



**Fujisawa Healthcare, Inc.**  
**Legal Department**  
Catherine J. Wertjes  
Associate General Counsel  
Three Parkway North  
Deerfield, Illinois 60015-2548  
Tel. (847) 317-1256 Fax (847) 317-7288  
[www.fujisawa.com](http://www.fujisawa.com)  
E-Mail: [catherine\\_wertjes@fujisawa.com](mailto:catherine_wertjes@fujisawa.com)

October 22, 2004

VIA HAND DELIVERY

Dockets Management Branch  
U.S. Food and Drug Administration  
5630 Fishers Lane, Room 1061  
Rockville, MD 20852

**Re: Supplemental Comments on Apotex Corp.'s Suitability Petition, Docket No. 2004P-0326/CP 1**

Ladies and Gentlemen:

Further to Fujisawa's letter of October 21, 2004, I attach the original signed copy of the declaration of Dr. Richard V. Aghababian for filing with the above docket. Dr. Aghababian's declaration is appended to the supplemental comments submitted yesterday (October 21, 2004) to the above-referenced docket. In the supplemental comments filed yesterday, Fujisawa included a facsimile copy of Dr. Aghababian's declaration.

Respectfully submitted,

  
Catherine Wertjes  
Associate General Counsel  
Fujisawa Healthcare, Inc.

2004P-0326

SUP 2

**Declaration of Richard V. Aghababian, M.D.,**  
**F.A.C.E.P.**

I, Richard V. Aghababian, M.D., F.A.C.E.P., hereby submit this declaration in order to provide information about the use of Adenocard<sup>®</sup> (adenosine injection) in the emergency room and ambulance settings. I have extensive experience in the use and administration of Adenocard<sup>®</sup> as well as with emergency room and ambulance practices. I am a Fellow and past President of the American College of Emergency Physicians and am Board certified by, among others, the American Board of Emergency Medicine. I am currently Associate Dean, Continuing Medical Education, of the University of Massachusetts Medical School, as well as the Chair of the Department of Emergency Medicine. My C.V. is attached hereto as Appendix A.

I hereby declare as follows:

1. I am familiar with the drug Adenocard<sup>®</sup>, which is indicated for conversion to sinus rhythm of paroxysmal supraventricular tachycardia (PSVT), including that associated with accessory bypass tracts (Wolff-Parkinson-White Syndrome). Adenocard<sup>®</sup> is primarily used in an emergency room or ambulance setting. In most cases, need for the product is sudden, and speed of administration is critical.
2. It is important in emergency situations to have the proper dose of adenosine prepared and ready to use, preferably in a pre-filled syringe or in a single use vial.
3. Adenocard<sup>®</sup> is available in pre-filled 2 ml and 4 ml syringes, or generically as adenosine in 2 ml and 4 ml vials, corresponding to the recommended dosages for the product.
4. I have been asked whether provision of adenosine for treatment of PSVT in larger 6 ml or 10 ml multidose vials would be beneficial or useful. It is my opinion that such larger vials would not be useful in an emergency setting and I would not use or purchase them for my emergency room for treatment of PSVT.
5. First, injecting the proper dose from a multi-dose vial will require additional time and measurement compared to the single dose vials or pre-filled syringes. Any dosage form that increases delivery time or requires multiple steps is not appropriate in an emergency setting.

6. Use of multi-dose vials raises the possibility of dosing errors and other safety hazards in administration. Indeed, the current pre-filled syringe packaging is ideal because it minimizes the chances of needle-stick injuries as well as dosing errors. The concern over injury or dosing error is heightened in an emergency room setting where speed of administration is critical. Delays or errors in administration can have serious results for patients.
7. Emergency room personnel learn to recognize drug packaging and rely, at least in part, on the similarity in packaging to confirm that they are providing the drug they intend to administer. Thus, I believe that it is important in emergency medicine for all makers of the same drug substance to provide the drug in the same or very similar format.
8. The introduction of a new larger vial size would require extensive retraining for emergency personnel. Emergency personnel are trained to respond in a reflexive, almost automatic fashion to emergency situations. Changing these conditioned responses would require extensive retraining. If you vary the routine, for example with different packaging or requiring injecting less than the entire vial or syringe, people will have to be retrained to respond in a different way.
9. In my experience, I try to avoid such retraining if at all possible. It is time consuming, and thus costly. It takes the already limited time of the emergency room personnel for a purpose other than treating patients. Retraining in the administration of an already familiar drug also causes confusion. If the retraining is not sufficient in the first instance, confusion can lead to errors in critical situations.
10. Multi-dose vials are particularly problematic where different nurses may treat the same patient. In such a case, the second nurse may not know the history of the vial that had been used for the first adenosine dose, and would be reluctant to reuse the vial where the second or third doses can be administered up to half an hour apart or longer. In addition, going back into a vial to draw an additional dose is not a good idea, as the vial may no longer be sterile.
11. A number of adverse effects are possible if a patient were mistakenly given a 30 mg dose of adenosine in a rapid injection. These could range from making the patient very uncomfortable to inducing an unstable rhythm that could deteriorate and even cause death. It is impossible to predict in advance who could be adversely affected by a large dose as certain patients can be unusually sensitive.
12. In summary, there is little need or justification for larger vial sizes of adenosine for the currently approved indication for Adenocard<sup>®</sup>. Use of these multi-dose vials would raise significant safety concerns as well as economic concerns related to retraining of personnel.

I declare under penalty of perjury that the foregoing is true and correct, to the best of my knowledge, information, and belief. Executed on October 21, 2004, in Worcester, Massachusetts.

Richard V. Aghababian  
Richard V. Aghababian, M.D., F.A.C.E.P.