January 10, 2013

ALL AGREEMENT STATES

NOTICE OF LICENSING DECISION ON RADIUM-223 DICHLORIDE (FSME-13-002)

Purpose: To inform Agreement States that the U.S. Nuclear Regulatory Commission (NRC) has issued a licensing decision on the medical use of radium-223 dichloride ($^{223}RaCl_2$) under 10 Code of Federal Regulations (CFR) Part 35 Subpart E, "Unsealed Byproduct Material – Written Directive Required". No action is required.

Background: $^{223}RaCl_2$ is currently an investigational radiopharmaceutical undergoing clinical trials in the United States. It is not yet approved by the U.S. Food and Drug Administration. $^{223}RaCl_2$ is being developed by Algeta ASA (Algeta) and will be commercialized, pending approval, under a global agreement with Bayer Pharma AG (Bayer). The intended application for $^{223}RaCl_2$ is for the treatment of skeletal metastases in advanced, castration-resistant prostate cancer. Radium-223 naturally self-targets bone metastases by virtue of its properties as a calcium-mimic and kills tumor cells by highly localized short-range alpha irradiation. $^{223}RaCl_2$ has the potential to be the first therapeutic radiopharmaceutical being administered primarily for its alpha emissions.

Discussion: NRC staff carefully reviewed the radiation safety aspects of the medical use of $^{223}RaCl_2$ to determine if the radiopharmaceutical should be licensed under Title 10 of the Code of Federal Regulations (10 CFR) Part 35, Subpart E, "Unsealed Byproduct material – Written Directive Required" or 10 CFR 35 Subpart K, "Other Medical Uses of Byproduct Material or Radiation From Byproduct Material". The Advisory Committee on the Medical Uses of Isotopes (ACMUI) evaluated the medical use of $^{223}RaCl_2$ and submitted a report recommending regulation under 10 CFR Part 35, Subpart E. See Enclosure 1. Bayer also submitted data and responses to questions from NRC staff for consideration. See Enclosure 2.

In addition to the data and responses provided by Bayer, NRC staff reviewed technical information obtained during meetings and other correspondence with Bayer and Algeta representatives. NRC staff'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. Bayer further indicated that at some future date it 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 doses) preclude the need for end users to manipulate $^{223}RaCl_2$. NRC staff also discussed and evaluated issues related to such matters as activity measurements, contamination surveys, long-lived contaminants, radon volatility, patient release criteria, training, available dosimetry information, and administrative procedures before reaching its licensing decision.

Based on available information, NRC staff agreed with the ACMUI recommendation and determined that licensing under 10 CFR Part 35, Subpart E is appropriate because the medical use of $^{223}RaCl_2$ is similar to other commonly used beta and photon-emitting therapeutic radiopharmaceuticals. The staff has also determined that 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 $^{223}RaCl_2$.

If NRC becomes aware of future developments related to the production, distribution, or medical use of $^{223}RaCl_2$ that may negatively impact radiation safety, NRC staff will consider revisiting this licensing decision for any additional actions.

If you have any questions regarding this correspondence, please contact me at (301) 315-3340 or the individual named below.

POINT OF CONTACT: Ashley M. Cockerham EMAIL: Ashley.cockerham@nrc.gov
TELEPHONE: (240) 888-7129

/RA/

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

Enclosures:
1. ACMUI Report on Licensing for Radium-223 Dichloride, November 20, 2012
2. Radium-223 Dichloride: Bayer Responses to NRC Questions, November 8, 2012

Based on available information, NRC staff agreed with the ACMUI recommendation and determined that licensing under 10 CFR Subpart E is appropriate because the medical use of $^{223}RaCl_2$ is similar to other commonly used beta and photon-emitting therapeutic radiopharmaceuticals. The staff has also determined that 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 $^{223}RaCl_2$.

If NRC becomes aware of future developments related to the production, distribution, or medical use of $^{223}RaCl_2$ that may negatively impact radiation safety, NRC staff will consider revisiting this licensing decision for any additional actions.

If you have any questions regarding this correspondence, please contact me at (301) 315-3340 or the individual named below.

POINT OF CONTACT: Ashley M. Cockerham EMAIL: Ashley.cockerham@nrc.gov
TELEPHONE: (240) 888-7129

/RA/

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

Enclosures:
1. ACMUI Report on Licensing for Radium-223 Dichloride, November 20, 2012
2. Radium-223 Dichloride: Bayer Responses to NRC Questions, November 8, 2012

DISTRIBUTION:
FSME/MSSA r/f

ML13008A151

OFC	MSSA/RMSB	MSSA/RMSB	MSSA/RMSB	MSSA	MSSA
NAME	A.Cockerham	M.Fuller	C.Einberg	P.Henderson	BJMcDermott
DATE	12/20/12	1/7/13	1/7/13	1/9/13	1/10/13

OFFICIAL RECORD COPY