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1998

IMPORTANT UPDATED INFORMATION FOR PHYSICIANS ABOUT PATIENTS WITH BJORK-SHILEY 70 DEGREE CONVEXO-CONCAVE HEART VALVES

Dear Doctor:

This letter provides new information about the risk of outlet strut fracture for 70 degree Bjork-Shiley Convexo-Concave (BSCC) heart valves and new recommendations from an independent expert panel regarding prophylactic valve replacement. The recommendations are described in detail in the enclosed attachments.

Under the Settlement Agreement that was entered into by a worldwide class of BSCC valve patients and Shiley Incorporated and approved by the U.S. District Court in Cincinnati, Ohio in Bowling v. Pfizer, an independent expert medical and scientific panel consisting of cardiothoracic surgeons, cardiologists, and epidemiologists was created called the Supervisory Panel. Under the terms of the Settlement Agreement, the Supervisory Panel is charged with the responsibilities of conducting studies and research, and of making recommendations regarding which BSCC heart valve patients should be considered for prophylactic valve replacement. The Supervisory Panel's recommendations also serve to determine which class members qualify for explantation benefits under the Settlement Agreement. The Panel's work has enabled it to develop these present guidelines for valve replacement surgery. The Panel's guidelines represent a departure from past reliance upon the valve replacement surgery guidelines developed by a Medical Advisory Panel created by Shiley Incorporated.

Recommendations Regarding Prophylactic Valve Replacement

Attachments A and B.

The Supervisory Panel's recommendations regarding prophylactic valve replacement are summarized in Attachment A, entitled "Summary of the Supervisory Panel's Prophylactic BSCC Valve Replacement Guidelines." The Panel's recommendations account for valve implant position (aortic vs. mitral), gender and current age of the patient, and patient-specific estimated annual fracture rate.

Table 1 in Attachment A provides certain threshold estimated annual fracture rates above which prophylactic explantation should be considered. If your patient's estimated annual fracture rate is higher than the corresponding rate in the table, the Supervisory Panel recommends that prophylactic explantation be considered. To use the table, you will need to obtain a patient-specific estimated annual fracture rate, as described below, and compare that rate to the rate listed in Table 1 for the patient's gender, valve position, and current age (rounded to the nearest five years).

In order for a Bowling class member to receive monetary benefits from the Bowling Patient Benefit Fund for prophylactic valve replacement, the valve replacement must meet the objective standards set forth in Attachment A. Qualification under these objective standards does **not** mean that replacement surgery is appropriate for a particular patient, but only that monetary benefits under the Bowling settlement are available should the surgery take place. It should be noted that benefits generally remain available for implantees who undergo explantation in accordance with the prior replacement surgery guidelines (January 1995) developed by the Medical Advisory Panel created by Shiley Incorporated. If you want a copy of the 1995 guidelines, please contact the Claims Administrator.

As discussed above, the recommendations regarding prophylactic valve replacement require the calculation of patient-specific estimated annual fracture rates. Attachment B, entitled "Summary of Factors and Methodology Used to Calculate 70 Degree BSCC Valve Fracture Rates," sets forth a formula based upon current information that can be used to identify 70 degree BSCC heart valves that may have a significantly greater risk of outlet strut fracture. The Supervisory Panel has identified five risk factors to be used in calculating estimated annual fracture rates for 70 degree BSCC heart valves: valve size, valve implant position (mitral vs. aortic), welder identity, valve shop order, and current patient age. This is the first time that two of these risk factors, valve shop order and current patient age, are used in the calculation of estimated annual fracture rates. Because current age must be included in the calculation, estimated annual fracture rates for each patient must be calculated on a case-by-case basis.

In order to obtain the estimated annual fracture rate for a specific patient, or to determine if the patient qualifies for benefits for reoperation under the Settlement Agreement, you will need to communicate the valve serial number, valve implant position, and the patient's gender and current age to the Bowling Claims Administrator. A telephone number, fax number, and mailing address for the Claims Administrator are provided at the end of this letter. A prompt response will be provided, including a copy of the calculation of the estimated annual fracture rate and whether the patient qualifies for the payment of the costs of reoperation.

Attachment C.

Attachment C contains the Supervisory Panel's recommendations and guidelines. That document is intended to provide valve implantees and their treating physicians with additional information that is relevant and important to the explantation decision. For example, it sets forth factors which should

be seriously considered by the patient and physician when deciding whether or not explantation of a heart valve identified to be at a greater risk of outlet strut fracture may be beneficial for a particular implantee. The guidelines contain additional information that the Supervisory Panel believes is helpful in the clinical management of BSCC valve patients, so please read them carefully.

Since guidelines development is a dynamic process, the guidelines will be continuously reviewed by the Supervisory Panel as new data become available. They will be modified when appropriate in accord with the best scientific, epidemiological and clinical information made available to the Panel.

The Supervisory Panel's recommendations are based upon the best data available at the present time and are not meant to be absolute recommendations for individual patients. The final decision regarding explantation in an individual patient must be made by the patient in consultation with the treating cardiologist or cardiovascular surgeon, after careful examination and explanation of the available data.

The Supervisory Panel will soon send letters to BSCC valve patients to inform them that new information regarding their heart valve is available. In the letter, we recommend that patients contact their physicians to discuss this new information. **The Supervisory Panel encourages you to obtain estimated annual fracture rates for your BSCC valve patients and to speak with them about this new information.** Also note that in the event that you or any of your patients disagree with the decision rendered regarding qualification for valve replacement surgery, please contact the Claims Administrator for information regarding an appropriate appeal process.

