

1.1 Safety and Effectiveness Summary

SYNOX passive-fixation endocardial leads are safe and effective bipolar leads designed for use with implantable pulse generators which require bipolar 3.2 mm IS-1 compatible pacing leads. SYNOX bipolar passive-fixation endocardial leads are available in straight and "J"-shaped conformations, for pacing and sensing in the ventricle and atrium, respectively. The designation SX xx-JBP refers to SYNOX "J"-shaped leads, which are available in lengths of 45 and 53 cm; SX xx-BP refers to SYNOX straight leads, which are available in lengths of 53 or 60 cm.

The SX xx-JBP model has a permanent bend proximal to both lead electrodes, approximately 40 mm from the lead tip, resulting in the distal portion of the lead body having what is commonly referred to as a "U" or "J" shape. This lead shape facilitates placement in the right atrial appendage.

These leads provide long-term safe and effective pacing through overall quality of design, manufacture and material biocompatibility. All SYNOX patient contact materials are commonly used in market-released leads. Acute and chronic biocompatibility tests have been performed, as well as long-term implantation studies. In addition, corrosion studies have been completed to address both long-term toxicity and durability of the surface iridium treatment. The testing conducted for biocompatibility as well as extensive clinical experience confirms that iridium is safe for use as an implantable material, and analyses supporting this view have been published within technical journals. Long-term corrosion testing results substantiate that iridium is a non-toxic and durable material for use in implantable devices.

Additional qualification testing results validate the safety and effectiveness of the lead design and materials used. In all cases the lead or lead component met or exceeded test specifications.

Field clinical experience as well as the *in vitro* and qualification testing performed on the SYNOX lead show that the risk to the patient in using these leads is no greater than that of comparable endocardial leads. Potential adverse effects associated with the implantation of endocardial leads include, but are not limited to: fibrotic tissue formation, thrombosis, embolism, elevated thresholds, lead dislodgment, fibrillation, body rejection phenomena, cardiac tamponade, pneumothorax, muscle/nerve stimulation, infection, skin erosion, valve damage and ventricular ectopy.

Table 2 below summarizes some of the potential symptoms indicating a complication and possible corrective actions:

**Table 2
Lead Complications**

SYMPTOM	POTENTIAL COMPLICATION	POTENTIAL CORRECTIVE ACTION
Loss of pacing or sensing	<ul style="list-style-type: none"> • Electrode dislodgement • Lead fracture • Setscrew penetration of lead insulation • Improper lead to pacemaker connection 	<ul style="list-style-type: none"> • Reposition lead • Replace lead • Replace lead • Reconnect lead to pacemaker
Increase or decrease in threshold	<ul style="list-style-type: none"> • Fibrotic tissue formation 	<ul style="list-style-type: none"> • Adjust pulse generator output; • Reposition lead

1.2 Summary of Studies

1.2.1 NONCLINICAL STUDIES

Qualification testing was performed to evaluate the final device as well as various manufacturing processes. All applicable national and international standards and/or criteria were evaluated. In all cases, test specifications were met. Tests were performed in the following categories:

- mechanical, electrical and environmental testing
- IS-1 BP connector testing
- Si tube abrasion testing
- transport and sterility testing
- introducer and stylet testing

Further, in order to address the issue of constant flexion experienced by endocardial leads, the SYNOX lead body was subjected to accelerated flex testing to evaluate its performance relative to other market-released BIOTRONIK leads. SYNOX conductor coils exhibited superior fatigue resistance as compared to the market-released control lead; therefore, fatigue resistance of the SYNOX lead is expected to be at least as good as the control lead.

An additional test was developed to evaluate the rigidity of the lead in its distal portion, as suggested in recent FDA guidance¹. Test results demonstrate that SYNOX lead tip rigidity is less than that of other marketed endocardial leads.

¹ Draft Guidance for the Submission of Research and marketing Applications for Permanent Pacemaker Leads, Version 2.1, March 24, 1997. U.S. Department of Health and Human Services, Food and Drug Administration.

An *in vivo* endocardial lead clinical study was sponsored by BIOTRONIK GmbH & Co in Hungary. Ten dogs were chronically implanted with three different configurations of endocardial leads with the objective to assess the electrical performance, biocompatibility, and biostability, including corrosion resistance, of endocardial leads with fractal iridium surface structured electrodes. The fractal surface lead results were compared to results from a control lead which contained porous, sintered electrode surfaces. The implant duration was three months for half of the study group and six months for the rest of the study population. The SYNOX tip electrode with a surface area of 1.3 mm² was one of the lead configurations tested.

Electrochemical and corrosion resistance analysis results from the *in vivo* Hungarian dog investigation indicate that fractal iridium structured electrode surfaces are stable against any measurable corrosion attack when electrically loaded and chronically implanted. Results from a histological evaluation of the tissue in the vicinity of the electrode tips showed no observable iridium, titanium or platinum in either the three month implant samples or the six month samples. Based upon these findings and other performance data collected, the investigators concluded that the endocardial leads tested have excellent long term electrophysiological properties.

