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April 16, 2012

The Honorable Margaret Hamburg, MD
Commissioner
Food and Drug Administration
5630 Fishers Lane, room 1061
Rockville, MD 20852

**Re: Circulatory System Devices Panel of Medical Devices Advisory
Committee
[FDA-2011-N-0001]**

Dear Dr. Hamburg:

The American College of Cardiology (ACC) is pleased to submit comments in response to the consideration of safety concerns pertaining to atrial septal defect (ASD) occlusion devices by the Circulatory System Devices Panel. The College is a 41,000-member nonprofit medical society composed of physicians, nurses, nurse practitioners, physician assistants, pharmacists and practice managers, and bestows credentials upon cardiovascular specialists who meet its stringent qualifications. The ACC is a leader in the formulation of health policy, standards and guidelines, and is a staunch supporter of cardiovascular research. The College provides professional education and operates national registries for the measurement and improvement of quality care. We appreciate the opportunity to furnish input to the Food and Drug Administration (FDA) and the Circulatory System Devices Panel of the Medical Devices Advisory Committee on this critical issue.

Cardiologists care deeply about the quality of the care their patients receive. Not only do they regularly take stock of their own performance, but they also pay close attention to the quality of the products they use in their treatment of patients. As such, safety of the devices implanted in patients is of paramount importance. Thus, the ACC has closely followed recent discussions and reports of potential safety concerns arising from the implantation of ASD occlusion devices.

Clinical discussion

Atrial septal defects, although recognized as a relatively benign form of cardiac disease, if left untreated can eventually contribute to significant morbidity and mortality, as borne out by the natural history studies.^{1,2} The current reported prevalence of ASD is around 10 percent of congenital cardiac defects.³ A study of the natural history of surgically corrected atrial septal defects by Murphy et al showed actuarial 27 year survival rates among patients younger than 25 years (97 percent in <12 years and 93 percent in 12-24 years) to be better than patients aged over 25 years (84 percent in 25-41 years and 40 percent in >41 years).⁴ The pivotal studies for both the Amplatzer Septal Occluder (St Jude Medical Inc., St. Paul,

Minnesota, USA) and the HELEX Septal Occluder (W.L. Gore & Associates, Flagstaff, Arizona, USA), which compared safety and efficacy, showed no statistical difference between surgical versus device closure of secundum atrial septal defects.^{5,6} The routine closure of atrial septal defects in childhood is therefore justified due to the availability of low risk, curative transcatheter and surgical options.

The devices currently approved in the United States and widely used for closure of atrial septal defects are the Amplatzer Septal Occluder (ASO) and the HELEX Septal Occluder (HSO). The instructions for use (IFU) for both these devices provide a list of potential adverse events and include the data from the pivotal studies.

The ASO pivotal study was a multicenter nonrandomized trial performed in 29 pediatric cardiology centers from March 1998 to March 2000 with 442 patients enrolled in the device group and 154 in the surgical group. This study sought to compare the safety, efficacy and clinical utility of the ASO for closure of secundum atrial septal defect with surgical closure. The inclusion criteria for both groups included: (1) presence of a secundum ASD (diameter \leq or $>$ 38mm by echo for the device group, no limit for the surgical group), (2) a left-to-right shunt with a Qp/Qs of \geq or $>$ 1.5:1 or presence of right ventricular volume overload and (3) patients with minimal shunt in the presence of symptoms. Additional inclusion criteria for the device group required the presence of a distance of $>$ 5 mm from the margins of the ASD to the coronary sinus, atrioventricular valves and right upper pulmonary vein as measured by echocardiography.

Exclusion criteria for both groups included:

1. The presence of associated congenital cardiac anomalies requiring surgical repair
2. Primum ASD
3. Sinus venosus ASD (including partial anomalous pulmonary venous drainage)
4. Pulmonary vascular resistance $>$ 7 Woods units
5. Right-to-left shunt at the atrial level with peripheral arterial saturation $<$ 94 percent
6. Patients with recent myocardial infarction
7. Unstable angina and decompensated congestive heart failure and patients with right and/or left ventricular decompensation with ejection fraction of $<$ 30 percent.

