August 13, 2010

Mr. Burke Lucy
Integrated Waste Management Specialist
Department of Resources Recycling and Recovery (CalRecycle)
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Re: Comments regarding CalRecycle's Research on Pharmaceutical Take-Back Programs (SB 966)

Dear Mr. Lucy:

Thank you for the opportunity to submit comments on behalf of Eisai Inc. (Eisai) regarding CalRecycle's findings as a result of the research and surveys conducted in compliance with SB 966.

As a research-based bio-pharmaceutical company, Eisai is proud of its *human health care* (*hhc*) mission to give first thought to patients and their families and to increasing the benefits that healthcare provides. Eisai's U.S. commercial presence was established in 1997 with the launch of Aricept® for Alzheimer's disease. Today, Eisai's U.S. portfolio has grown to include a broad spectrum of treatments for gastrointestinal disorders, epilepsy, and prevention of deep vein thrombosis as well as several oncology and supportive care products. Of these, four medicines carry "orphan drug" status, with patient populations of fewer than 200,000 people. These include three oncology treatments and also, BANZEL®, a medication approved for the adjunctive treatment of Lennox-Gastaut Syndrome in children four years and older and adults.

After reviewing the materials that CalRecycle compiled for its July 20, 2010 workshop, Eisai would like to comment on the arguably undue emphasis CalRecycle seems to be placing on existing foreign drug take-back programs, particularly in European countries.[1] These programs are fundamentally different from U.S. programs because their history and purpose have developed differently. At the time European drug take-back programs began, there were issues regarding the lack of space and development of waste management technology to adequately control waste output at landfills. While the collection programs have been operational, many are not as successful as implied nor are they seen as having a significant impact on the amount of compounds found in landfills, sewage, or water runoff.

European Take-back Programs

As indicated in CalRecycle's background paper, "Evaluation of Home-generated Pharmaceutical Waste Programs in California," programs in Europe and other areas have had varied results. While nearly all countries in Europe have take-back programs, the documents seem to examine only four (4) of the more successful in terms of collection and model. And even amongst those four, the results are varied.

In January 2010, a workshop was held by the European Environmental Agency (EEA). During this workshop, the survey results were discussed regarding take-back programs in all European member

[1] CalRecycle Backgrounder, page 28, July 2010.

states, as well as Albania, Croatia, Serbia, Iceland, Lichtenstein, Norway, and Switzerland. Twenty-eight European states responded to this survey. The results were quite varied ranging from 0.19 tonnes per million per capita in Croatia to 237 tonnes per million per capita in Switzerland. The size and scope of these programs were also in question.

Based on this and other recent surveys, even with public programs in most European states, it is estimated that less than 50% of all unused pharmaceuticals are collected in best-case scenarios.[2] However, a study funded by the European Commission's Research Director-General known as KNAPPE, the Knowledge and Need Assessment on Pharmaceutical Products in the Environment, determined after 18-months that there is no real evidence that concentrations of pharmaceuticals in the environment are harmful to humans nor has a resolution been found to reduce the amount of pharmaceutical concentrations in the environment.

A presentation at the same January 2010 workshop also suggested that the only reason programs are in place, and will continue, is to address public perception that the concern about the issue is valid.[3] It implied heavily that any recommendation for additional stewardship programs or changes in existing programs to address environmental risk will be to placate public fears that a risk exists. One of the evaluations of the environmental impact of pharmaceuticals reviewed 60 compounds in the drinking water of the United Kingdom. Using worst-case scenarios, it was determined that for more than 80% of the compounds, a lifetime ingestion would be less than the daily therapeutic dose for those compounds.[4] With the risk of harm to the general public so low, it does not appear economical or practical to presume these take-back programs can ameliorate concerns on the issue of pharmaceuticals in the environment.