1.2.2 CLINICAL STUDIES

A prospective, non-randomized clinical study was initiated on January 27, 1997, under IDE G960236 to evaluate the safety and effectiveness of the SYNOX pacing lead. This study is currently ongoing; the control lead used in this clinical investigation is the BIOTRONIK POLYROX lead, which is the predicate device to the SYNOX lead.

The primary objective of the investigation is to determine whether the SYNOX pacing leads are safe and effective endocardial pacing leads. Results from the clinical investigation provide valid scientific evidence and reasonable assurance that SYNOX pacing leads are safe and effective when used in accordance with their labeling.

To date, the main objectives of the clinical investigation have been achieved:

- There were no reports of any unanticipated adverse device effects occurring during the clinical investigation.
- There have been no reports of safety issues related to the chronic use of the pacing lead. One lead that was explanted due to loss of capture met all electrical specifications upon analysis. The other two SYNOX lead explants were not due to lead performance but rather because the patient required an ICD implant. The four patient deaths during the study have not been related to the pacing system.
- All of the anticipated adverse events reported, except for the one lead explant described above, were resolved by the investigator through reprogramming, drug therapy, or lead repositioning.

- The combined rates of anticipated and unanticipated adverse events for the SYNOX leads are not statistically different from the rates for the control leads.

All lead performance endpoints of the clinical investigation have been achieved:

- As expected, due to the decreased lead tip area (1.3 mm² for SYNOX vs 3.5 mm² for POLYROX) the mean measured atrial and ventricular lead pacing impedance for SYNOX leads was more than 150 ohms over the mean measured atrial and ventricular lead pacing impedance for the control leads at all of the follow-up intervals.
- The mean capture and sensing thresholds of the SYNOX leads were equal to or better than the control leads for all of the follow-up intervals.
- The atrial sensing and pacing performance of the SYNOX leads were comparable to the control leads.
- The ventricular sensing and pacing performance of the SYNOX leads were comparable to the control leads.

In addition to the SYNOX IDE lead study, another SYNOX lead study was conducted in France to evaluate the performance of the ventricular SYNOX pacing leads. Study results were consistent with the findings of the SYNOX IDE clinical study.



DEPARTMENT OF HEALTH & HUMAN SERVICES

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SEP 10 1998

Mr. David Makanani
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Re: K980869
Trade Name: SYNOX SX 53-BP, SX 60-BP, SX 45-JBP, SX 53-JBP,
Models 12
Regulatory Class: III
Product Code: DTB
Dated: June 4, 1998
Received: June 5, 1998

Dear Mr. Makanani:

We have reviewed your Section 510(k) notification of intent to market the device referenced above and we have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments. You may, therefore, market the device, subject to the general controls provisions of the Federal Food, Drug, and Cosmetic Act (Act). The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, and labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (Pre-market Approval) it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 895. A substantially equivalent determination assumes compliance with the Current Good Manufacturing Practice requirements, as set forth in the Quality System Regulation (QS) for Medical Devices: General regulation (21 CFR Part 820) and that, through periodic QS inspections, FDA will verify such assumptions. Failure to comply with the GMP regulation may result in regulatory action. In addition, the Food and Drug Administration (FDA) may publish further announcements concerning your device in the Federal Register. Please note: this response to your premarket notification submission does not affect any obligation you might have under section 531 through 542 of the Act for

devices under the Electronic Product Radiation Control provisions, or other Federal Laws or Regulations.

On August 16, 1993 the Final Rule for Device Tracking was published in the Federal Register, pages 43442-43455 (copy enclosed). Be advised that under Section 519(e) of the Act as amended by the Safe Medical Devices Act of 1990, FDA has identified the above device as a device which requires tracking. Because the device is subject to tracking, you are required to adopt a method of tracking that follows the devices through the distribution chain and then identifies and follows the patients who receive them. The specific requirements of the regulation are found in 21 CFR 821 as described in the August 16, 1993 Federal Register beginning on page 43447.

This letter will allow you to begin marketing your device as described in your 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR part 801 and additionally 809.10 for in vitro diagnostic devices), please contact the Office of Compliance at (301) 594-4586. Additionally, for questions on the promotion and advertising of your device, please contact the Office of Compliance at (301) 594-4639. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 807.97). Other general information on your responsibilities under the Act, may be obtained from the Division of Small Manufacturers Assistance at its toll free number (800) 638-2041 or (301) 443-6597, or at its internet address "<http://www.fda.gov/cdrh/dsma/dsmamain.html>".

Sincerely yours,



Thomas J. Callahan, Ph.D.
Director
Division of Cardiovascular, Respiratory
and Neurological Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosures

1.2 Indications for Use

SYNOX leads are designed for use with implantable pulse generators which require pacing leads with a bipolar 3.2 mm IS-1 connector configuration; they may be used with single or dual chamber pacing systems. The leads are designed for use in patients for whom single or dual chamber pulse generator therapy is medically indicated. This indication follows that recommended in the Class I definition of the ACC/AHA Task Force Report, entitled "Guidelines for Implantation of Cardiac Pacemakers and Antiarrhythmic Devices" (JACC, Vol. 18, No. 1, July 1991:1 - 13).

Judy Amelsson for Doyle Hantt
(Division Sign-Off) *Acting Branch Chief*
Division of Cardiovascular, Respiratory,
and Neurological Devices
510(k) Number K980869