January 10, 2013

Deepika Jalota, PharmD
Bayer HealthCare Pharmaceuticals Inc.
Global Regulatory Affairs, Specialty Medicine
Montville, Building 100 / Office 268
340 Changebridge Road
Pine Brook, New Jersey 07058

Dear Dr. Jalota,

I am writing to inform Bayer that the U. S. Nuclear Regulatory Commission's (NRC) staff has reviewed the radiation safety aspects of radium-223 dichloride ($^{223}RaCl_2$) and determined, based on available information, that licensing under Title 10 of the Code of Federal Regulations (10CFR) Part 35, Subpart E "Unsealed Byproduct Material – Written Directive Required" is appropriate. Under current regulations, physicians who are approved for the use of any beta emitter or any photon-emitting radionuclide with a photon energy less than 150 keV under 10 CFR 35.390 "Training for use of unsealed byproduct material for which a written directive is required" or 10 CFR 35.396 "Training for the parenteral administration of unsealed byproduct material requiring a written directive" can be authorized for the medical use of $^{223}RaCl_2$.

The NRC staff gained a better understanding of the clinical and radiation safety aspects of $^{223}RaCl_2$ for the treatment of skeletal metastases in advanced, castration-resistant prostate cancer through meetings, teleconferences, and written correspondence with Bayer. The staff discussed and evaluated issues related to matters such as activity measurements, contamination surveys, long-lived contaminants, radon volatility, patient release criteria, training, available dosimetry information, and administrative procedures before reaching a licensing decision. The staff also considered the Advisory Committee on the Medical Uses of Isotopes (ACMUI) Report on Licensing for Radium-223 Dichloride and accepted the recommendation of the ACMUI to regulate the medical use of $^{223}RaCl_2$ under 10 CFR Part 35, Subpart E.

The NRC's current understanding is that unit dosages of $^{223}RaCl_2$ will be shipped to clinical trial sites from Algeta's manufacturing facility in Norway. It is also our understanding that at some future date, Bayer may ship multi-dosage vials to the United States for commercial distribution of unit dosages to medical use licensees. The current methods of distribution (unit dosages) preclude the need for end users to manipulate $^{223}RaCl_2$.

If there are future developments related to the production, distribution, or medical use of $^{223}RaCl_2$ that may negatively impact radiation safety, the NRC will consider revisiting this licensing decision for additional actions. I appreciate the time and effort Bayer has taken to provide the NRC staff with the clinical and technical data needed to make a well-informed licensing decision. If you have any questions or need clarification, please contact Ashley Cockerham of my staff at (240) 888-7129 or Ashley.Cockerham@nrc.gov.

Sincerely,

**/RA/**

Brian McDermott, Director
Division of Materials Safety and State Agreements
Office of Federal and State Materials
and Environmental Management Programs

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| **OFFICE** | MSSA/RMSB | MSSA/RMSB | MSSA/RMSB | MSSA | MSSA |
|---|---|---|---|---|---|
| **NAME** | ACockerham | MFuller | CEinberg | P.Henderson | B.McDermott |
| **DATE** | 12/14/12 | 1/7/13 | 1/7/13 | 1/9/13 | 1/ /13 |

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