The rates of detection of pharmaceuticals in the environment in Europe are still being measured in amounts so small that they could be considered "trace amounts."[5] This is no different from those in the United States where fewer programs exist for take-back of unused medicines. The vast majority of prescription drugs in the environment are not from unused medicines being disposed of in landfills or sewage. The overwhelming majority of drug compounds found in the environment exist because of human and animal excretion of drugs that have not metabolized and have been secreted into the environment. A study of active pharmaceutical ingredients (APIs) in the environment and their impact on landfills, demonstrated that 99.9% of drug compounds found in landfills and surrounding waterways are attributed to patient use and excretion. Disposal of unused medicines accounts for only 0.1%.[6]

SMARxT Disposal

Because there is the need to balance the needs for patient access to affordable medicines with those of being responsible corporate citizens, Eisai is committed to educating the general public on the proper disposal of unused medicines pursuant to the White House Office of National Drug Control Policy (ONDCP). Eisai supports the "SMARxT Disposal" campaign to educate patients to not "flush" their unused

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[2] Vollmer, Gerald, Denmark, European Environmental Agency, "Pharmaceuticals in the Environment Workshop," January 2010.
[3] Roig, Benoit, Head of the Biodiagnostic and Metrology Department, Ecole des Mines d'Alès, Alès France, KNAPPE Findings at the "Pharmaceuticals in the Environment Workshop," January 2010.
[4] Webb, Simon, et al., "Indirect Human Exposure to Pharmaceuticals via Drinking Water," *Toxicology Letters*, January 2003.
[5] "Environmentally Classified Pharmaceuticals," Stockholm City Council, 2009.
[6] Tischler/Kocurek, "Potential Contribution of Unused Medicines to Environmental Concentrations of Pharmaceuticals," Round Rock, TX, 2007.

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medications into the sewer system unless the FDA-approved packaging specifically recommends doing so (which happens at times with medications that have a high potential for abuse). Patients are encouraged to look for any available local take-back programs. If no such programs are available, patients are encouraged to place their medications in an opaque container, diluted and/or mixed with an undesirable substance such as kitty litter, and dispose of them in a trash receptacle. The SMARxT Disposal campaign is a collaboration between the U.S. Fish and Wildlife Service, the American Pharmacists Association (APhA), and the Pharmaceutical Research and Manufacturers of America (PhRMA). Additional information on SMARxT Disposal may be found at www.smarxtdisposal.net.

Diversion and Counterfeits

As your findings note, there are many legal concerns associated with take-back programs. Under federal regulations, Pharmacists are not permitted to take back controlled substances, except under strict circumstances. These rules exist because of concerns over diversion. Interestingly, counterfeit and diversion schemes can take place just as easily when medicines are placed in return receptacles, or returned through the mail via a take- back program.[7] It could also be very easy for diversion to take place through the mail system once common envelopes are printed with the same reverse distributor(s) or other entity to receive them. Over time, as the envelopes become recognizable and known to the general public, it would be easy for a person to identify that a package contains drugs. Stated simply, there is no guarantee these programs could be successful in avoiding the diversion of unused medications.
The risk is even more pronounced when dealing with home-generated sharps devices. In the past, there have been reports of fraud and counterfeit schemes in which vials from sharps devices were simply filled with water and sold as the original drug.[8] How much easier it would be to conduct these schemes if the vials that were recovered and used by criminals had original manufacturer labels? Depending upon the take-back scheme is developed around home-generated sharps waste, this is a valid concern.

Thank you for the opportunity to provide comments on your findings. Please contact me at cher_gonzalez@eisai.com or at 916-397-4734 should you have any questions regarding Eisai's comments on CalRecycle's findings.

Sincerely,
/s/
Cher Gonzalez
Senior Manager
State Government Affairs

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[7] Daughton, Christian G., "Drug Usage and Disposal: Overview of Environmental Stewardship and Pollution Prevention," prepared for Research Triangle Environmental Health Collaborative, Health Summit, November 2008. (Abstract)
[8] Rudolf, Paul, Ph.D. and Ilisa B.G. Bernstein, "Counterfeit Drugs," *New England Journal of Medicine*, 350; 14, April 1, 2004.