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Joan Claybrook, President

January 13, 1994

Dr. David Kessler
Commissioner
Food and Drug Administration
5600 Fishers Lane
Rockville MD 20857

Re: Need for Renotification to Patients With the Bjork-Shiley Convexo-Concave Valve in Light of New Findings of Extremely High Failure Rates

Dear Dr. Kessler:

As you know, the Bjork-Shiley Convexo-Concave (BSCC) artificial heart valve was implanted in approximately 80,000 patients worldwide between 1979 and 1986. The valves were withdrawn from the market in 1986 after it was clear that they were defective and one of the valve's struts had a tendency to fracture. These fractures result in death in approximately two-thirds of all fracture cases. As we explain below, important new information indicates that the valves are far more dangerous than previously believed. We urge the FDA to take immediate steps to ensure that this information is made available to BSCC patients and their doctors so that they will be fully informed concerning the decision to replace their valves.

Since 1984, we have urged the FDA to require that the valves be removed from the market and that patients be notified of the problems with the valves and the signs and symptoms of imminent valve failure. As explained in the January-February 1994 issue of the FDA Consumer ("Shiley Saga Leads to Improved Communications," pp. 13-17), patient notification is critical so that patients can take steps to reduce the likelihood of serious injury and death in the case of valve failure.

After years of resistance and the filing of a lawsuit seeking notification in California, in mid-1990, the valve's manufacturer, Shiley Incorporated, and its parent corporation, Pfizer, Inc., agreed to notify patients. Under FDA auspices, the companies set up a notification and registry program through the MedicAlert Foundation, which now has the capability of contacting thousands of BSCC patients with the latest information concerning the defective valves. When the first round of new information indicating that the risk of fracture was much higher than previously believed

became available,[1] the FDA directed that Shiley renotify patients through the MedicAlert system. The principal reason for renotification was that the higher incidence of strut fracture made elective valve replacement surgery a viable option for many more patients. In short, for more patients, the risks of open heart surgery were outweighed by the risk of valve failure.

Important new information has just been published in The Lancet on January 1, 1994 (see attached), which indicates that fracture rates are much higher than previously believed.[2] In this study, a group of Dutch investigators looked at 24 valves explanted from BSCC patients. The data includes all patients studied and was, in the authors' words, "a random sample of patients at risk and ... therefore, an unbiased study." Eight 60 degree valves and sixteen 70 degree valves were explanted. The valves were then viewed by stereoscope and by scanning electron microscopy. The findings are astounding: two of the 60 degree valves and five of the 70 degree valves had single-leg strut fractures, the precursor for complete valve failure (the tearing away of the strut from the valve ring). The most significant findings are:

1. Although the sample is a small one, the fracture rates percentages (25% of the 60 degree valves, and 31% of the 70 degree valves) are well in excess of previously reported fracture rates, which were based only on reported fractures.

2. These findings tend to confirm that the fracture rates have been generally underreported because of the so-called "hidden fracture" phenomenon. Since the symptoms of valve fracture are not dissimilar from other catastrophic cardiac events, such as myocardial infarction, BSCC patients' physicians may not consider the possibility of valve fracture as a cause of death. This is compounded, of course, by the low autopsy rate, especially in this country, where about 40,000 of the 60 degree valves were implanted.

3. Some of the fractures occurred in BSCC valves not previously believed to be at high risk (i.e., small valves and 60 degree aortic valves). The first Dutch study (see note 1) found that young patients with large 60 degree valves were most at risk.

4. The data confirm prior information indicating that many of the most problematic valves were welded, or at least purportedly welded, by one particular Shiley welder, employee number 2295.

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[1] See van der Graff Y, de Waard F, van Herverden LA, Defauw JJ, "Risk of strut fracture of Bjork-Shiley valves," Lancet 1992, **339**: 257-61.

[2] See Mol BA, Kallewaard M, McLellan RB, van Herweden, LA, Defauw JJ, van der Graaf Y, "Single-leg strut fractures in explanted Bjork-Shiley valves," Lancet 1994, **343**: 9-12.