An additional exclusion criterion for the device group was patients with multiple defects that could not be adequately covered by device(s).

Also excluded from the study were patients with:

1. Sepsis
2. History of repeated pulmonary infection
3. Any type of serious infection $<$ one month before the procedure
4. Malignancy where life expectancy was $<$ 2 years
5. Intracardiac thrombi
6. Weight $<$ 8 kg
7. Inability to obtain informed consent
8. Other contraindications to aspirin or other antiplatelet agents.

While the procedural attempt success rate was 95.7 percent for the device group and 100 percent for the surgical group, the early (lack of residual shunt, device embolization, and major complication), primary (lack of residual shunt) and secondary efficacy (lack of major complication, cardiac arrhythmia treated, and surgical re-intervention) success rates were 94.8 percent, 98.5 percent and 91.6 percent respectively for the device group and 96.1 percent, 100 percent and 89 percent for the surgical group. The overall complication rate was 7.2 percent for the device group and 24 percent for the surgical group with mortality of zero percent for both

groups. One death that occurred in the device group was found to be unrelated to the device. The major adverse event rate was 1.6 percent for the device group as compared to 5.2 percent for the surgical group.⁵

The HSO pivotal study was a multicenter nonrandomized trial performed in 14 US medical centers from March 2001 to April 2003 with 119 patients enrolled in the device group and 128 in the surgical group. This study sought to compare the safety and efficacy of the HELEX septal occluder with the surgical repair of secundum atrial septal defects. Inclusion criteria for enrollment included the presence of an ostium secundum ASD and evidence of right heart volume overload. Additional criteria for the device arm patients was a balloon occlusion defect diameter less than or equal to 22 mm and the presence of adequate septal rims to secure the device as judged by the individual investigator at the time of implantation. In the surgical arm, patients could be enrolled retrospectively within 12 months of institutional review board approval. Exclusion criteria for the study included the presence of concurrent cardiac defects requiring surgical repair or significant comorbidities including a history of stroke, pulmonary hypertension, pregnancy, or the presence of multiple ASDs requiring the use of more than one device (device arm only). The primary endpoint of this study was clinical success, which was achieved in 91.7 percent in the device group and 83.7 percent in the surgical group. The major adverse event rate was 5.9 percent for the device group and 10.9 percent for the surgical group. There were no deaths in the device group with one death in the surgical group from pericardial tamponade.⁶

The following are the potential device or procedure related adverse events listed by the manufacturer for the ASO: air embolus, allergic reaction, anesthesia reactions, apnea, fever, hypertension/hypotension, infection including endocarditis, perforation of vessel or myocardium, pseudoaneurysm, blood loss requiring transfusion, stroke, valvular regurgitation and death. The major adverse events attributed to the transcatheter group in the pivotal ASO study included device embolization requiring surgical (0.7 percent) or percutaneous retrieval (0.2 percent), cardiac arrhythmia requiring major treatment (0.5 percent), pericardial effusion with tamponade (0 percent), tissue erosion/ cardiac perforation (0 percent) and delivery system failure (0.2 percent). The minor adverse events included cardiac arrhythmias requiring minor treatment, allergic reaction, headaches/possible TIA, extremity tingling/numbness, delivery system failure and thrombus formation.^{5,7}

