

Eisai Sharps Disposal Plan

Chapter 591 of the California Public Resources Code (SB 486-2009)

June 30, 2010

Background

Eisai Inc. (Eisai or “the company”) takes environmental management and safety seriously and has long supported programs that protect our environment. Eisai established formal environmental policies in 2002 and created its worldwide Environmental Management and Safety Committee specifically to address concerns of the company and the neighborhoods in which it lives.

Sound environmental policy is central to maintaining Eisai’s *human health care (hhc)* mission. During the course of our research, discovering, and developing new and innovative cures and treatments for debilitating diseases, Eisai uses chemicals, compounds, and materials (including live organisms) that could be hazardous if not properly handled. Eisai and all its employees abide by federal and state laws and regulations, and internal rules and procedures that regulate the handling of certain classes of these chemicals and compounds, and other hazardous materials. The company views global environmental protection as an important component of its business operations and strives to protect the environment. Eisai not only complies with local, state, federal, international laws, regulations and agreements concerning environmental protection, it also implements voluntary standards that exceed these requirements. Because there are a variety of standards, we believe it is essential to focus on voluntary efforts in the area of environmental stewardship.

Eisai understands the impact a pharmaceutical company can have on its surrounding environment as a result of its research and development activities. Accordingly, Eisai conducts its business in a manner that is as environmentally safe and friendly as possible. Historically, Eisai has strived to voluntarily dispose of its pharmaceutical waste through incineration whenever possible. Eisai also ensures that the company abides by Food and Drug Administration (FDA) Standards for Good Manufacturing Practices.

Eisai Practices Regarding Sharps: Disposal Container and Self-Retractable Syringes

A great example of Eisai’s attention to the environment can be found with Eisai’s clot-preventing agent, Fragmin®. (Please see “Fragmin: Important Safety Information,” Appendix B.) Since the company began marketing Fragmin® in 2005, Eisai has provided a self-retractable needle and “sharps” disposal containers within its “patient kits” so patients can safely dispose of their syringes. Each Fragmin® patient kit provides patients with written instructions and an instructional DVD that not only demonstrates how to safely administer the drug, but also how to dispose of it in the disposal container. In addition, the needles themselves are self-retractable. This technology protects both patients and others from being stuck by a needle not properly disposed of in a sharps container.

This self-retractable needle encompasses “anti-needlestick” technology that renders it a passive device. Patients or healthcare professionals administering Fragmin® do not need to proactively prompt the needle sheath. (The sheath covers the needle to protect the patient and others from “sticks.”) With the Fragmin® syringe, a protective sheath automatically encompasses the needle in one action once the drug has been fully administered. This is unique in that most protective needles are not passive, but rather require the individual to intentionally focus on covering the device while using two hands and a hard surface to secure. With the Fragmin® syringes, however, a patient can inject with one hand and the safety sheath is automatically employed in one action. This “anti-needlestick” technology saves healthcare workers, waste management workers, and patients from unwanted “sticks” which can result in many months of waiting for blood testing to ensure they have not contracted an illness.

Notably, Eisai has and continues to support patient education on safe medication disposal. We support the SMARTRx campaign sponsored by the U.S. Fish and Wildlife Service, American Pharmacists Association, and the Pharmaceutical Research and Manufacturers of America (PhRMA), which is designed to help patients dispose of their medicines with minimal impact on the environment. Through its support of SMARTRx, Eisai is working to ensure consistent messaging for patients on the safe disposal of their medical waste.

Plan

Providing for Effective Safe Needle Disposal

Eisai works daily to fulfill its *human health care* mission, which is achieved when we can provide access to safe, effective medicines to patients in need. Safety weighs heavily on Eisai's decisions when providing all their products, which is why we currently use the passive self-retraction needle for the administration of Fragmin®, and also provide patient kits that include a sharps disposal container for Fragmin® syringes.

While the vast majority of Fragmin® patients receive their drug therapies in a hospital or clinical setting, the company will be further enhancing its efforts to ensure patients understand how to dispose of home-generated sharps waste.