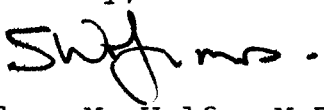
* * *

In light of these very important findings, we ask that the FDA require Shiley and Pfizer to immediately renotify BSCC patients, as well as all cardiologists, cardiovascular surgeons, and primary care physicians. These individuals have a right to know of this information in making reoperation decisions. Furthermore, the FDA should order Shiley and Pfizer to provide the Agency with all manufacturing data concerning the BSCC valves, if that has not occurred already. That data should reveal which valves were welded by employee number 2295. That information, in turn, should be listed on any new notification so that patients who know their valve serial number can take appropriate action. Finally, given the extraordinary rate of single-leg fracture among 70 degree valves, FDA should demand that Shiley and Pfizer take immediate steps to notify BSCC patients abroad (where all of the 70 degree valves, and about half of all the BSCC valves, were implanted). The companies should be required to set up MedicAlert-type systems around the world both to increase patient awareness and to allow patients to make informed decisions regarding reoperation.

As of three months ago, 386 fractures had been reported to the FDA but, because of the gross underreporting -- confirmed by the earlier Dutch study -- the actual number of fractures is likely to be at least 1,500, meaning that at least 1,000 patients have already died. Prompt action to notify patients and their doctors about these extraordinary new findings will surely prevent some future deaths in those patients who choose to have their valves replaced before it is too late.

I look forward to a prompt response to this letter.

Sincerely,



Sidney M. Wolfe, M.D.
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Articles

Single-leg strut fractures in explanted Björk-Shiley valves

B A de Mol, M Kallewaard, R B McLellan, L A van Herwerden, J J Defauw, Y van der Graaf

Summary

A retrospective follow-up study in the Netherlands on the risk of fracture of Björk-Shiley convexoconcave valves concluded that prophylactic replacement is advisable for certain groups of patients. We have examined valves explanted from twenty-two patients because they met epidemiological criteria for reoperation, with or without the presence of moderate cardiac impairment, or because there were other cardiac complaints not related to the valve. No information was available before explantation to suggest a valve defect.

All patients survived their operations. Of the twenty-four valves, seven (29% [95% CI 13–52]) had fracture of one of the legs of the outlet strut (single-leg strut fracture [SLF]). Two other valves had features that suggested fatigue defects. As in the previous study, 70° valves had the highest risk of SLF (five of sixteen, two aortic and three mitral). However, two of eight 60° valves (both aortic) also had SLF.

Current hazard calculations and explantation recommendations may need to be revised. Since several of the defective valves were welded by the same person, knowledge of manufacturing details may help in estimation of fracture risk for an individual patient.

Lancet 1994; **343:** 9–12

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Correspondence to: Dr B A de Mol, Department of Cardiopulmonary Surgery, Academic Medical Center, Meibergdreef 9, 1105 AZ Amsterdam, Netherlands

Introduction

In the Netherlands between 1979 and 1986, 2303 patients underwent heart-valve replacement by implantation of Björk-Shiley convexoconcave (BS cc) artificial heart valves with opening angles of 60° or 70°. These valves are manufactured by Shiley Inc (Irvine, California, USA), a subsidiary of Pfizer Inc. Escape of the valve occluder caused by fracture of the outlet closure strut was periodically reported; thus patients with implanted valves were subject to a lethal risk. Our epidemiological study[1] found 42 strut fractures during mean follow-up of 6·6 years. The highest risk was for large ($\geq$29 mm) 70° BS cc mitral valves, which had a cumulative risk of outlet strut fracture after 8 years of 17·4% (95% CI 9·1–31·6). One of our conclusions was that decisions on explantation of large 60° and 70° cc valves should be made by weighing the risk of fracture against the risk of morbidity and mortality related to the operation. Several studies have focused on the metallurgical assessment of fatigue fractures of BS cc valves.[2,3] The purpose of such technical assessment is to confirm the possible existence of valve defects preceding strut fracture. We report here the outcome of twenty-two elective explantations and the subsequent examination of twenty-four retrieved BS cc valves.

Patients and methods

The decision to explant a BS cc valve was taken by the cardiac surgeon, cardiologist, and the patient on an individual basis. Our epidemiological study[1] found that the age of the patient and size, opening angle, and position of the valve were risk factors for strut fracture. The indication for reoperation in the individual patient was based on these epidemiological considerations, alone or together with the presence of moderate cardiac impairment, or on cardiac complaints due to causes other than the prosthesis.