If you have any questions about this letter or want to obtain an estimated annual fracture rate for a specific patient, please contact the Claims Administrator at 1-513-421-4415. The Claims Administrator will accept calls that reverse the charge. Someone will be available to answer questions between 9:00 a.m. and 5:00 p.m. Eastern Time, Monday through Friday. You can also contact the Claims Administrator by fax at 1-513-421-7696, or by mail at Claims Administrator, Offices of Bowling-Pfizer Trust, 525 Vine Street, Suite 1300, Cincinnati, Ohio 45202, U.S.A.

Sincerely,

J. Kermit Smith
Chairman
Supervisory Panel
Bowling-Pfizer Settlement

Attachment A

Summary of the Supervisory Panel's Prophylactic BSCC Valve Replacement Guidelines

TABLE 1 Estimated Outlet Strut Fracture Rates (% Per Year) By Age, Gender and Position Above Which Reoperation Should be Considered				
	Male		Female	
Age	Aortic	Mitral	Aortic	Mitral
30	0.80	0.93	0.73	0.85
35	1.15	1.32	1.03	1.19
40	1.32	1.50	1.16	1.33
45	1.55	1.74	1.34	1.52
50	1.87	2.09	1.58	1.78
55	2.33	2.58	1.92	2.14
60	3.01	3.29	2.40	2.64
65	4.02	4.37	3.10	3.39
70	5.65	6.09	4.19	4.53
75	8.42	9.01	5.96	6.40

To use this table, communicate your patient's valve serial number and implant position, along with the patient's gender and current age, to the Claims Administrator by telephone at 1-513-421-4415, by fax at 1-513-421-7696, or by mail at Claims Administrator, Office of Bowling-Pfizer Trust, 525 Vine Street, Suite 1300, Cincinnati, Ohio 45202, U.S.A.

Once you have received your patient's estimated annual fracture rate from the Claims Administrator, compare that rate to the rate listed in Table 1 for the patient's gender, valve position, and current age (rounded to the nearest five years). If your patient's estimated rate is higher than the corresponding rate in the table, prophylactic explantation should be considered. For example, if your patient is a 30 year-old male with a 70 degree aortic BSCC valve and a 0.75 estimated annual fracture rate, prophylactic explantation should not be considered. On the other hand, if your patient is a 30 year-old male with a 70 degree aortic BSCC valve and a 0.85 estimated annual fracture rate, prophylactic explantation should be considered.

There are two other subgroups of patients for whom prophylactic explantation should be considered: (1) patients currently under the age of 35, implanted with a size 29, 31 or 33mm mitral valve with an unknown serial number, and (2) patients in whom x-ray images definitively show that one leg of the outlet strut has separated from the valve flange. These recommendations are discussed in greater detail in Attachment C.

Attachment B

**Summary of Factors and Methodology Used to Calculate
70 Degree BSCC Valve Fracture Rates**

Fracture rates (%/yr) are adjusted for underreporting and are calculated by multiplying the factors listed below with the factor 0.75078.

<u>Valve Size (mm)</u>	<u>Factors</u>
21 or 25	1.00
23 or 27	1.94
29	3.20
31 or 33	5.69
<u>Implant Position</u>	
Aortic	1.00
Mitral	1.51
<u>Welder Group</u>	
D	1.00
E	2.23
<u>Shop Order</u>	
Low Risk	1.00
High Risk	2.94
<u>Current Age of Patient</u>	
<35	1.00
>35	(0.942) ^(Age-35)

EXAMPLE

size 31mm	5.69
mitral	x 1.51
welder group=D	x 1.00
shop order=low	x 1.00
age=63	x 0.942 ⁽⁶³⁻³⁵⁾ = .942 ²⁸ = .19
	x 0.75078
	= 1.23% per year
	(adjusted for underreporting)

**Guidelines to Assess Patients with
Bjork-Shiley Convexo-Concave Heart Valves
for Elective Explantation
Proposed by the Bowling-Pfizer Supervisory Panel
and
Approved by the
U.S. District Court, Southern District, Western Division
Cincinnati, Ohio**

INTRODUCTION

The Bowling-Pfizer litigation arising from strut fracture of Bjork-Shiley Convexo-Concave (BSCC) heart valves was ended by a Settlement Agreement entered into as of January 23, 1992, later approved by the U.S. District Court in Cincinnati, Ohio. The Settlement Agreement provides, among other things, for the payment of certain financial benefits for patients undergoing reoperation to replace a BSCC heart valve due to the risk of strut fracture if the patients fall within certain guidelines. In the past, the guidelines have been those developed by a Medical Advisory Panel created by Shiley Incorporated. Pursuant to the Settlement Agreement, a Supervisory Panel was appointed in May, 1994, charged with the responsibilities, among others, of conducting research on diagnostic techniques to identify high risk valves as well as the risks of replacement surgery, and of adopting new guidelines for recommendations for reoperation which would determine eligibility for payment of benefits. All new guidelines must be approved by the U.S. District Court. The specific direction to the Supervisory Panel is as follows:

"In its guidelines for valve replacement surgery, the Supervisory Panel is to identify those circumstances in which prophylactic replacement of a Bjork-Shiley Convexo-Concave heart valve would reasonably offer a meaningful extension of life expectancy because of the risk of strut fracture. The Panel shall, to the extent possible, establish these guidelines premised on an implantee whose health history and status presents the optimal estimated risks for valve replacement surgery; the Panel shall also, to the extent possible, separately identify those factors of an implantee's health history or status that might increase these risks. Additionally, the Panel shall establish these guidelines on the assumption that the experience of the facility at which the surgery will be performed presents the optimal estimated risks for valve replacement surgery; the Panel may also, to the extent possible, separately identify those factors of facility experience that might increase these risks." (From the Court Settlement of January 23, 1992.)

