**DE NOVO CLASSIFICATION REQUEST FOR**

**BloXR X-ray Attenuating Cream**

**DECISION SUMMARY**

## 1. Regulatory Information:

**a. Identification**

FDA identifies this type of device as:

**Cream for x-ray attenuation**

A cream for x-ray attenuation is a cream intended for use as a radiation shield. It is intended to be applied to the user's hand before donning gloves, or it may be applied on a glove on the hand, followed by donning a second glove. Cream for x-ray attenuation is intended to be used during medical procedures in which hands are necessarily exposed to radiation to offer some degree of protection from radiation exposure in the diagnostic imaging range of up to 130 kVp. This may include surgical procedures that require the use of fluoroscopy or radiography or other procedures. Cream for x-ray attenuation is not intended to be used in or adjacent to the primary x-ray beam or the transmitted beam and should not be used in lieu of a Radiographic Procedure Glove, which is used in radiography for those studies requiring the physician's hand or forearm be in the direct path of the primary x-ray beam.

**b. New Regulation Number:** 21 CFR 892.6510

**c. Classification:** Class II

**d. Product Code:** PDK

## 2. Background

**a. Device Name:** X-ray Attenuating Cream

**b. Submission number:** K123422

**c. Date of De Novo Request:** February 4, 2013

**d.** **Contact in USA:** Mr. Prataprai (Rai) Chowdhary
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**e.** **Requester's Recommended Classification:** Class II

## 3. Indications for use

The X-ray Attenuating Cream is intended for use as a radiation shield. It is intended to be applied to the user's hand before donning gloves, or it may be applied on a glove on the hand, followed by donning a second glove. The X-ray Attenuating Cream is intended to be used during medical procedures where hands are necessarily exposed to radiation to offer some degree of protection from radiation exposure in the diagnostic imaging range of up to 130 kVp. This may include surgical procedures that require the use of fluoroscopy or radiography or other procedures. X-ray Attenuating cream is not intended to be used in or adjacent to the primary x-ray beam or the transmitted beam and should not be used in lieu of a Radiographic Procedure Glove, which is used in radiography for those studies requiring the physician's hand or forearm be in the direct path of the primary x-ray beam.

### a. Limitations

This is a prescription device regulated under 21 CFR 801.109.

**Note**: For use with natural rubber latex Surgeon's Gloves only.

- A warning statement placed in a black box must be prominently placed in all labeling material for this device. That warning statement must read:

> The device is **not** intended to be used in or adjacent to the primary X-ray beam or transmitted beam and should **not** be used in lieu of a Radiographic Procedure Glove, which is used in radiography for those studies requiring the physician's hand or forearm be in the direct path of the primary X-ray beam.

## 4. Device Description

### a. Device description:

The subject device is an X-ray attenuating cream that utilizes bismuth oxide powder as the X-ray absorber material. The subject device is provided sterile in a tube for single use. The end user is to squeeze all of the cream out, either directly to the health care professional's hands or onto a surgical glove before donning a second glove. The device provides protection from X-rays and scatter radiation during procedures where the health care professional's hands are necessarily exposed to radiation.

### b. Principle of Operation:

Radiation is blocked by the device via absorption of the photon energy from ionizing radiation. This photon energy is dissipated as phonon energy within the atomic lattice structure of the radiation absorber material (bismuth oxide).

## 5. Summary of Nonclinical/Bench Studies

Nonclinical performance data were provided to address the following areas:

### a. Biocompatibility/Materials

Biocompatibility testing was submitted for the subject device which is intended for skin contact with the health care professional for less than 24 hours. Testing included Cytotoxicity in accordance with ISO 10993-5, Sensitization in accordance with ISO 10993-10, Skin irritation in accordance with ISO 10993-10, and Acute Systemic toxicity in accordance with ISO 10993-11. Acute systemic toxicity testing was conducted in the event that the surgical glove fail and some of the subject device flakes off the healthcare professional's hand into an open surgical site into the patient.

### b. Shelf Life/Sterility

The subject device is sterilized via radiation sterilization in accordance with ISO 11137 and validated with bioburden method in accordance with ISO 11737-1. The sterility assurance level is SAL of $10^{-6}$. The device will have a starting shelf life of 9 months as stated on the device labeling this is based on 1 year accelerated testing. The accelerated testing, bubble leak testing and package strength testing were all done in accordance with ASTM F 1980, ASTM F 2096, and ASTM F 88 respectively.