The series consisted of the first twenty-four valves offered for examination so that we could give an expert opinion to support a claim for financial compensation. The explantations took place between November, 1991, and January, 1993. The mean age of the eight women and fourteen men was 51 (range 26–68) years. Explantation was carried out without any diagnostic or clinical indication that the valve might be defective. No welding or manufacturing information was available before the operations.

Three patients underwent concomitant coronary artery bypass grafting (CABG), in one because of angina pectoris. Three patients had paravalvular leak (one known relevant leak and two unknown, detected by preoperative screening). In one patient, further progression of complaints of tricuspid regurgitation was not awaited. Given her age (47 years), reoperation was advised, because she had a high-risk 70° mitral BS cc valve. Two patients underwent two reoperations. One of them had survived strut fracture of a 29 mm 60° mitral valve.

Non-destructive examination of the valves was completed in April, 1993. The metallurgical analysis was done in Houston, Texas (by R B McL) in collaboration with Delft University of Technology, the Netherlands (B A de M). The valves were studied stereoscopically and by scanning electron microscopy (SEM) to assess their structural integrity. The manufacturer (Shiley Inc)

Valve position and angle	Age*	Size (mm)	Damage	Time (yr) since implantation
Aortic 60°				
1	68	21	..	13
2	41	23	..	12
3†	36	23	..	9
4	40	25	SLF	10
5	51	27	..	9
6	41	29	SLF	10
Aortic 70°				
7	66	25	..	9
8†	66	25	..	9
9	26	27	..	9
10	60	27	..	9
11	50	27	..	9
12	42	27	SLF	9
13	54	27	..	8
14	66	27	SLF	9
15	48	29	Crack‡	9
Mitral 60°				
16	47	27	..	10
17†	36	31	..	9
Mitral 70°				
18	47	27	SLF	9
19	30	29	Extrusions/intrusions	9
20	53	29	SLF	9
21	55	29	SLF	8
22†	66	29	..	9
23	64	31	..	9
24	63	31	..	9

*Patient's age (yr) at explantation.
†Double valve replacements.
‡Visible at × 250 magnification and higher. This valve was also examined by the manufacturers, at magnification up to × 200; they did not, therefore, detect a crack. The relevance of the crack remains a matter of debate (see text).

Table: **Characteristics of explanted valves**

divides the 70° cc valves into three subgroups for analysis—group I consists of the early-production large (29–33 mm) valves, group II of the later-production large valves, and group III of the small (21–27 mm) valves.[4] Group I valves were originally manufactured as cc 60° models and later modified to cc 70° specifications, whereas group II valves were manufactured as cc 70° valves. Manufacturing data were available for twenty of the twenty-four explanted valves.

Results

All twenty-two patients in this series survived explantation. The postoperative course was extended in three patients, one of whom underwent two valve replacements and CABG. One patient had total atrioventricular block and required a pacemaker. Eight 60° and sixteen 70° valves were explanted (table). Two aortic 60° valves had single-leg fractures (SLF) without displacement. Five 70° valves, two aortic and three mitral, had SLF; three of these five valves were small (≤27 mm).

Thus, examination of this unselected series of explanted valves revealed SLF in seven, four (of fifteen) aortic and three (of nine) mitral. The prevalence of SLF is therefore 29% (95% CI 13–52). Two valves showed fatigue changes. Valve number 15 showed a crack at × 250 magnification or higher on SEM; the crack went through a carbid inclusion and branched out at one side into more ductile weld matrix. In valve 19 both legs of the small struts on the inlet side showed extrusions and intrusions, characteristics of incipient fatigue failure, visible on SEM at a magnification as low as × 250 and very clear at × 1000. These intrusions and extrusions are associated with the formation of microcracks. Figure 1 shows a BS cc valve (29 mm, 60°) that was explanted in 1987 (not part of this series);[3] it has an SLF of the minor strut with displacement. Figure 2 shows SLF in valve number 14 of this series. A fracture line is visible in one leg of the strut all the way through the wall. However,