The Supervisory Panel has monitored a number of clinical studies, continuously analyzed the worldwide database for BSCC valves, and undertaken extensive studies to understand the operative risk of elective explantation as it relates to age and cardiac functional ability. In addition, the Panel formed a new, independent Guidelines Committee composed of expert cardiovascular surgeons, cardiologists, biostatisticians, and ethicists to evaluate newly available data and formulate recommendations for revised guidelines. Input from all these groups was used to reach consensus on these recommendations.

The purpose of this document is to state the new guidelines which will be used to help patients and their cardiologists or cardiovascular surgeons in making decisions about elective explantation. *Although these guidelines will be used to establish compensation for reoperation, the decision to issue revised guidelines and their content was based on the mandate of the settlement and represents the best medical judgement of the Guidelines Committee and the Supervisory Panel, independent of any other considerations.*

All guidelines are clinical models based upon the best data for outlet strut fracture (OSF) and operative mortality for explantation available at the time of their development, and are not meant to be absolute recommendations for individual patients. The final decision regarding explantation in an individual patient must be made by the patient in consultation with the managing cardiologist or cardiovascular surgeon, after careful examination and explanation of the available data. However, under the Settlement Agreement, certain financial benefits are provided only for those patients falling within the guidelines who have their valves replaced due to the risk of strut fracture. All decisions about patients qualifying for benefits are made by the Claims Administrator appointed by the Court, subject to the appeal process set forth in section 5.2.3.1 (a) of the Settlement Agreement.

We emphasize that these guidelines will be continuously reviewed by the Supervisory Panel as new data become available. They will be modified when appropriate in accord with the best epidemiological and clinical information made available to the Panel.

PRIMARY CONSIDERATIONS IN NEW GUIDELINE DEVELOPMENT

The most important issue considered by the Supervisory Panel in developing these guidelines was identifying those circumstances in which prophylactic replacement of a BSCC heart valve would reasonably offer a meaningful extension of life expectancy because of the risk of OSF. These depend upon sets of data respectively dealing with expected valve fracture rates and operative mortality rates for various groups. The formulas developed to calculate fracture rates for 60 degree and 70 degree BSCC valves take into account valve size, valve position, weld date, welder, shop order and the patient's current age. A model for reoperative mortality that accounts for the patient's age is used to calculate expected gain in life expectancy. See Appendix I, Tables 1-4. The Supervisory Panel developed these guidelines by determining the estimated OSF rate for individual patient-valve combinations taking into consideration the estimated reoperative mortality for elective explantation. Outlet strut fracture rate was estimated separately for 60 and 70 degree valves. Models for expected extension of life were developed. Because these models are conservative and do not take into account post-operative morbidity or late post-operative mortality, or the possibility of survival from an OSF, together with the fact that many patients undergoing reoperation will not benefit from the

procedure (because they would not undergo strut fracture or will die as a result of the surgery), a projected extension of life expectancy of two years was chosen as significant. (The rationale for this decision is discussed in greater detail in Appendix I.)

In interpreting these guidelines, it is important to emphasize that the recommendations are based on biostatistical analysis of group data, and that the risk for an individual patient may differ from those of the group.

There are a large number of patients who, on medical grounds, generally would not be recommended for explantation. These include patients with valves welded after April 1984, those in NYHA Class III or IV, and any patient with a BSCC 60 degree valve over the age of 75 years. The panel has developed additional information to help physicians make decisions regarding patients, but not necessarily within the patient benefit settlement agreement. These are presented in Appendix II.

SPECIFIC GUIDELINES

The guidelines detailed below are for the elective explantation of BSCC valves in otherwise well-functioning patients (NYHA Class I or II). These guidelines account for patient gender (male or female), patient current age, valve position (aortic vs. mitral) and manufacturing characteristics of the valve. The risk of valve fracture depends on a number of manufacturing characteristics of each valve. Accordingly, it is absolutely necessary to know the valve serial number.

Use of these guidelines requires knowledge of the OSF rate for the specific patient in whom prophylactic explantation is being considered. In order to determine if the patient qualifies for benefits for reoperation utilizing the formula presented in Appendix I, the responsible physician managing the patient will need to communicate the valve serial number, along with the current age, gender and valve implant position of the patient, to the Claims Administrator. This may be accomplished by phone to (800) 977-0779 in the U.S.A. or Canada or 00 (1) 513-421-3517 internationally, by fax to (513) 421-7696, or by mail to Claims Administrator, P.O. Box 3598, Cincinnati, OH 45201-3598, U.S.A.

I. MALE AND FEMALE PATIENTS WITH 60 DEGREE OR 70 DEGREE BSCC VALVES.

ELECTIVE EXPLANTATION SHOULD BE CONSIDERED IF THE PATIENT'S OSF RATE IS GREATER PER ANNUM THAN THE RATES LISTED BELOW IN TABLE 1 FOR THE PATIENT'S GENDER, VALVE POSITION, AND CURRENT AGE (ROUNDED TO THE NEAREST 5 YEARS). IN ORDER TO OBTAIN THE ESTIMATED OSF RATE FOR EACH PATIENT, THE SERIAL NUMBER, THE IMPLANTED VALVE POSITION, AND THE PATIENT'S CURRENT AGE AND GENDER SHOULD BE SENT TO THE CLAIMS ADMINISTRATOR AS OUTLINED ABOVE. THE ESTIMATED OSF RATE PER ANNUM AND THE AVAILABILITY OF PATIENT BENEFITS FOR REOPERATION WILL BE FORWARDED TO THE MANAGING PHYSICIAN MAKING SPECIFIC EXPLANTATION RECOMMENDATIONS TO HIS/HER PATIENTS.