## c. Electromagnetic Compatibility and Electrical Safety

Not applicable

## d. Software

Not applicable

## e. Performance Testing – Bench

Glove compatibility testing was provided to evaluate the compatibility of the subject device with latex gloves. (1) The first study covered the gloves with the X-ray attenuating cream and incubated at 37° C for two hours then tested for tensile strength to ASTM D3577-09. Results showed that the gloves were still within specification for tensile strength. (2) The second glove compatibility study was a glove leakage study done in accordance with the ASTM D5151 protocol and FDA 21 CFR Part 800.20. The result showed that the subject device is compatible with latex gloves.

Radiation attenuation property testing: (1) Bench testing comparing the cream with two brands of X-ray attenuating gloves using a phantom hand model and a clinical C-arm as the X-ray source. To determine the effect of user-to-user variation in cream application on attenuation, a study was conducted using a modified ASTM F2547-06 protocol. An X-ray cabinet (Faxitron, IL) and a 0.6 cc ion chamber detector (Radcal, CA) were used. Owing to the size limitations of the X-ray cabinet, the ion chamber was placed proximally below the attenuating specimen. Data from two sterile attenuating surgical gloves, Radion-X (Medline Industries, Mundelein, IL) and International Biomedical (Austin, TX) were used for comparison. The cream was applied onto a glove donned on an anthropomorphic anatomic phantom hand (Radiology Support Devices,CA) modified to accommodate the ion chamber. The desired cream thickness was 0.010 inches. Results shown below:

Table 1: Mean % Attenuation, BloXT vs. Predicate Gloves

| | | BloXR | | | Manufacturer performance claims | |
|---|---|---|---|---|---|---|
| | | **Operator 1** | **Operator 2** | **Operator 3** | **Int. Biomed.[2]** | **Radion-X[3]** |
| 60 kVp | **Mean** | 81.1 | 83.5 | 85.3 | 56.5 | 55 |
| | **SD** | 8.4 | 9.1 | 7.7 | N/A | N/A |
| 80 kVp | **Mean** | 72 | 74.5 | 77.2 | 47.1 | 43 |
| | **SD** | 8.6 | 11 | 9.6 | N/A | N/A |
| 100 kVp | **Mean** | 62.6 | 67.2 | 69.9 | 41.6 | 34 |
| | **SD** | 8.2 | 11.1 | 9.9 | N/A | N/A |
| 120 kVp | **Mean** | 58.3 | 57.5 | 64.4 | 37.7 | 26 |
| | **SD** | 8.4 | 17.2 | 11.5 | N/A | N/A |

(2) A bench study comparing the variation in X-ray attenuation by the subject device arising from user variability in application technique. This study examined the attenuation of void free films of the subject device at 0.005, 0.010 and 0.015 inch thicknesses. In accordance with ASTMF2547-06 protocol, transmitted dose was measured using nanoDot™ dosimeters (Landauer, IL) placed under the films or radiation glove specimens. Incident dose was measured separately. Five replicate measurements were made. Attenuation was calculated as a ratio of blocked dose to incident dose expressed as percent attenuation. Results showed that the attenuation at all thicknesses were equivalent or better than current surgical attenuating gloves. Results shown below:

Table 2: Average% Attenuation of Cream and Radion-X Glove

| | **60 KVp** | **95 KVp** | **110 KVp** |
|---|---|---|---|
| Cream (.005" thick) | 37.4 | 36.6 | 36.1 |
| Cream (.010" thick) | 62.6 | 58.1 | 49.9 |
| Cream (.015" thick) | 76.6 | 63.0 | 63.2 |
| Radlon-X Glove | 42.4 | 30.1 | 26.5 |

(3) A study evaluating the length of effectiveness was also provided. This study provided a measure of the amount of time the end user could use the subject device and still be shielded, before having to remove and reapply the X-ray attenuating cream. A disposable glove was donned and 22 g of cream was spread over the surface of the glove. The covered gloves were exposed to a 53 kVp beam for 4 hours and attenuation was measured for each cream covered glove using a 0.6 cc ion chamber. Results showed consistent attenuation throughout the 4 hours of exposure. Based on this study, the labeling states, "the cream shall be used for a maximum of 3 hours."