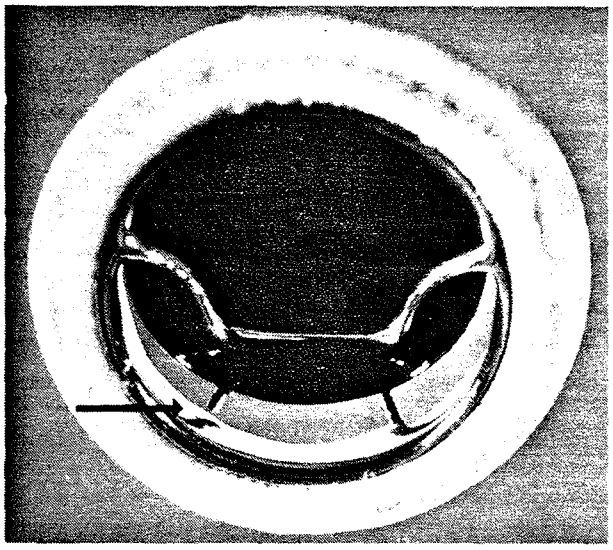

Figure 1: **Mitral BS cc valve (29 MBRC; 10032) with occluder in situ**

Note displacement due to SLF of minor strut (arrow).[3]

contact between the flange end and the leg of the strut is maintained.

From production information provided by Shiley Inc, the person who did the welding of the outlet strut could be identified for twenty valves. We concluded that in ten cases the strut had been welded by welder number 2295. Of these valves, six showed SLF. Eight valves had been welded by

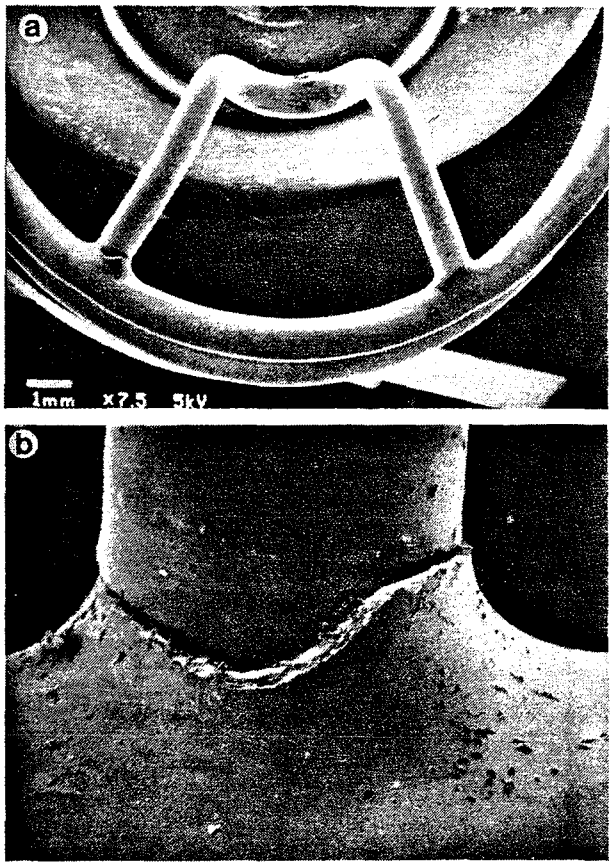

Figure 2: **SEM of valve number 14 in this series (27 ABCB; 10168)**

One leg of minor outlet strut is fractured through wall from flange. Note bend in fractured strut leg and its asymmetrical position in comparison with intact leg of strut. Reduced by a third from a = × 7·5, b = × 62.

welder number 2013; only one of these showed defects (intrusions and extrusions). The two remaining valves were made by different welders; one valve showed SLF.