TABLE 1
Outlet Strut Fracture Rates (% Per Year)
by Age, Gender and Position Above Which
Reoperation Should be Considered
(Calculated Using the Method
Described in Appendix I)

Age	Male		Female	
	Aortic	Mitral	Aortic	Mitral
30	0.80	.93	0.73	.85
35	1.15	1.32	1.03	1.19
40	1.32	1.50	1.16	1.33
45	1.5	1.74	1.34	1.52
50	1.87	2.09	1.58	1.78
55	2.33	2.58	1.92	2.14
60	3.01	3.29	2.40	2.64
65	4.02	4.37	3.10	3.39
70	5.65	6.09	4.19	4.53
75	8.42	9.01	5.96	6.40

II. PATIENTS WITHOUT SERIAL NUMBERS.

FOR PATIENTS WITH BSCC VALVES WHERE THE VALVE SERIAL NUMBER IS NOT KNOWN AND NO IMPLANT CARD IS AVAILABLE, EVERY EFFORT SHOULD BE MADE TO OBTAIN THE SERIAL NUMBER, OR AT LEAST DETERMINE THE VALVE SIZE, BY CONTACTING THE HOSPITAL WHERE THE VALVE WAS IMPLANTED OR THE CARDIAC SURGEON INVOLVED IN THE INITIAL IMPLANT. IF THIS INFORMATION IS UNOBTAINABLE, ONLY AN ESTIMATE OF THE RISK OF OSF CAN BE MADE. IF THE PATIENT CAN PROVE THAT HE OR SHE IS CURRENTLY UNDER THE AGE OF 35 AND HAS A 29-31-33 MM 60-DEGREE OR 70-DEGREE MITRAL BSCC VALVE IMPLANTED, HE OR SHE WILL QUALIFY FOR THE BENEFITS UNDER THE SETTLEMENT AGREEMENT. PROOF OF THE CHARACTERISTICS OF THE VALVE MAY BE MADE BY X-RAY, FLUOROSCOPY OR TRANSESOPHAGEAL ECHOCARDIOGRAPHY.

III. PATIENTS WITH DOCUMENTED SINGLE LEG SEPARATION (SLS).

WEIGHING ALL THE DATA, IF THERE IS CLEAR EVIDENCE OF SINGLE LEG SEPARATION, AS DOCUMENTED BY X-RAY IMAGES DEFINITELY SHOWING OFFSET

OF THE STRUT SECTIONS, WHICH IS CLASS V IN THE PREVIOUSLY REPORTED IMAGING STUDIES, AND THE PATIENT HAS RELATIVELY LOW PREDICTED MORTALITY FROM EXPLANTATION, SHOULD BE CONSIDERED FOR ELECTIVE EXPLANTATION. IF THE PATIENT IS AT HIGHER OPERATIVE RISK, THEN THE DECISION TO REOPERATE MUST REST WITH THE PATIENT AFTER CONSULTATION AND EXPLANATION BY THE RESPONSIBLE PHYSICIAN. NEW TECHNOLOGIES ARE BEING STUDIED WHICH MIGHT LEAD TO A MORE PRECISE DOCUMENTATION OF SINGLE LEG SEPARATION AND DETERMINATION OF ITS NATURAL HISTORY. (THE RATIONALE FOR THIS IS EXPLAINED IN APPENDIX I.)

IV. PATIENTS QUALIFYING FOR BENEFITS UNDER PREVIOUSLY EXISTING GUIDELINES

IN ADDITION TO THE FOREGOING GUIDELINES, THE SUPERVISORY PANEL CONCLUDES THAT THE PREVIOUSLY EXISTING GUIDELINES OF THE BJORK-SHILEY 60° AND 70° C/C HEART VALVE MEDICAL ADVISORY PANEL (60° GUIDELINES OF JANUARY 1995 AND 70° GUIDELINES OF AUGUST 1994) HAD SCIENTIFIC BASIS, AND THAT REPLACEMENT SURGERY COMPLYING WITH THOSE GUIDELINES WILL QUALIFY THE PATIENT FOR THE VALVE REPLACEMENT SURGERY BENEFITS. THERE ARE TWO EXCEPTIONS: 1. THOSE 60° PATIENTS WHO WOULD QUALIFY ONLY BECAUSE OF REPEAT CARDIAC SURGERY FOR OTHER REASONS AND 2. THOSE 70° PATIENTS WHO WOULD QUALIFY ONLY BECAUSE OF SURGERY FOR ANOTHER PROBLEM RELATED TO THEIR C/C 70° PROTHESIS. THE PANEL CONCLUDES THAT IT IS INAPPROPRIATE TO RESCIND BENEFITS THAT WERE PREVIOUSLY AVAILABLE UNDER THOSE GUIDELINES, EXCEPT FOR THE TWO CONDITIONS OUTLINED ABOVE. THESE PREVIOUSLY EXISTING GUIDELINES SHOULD BE APPLIED TO OLDER PATIENTS WITH CAUTION BECAUSE OF OBSERVED HIGH MORTALITY RATES IN OLDER AGE GROUPS AND SHOULD BE UTILIZED ONLY FOR OPTIMUM SURGICAL CANDIDATES.