The following are the potential device or procedure related adverse events listed by the manufacturer for the HSO: device embolization, new arrhythmia requiring treatment, repeat procedure to the septal defect, intervention for device failure or ineffectiveness, access site complications requiring surgery, interventional procedure, transfusion or prescription medication; thrombosis or thromboembolic event resulting in clinical sequelae, impingement on, damage to or perforation of a cardiovascular structure by the device, device fracture resulting in clinical sequelae or surgical intervention, air embolism, myocardial infarction, pericardial tamponade, cardiac arrest, renal failure, sepsis, significant pleural or pericardial effusion requiring drainage, significant bleeding, endocarditis, headache or migraine, TIA or stroke and death. In the pivotal HSO study the major adverse events attributed to the transcatheter group included device embolization (1.7 percent), allergic reaction (0.8 percent), migraine (1.7 percent), paresthesia (0.8 percent), inappropriate device size (1.7 percent) and hemorrhage (0.8 percent). The minor adverse events included arrhythmia, chest pain, pericardial effusion, syncope, vaso-vagal reaction, headache, migraine, paresthesia, visual field disturbance or defect, access site bleeding, delivery system failure and device fracture.^{6,8}

Both pivotal studies showed that the rate of major adverse events was lower in the device group as compared to the surgical group. The Mid-Atlantic Group of Interventional Cardiology

(MAGIC) atrial septal defect study (2004-2007), which reported the results of unrestricted multi-institution routine use of ASO in 478 patients from 2004 to 2007 showed a major adverse event rate of 1.1 percent⁹. The interim results of the post-approval study for the ASO reported in July 2011 showed a serious adverse event rate of 0.4 percent related to the device or delivery system in 564 patients¹⁰. In the continued access study for the HSO the rate of major adverse events was 2.2 percent in 137 patients¹¹. A recent HSO report on combined data of feasibility, multicenter pivotal and continued access studies showed a composite success of 91.5 percent with a major adverse event rate of 5.8 percent. The embolization rate was 2.3 percent, wire fracture rate of 8 percent and significant residual shunt of 2.6 percent.¹²

A retrospective review of all adverse events reported to the FDA Manufacturer and User Facility Device Experience (MAUDE database) and Health Canada and published in the literature including a review of institutional cases by Divekar et al in 2005 found a total of 24 cardiac perforations¹³. These cardiac events occurred early in 20.8 percent and late in 66.6 percent. A total of five events occurred within one day, 10 within three days and six after three days (three weeks to three years). A good outcome was reported in 14 patients, whereas three patients had neurological deficits and three died. The outcome was not known in four patients.

A recent analysis of the MAUDE database maintained by the FDA revealed that there was no difference between overall mortality for surgical and device closure.^{14,15} There were 17 deaths (0.09 percent) among the 223 adverse events reported to the FDA. The estimated number of implants used for this analysis was 18,333. The percentage of reported events between January 1, 2002 to June 30, 2007 for the various major adverse event categories were:

- 51 percent device embolization
- 23 percent cardiac perforations
- Five percent thromboembolic complication
- Four percent residual/recurrent defect
- Two percent device related infection

The Society for Thoracic Surgery (STS) database was analyzed for ASD closures over a contemporaneous time period. Out of 1537 primary operations, there were two deaths (0.13 percent). However, the surgical closure group may have included patients not suitable for device closure. The mortality for surgical management of a device adverse event was 2.6 percent. Device embolization was the most prevalent adverse event with an estimated rate of 0.62 percent, which is similar to the rate of embolization determined by a survey of AGA proctors in 2004 of 0.55 percent.¹⁶

An analysis of the device embolizations reported to the MAUDE database found that the device was retrieved surgically in 77.2 percent of cases and using a transcatheter approach in 16.7 percent of cases. There were 2 deaths related to embolization. A survey of AGA proctors carried out in 2003 revealed that there were 21 embolizations out of 3,824 ASO implants. Of those, 15 were retrieved using a transcatheter approach (71.4 percent) and six were retrieved surgically (28.5 percent)¹⁶. There were 51 cardiac perforations/erosion or rupture reported to the MAUDE database; 10 of those patients died. The most common site for perforation documented was a combination of the atrium and aorta adjacent to the device suggesting erosion. By similarly applying the previous estimates for total number of implants, the national erosion rate is 51 of 18,333 (0.28 percent). A 2004 publication by Amin et al determined the erosion rate to be nine in the known 9000 US implants, giving a rate of 0.1 percent. Only four events occurred at implant. Most were clustered in the first 6 months (16 within 24hrs, 11 within one month and eight between one and six months), but erosions and ruptures are still being reported as late as three

years after deployment. The mortality from erosions from this MAUDE database analysis is 0.05 percent, which, as an isolated cause for mortality, is still at a lower rate than the overall surgical mortality of 0.13 percent determined from the STS database. The data from the STS database is not longitudinal and includes approximately half of the congenital centers in this country.