Discussion

Thus seven of twenty-four BS cc valves seemed to be defective, with one leg of the outlet strut completely fractured. Before explantation, there was no indication of a valve defect; explantation was justified simply on the basis of an increased risk of strut fracture found in epidemiological studies. Although this was a small series of valves, there was no selection of patients, no knowledge of manufacturing data, and no metallurgical examination. Within the time of the study, five other valves were explanted but not offered to us for examination. The decision on whether to ask for an opinion was determined by patients' desire to claim compensation. We believe that the twenty-four valves studied were obtained from a random sample of patients at risk and are therefore, an unbiased sample. Sixteen of the valves we examined were 70° valves, and five of the seven compromised valves were 70°. Thus, as in our epidemiological study,[1] 70° BS cc valves carried the highest risk of fracture. Among patients with 70° cc valves, we observed an adjusted excess mortality of 50% by comparison with patients who had 60° valves.[1] We concluded from the epidemiological study that prophylactic reoperation should be considered in patients with large 70° mitral valves and in young patients with large 60° mitral valves. Data were too limited for us to draw up guidelines about the large aortic valves. However, the Medical Advisory Panel appointed by Shiley judged the large aortic valves to be at high risk of SLF too.[4] Four of the 70° heart valves in this series (7, 10, 13, and 14) were explanted from patients older than 50 years, and were small valves in the aortic position. On the basis of our epidemiological study, surgeons would not be advised to explant such valves. However, one of them (number 14) had an SLF.

In our epidemiological study,[1] only 7 of the 1458 aortic valves had documented fractures. By contrast, in this series four of thirteen aortic valves had SLF and one had a crack. This finding supports our hypothesis that, owing to the lethal character of the failing aortic valve strut, fractures remain under-reported; few such patients reach hospital and necropsy is rarely done.

Since 60° aortic valves are not considered to be at high risk of fracture, our finding of SLF in two of six 60° aortic valves is important. It is not sufficient to decide about explantation on the basis of the epidemiological risk profile. The presence of coronary artery disease, paravalvular leakage, other valve disease, or anxiety influenced decisions about reoperation to a variable degree. The Medical Advisory Panel set up by Shiley Inc did not support the decision on explantation of 60° BS cc valves.[4-6] One exception was made for a small subgroup of patients under 40 years old who had 33 mm mitral valves, welded between July, 1981, and June, 1982. The panel recommended explantation be considered for group I valves (the early-production 70° cc large-size valves), which had an annual risk of strut fracture of 1·4%. Both group I valves in our series (20 and 21) had SLF. The cracked valve we found (number 15) was from group II (the late-production 70° cc large size valves), which have an annual risk of strut fracture of 0·9%; for these explantation was recommended if the patient's life expectancy was otherwise good. Elective explantation of group III (21–27 mm) valves, with an annual strut fracture risk of 0·3%, was not recommended, although in our study three of the nine group III valves had SLF.

Birkmeyer et al[7] did decision analysis based on data from three large studies.[6] The conclusions accorded with those of our follow-up study.[1] Some recommendations for elective explanation of BS cc valves carry a more conservative message.[8] Others are based on the clinical observations that some subgroups of valve carriers face a definite lethal risk,[9] or emphasise the risk of morbidity and mortality of elective explantation.[10] In the Netherlands, the presence of a database on patients with BS cc valves, the results of our epidemiological study,[1] decision support expertise,[11] and the availability of reoperation data in various centres, may have encouraged surgeons to explant at-risk valves.

This study also shows that complex decision-making on the basis of guidelines requires adjustments for the individual patient. However, the high proportion of defective valves in this series justifies a closer look at the welding process. SLF cannot be seen with the naked eye, but can easily be made visible by stereoscopic inspection at ×25 magnification. SEM did not show any pitting or damage that could be related to surgical mishandling during implantation or explantation.[12]

At high magnification, two valves (15 and 19) showed features that can be interpreted as developing fatigue fracture. The other fifteen valves did not reveal defects on SEM. Intrusions and extrusions result in cracks that propagate in a characteristic way in metallic materials subject to alternating loading.[12] After failure, they can be identified as the narrow initiation zone on fracture surfaces. Although a fatigue life cycle model is available for the alloy (Haynes 25), of which the BS cc valve is made, its use is questionable for the weaker welded area.[13] So, it remains uncertain and a matter of debate how fast such a crack would grow under physiological conditions and how it would evolve towards SLF.