For subgroups of patients with BSCC valves warranting special consideration, see Appendix II.

For general recommendations for all BSCC patients, see Appendix II.

For patients whose previous valve replacement surgery did not qualify for benefits under the old guidelines but will qualify under the new guidelines, see Appendix II.

EFFECTS OF THE NEW GUIDELINES ON THE TOTAL PATIENT GROUP WITH BSCC VALVES

It should be emphasized that these guidelines differ in several significant ways from the old guidelines. The new guidelines include new variables that have modified risk groups. Accounting for the well documented effects of decreasing fracture risk and of increasing valve explantation operative mortality risk with each advancing year of age has allowed more detailed analysis of patients who will benefit from prophylactic surgery. Many more patients were identified in the old guidelines that were

of advanced age and were not actually reasonable operative candidates, although they were eligible for benefits. The new guidelines identify patients of younger age as having the greatest likelihood of meaningful extension of life, and a much higher number of these patients will be suitable candidates for elective valve explantation. Ninety-eight percent of the patients identified in the new guidelines are under the age of 50 which is in marked contrast to the previous guidelines where 6% of the patients were <50 years of age and 55% were >70.

CONCLUSIONS

The present guidelines suggest consideration for elective reoperation and explantation of BSCC 60 and 70 degree valves with high risk for fracture primarily in younger patients. As emphasized previously, the final decision for elective explantation of a BSCC valve rests with the patient and his or her managing physician. The Supervisory Panel believes that the guidelines presented above and explained in Appendices I and II represent the present state-of-the-art knowledge relating to BSCC valves. Considerable work on new diagnostic techniques, on cohort studies of well-defined populations, and on further refinement of reoperative mortality are in progress. The data from these studies may result in further refinement of recommendations in the future.

Since the guidelines development is a dynamic process, the guidelines will be reviewed and amended in the months and years ahead, and the panel should establish a study to review the impact of these guidelines and any changes that might be indicated be made to the guidelines for the health of the implantees.

APPENDIX I

Background and Detailed Explanation for Recommendations for Explantation of BSCC Valves

INTRODUCTION

Several detailed observations and considerations made by the Supervisory Panel in reaching the recommendations for elective explantation of BSCC valves are contained in this appendix. The Supervisory Panel has reviewed the relevant clinical data at several meetings each year since 1994, has relied on the advice of an independent Guidelines Committee, and has engaged the services of several biostatistical consultants. In all instances, the expert clinical judgement of physicians who are daily managing patients with complex cardiovascular conditions was the final arbiter for these guidelines as opposed to concerns about financial benefit payment to patients.

RATIONALE FOR USING A TWO-YEAR INCREASE IN PREDICTED LIFE EXPECTANCY

The decision by the Supervisory Panel to use an increase in life expectancy of two years (as opposed to one year or one day, for example) as a threshold for recommending prophylactic explantation was made because some of the assumptions underlying the calculations were conservative in that they tend to overestimate the gains in life expectancy from reoperation. These assumptions are listed below.

First, the reoperative mortality rates used in constructing the tables in this appendix were conservative because they account for mortality only in the first 90 days after surgery. The 90-day cut-off was chosen to be consistent with the reference data in the literature. Additional mortality has been demonstrated to occur in the 90-day to one-year period. Thus, if the one-year figures were used instead of 90 days, estimated reoperative mortality would increase. While there are small differences in reoperative mortality between genders, these were insignificant when compared to age, cardiac status, and the other uncertainties in these estimates.

Second, morbidity was also not considered in the recommendation for elective explantation. Morbidity includes the long recovery time which is frequently required in patients undergoing a second major open-heart surgery. In many instances, this could be as much as six months. It also includes complications of open heart surgery such as stroke and other neurological dysfunction which have recently been reported to be much higher than previously recognized, infection, embolism, and other complications of valve replacement.(1)

Third, it was assumed that all outlet strut fractures would be lethal. This has not proven to be the case, and hence the risk of death from OSF is actually less than estimated.

Furthermore, it must be emphasized that any gain in meaningful life expectancy for the group of patients could only be achieved by accepting significant numbers of operative deaths among individual patients. In addition, it must be recognized that even among those patients who survive reoperation,

there would be many patients who would not have their life prolonged because it is unlikely that they would have had a strut fracture had the valve been left in place, and yet, they would be subject to all of the morbidity of a second reoperation. This is illustrated in Figure 1, which is a simulated distribution of the potential gains and losses of years of life from reoperation in the subpopulation of BSCC patients qualifying under these guidelines. The negative gains in survival represent those patients who die at reoperation. The positive bars represent the patients who avoided fracture by elective explantation. The large bar at zero represents the large group of patients who survived reoperation but did not receive benefit from the procedure because they would not have had an outlet strut fracture had the valve been left in place. The graph also shows that although on average the duration of life will increase by at least two years in this population, for individual patients there can be a significant loss of life (if death results from reoperation) or a significant gain (if an OSF is avoided by a successful operation).

All of these considerations entered the Supervisory Panel's deliberations on meaningful extension of life expectancy and the Panel's decision to use two years as the basis for the guidelines.

METHODOLOGY FOR OSF RISK

Table 1 outlines the factors utilized to calculate the OSF rates (percent per year) for 60 degree BSCC valves. The rates are calculated by multiplying the factors corresponding to valve characteristics and patient current age together with a statistical adjustment factor to give the risk in terms of percent per year. The rates are adjusted for under-reporting of fractures using the figures from the Dutch epidemiological studies which are 2.29 times higher than U.S. rates.