A more recent systematic review and meta-analysis of currently available clinical evidence on percutaneous versus surgical closure of secundum atrial septal defects was performed by Butera et al.¹⁸ The authors reviewed all relevant articles from January 1998 to December 2008 and included thirteen original studies (3082 patients: 1270 treated surgically and 1812 treated with a device). All studies were nonrandomized. The postprocedural major complication rate was 1.9 percent in the device closure group, as compared to 6.8 percent in the surgical closure group. There was one death in the surgical group from cardiac tamponade six days after surgery. The most frequent major complication in the device group was device embolization or malposition needing surgical or transcatheter retrieval in 30 patients. In three patients, cardiac perforation due to device erosion was reported (one treated with the Angel Wing device and two treated with Amplatzer septal occluder). This large cohort analysis, although retrospective and nonrandomized, showed that the safety and efficacy of device closure was comparable to the surgical closure but with significantly lower rate of major early postprocedural complications.

As expected the MAUDE database compiled many reports of adverse events encountered in the pivotal studies of septal occluders. In addition, MAUDE reports eventually identified cardiac perforation resulting in hemodynamic compromise as a rare serious adverse event caused by the ASO. This rare complication that was not encountered in the pivotal or postmarket approval studies is particularly troubling because it may occur late after device implant and may be catastrophic resulting in patient's death.

AGA Medical Corporation focused on the issue of cardiac perforation when it selected an expert panel to review all cases of hemodynamic compromise reported to the Corporation by 2004. The panel's mandate was to analyze the cases of device erosion, to alert the medical community about this rare but potentially fatal complication, to better understand factors contributing to device erosion and to minimize the risk of such complications in the future.¹⁷ A total of 28 cases of hemodynamic compromise were reported with Amplatzer septal occluder by 26 physicians between 1998 and March 2004. In 25 patients the aortic rim was deficient and/or described as high ASD suggesting deficient superior rim. Of the 28 cases with hemodynamic compromise, five involved perforation of the roof of the left atrium and the aorta, six involved perforation of the roof of the atrium and the aorta, both atria were involved in one case, no atrial perforation in three cases and in three cases with aortic perforations, a fistulous communication was noted. 19 out of 28 patients' symptoms developed within 72 hours. In eight patients, diagnosis was made between five days and eight months, and in one patient, pericardial effusion developed after three years. The therapeutic approach to erosion varied with 21 patients requiring surgery. Of those 21 patients requiring surgery, 16 had device removal in addition to perforation or fistula repair. The device was left in place in five patients because it appeared to be in optimal position, but the perforation was repaired. In seven out of 28 cases with hemodynamic compromise, the patients were managed medically with pericardiocentesis and/or observation. The expert panel determined that implantation of oversized devices may have a cause/effect relationship and made the following recommendations:

- Follow instructions for use when performing balloon sizing
- Avoid overstretching the balloon when balloon sizing the defect
- Use stop-flow technique for maximum inflation of sizing balloon

- Be gentle with to and fro movement of the device to assess stability while the device is attached to the delivery cable
- Follow more closely the categories of patients listed below:
 - Those with significantly larger ASO (>1.5 times) than native diameter of ASD
 - Those even with development of small pericardial effusion
 - Those with deformation of the ASO at the aortic root (significant splaying of the device edges by the aorta)
 - Those with high defects (minimal aortic and superior rims)
- Conduct follow-up in all patients
- Educate patients about the risk and need for echocardiography with symptoms.