The high prevalence of SLF and data from previous metallurgical analyses point to manufacturing problems. Additional evidence for manufacturing incidents being associated with a high risk of strut fracture was obtained from the US Food and Drug Administration (FDA). In 1991, the FDA urged Shiley Inc, to draw physicians' attention to a subgroup of large 60° BS cc mitral valves that seemed to have an increased risk of fracture.[14] These valves were apparently welded by the same operator. Also in our small group of valves, a disproportionate number of defective outflow struts could be related to a particular welder. If SLF exists as a defective stage resulting in strut fracture, can it be detected by means of non-invasive techniques such as spectral analysis of emitted acoustic waves or enhanced digital imaging techniques on the basis of X-ray investigation of patients?[6] In the short term, none of these techniques is likely to be available for large-scale and reliable use. However, the method of individual risk analysis on the basis of epidemiology is valid only if there is a design problem alone.[1,11] Manufacturing information, in combination with the method of individual risk analysis, may further improve medical advice to patients, possibly including those currently thought to be at low risk of strut failure.

We thank the Cardiopulmonary Surgical Center of Amsterdam (Dr L Eijsman), University Hospital Leiden (Dr H Huysmans), Dijkzigt Ziekenhuis Rotterdam (Dr E Bos, Dr N Verbaan), Sint Antonius Ziekenhuis, Nieuwegein (Dr F Vermeulen), Medisch Centrum De

Klokkenberg, Breda (Dr Th R van Geldorp), Ziekenhuis De Weezenlanden Zwolle (Dr M M P Haalebos), Mrs G L van Gaalen, and Mr Klaas Koch.

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Haemophilus parainfluenzae antigen and antibody in renal biopsy samples and serum of patients with IgA nephropathy

Satoru Suzuki, Yasuo Nakatomi, Hirokazu Sato, Hiroki Tsukada, Masaaki Arakawa

Summary

IgA nephropathy may be associated with colonisation with *Haemophilus parainfluenzae*. In patients with glomerular diseases, we examined renal-biopsy specimens for presence of bacterial antigen by immunofluorescence microscopy with rabbit antiserum against *H parainfluenzae*, and by enzyme-linked immunosorbent assay looked for IgA antibody against *H parainfluenzae* in patient sera.

The rabbit antiserum recognised by immunoblotting four components of *H parainfluenzae* outer membranes (OMHP) of molecular weights 19·5, 30, 33, and 40·5 kDa. All 44 patients with IgA nephropathy and 2 of 39 patients with other glomerular diseases showed mesangial deposition of OMHP antigens ($p < 0.001$). Patients with IgA nephropathy had significantly more IgA antibody against *H parainfluenzae* than did patients with other glomerular diseases. IgA antibody in the sera of patients with IgA nephropathy recognised by immunoblotting the same four components of OMHP as recognised by rabbit antiserum.

Glomerular deposition of OMHP antigens and the presence of IgA antibody against OMHP in patients with IgA nephropathy suggest that *H parainfluenzae* has a role in the aetiology of this disease.

Lancet 1994; **343:** 12–20.

Introduction

IgA nephropathy is characterised by IgA deposits, predominantly in the glomerular mesangium, and mesangial-proliferative glomerulonephritis (GN).[1] The mesangial IgA deposits are dimers or polymers of IgA1 and are probably complexed with antigens. These IgA deposits are derived from the circulation and may be deposited in "showers" after mucosally presented antigen exposure. In IgA nephropathy, there is increased production of IgA and its polymers by mucosal and peripheral blood lymphocytes. We have shown that mucosal infections such as pharyngitis and tonsillitis are frequently associated with acute onset of IgA nephropathy.[2] We believe that, in the main, IgA nephropathy is an immune-complex disease resulting from a poorly controlled mucosal immune response to environmental antigens to which the patient is chronically exposed, although no convincing cause for IgA nephropathy has come to light. In addition, we have found that *Haemophilus parainfluenzae* is more frequently isolated from the pharynx of patients with IgA nephropathy than from those with other diseases. We describe a study that investigated patient with IgA nephropathy for glomerular deposition of *H parainfluenzae* antigens and for circulating IgA antibody against *H parainfluenzae*.