Table 2 illustrates the calculation of an OSF rate for a hypothetical patient with a size 31 mm BSCC mitral valve, welded in 1983 by Welder Group B, in a shop order with a low risk at the present age of 63 years. In order to obtain the manufacturing data necessary to apply the calculations, the serial number for the valve must be known as well as the implanted valve position. As noted above, once this information and the current age, gender and valve implant position of the patient are communicated to the Claims Administrator, this calculation will be made and transmitted to the physician managing the patient.

Table 3 presents the factors utilized in calculating potential OSF rates for 70 degree BSCC valves. The same technique as for 60 degree valves is employed. Note that the statistical factor used to adjust to a rate per year is larger than for 60 degree valves, reflecting the greater risk of OSF in 70 degree valves.

METHODOLOGY FOR ESTIMATING REOPERATIVE MORTALITY

Table 4 provides a model for estimating mortality for elective explantation of BSCC valves. This model was based upon the logistic regression model of Piehler, et al (2), which was normalized to a predicted reoperative mortality of 6% at an approximate age of 58. The average reoperative mortality rate from the clinical experience for elective BSCC valve replacement from the worldwide databases reported to the Supervisory Panel was 9% at approximately mean age of 58. In the Panel's

judgement, 6% is the lowest plausible reoperative mortality rate that can be achieved in this population. These mortality rates vary with age as illustrated in Table 4 and the accompanying figure. Column B and Curve B represent the 6% model and is the one used to determine patients qualifying for replacement surgery benefits. Column A and Curve A are the values from the worldwide database experience.

RATIONALE FOR PATIENTS WITH DOCUMENTED SINGLE LEG SEPARATION (SLS)

Patients with a documented break of one leg of a BSCC outlet strut are generally considered to be at significantly increased risk for complete OSF and prophylactic reoperation has been recommended in these patients. However, documentation of SLS before surgery is rarely unequivocal, as has been amply proven in the nearly 1,000 patients undergoing special imaging techniques where both false-negative and false-positive diagnoses were relatively common. The false positive rate was 18% in the imaging studies and the test had a specificity of 76%. Based on data relating to the removal of BSCC valves for reasons other than suspected SLS, it is estimated that the prevalence of SLS in the total BSCC population is roughly 10%. The prevalence detected in the imaging studies was 3%. This suggests a sensitivity of approximately 30%. In addition, the natural history of SLS is not truly known, and while some SLS valves have rapidly progressed to complete fracture, breakage of one leg of the outlet strut may mechanically decrease the stress on the other, and many clinical or artificially fractured SLS valves have continued to function indefinitely in in-vitro pulse duplicator studies and have remained intact for years when implanted in animals.

Figure 1: Simulated Distribution of Potential Gains and Losses of Years of Life from Reoperation Among Patients Satisfying the Guidelines for Reoperation

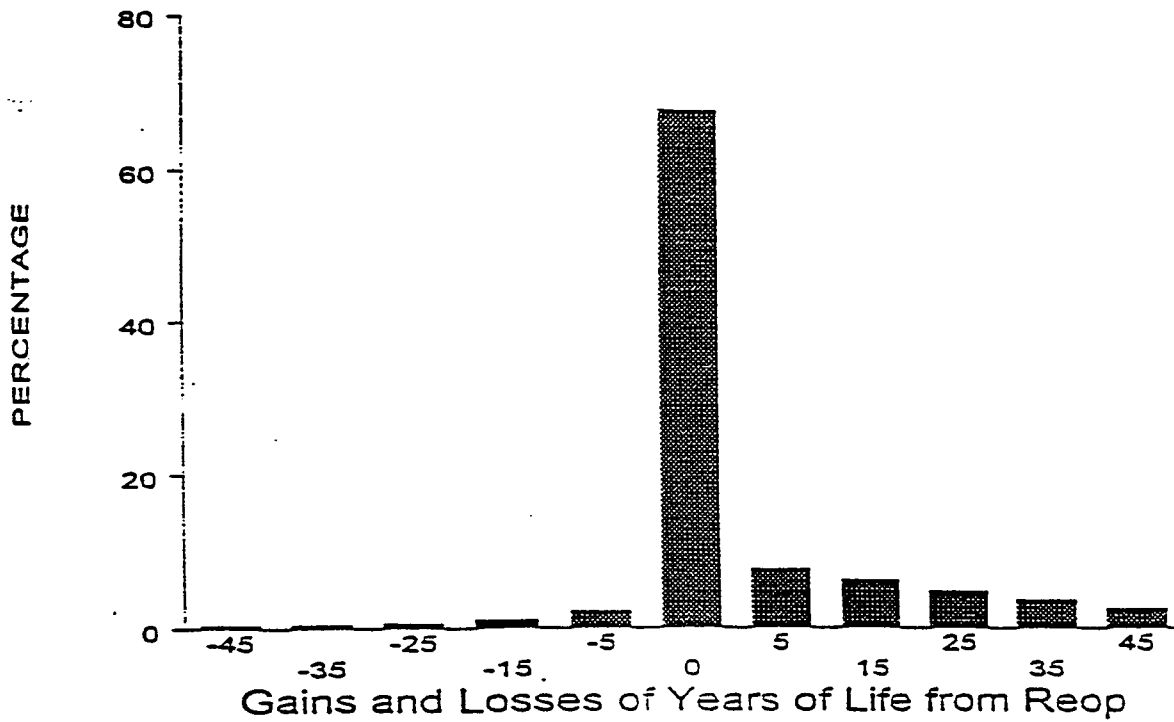


Table 1: Factors for calculation of fracture rates of 60° BSCC valves. Fracture rates (%/yr) are adjusted for underreporting and are calculated by multiplying factors together with the factor 0.05470¹