Education and Outreach

Patients

Eisai will enhance its current educational communications to patients through its distribution of more robust patient kits for patients administering Fragmin® at home. These patient kits currently include a disposal container and instructions on how to use the container to dispose of sharps. The information given to the patient in the instructional booklet and the video provided to patients will be modified to inform consumers even more fully about how to dispose of their needles properly using the disposal container provided at no extra charge with the kit. We will also include a statement explaining that the State of California bans the disposal of sharps medical waste in landfills. This information will be phased in as newer patient kits are assembled and distributed.

Eisai's web site (www.eisai.com) will be updated to provide effective instructions on how to safely dispose of the needles into the disposal container provided in the patient kit. Additionally, a separate web page will be created to provide information about how to safely dispose of syringes in their disposal containers and after the containers are full. The web site will also inform viewers about the California ban on disposing sharps in landfills, and provide information about appropriate sites to dispose of the containers according to the law.

As noted, changes to patient communications in Eisai's patient kits will be phased-in as stock is replenished. Modifications to Eisai's web site and other patient communications will be made by January 1, 2011.

Healthcare Practitioners

The company is in the process of working with professional associations that address thrombophilia and other venous conditions, not only to educate physicians about safe sharps and Eisai's plans in this regard, but patients as well. Eisai will also work with pharmacy associations to

ensure pharmacies and pharmacists are aware of Eisai's efforts as well. Educating healthcare practitioner organizations about Eisai's plans may ultimately enhance patient initiative because patients may be more apt to follow the plan if a trusted healthcare practitioner is giving guidance.

Eisai will also ensure its web site (www.eisai.com) contains specific information for healthcare practitioners. There will be a page focused exclusively on the new requirements or recommendations for disposal and we will inform practitioners on the most appropriate means to instruct their patients to dispose of sharps containers.

Government Officials

Eisai will notify the state and local waste management departments about its plan to help patients dispose of sharps medical waste. This notification will include a contact name referring any inquiries regarding Eisai's actions to the most appropriate company personnel. Government officials will also be directed to Eisai's web page on sharps disposal.

Community Involvement

Eisai plans to place a link on its web site permitting patients and others the opportunity to offer suggestions about how Eisai might improve its waste disposal plans. Eisai will review these suggestions as it continues to monitor its plan for collecting and disposing of sharps waste.

Eisai Contact Information

Please contact the following person with any inquiries:

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Appendix A:

The only prescription drug Eisai manufactures and distributes that is administered via a sharps device at home is Fragmin®. Fragmin® is administered through a passive self-retractable needle. Eisai provides Fragmin® patients with a “patient kit” when they are given the drug to self-administer at home. This kit provides the patient with instructions, both written and through video, on how to dispose of the needles in the container that is provided within the kit free-of-charge. Eisai’s Fragmin® web site will provide for these same instructions.

Provided Plan Elements	Enhanced Company Activity
Patient Education	<p>Eisai will educate patients in a manner reflecting appropriate means of communication and use, including:</p> <ul style="list-style-type: none"> • Via Eisai.com Eisai will: <ul style="list-style-type: none"> - Create a new web page for patients regarding sharps disposal. - Explain the importance of proper sharps disposal for safety and the environment. - Provide contact information of additional groups that may have information on the issue. • Improved written and video materials provided in the patient kit, including information on how to administer as well as dispose of the passive, self-retracting needles. • The educational materials will explain that California has a ban on sharps in landfills and inform patients of the types of facilities at which it is appropriate to dispose of containers.
Local and state Coordination	<ul style="list-style-type: none"> • Eisai will send letters or electronic communication to waste management personnel in the state and local programs informing them of its activities. Provide information regarding Eisai’s web site page for sharps disposal.
Consumer/Community Involvement	<ul style="list-style-type: none"> • Eisai plans to place a link on its web site permitting patients or others the opportunity to offer the company suggestions on ways to improve the plan. Eisai will review these suggestions as it continues to monitor this plan for collecting and disposing of sharps waste. • Eisai’s web site will explain the California Code banning sharps waste from landfills and where it is best to dispose of sharps containers. • Eisai will be working with appropriate professional associations, such as the pharmacy trade associations and physician associations to ensure there will be a commitment from trusted healthcare practitioners in order to provide a safe manner of disposal, and patient education on the provider level. The Eisai web site will be modified to ensure appropriate information addressing issues for healthcare practitioners.