Patients and methods

All patients were monitored at Niigata University Hospital. IgA nephropathy was diagnosed in 44 patients (21 men and 23 women, age range 19–54 years, mean age 32·7 years). For comparison, 39 patients with glomerular disease other than IgA nephropathy (19 males and 20 females, age range 5–63 years, mean age 36·7 years) were also examined. Patients in the control group had non-IgA mesangial-proliferative GN (non-IgA GN; 15 patients), membranous nephropathy (MN; 8), systemic lupus erythematosus (SLE; 5), membranoproliferative GN (MPGN; 4), focal glomerulosclerosis (FGS; 3), minimal-change nephrotic syndrome

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PERSONAL AND CONFIDENTIAL

March 30, 1993

David A. Kessler, M.D., J.D.
Commissioner
U.S. Food & Drug Administration
5600 Fishers Lane
Rockville, Md. 20857

BY FAX: 301 443 3100

Re: Request for Assistance From the U.S. Food & Drug Administration Regarding Matter of Major Health Concern Pertaining to Björk Shiley 60° and 70° Convexo/Concave Heart Valves Implanted in Dutch Citizens.

Dear Dr. Kessler:

I am a cardiopulmonary surgeon practicing medicine in the Netherlands in Amsterdam at the Academic Medical Centre. I am also associate professor at the Safety Science Department of the Delft University of Technology. We are involved in metallurgical, epidemiological and safetey managements studies regarding the Björk Shiley Convexo/Concave problems. I am appointed by the Dutch Society of Cardiology and the Dutch Society of Cardiothoracic surgeons as the liason officer on the retrieval and exchange of technical data in this matter. I am writing you this letter to advise you of a Major Public Health concern we have in the Netherlands with reference to the Björk Shiley 60° and 70° Convexo/Concave prosthetic heart valves presently implanted in approximately 1,200 or more of our citizens. We also ask you to use your office to provide our physicians assistance in the Netherlands in dealing with this immediate major medical problem. I will provide you with the basis for our request in the following paragraphs.

I am certain that your officers are aware of the Lancet articles containing the studies published in February and August 1992 in reference to the problems that our cardiac surgeons and physicians in the Netherlands are having with the fractures of Björk Shiley 60° and 70° Convexo/Concave heart valves. In general, the cardiac surgeons in the Netherlands have been dealing with the decision whether or not to explant a patient's Björk Shiley valve on an individual patient-by-patient basis, using guidelines established by the authors of the Lancet articles. The details of how the model was designed and operate will be published in the June issue of Circulation. As of this date, we have explanted approximately 30 of the Björk Shiley 60° and 70° Convexo/Concave prosthetic heart valves previously implanted in the Netherlands, with no substantial resulting injuries or deaths from the explant surgery. The primary doctors responsible for explanting the majority of these valves are Dr. Jo Defauw in Nieuwegein; Professor Dr. E.Bos in Rotterdam and Dr. Klaas Ten Have in Amsterdam. There are a number of other cardiac surgeons in the Netherelands, explanting these valves from their patients.

Recently, metallurgical examination was performed on a total of 24 of these Björk Shiley 60° and 70° Convexo/Concave prosthetic heart valves which had been explanted from patients by our Netherlands cardiac surgeons. Explantation took place on the basis of the outcome of the epidemiological study, adjusted for patient and hospital related circumstances. These prosthetic CC heart valves were explanted from patients over a fifteen-month period of time, from November 14, 1991 to January 25, 1993. The preliminary results of this metallurgical examination were shocking to us and generate a great major health and public concern to the citizens of the Netherlands and to their physicians. I assume that the results of this study and our conclusions are also of a major health concern to your office and citizens of the United States and other countries who have these valves implanted in their citizens' hearts. In the following paragraphs, I will summarize our findings.

A total of 24 Björk Shiley 60° and 70° Convexo/Concave prosthetic heart valves which had been explanted from Netherlands citizens by their cardiac surgeons over a fifteen-month period of time were examined in Houston, Texas by the Department of Metallurgy at Rice University. The Delft University departments of Safety Science and Metals Science are participating in the study. The preliminary result of this SEM examination of these specific 24 Björk Shiley 60° and 70° Convexo/Concave prosthetic heart valves is as follows:

1. The preliminary conclusions from SEM examination of 24 these explanted C/C valves is that a total of eight or one third of these implantees were to be considered in immediate danger of death or serious injury.

2. A total of seven of these Björk Shiley 60° and 70° Convexo/Concave heart valves had one leg of their outlet strut completely severed all the way through and that the only material holding the Convexo/Concave disc in place was the remaining leg of the outlet strut, which was beginning to give way;

3. An additional Björk Shilcy 70° Convexo/Concave heart valve previously implanted in the aortic position of a Dutch patient had a crack located in the weld area of one leg of its outlet strut which it attacks to the flange, which crack would definitely have promulgated and have ultimately led to a complete strut fracture of this aortic valve. An examination of this valve made under SEM examination revealed a deep crack in the weld area of one leg of its outlet strut.