In order to better understand factors causing device erosion with ASO, a survey was sent by email to all members of the Congenital Cardiovascular Interventional Study Consortium (CCISC). CCISC was originally founded to design, conduct and report the findings of scientific studies in interventional cardiovascular care of patients with congenital heart disease. The 57 survey responders had cumulative experience of 12,006 ASO implants. Of those responders, 12 reported 14 erosions out of 3,010 implants. The findings of this survey revealed that the opinions of experienced operators were at odds with the manufacturer's recommendations made following the expert review in 2004.¹⁷ A deficient aortic rim was noted in 90 percent of patients with erosion. The results of the survey regarding the mechanism of the erosion indicated:

- Devices with lower risk of erosion are those which straddle the aorta, are somewhat oversized and do not move relative to the heart
- Devices with higher risk are those with protruding left atrial disc into the aortic root, are somewhat undersized and may have motion relative to adjacent heart structures

The CCICS members were divided in their opinion of the leading risk factor. 84.7 percent agreed that the motion of the device relative to the heart causes erosions, while 71.7 percent felt that a somewhat undersized device with tip disc protrusion into the aortic root was more likely to cause erosions.¹⁹

A study from the National Cardiovascular Center in Osaka, Japan sought to answer this question by conducting a prospective investigation into the morphological changes in the ASO over time and the influences of these changes on the atrial and aortic walls after ASD closure.²⁰ The study classified the relationship of the discs to the atrial and/or aortic walls into four types:

- No touch (NT) if a disc never touched any part of the atrial wall during cardiac cycle
- Touch (T) if a disc touched part of the atrial wall either intermittently or continuously during the cardiac cycle
- Intermittent pressure (IP) if a disc compressed and deformed a part of the atrial (and aortic) wall(s) intermittently during the cardiac cycle and continuous pressure if a disc compressed and deformed a part of the atrial (and aortic) wall(s) continuously during the cardiac cycle

Researchers also looked at any residual shunts. They enrolled 78 patients and performed TEE under anesthesia before and soon after device placement on all patients. 50 out of 78 had TEE three months after deployment, four out of 78 had TEE at six months follow-up and 24 out of 78 had TEE at 12 months. In nine cases, the relation of the left atrium (LA) discs to the atrial and aortic walls changed from T immediately after deployment to IP at the last follow-up. In 10 cases, the relation of the right atrium (RA) discs to the atrial and aortic walls changed from T to IP. In five of these cases, both the relations of the LA and RA discs to the atrial and aortic walls changed from T to IP. Between these 14 cases showing T-to-IP change and the other 64 cases

without such a T-to-IP change, there were no significant differences in age, weight, maximum unstretched ASD diameter, device diameter/maximum unstretched ASD diameter ratio, lengths of the superior and posterior rims, or the ratio of the number of cases showing residual leakage to the number of cases without leakage. However, there were significant differences in the device diameter ($P = 0.003$), the aortic rim length ($P < 0.001$), the ratio of the number of devices with a flare shape on the aortic side to the number of devices with a closed shape on the aortic side ($P < 0.001$) and change in maximum device thickness at the middle part ($P = 0.002$). This study showed that those with deficient aortic rim, flare device shape on the aortic side immediately after deployment, and thicker device profile at the middle part immediately after deployment were significantly more likely to show a possible worsening in the relation of the discs to the atrial and aortic walls. No major complications such as erosion or device migration were recognized in the 78 patients.

In spite of recent focus on the issue of erosions, current registry data obtained by e-mail queries shows that erosion continues to occur at rates ranging from 0.1 percent (1/922 implants MAGIC registry data from 2004-2011)²¹ to 0.5 percent (3/590 implants C3PO registry data from 2007-2010).²² The Improving Pediatric and Adult Congenital Treatment (IMPACT) Registry®, launched in December 2011 and received its first patient records in January 2011, contains 252 cases involving the implantation of the ASD device. To date, there have been no reports of erosion, but it is still early and the number of cases in the Registry too small to be considered definitive, especially in light of the apparently relatively low incidence of this problem.