(4) As part of a risk assessment provided by an outside expert a peer review published paper was also included that replicated the results from tables 1 and 2. This paper represents good scientific experimental design: "Radiation shielding materials and radiation scatter effects for interventional radiology (IR) physicians". J.P. McCaffrey, F. Tessier and H. Shen, Med. Phys. **39**(7), 4537-4546 (2012).

f. **Performance Testing – Animal &/or Cadaver**

As a proof of concept a cadaver hand investigation was conducted. Dosimeters were implanted on the ipsilateral and contra lateral sides of 5 cadaver hands. The implanted dosimeters were shielded with the cream. Each hand also had a bare dosimeter to measure incident radiation does. There were also four bare and four shielded dosimeters placed symmetrically around a 250 mm perimeter around the hand to measure scatter radiation. The cadaver hands were exposed for 300 seconds at 53 kVp. The measured attenuation ranged from 30 - 92% for the shielded dosimeters on the hand.

## 6. Summary of Clinical Information

A clinical study was conducted at a level 1 trauma center to determine the amount of radiation that the hands of orthopedic traumatologists experience during routine clinical practice and to evaluate the ability of the subject device to decrease this radiation exposure. This was an IRB-approved low-risk clinical study involving three trauma surgeons. The surgeons wore dosimeters on their dominant hand and either was shielded with the subject device or unshielded during surgical procedures involving C-arm Fluoroscopy. The study was considered low-risk because the standard operating procedure at the center was to not wear any shielding during C-arm Fluoroscopy. The results showed an average of 54% reduction in ionizing radiation exposure with the use of the subject device for full coverage compared to no shielding (Table 3) when looking at the cumulative dose. Results shown below:

Table 3: Dominant Hand Exposure and Attenuation during Cumulative Case Series

| Surgeon | Dosimeter | Cumulative Unshielded Dose (mRem) | Cumulative Shielded Dose (mRem) | Attenuation % |
|---|---|---|---|---|
| A | A5 | 128 | 53 | 58.6% |
| B | A1 | 92 | 46 | 50.0% |
| C | A2 | 81 | 39 | 51.9% |
| | MEAN | 100 | 46 | 53.5% |
| | Std. Dev. | 25 | 7 | 4.5% |

## 7. Labeling

The labeling is sufficient and satisfies the requirements of 21 CFR 801.109 Prescription devices.

Of particular note the labeling meets the requirements in the special controls:

**a. The device labeling must include a statement notifying the end user that the device is sterile and provide an expiration date.**

The labeling includes an expiration date which has been specified as 9 months and states that the device is sterile until opened. The device labeling also states that it is for single use.

**b. A warning statement placed in a black box must be prominently placed in all labeling material for these devices. That warning statement must read:**

> The device is **not** intended to be used in or adjacent to the primary X-ray beam or transmitted beam and should **not** be used in lieu of a Radiographic Procedure Glove, which is used in radiography for those studies requiring the physician's hand or forearm be in the direct path of the primary X-ray beam.

The labeling has included the contraindication statement as requested in a black box warning.

**c. Labeling must present the methods and results from nonclinical and/or clinical performance testing representative of "as use" conditions**

**demonstrating the amount of attenuation the device provides to the end user at 60, 80, 100, and 120 kVp.**

The labeling includes the table shown below of the % attenuation the end user can expect the device will provide if applied correctly.

| kVp | % Attenuation |
|---|---|
| 60 | 80 |
| 80 | 75 |
| 100 | 65 |
| 120 | 60 |

The sponsor has also provided Tables 1 – 3 shown above in the labeling along with the testing method.

**d. Labeling must include validated instructions for use for device application and state how often the device must be removed and re-applied for effective shielding.**

The instructions for glove application include the following: Squeeze out entire contents of tube and apply to hands evenly to create a uniform opaque coating. Allow to dry for up to 60 seconds before putting on surgeon's gloves. Or, you may apply the cream to uniformly coat the first glove; allow to dry for up to 60 seconds, before putting on the second surgeon's glove. Check to make sure cream is completely encapsulated within gloves. Once applied on the hand or glove, the cream shall be used for a maximum period of three hours.

