that the activity and dose rate values in Tables 1 and 2 be calculated with an occupancy factor of 0.25 at 1 meter, to be more realistic and compatible with 10 CFR 35.2075(a).</u>"[ii]

Novartis respectfully requests the NRC follow the recommendations of the ACMUI and revert to applying 0.25 at 1 meter for the occupancy factor default value in Table 1.

Second Tier Approach – Overly Burdensome Patient Release Calculations

The NRC acknowledges that the thresholds applied in the first-tier approach include conservative estimates and therefore provides a second-tier approach whereby treating facilities may apply patient-specific modifying factors to determine patient release. The NRC proposes that treating facilities must justify the specified value of each patient's modifying factors which include the occupancy factor. Unfortunately, the proposal fails to recognize the burden this patient-by-patient calculation will place on treating facilities. Indeed, many community hospitals and treating facilities do not currently employ on-site expert support which would be needed to calculate the patient-specific modifying factors.

If treating facilities are unable to provide documented support supplied by highly trained technical professionals, they will be faced with two choices: hospitalizing patients or denying access to critical therapies, as many treating facilities do not have the physical infrastructure nor

staffing capabilities to admit patients for even one night. As proposed, DG-8061 would create significant changes that hospitals and other sites of care would need to operationalize. In addition, the impact to insurers, including Medicare and Medicaid could be significant if drugs currently being reimbursed on an outpatient basis are suddenly required to become part of a more expensive inpatient stay. Some therapies require multiple treatments, which would require multiple hospital stays.

The ACMUI made the following recommendations to the NRC regarding the second-tier approach:

"The Patient-Specific Modifying Factors and Methods presented in Appendix B, and Example Calculations illustrated in Appendix C, are overly complex and require an unrealistic level of knowledge of extended patient behavior following release. While this calculational methodology is an admirable academic exercise, it is not practical for licensees to use for authorizing and documenting patient release using patient specific factors. Determining "Time Durations" for Travel, Instruction, and Afterward in units of effective half-lives, and the corresponding fraction of time a bystander spends in close contact with the patient during these periods would be unworkable. While the Geometric Modifying Factor accounts for varying bystander separation distances and source-receptor configurations, it again requires an unrealistic detailed knowledge of patient and bystander behavior following release. The Attenuation Modifying Factor tables account for photon scatter, buildup, and absorption at different patient tissue thicknesses, however, buildup is not applicable for distributed sources within the body and accurately determining the overlying tissue thickness would be much more challenging than simply measuring the dose rate from the patient after administration of the radiopharmaceutical. To be of practical operational value, the model needs to be simplified, such as that in the current RG 8.39 or the RADAR Patient Exposure Radiation Dose Calculator."[iii]

Novartis respectfully requests that the NRC follow the recommendations of the ACMUI and simplify the overly burdensome Patient-Specific Modifying Factors and Methods in Table 2.

Conclusion

The NRC plays an indispensable role in protecting public health and safety. Unfortunately, the proposed revisions to DG-8061 could impose significant and unjustified burdens on both patients and providers. Novartis respectfully requests the NRC consider revising their conservative assumptions used to calculate administered activity and dose rate values in DG-8061, which would include applying a 0.25 occupancy factor to the calculations.

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[i] Advisory Committee On The Medical Uses Of Isotopes | NRC.gov

[ii] https://www.nrc.gov/docs/ML2202/ML22021B300.pdf

[iii] https://www.nrc.gov/docs/ML2202/ML22021B300.pdf