In reviewing the literature and available registry data, it is evident that there is neither conclusive data nor consensus about incidence or root cause(s) of cardiac perforation or erosion by the ASD. Potential risk factors may be:

- Rotation of the device around its central pins during atrial contraction (translational movement of the device relative to the motion of the heart) after implantation
- Splaying or flaring of the device around the aortic root following implantation
- Contact by the edge of the device with the atrial wall causing protrusion of the device into wall and into adjacent structures such as the aorta
- Absent and/or deficient aortic (anterior-superior) rim
- Thicker device profile at the time of deployment.

These factors individually or in combination may be predictors of early and late erosions; thus, they warrant close monitoring.

Recommendations

The ACC believes that there is insufficient data and no consensus as to whether or how to change clinical practice or alter labeling of ASD occlusion devices. Given the lack of available data pertaining to the potential risk factors for erosion and frequency of adverse events in patients with ASD occlusion devices, the ACC makes the following two recommendations:

1. That the FDA require that a prospective study of potential risk factors for erosion in relation to the implantation of ASD occlusion devices and that the NCDR® provide the infrastructure for that study.
2. That the FDA to fund a registry study to assess adverse events in patients with implanted devices after discharge to better ascertain if and when problems occur that may not have been identified in the initial studies and what the risk factors for such problems may be.

Post approval study

While not a new technology, there is still much to be learned about patient risk factors for documented safety issues. Critical to learning about those risk factors and other potential safety concerns is a mechanism for collecting data on patients who receive a procedure and have devices implanted. Clinical trials can provide information on immediate outcomes and even short-term or intermediate follow-up in a selected patient population using a particular device in a procedure performed by a specific pool of physicians at specific facilities. While these trials provide invaluable efficacy information, they are expensive to conduct and do not necessarily provide the full gamut of information needed. Additionally, they are of limited use when affected patient populations are not of a certain size so as to rise to the level of statistical significance, as in the case of ASD.

Instead, the ACC recommends that the FDA leverage existing clinical data repositories for the development of this dataset. As the FDA is well aware, the ACC's National Cardiovascular Data Registry® (NCDR®) is a viable option for such an endeavor. While more details are provided below, the FDA can be confident in the knowledge that using NCDR data as the basis for research and study is not foreign territory for the NCDR.

In 1997 the ACC launched the NCDR as a result of its exploration of various strategies for collecting and implementing clinical data to improve cardiovascular care. The outgrowth of that effort focused on quality patient care through standardized measurement of clinical practice and patient outcomes. Then, as now, NCDR is committed to including clinicians and care providers in its leadership and to using standardized, clinically relevant data elements and scientifically appropriate methods to collect, analyze and report clinical outcomes.

Today, more than 2,200 hospitals nationwide participate in the NCDR. As the US' preeminent cardiovascular data repository, the NCDR provides evidence-based quality improvement solutions for cardiologists and other medical professionals who are committed to measurement, improvement and excellence in cardiovascular care. As a trusted, patient-centered resource, the NCDR has developed clinical modules, programs and information solutions that support the areas of cardiovascular care where quality can be measured, benchmarked and improved to make a difference in patients' lives.

NCDR data has been studied for a variety of purposes, including consistency with guidelines,¹ appropriateness,² and comparative effectiveness, to name a few.³ The FDA has long been a supporter of NCDR, providing funding for the IMPACT Registry and development of a possible atrial fibrillation registry. The IMPACT Registry is the first national registry designed to track outcomes for patients undergoing a cardiac catheterization procedure for congenital heart disease. Presently, there is no evidence-based research to guide practice standards. Most guidelines are derived from expert opinion. The IMPACT Registry will collect data and report on outcomes for

¹ Chan PS, Patel MR, Klein LW, et al. Appropriateness of Percutaneous Coronary Intervention. JAMA 2011; 306(1):53-61.