**e. Labeling must identify the type(s) of surgical glove (i.e., latex, nitrile, vinyl, etc.) that are compatible for use with the device.**

The labeling states that the cream is for use with latex gloves only.

## 8. Risks to Health and Required Mitigation Measures

FDA has identified the risks of cream for x-ray attenuation as:

**a.** Adverse tissue reaction to health care professionals and patients as a result of direct contact to the skin. Health care professionals may apply the cream directly to their hands for use. Patients may be exposed to the cream as a result of glove failure due to incompatibility with the cream formulation weakening the mechanical characteristics of the surgical gloves. The adverse tissue reaction would be due to toxic, irritating, or sensitizing agents present in the cream formulation.

**b.** *Infection risk to patient as a result of patient contact with contaminated/compromised cream due to glove failure.* Glove failure could occur due to incompatibility with the cream formulation weakening the mechanical characteristics of the surgical gloves. Infection to the patient could occur as a result of non-sterile cream, contaminated/compromised cream and loss of the sterile boundary due to glove failure.

**c.** *Radiation exposure to health care professionals due to lack of radiation attenuation. Lack of radiation can occur due to inadequate or inconsistent cream formulation.* The radiation attenuating agent in the cream may not be present in high enough concentration or is not appropriate to provide the amount of protection needed.

**d.** *Radiation exposure to health care professional during actual use (lack of effectiveness).* Lack of continuous protection during actual use can result from poor cream composition such that the cream will absorb, crack, flake off, etc. during use in a clinical setting.

f. *Radiation exposure to health care professionals due to inconsistent device application.* Radiation exposure can result due to inadequate instructions describing how to apply the cream and how often to reapply the cream to ensure that the hands are completely covered and covered with enough cream to provide the amount radiation protection stated in the labeling.

Table - Identified Potential Risks and Required Mitigation Measures

| Identified Potential Risks | Required Mitigation Measures |
|---|---|
| Adverse tissue reaction to health care professionals | (1) Biocompatibilitv testing |

| | |
|---|---|
| and patients as a result of direct contact to the skin. | (2) Surgical glove compatibility performance testing<br>(3) Identification of compatible surgical gloves in labeling |
| Infection risk to patient as a result of patient contact with contaminated cream due to glove failure and the cream flaking off onto the patient. | (1) Sterilization, packaging, and expiration date testing.<br>(2) Sterile device and expiration date statement in labeling<br>(3) Surgical glove compatibility performance testing<br>(4) Identification of compatible surgical gloves in labeling |
| Radiation exposure to health care professionals due to lack of radiation attenuation because of cream formulation. The radiation attenuating agent in the cream may not be present in high enough concentration or is not appropriate to provide the amount of protection needed. | (1) Black box warning in labeling<br>(2) Attenuation information in labeling<br>(3) Surgical glove compatibility performance testing<br>(4) Attenuation performance testing<br>(5) Application performance testing |
| Radiation exposure to health care professional during actual use (lack of effectiveness). Lack of continuous protection during actual use can result from poor cream composition such that the cream will absorb, crack, flake off, etc. during use in a clinical setting. | (1) Black box warning in labeling<br>(2) Attenuation information in labeling<br>(3) Surgical glove compatibility performance testing<br>(4) Attenuation performance testing<br>(5) Application performance testing<br>(6) Validated device application instructions for effective shielding in labeling |
| Radiation exposure to health care professionals due to inconsistent device application. Radiation exposure can result due to inadequate instructions describing how to apply the cream to ensure that the hands are completely covered and covered with enough cream to provide the amount of radiation protection stated in the labeling. | (1) Validated device application instructions for effective shielding in labeling |

## 9. Special Controls

In addition to the general controls of the FD&C Act, the X-ray Attenuating Cream is subject to the following special controls:

(1) Design verification and validation must include documentation of results from safety and effectiveness testing. The results from safety and effectiveness testing must include:
  (i) Biocompatibility data consistent with the intended use for the device;
  (ii) Sterilization, packaging, and expiration date testing; and,
  (iii) Nonclinical and/or clinical performance testing representative of "as use" conditions demonstrating:
    (A) Compatibility to the type(s) of surgical glove (i.e., latex, nitrile, vinyl, etc.) to be used with the device;
    (B) Attenuation performance; and
    (C) Proper application of the device.