<u>Size (mm)</u>	<u>Factors</u>
21 or 25	1.00
23 or 27	4.16
29	7.64
31	12.11
33	23.04
<u>Position</u>	
Aortic	1.00
Mitral	2.11
<u>Weld date</u>	
< 1980, July 82 - Mar 84	1.00
1980	.51
Jan 81 - June 82	1.73
> April 84	0.0
<u>Welder group</u> ²	
A	1.00
B	1.63
C	2.42
<u>Shop order</u> ³	
Low Risk	1.00
High Risk	3.58
<u>Current Age</u> ⁴	
< 35	1.00
> 35	(.942) ^(Age-35)

Table 2

METHOD TO PREDICT FRACTURE RATES (%/YEAR) FOR 60° BSCC VALVES

- (1) MULTIPLY FACTORS FOR
SIZE, POSITION, WELD DATE, WELDER,
SHOPORDER, CURRENT AGE
- (2) MULTIPLY BY CONSTANT 0.05470¹

EXAMPLE

size 31 mm		12.11
mitral	x	2.11
weld 1983	x	1.00
welder=B	x	1.63
shop=low	x	1.00
age=63	x	$0.942^{(63-35)} = .942^{28} = .19$
	x	<u>0.05470</u>
		= 0.43 %/year
		(adjusted for under-reporting)

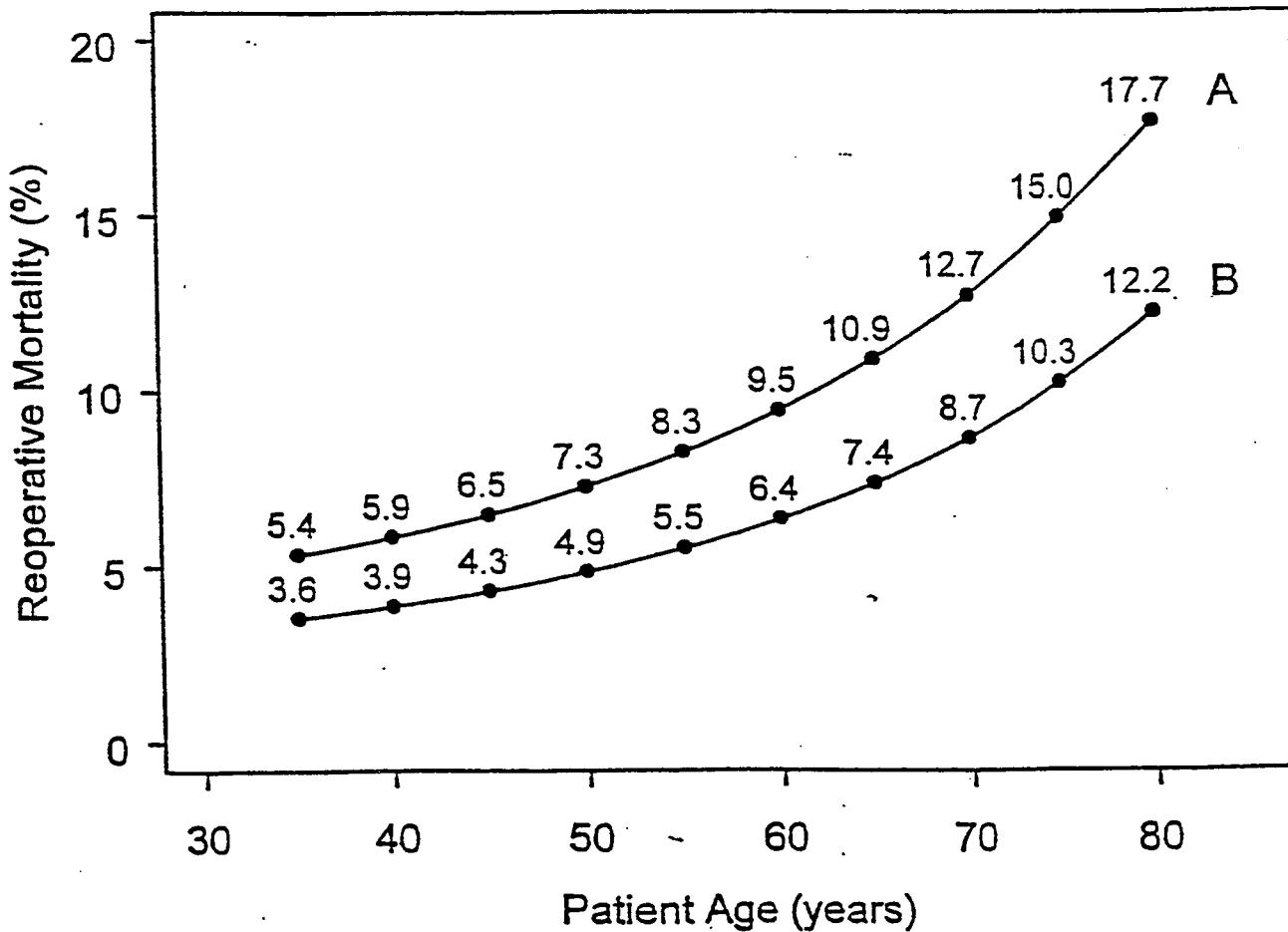
¹The constant 0.05470 is the fracture rate (%/year) for an individual whose factors are all 1.0 (size 21 or 25; aortic; <1980, Jul 82-Mar 84; welder groupA; low risk shop order; age <35.