² Al-Khatib SM, Hellcamp A, Curtis J, et al. Non-evidence-based ICD implantations in the United States. JAMA 2011; 305(1):43-49.

³ Funded by a National Heart, Lung, and Blood Institute American Recovery and Reinvestment Act Grant, the ASCERT Study represents a unique collaboration between the ACCF and STS to study the comparative effectiveness of percutaneous coronary intervention and coronary artery bypass graft surgery in patients with stable coronary artery disease.

pediatric and adult congenital disease patients. The IMPACT Registry will provide guidelines and improve the outcome for all congenital heart disease catheterization-based treatments. NCDR is also a participant in the FDA's Sentinel Initiative, looking at methods of drawing on registry data as a mechanism of providing safety signals to the FDA. We look forward to continuing to work collaboratively on these initiatives.

NCDR powers what has the potential to be a powerful research resource: the National Cardiovascular Research Infrastructure (NCRI). Created through a federal grant, the ACC Foundation, in partnership with the Duke Clinical Research Institute, is working to build a cardiovascular research infrastructure, including the standards for data definitions and elements. Among its goals, the NCRI project aims to develop a large simple clinical trials platform to solicit and advance research questions that fill critical evidence gaps, as well as an integrated electronic repository of tools and programs to assist clinical research site activities accessible by a web-based informatics structure. Ideally, NCRI powered by NCDR has the potential to streamline data collection, so industry, government and research entities are not competing for valuable limited resources.

There are certain efficiencies to be gained from using registries, such as NCDR, for post-market research and surveillance. It increases the collaboration between industry and the professional societies, providing an increased level of credibility to the data and findings. NCDR has the ability to conduct site recruitment, patient randomization and data audits. With some modifications, the IMPACT Registry, referenced above, would offer the FDA an excellent opportunity to collect the necessary data on ASD occlusion devices pertaining to patient risk factors and safety concerns. While the IMPACT Registry does not presently collect all of the necessary data, it would be much more cost-effective to make the necessary modifications for such a study rather than to create a new infrastructure from scratch. Given the FDA's history of involvement with the IMPACT Registry, the ACC believes that it would be a natural fit for such a study.

Adverse events and patient follow-up

One of the reasons why there is a dearth of information pertaining to potential risk factors for erosion resulting from the implantation of an ASD occlusion device is that adverse events such as erosion typically do not occur until a great deal of time has passed, rather than occurring within a few days of the procedure and ASD device implantation. This translates into a lack of patient follow-up with respect to the particular ASD device. Patients receive the appropriate procedure follow-up and any additional care associated with their condition as needed, but there is no mechanism for following up with the patient on the continued functioning of the implanted device. This patient population is particularly difficult, given the young age at which they are diagnosed and treated for ASD.

What constitutes the most effective mechanism for conducting such follow-up remains unclear, and this problem is not uncommon across the spectrum of implanted devices. Patients with pacemakers, implantable cardioverter defibrillators (ICDs), and other cardiac devices face similar challenges. They are followed for the management of their particular issue, but the device itself is not always monitored. Thus, the ACC urges the FDA to fund a registry study to assess adverse events in patients with implanted devices after discharge, so we may better ascertain if and when problems occur that may not have been identified in the initial studies and what the risk factors for such problems may be. The College would welcome the opportunity to work with the FDA on developing such a study.

Conclusion

The College looks forward to addressing the Circulatory System Devices Panel of the FDA Medical Devices Advisory Committee to further discuss concerns and recommendations pertaining to ASD occlusion devices. In the interim, please direct any questions or concerns to Lisa P. Goldstein at (202) 375-6527 or lgoldstein@acc.org.

Sincerely,

A handwritten signature in black ink, appearing to be 'W. A. Zoghbi', written over a horizontal line.

William A. Zoghbi, M.D., F.A.C.C.
President

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