Appendix B:

FRAGMIN®: IMPORTANT SAFETY INFORMATION

WARNING: SPINAL/EPIDURAL HEMATOMA

Epidural or spinal hematomas may occur in patients who are anticoagulated with low molecular weight heparins (LMWH) or heparinoids and are receiving neuraxial anesthesia or undergoing spinal puncture. These hematomas may result in long-term or permanent paralysis. Consider these risks when scheduling patients for spinal procedures. Factors that can increase the risk of developing epidural or spinal hematomas in these patients include:

- Use of indwelling epidural catheters
- Concomitant use of other drugs that affect hemostasis, such as non-steroidal anti-inflammatory drugs (NSAIDs), platelet inhibitors, other anticoagulants
- A history of traumatic or repeated epidural or spinal punctures
- A history of spinal deformity or spinal surgery

Monitor patients frequently for signs and symptoms of neurological impairment. If neurological compromise is noted, urgent treatment is necessary.

Consider the benefits and risks before neuraxial intervention in patients anticoagulated or to be anticoagulated for thromboprophylaxis [see **Warnings and Precautions** and **Drug Interactions**].

- FRAGMIN® is contraindicated in patients with active major bleeding, history of heparin induced thrombocytopenia, hypersensitivity to dalteparin sodium, heparin, or pork products.
- FRAGMIN® is contraindicated in patients undergoing epidural/neuraxial anesthesia as a treatment for unstable angina and non-Q-wave MI and for prolonged VTE prophylaxis due to an increased risk of bleeding associated with the dosage of FRAGMIN® recommended for these indications.
- FRAGMIN®, like other anticoagulants, should be used with extreme caution in patients who have an increased risk of hemorrhage; bleeding can occur at any site during therapy. An unexpected drop in hematocrit or blood pressure should lead to a search for a bleeding site.
- FRAGMIN® should be used with caution in patients with bleeding diathesis, thrombocytopenia or platelet defects, severe liver or kidney insufficiency, hypertensive or diabetic retinopathy, and recent gastrointestinal bleeding.
- **FRAGMIN® should be used with extreme caution in patients with history of heparin-induced thrombocytopenia.**
 - In FRAGMIN® clinical trials supporting non-cancer indications, platelet count of $<50,000/\text{mm}^3$ occurred in $<1\%$ of patients.
 - In FRAGMIN® clinical trials supporting the extended treatment of symptomatic VTE in patients with cancer, platelet counts of $<100,000/\text{mm}^3$ occurred in 13.6% of patients, including 6.5% who also had platelet counts less than $50,000/\text{mm}^3$. In the same clinical trial, thrombocytopenia was reported as an adverse event in 10.9% of patients in the FRAGMIN® arm and 8.1% of patients in the oral anticoagulant arm. FRAGMIN® dose was decreased or interrupted in patients whose platelet counts fell below $100,000/\text{mm}^3$.

- Thrombocytopenia of any degree should be monitored closely. Heparin-induced thrombocytopenia can occur with administration of FRAGMIN®. The incidence of this complication is unknown at present. In clinical practice, rare cases of thrombocytopenia with thrombosis have also been observed.
- Each multiple-dose vial of FRAGMIN® contains benzyl alcohol as a preservative. Benzyl alcohol has been reported to be associated with a fatal "Gasping Syndrome" in premature infants. Because benzyl alcohol may cross the placenta, use caution when administering FRAGMIN® preserved with benzyl alcohol to pregnant women. If anticoagulation with FRAGMIN® is needed during pregnancy, use preservative-free formulations, where possible.
- Periodic routine complete blood counts, including platelet count, blood chemistry, and stool occult blood tests are recommended during the course of treatment with FRAGMIN®.
- The most commonly reported side effect is hematoma at the injection site.
- Allergic reactions (i.e., pruritus, rash, fever, injection site reaction, bulleous eruption) have occurred. A few cases of anaphylactoid reactions have been reported.
- Use FRAGMIN® with care in patients receiving oral anticoagulants, platelet inhibitors, and thrombolytic agents because of increased risk of bleeding.
- FRAGMIN® cannot be used interchangeably (unit for unit) with unfractionated heparin or other low molecular weight heparins.
- FRAGMIN® Injection is not intended for intramuscular administration.