(2) Labeling must include:
  (i) A statement that the device is sterile and an expiration date.
  (ii) A boxed warning statement prominently placed in all labeling material for these devices. That boxed warning statement must read:

> The device is **not** intended to be used in or adjacent to the primary X-ray beam or transmitted beam and should **not** be used in lieu of a Radiographic Procedure Glove, which is used in radiography for those studies requiring the physician's hand or forearm be in the direct path of the primary X-ray beam.

  (iii) The methods and results from nonclinical and/or clinical performance testing representative of "as use" conditions demonstrating the amount of attenuation the device provides to the end user at 60, 80, 100, and 120 kVp.
  (iv) Validated instructions for use for device application and state how often the device must be removed and reapplied for effective shielding.
  (v) Identification of the type(s) of surgical glove (i.e., latex, nitrile, vinyl, etc.) that is compatible for use with the device.

## 10. Benefit/Risk Determination

### a. Risks

The risks of the device are based on the indications for use for the device and the data collected from the bench and clinical data described above. These risks include:

- Adverse tissue reaction to health care professionals and patients as a result of direct contact to the skin.
- Infection risk to patient as a result of patient contact with contaminated cream due to glove failure and the cream flaking off onto the patient.
- Radiation exposure to health care professionals due to lack of radiation attenuation because of cream formulation. The radiation attenuating agent in the cream may not be present in high enough concentration or is not appropriate to provide the amount of protection needed.
- Radiation exposure to health care professional during actual use (lack of effectiveness). Lack of continuous protection during actual use can result from poor cream composition such that the cream will absorb, crack, flake off, etc. during use in a clinical setting.
- Radiation exposure to health care professionals due to inconsistent device application. Radiation exposure can result due to inadequate instructions describing how to apply the cream to ensure that the hands are completely covered and covered with enough cream to provide the amount of radiation protection stated in the labeling.

**b. <u>Benefits</u>**

The probably benefits of the device are also based on the indications for use of the device, known standard operating procedures of health service providers, and the bench and clinical testing date described above. The summary benefits include:

- Improved X-ray radiation attenuation properties compared to most X-ray attenuating gloves currently on the market.
- Allows the health care professional to maintain their tactile dexterity that would be lost with the thicker Radiographic procedure gloves.
- The device is biocompatible for the intended use
- The device is compatible with latex gloves
- The device is provided sterile

**c. <u>Summary of Other Factors</u>**

- The device is intended to be used only with latex gloves and no other glove type.

- The sponsor has added the black box warning statement that the subject device is not to be used in or adjacent to the primary x-ray beam or the transmitted beam and should not be used in lieu of a Radiographic Procedure Glove, which is used in radiography for those studies requiring the physician's hand or forearm be in the direct path of the primary x-ray beam.

- Labeling includes the expected amount of attenuation the device provides to the end user at 60, 80, 100, and 120 kVp.

- Labeling includes instructions for device application and also states how often the device must be removed and reapplied for effective shielding.

- Labeling includes a statement that the device is sterile and provides an expiration date.

- Biocompatibility data was included in the premarket notification submission consistent with the intended use for the device.

- Nonclinical and clinical performance testing was included in the premarket notification submission demonstrating (a) the device's compatibility to surgical gloves (i.e., latex, nitrile, vinyl, etc.), (b) the device's attenuation ability and efficacy, and (c) testing to ensure proper application of the device.

**d. <u>Assessment of Benefit and Risks</u>**

In conclusion, the bench testing and clinical testing indicate that the probability of risks for the subject device is similar to those for X-ray attenuating gloves. The benefits the subject device provides in terms of X-ray attenuation are equivalent or better than the X-ray attenuating gloves currently available on the market. As such the benefit to risk ratio is high for the subject device.

## 11. Other comments

None

## 12. Conclusion:

The de novo for the BloXR X-ray Attenuating Cream is granted and the device is classified under the following:

a. **Product Code:** PDK

b. **Device Type:** Cream for x-ray attenuation

c. **Class:** Class II

d. **Regulation:** 21 CFR 892.6510