4. We have reached the following conclusions with reference to these eight (8) Björk Shiley Convexo/Concave heart valves:

a. Six of these valves were 70° Björk Shiley Convexo/Concave prosthetic heart valve and two were 60° Björk Shiley Convexo/Concave prosthetic heart valves;

b. Two of these valves are large size (29) 70° mitral valves which Shiley and Pfizer classify as "Group I" valves;

c. Three of these valves are size (27) 70° Björk Shiley Convexo/Concave valves, two of which are aortic valves and the remaining one of which is a mitral valve, all of which valves Shiley classifies as "Group III" 70° CC valves;

d. One of these valves is a size (29) 60° Björk Shiley Convexo/Concave heart valve that was implanted in the aortic position in the patient;

e. One of these valves is a size (25) 60 ° Björk- Shiley Convexo/Concave prosthetic heart valve that was previously implanted in the aortic position in the patient; and

f. The remaining valve with a crack in the weld area of its strut is a Size (29) 70° Convexo/Concave heart valve implanted in the aortic position.

It is my information that at the present time Shiley and Pfizer's official position regarding explantation of any Björk Shiley Convexo/Concave heart valve is that none of these 24 explanted valves should ever have been explanted by Dutch surgeons because it was not medically reasonable. Stated another way, Shiley's and Pfizer's public official position today is that while they do not oppose explantation of group I and II 70° C/C valves and size 33 mm 60 ° C/C mitral valves with weld dates from July 1, 1981 through June 30, 1982, they would not have recommended explant of any of these valves by Dutch phycisians. (Pfizer and Shiley claim that their conclusions are based upon the opinions stated in an article entitled, "Strut Fracture With Björk-Shiley 60° Convexo/Concave Valve" which appeared in the European Journal of Cardiac-Thoracic Surgery in Spring 1992 which was authored by Dr.A. Ericsson, Dr. Lindblom and Others. Their opinions are also allegedly based upon a letter dated August 6, 1992 from Mr. Graeme Bennett, a consultant cardiac surgeon from the Royal Brompton and National Hospital in London, England).

In conclusion, the detailed metallurgical analysis of these 24 Björk Shiley 60° and 70° Convexo/Concave prosthetic heart valves that were explanted by different surgeons in the Netherlands is continuing forward in an effort to determine how many more of the remaining 16 valves from this explanted large population of CC valves also had a very high probability strut fracture.

I have personnally spoken with Professor McLellan concerning his preliminary findings generated by his non-destructive metallurgical examination of these 24 explanted valves and discussed this matter with him. I understand that Dr. McLellan plans to perform further non-destructive metallurgical testing on these valves.

I would request that you and your office order Shiley and Pfizer to immediately produce at their expense in the Netherlands a good readable copy of all manufacturing records pertaining to all Björk-Shiley 60° and 70° Convexo/Concave prosthetic heart valves ever implanted in the Netherlands. Specifically, I ask for the manufacturing records of each specific valve, since I understand that each valve has its own specific individual manufacturing record. Of course, I will provide you with a detailed list of the serial number for the CC valves manufacturing records I will need. The sole purpose of obtaining these records is to correlate the findings of Dr. McLellan, along with the findings of the authors of the Lancet studies for the purpose of performing further research to have the enhanced X-ray investigation by means of digital imaging evaluated and for the purpose of trying to determine which of these valves have a high risc of fracture. This matter is of utmost importance and I would ask you to intervene personally and keep us advised as to your progress. I am certain that we make these valves available for your officers' examination and inspection in Houston if they wish. If they would be so kind as to telephone me at my office at 020-5666005, I am certain I can arrange to make these valves available for your officers' inspection.

I would also request you to instruct and order Pfizer and Shiley to cooperate with the Dutch cardiac surgeons and physicians in the production of these records, as well as dealing with the situation. You will receive this letter and a confidential summary of preliminary results of the scanning electron microscope examination by Federal Express Mail.

Sincerely,

Amsterdam / Delft
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