Table 3: Factors for calculation of fracture rates of 70° BSCC valves. Fracture rates (%/yr) are adjusted for underreporting and are calculated by multiplying factors together with the factor 0.75078¹

<u>Size (mm)</u>	<u>Factors</u>
21 or 25	1.00
23 or 27	1.94
29	3.20
31 or 33	5.69
<u>Position</u>	
Aortic	1.00
Mitral	1.51
<u>Welder group</u> ²	
D	1.00
E	2.23
<u>Shop order</u> ³	
Low Risk	1.00
High Risk	2.94
<u>Current Age</u>	
< 35	1.00
> 35	(.942) ^(Age-35)

Table 4 Reoperative Mortality Rates by Age					
Age	A Rate %	B Rate %	Age	A Rate %	B Rate %
35	5.4	3.6	60	9.5	6.4
40	5.9	3.9	65	10.9	7.4
45	6.5	4.3	70	12.7	8.7
50	7.3	4.9	75	15.0	10.3
55	8.3	5.5	80	17.7	12.2

Reoperative Mortality by Patient Age



APPENDIX II

Additional Information to Help Physician Make Decision Regarding Patients but not Necessarily within the Patient Benefit Settlement

1. SUBGROUPS OF PATIENTS WITH BSCC VALVES WARRANTING SPECIAL CONSIDERATION:

- A) Patients with moderate or severe left ventricular dysfunction (NYHA Class III or IV).

For patients with heart failure due to left ventricular dysfunction (NYHA Class III or IV) the risk of reoperation is increased as much as two-fold and expected long-term survival is reduced. Given the increase in operative mortality, these patients would not achieve the two-year gain in expected survival considered necessary to justify elective explantation, and therefore, elective reoperation is not recommended. *For patients with heart failure (NYHA Class III or IV) due to dysfunction of the BSCC valve, the procedure would not be elective and the decision to reoperate should be based on physician judgement and patient consent.*

- B) Concomitant valve replacement in patients undergoing cardiac surgery for another cause.

In the past, it has been recommended that certain patients with BSCC valves who are undergoing heart surgery for unrelated conditions should be considered for concomitant prophylactic BSCC valve explantation. Concomitant valve replacement (BSCC or other) has been demonstrated to increase mortality for the primary procedure, and this risk is, in the opinion of the Supervisory Panel, higher for mitral explantation than for aortic. Therefore, careful consideration of the individual risks and benefits must be made by the cardiologist and cardiac surgeon at the time of the primary surgery before prophylactic BSCC valve replacement is undertaken under these circumstances.

- C) Patients with more than one BSCC valve in place who have one valve qualifying for explantation should be considered at higher risk for operative explantation than the same patient if that patient had only one valve. This risk is not quantifiable. Decisions to operate on these patients should be made with this consideration. Removal of the lower risk non-qualifying second valve should only be performed if the surgeon feels that the risk will not substantially be increased by this decision.

- D) Patients with BSCC valves in aortic valve conduits that were manufactured by Shiley Incorporated should not be considered for explantation as there are no known fractures in this clinical situation.
- E) There are some patients who maintain remarkable health status in older age groups. In this appendix the panel provides their best medical judgements to help patients and physicians make individual decisions. It should be emphasized that patients with the aid of their physicians should select explantation in centers with large experience in explantation. Factors of comorbidity that may increase operative mortality should be carefully weighed by the surgeon prior to proceeding with explantation.

2. **GENERAL RECOMMENDATIONS FOR ALL BSCC PATIENTS:**

All patients with BSCC valves should regularly consult their physicians and should have a clear understanding of the symptoms which occur at the time of OSF. These should be made known to those relatives or friends in contact with the patient. These patients should also be made aware of the nearest center with high-volume, low-mortality cardiovascular surgery, since early recognition and prompt surgical intervention may be lifesaving for the small percentage of BSCC valve recipients who actually experience OSF.

3. **FOR PATIENTS WHOSE PREVIOUS VALVE REPLACEMENT SURGERY DID NOT QUALIFY FOR BENEFITS UNDER THE OLD GUIDELINES:**

The Settlement Agreement provides (Section 5.2.3.1[c]): "If the Panel at any time modifies its guidelines for valve replacement surgery, then a Settlement Class Member may request that his or her previously non-qualifying valve replacement be re-evaluated under the modified guidelines. If the surgery would have been qualifying under the modified guidelines then the Settlement Class Member shall be entitled to the applicable benefits for qualifying valve replacement ..., if not previously waived by bringing an action for damages from the valve replacement."

Some publications which may be of interest to physicians managing patients with BSCC valves are referenced below.

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14. Van de Graaf Y, deWaard F, van Herwerden LA, et al. Risk of strut fracture of Bjork-Shiley valves. Lancet 1992, 339:257-261.
15. Pansini S, Ottino G, Gorsemati PG, et al. Reoperations on heart valve prostheses: an analysis of operative risks and late results. Ann Thorac Surg 1990, 50:590-6.
16. Lytle BW, Cosgrove DM, Taylor PC, et al. Reoperations for valve surgery: perioperative mortality and determinants of risk for 1000 patients, 1958-1984. Ann Thorac Surg 1986, 42:632-43.