

September 27, 2004

VIA UPS

Dear Doctor:

On behalf of St. Jude Medical, I write to provide you with information on the Artificial Valve Endocarditis Reduction Trial (AVERT). This clinical study has enabled us to compare the experience of a group of patients with Silzone® coated mechanical heart valves to another group with non-Silzone® coated valves. We believe the latest data concerning the Silzone® coated valve are reassuring and will be of interest to you.

If there is another physician who is following a patient with a Silzone® coated heart valve and you would like us to forward this updated information to that physician, please contact the Associate Silzone Communications Coordinator at the St. Jude Medical office (phone 800-922-9219) or email: heartvalves@sjm.com and we will send the information to the physician(s) you request.

A. Background Information Re: AVERT

AVERT is the international, multi-center, randomized clinical trial that was designed to determine whether the Silzone® coating on the sewing ring on certain St. Jude Medical mechanical heart valves reduced the incidence of prosthetic valve endocarditis. Based on the data reviewed on January 21, 2000, the AVERT Data Safety and Monitoring Board recommended discontinuing patient enrolment in the trial because of a small but statistically significant increase in the incidence of paravalvular leak (PVL) leading to explant in patients with Silzone® coated valves compared to those with non-Silzone® coated valves. On the same day, St. Jude Medical acted immediately and voluntarily to withdraw all non-implanted Silzone® coated products from the market.

At the time of the recall, the Data Coordinating Center (DCC) for AVERT at the University of Pittsburgh's Department of Epidemiology analyzed over 200 factors in an attempt to determine similar characteristics among patients with Silzone® coated valves who developed PVL that led to an explant. At that time, the AVERT DCC did not reach any conclusions as to the cause of the increase in explant due to PVL or identify any specific patient group with Silzone® coated valves that was at a greater risk.

The AVERT investigators have continued to follow those patients who were already enrolled in AVERT at the time enrolment was suspended. As part of this follow-up, the AVERT investigators have initiated periodic database closures in order to collect and analyze the AVERT data, most recently on January 21, 2004.

Dr. Hartzell Schaff and the other AVERT investigators reported on their analysis of the AVERT data in *Paravalvular Leak and Other Events in Silzone-Coated Mechanical Heart Valves: A Report From AVERT*, *Annals of Thoracic Surgery* (73:785 2002). This analysis was based principally on the November 30, 2000 database closure that included 804 patient-years of follow-up data. (The Addendum included with the article briefly commented on the data through the December 5, 2001 database closure).

B. Data as of January 21, 2004

Although the AVERT investigators are continuing to analyze the more recent data, except for the Addendum mentioned above, they have not yet published an analysis of the data collected after November 30, 2000. AVERT recently provided St. Jude Medical with the information below from the January 21, 2004 database closure, which now includes 2,851 patient-years of follow-up. The following sets forth the number of reports of major PVL and thromboembolic events experienced by patients in AVERT over time:

Major Paravalvular Leaks

Months After Implant	SILZONE® COATED		NON- SILZONE® COATED	
	Major PVL Events	# at Risk	Major PVL Events	# at Risk
0--6	8	391	2	387
6--12	2	365	1	362
12--18	2	352	0	352
18--24	1	343	0	347
24--30	0	334	1	341
30-36	1	325	0	327
36++	0	160	2	160

Thromboembolic Events

Months After Implant	SILZONE® COATED		NON- SILZONE® COATED	
	TE Events	# at Risk	TE Events	# at Risk
0—6	17	389	13	388
6—12	7	352	4	352
12—18	2	334	3	339
18—24	2	325	3	331
24—30	4	316	3	324
30-36	2	303	2	310
36++	5	151	6	153

The information from the January 21, 2004 database closure should be reassuring in a number of respects. Significantly, the data show that the small early increased risk of major PVL seen in AVERT patients with Silzone® coated valves appears to have declined with the passage of time. As a result, a statistical analysis of the above major PVL data shows that the overall difference in the major PVL rates between the two arms of the trial is no longer statistically significant ($p = 0.075$ by the log-rank test). Furthermore, in the AVERT patients who have had their valves implanted for more than 18 months without experiencing major PVL, there have been fewer subsequent reports of major PVL in the patients with Silzone® coated valves (two cases) than in those with non-Silzone® coated valves (three cases).

In addition, a statistical analysis of the above thromboembolic event data shows that there continues to be no statistically significant difference between recipients of Silzone® coated valves and non-Silzone® coated valves ($p = 0.54$ by the log-rank test).

The AVERT investigators are analyzing a number of factors in AVERT patients with Silzone coated valves that now appear to be predictors of an increased risk for major PVL. The analysis of this data is not complete, but it is our understanding that the AVERT investigators expect to publish additional information concerning these factors, as well as the above data, in the future.

C. Status of AVERT Data Adjudication

The majority of the data obtained by AVERT has been adjudicated for both endocarditis and thromboembolic events. All members of the events adjudication committee were blinded to valve type (i.e. Silzone or conventional). As a result, events in two patients with Silzone® coated valves previously categorized as major PVL in the data from the November 30, 2000 database closure (and discussed as such in the article by Dr. Schaff, et al.), are now classified as endocarditis, rather than major PVL. Therefore, these two events are no longer reflected as cases of major PVL in the data above. Likewise, adjudication of the thromboembolism cases resulted in a reduction in the number of thromboembolic events for both Silzone® coated and non-Silzone® coated valve recipients because certain of those incidents did not meet the criteria for a thromboembolic event. The adjudication process for these complications will be continuing as additional data are obtained for the patients in AVERT.

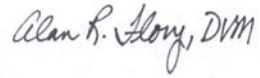
D. Continued Follow-Up

Although the data from the January 21, 2004 database closure appear reassuring, the diligent normal monitoring recommended for all patients with mechanical heart valves should continue for those with Silzone® coated valves. St. Jude Medical believes that such normal monitoring should detect the types of PVL complications observed in the AVERT study. Our company also continues to recommend that clinicians emphasize to patients the importance of keeping scheduled appointments and of reporting all changes in symptoms to their reviewing physicians.

If information from the continuing AVERT review results in any change in the recommended patient follow-up provided here, St. Jude Medical will report this to you. We also continue to post information concerning Silzone® coated valves on our web site (www.sjm.com) and to maintain our Silzone information line (1-800-922-9219) (as we have since the time of our voluntary recall of all non-implanted Silzone® coated valves in January of 2000).

Please do not hesitate to contact me if you have any questions or if I can be of further assistance.

Yours sincerely,

A handwritten signature in black ink that reads "Alan R. Flory, DVM". The signature is written in a cursive style with a loop at the end of the last name.

Al Flory, D.V.M.
Vice President, Corporate Clinical Services
St. Jude Medical, Inc.