This guidance was written prior to the February 27, 1997 implementation of FDA's Good Guidance Practices, GGP's. It does not create or confer rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statute, regulations, or both. This guidance will be updated in the next revision to include the standard elements of GGP's.

DRAFT

Amendment to
Guidance on Discretionary Postmarket Surveillance
on Pacemaker Leads

3/30/94 Draft - Guidance for TTM-Based Studies

Introduction

Manufacturers of implantable cardiac pacemaker leads, are required to carry out Discretionary Postmarket Surveillance (DPS) on their lead models sold after 1982 and introduced into commerce before January 1, 1991. In its Guidance to Sponsors on the Development of a Discretionary Postmarket Surveillance Study for Permanent Implantable Cardiac Pacemaker Electrodes (Leads), FDA recommended that DPS studies be organized around a group of clinical centers involved in pacemaker/lead implants. Patient follow-up for the purposes of the DPS study in this recommended approach would be the responsibility of the patient's standard medical care follow-up system.

Several manufacturers have suggested that clinical center-based DPS studies would be impossible for studying their lead models because the distribution of the lead is not sufficiently concentrated in any group of clinical centers. These companies have suggested an alternate approach to DPS studies, organized around transtelephonic monitoring (TTM) services.

TTM is often used to monitor the status of pacemaker/lead patients periodically as an adjunct to the schedule of in-office evaluations. The patient is provided with a portable ECG transmitter which can transmit an ECG over the telephone to a central receiving station where it can be evaluated. While TTM is widely used as an adjunct to clinical examination and as a screening tool, it is generally understood that it is not as sensitive as evaluations in an electrophysiology clinic in detecting complications. The relevant scientific literature suggests that 60-80% of potential problems with the pacer leads or the generator can be detected by TTM. Whenever a complication is suggested by a TTM transmission, the normal procedure is referral for clinical follow-up where the complication can be checked and confirmed.

An advantage of a TTM-based study is that the low-volume/wide distribution lead models can still be studied when a center-based study is not possible. A TTM service under contract to the manufacturer becomes responsible for follow-up *for the purposes of the DPS study* (not for normal medical care follow-up, though the results of TTM may affect the course of medical care for the patient). A TTM-based study has the potential additional advantages of suffering fewer patients lost to follow-up, and having greater geographic representativeness.

FDA continues to believe that the preferred approach for DPS studies of pacemaker leads is one organized around a group of clinical centers involved in pacemaker/lead implants. In cases where a center-based approach is not feasible, a well-designed study organized around TTM may be acceptable. However, FDA believes that for a DPS study to be scientifically valid, TTM cannot be used alone for follow-up. There are a number of potential problems

with the TTM approach which must be addressed by imposing special requirements on TTM-based studies. In the following section, these special requirements are discussed.

Potential Problems and Special Requirements for TTM-Based Studies

Problem 1. TTM does not have the specificity of an in-office evaluation.

Requirement: When a complication is suggested by TTM, a subsequent clinical follow-up evaluation must occur to confirm the complication.

Problem 2. TTM does not have the sensitivity of an in-office examination, so there is the possibility that some complications may not be detected for many months. There are some suggestions that the use of a properly designed (voice) telephone interview can improve the sensitivity of TTM [NASPE Policy Conference Report, Antibradycardia-Pacemaker Follow-Up: Effectiveness, Needs, and Resources].

Requirement: The study monitor must obtain a follow-up report of a clinical evaluation at least every other year, i.e. at years two and four post-implant.

When no complications are suggested by TTM, this status should be noted as unconfirmed until the next clinical evaluation confirms a functioning lead.

Each DPS TTM monitoring session should include a telephone (voice) interview and should include questions to ascertain at a minimum, all of the following: The name, address, and telephone number of the current follow-up physician; the date of the last office visit to the follow-up physician and whether the visit was routine or symptom-driven; all symptoms related to the patient's cardiac health, whether or not the TTM suggests a problem.

Problem 3. Patients may not be enrolled in the TTM service during the first several weeks post-implant, so some early complications such as dislodgment may not be detected.

Requirement: As patients enter the study, their early status (post 3 months implant) must be determined . Since TTM, as an assessment method, may not be conducted until much later in the study and because early disposition in the follow-up program needs to be documented, a 3-month clinical evaluation must be performed to assess the possible occurence of early events such as dislodgement.

Problem 4. Because patients may not receive clinical evaluation every year, the

determination of the dates of significant events becomes more difficult, and the length of observation becomes less well defined.

Requirement: For the purposes of data analysis, sponsors may only count satisfactory lead performance up to the date of the patient's last satisfactory clinical evaluation. A result of this requirement would be that every patient's status would have to be determined from a clinical evaluation at study completion (so that the total schedule for follow-up based on clinical evaluation is: at 3 months, two years, and four years post implant, and at the end of the study). In determining the date of the last satisfactory clinical evaluation, the sponsor would not have to rely on the last DPS clinical follow-up form only, but could base the determination on an examination of the patient's complete medical record, if available.

Problem 5. Retrospective studies based on TTM would be potentially biased because some of the requirements for a DPS study, such as the interview and clinical evaluation, could not be imposed retroactively.

Requirement: Sponsors may not base a retrospective study solely on the records of TTM services.

Additional Miscellaneous Requirements:

The sponsor should develop a plan, including indications for any modifications to the follow-up schedule, which adequately deals with the following situations: (1) TTM suggests a complication, but clinical evaluation fails to confirm it; (2) the patient requests unscheduled TTM because of the occurrence of symptoms, but TTM fails to indicate any problem; (3) the patient experiences symptoms and is evaluated by a physician without the involvement or knowledge of the TTM service.