final

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SUPPLEMENT 1

generic environmental statement

on

ROUTINE USE OF PLUTONIUM-POWERED CARDIAC PACEMAKERS

MAY 1979

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FINAL
GENERIC ENVIRONMENTAL STATEMENT ON THE ROUTINE USE OF PLUTONIUM-POWERED CARDIAC PACEMAKERS

UPDATE OF INFORMATION ON POWER SOURCES FOR PACEMAKERS

U.S. NUCLEAR REGULATORY COMMISSION
OFFICE OF STANDARDS DEVELOPMENT

Issued: May 1979

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SUMMARY

The Final Environmental Statement on Routine Use of Plutonium-Powered Cardiac Pacemakers (FES) issued July 1976 states, "Plutonium-powered pacemakers have sufficient longevity to eliminate the need for surgical replacement operations that are necessitated by depletion of chemical batteries." This benefit of longevity for plutonium pacemakers has become less significant with technological advances in chemically powered pacemakers. Lithium-powered pacemakers, first implanted in 1972, have proved capable of providing lifetime pacing to the majority of patients. The industry confidently speaks of lithium-powered pacemakers lasting 10 years or more.

In Germany, reportedly by choice of the medical profession, no more nuclear-powered pacemakers are being implanted. Physicians are implanting lithium-powered pacemakers.

In certain Provinces in Canada, reportedly because of relative costs of nuclear- and lithium-powered pacemakers, nuclear pacemakers are not implanted.

In the U.S., there were five manufacturers/distributors of nuclear-powered pacemakers when the FES was issued. Today there are two.

Industry and medical profession interest in lithium-powered pacemakers has developed notwithstanding the achievement of an excellent performance record by nuclear-powered units. There is no reported instance of failure of a nuclear power source in a pacemaker. In May 1978, there were 1161 nuclear pacemakers in use in the U.S. There has been 100% accountability for nuclear pacemakers used in the U.S.

Industry and medical profession opinions about the need, if any, for nuclear-powered cardiac pacemakers in view of the availability of lithium pacemakers appear to be strongly influenced by the significance attached to re-implant operations. A person considering such operations to present only minor medical risks, psychological concern, and financial costs would be inclined to find little benefit in a nuclear pacemaker that is not found in a lithium pacer. If a person attaches greater significance to these factors and accordingly feels more strongly about avoiding re-implant operations, he may see a need for a nuclear pacemaker that may not be met by lithium pacers. Medical judgment is involved in this question of need and there are differing opinions.

STAFF CONCLUSIONS

Following the update of information on alternatives to nuclear-powered pacemakers, the staff re-examined the FES. The FES, as published in July 1976, concludes that the benefits to be derived from the use of plutonium-powered cardiac pacemakers are greater than the risk to the environment and that the routine use of plutonium-powered pacemakers should be authorized. The update of information on power sources does not change that conclusion. Although lithium-powered pacemakers may be adequate for most patients, they do not entirely eliminate replacement operations required because of power-source depletion. For a patient who may require long-term pacing but is ill-suited for replacement operations, the plutonium pacemaker may be the pacemaker preferred by his physician. The plutonium pacemaker provides physicians with an alternative choice of medical treatment for patients. The Commission recently stated in a general policy for regulating medical uses, that NRC will minimize intrusion into medical judgments affecting patients.[1] Accordingly, and since the risk to the environment is low, distribution of plutonium-powered pacemakers for routine use should be authorized subject to specific conditions. (See page vii of the FES (NUREG-0060, issued in July 1976) for complete staff conclusions and conditions.)

Supplement 1

UPDATE OF INFORMATION ON POWER SOURCES FOR PACEMAKERS

INTRODUCTION

The Final Environmental Statement on Routine Use of Plutonium-Powered Cardiac Pacemakers (FES) for this rulemaking action was issued in July 1976. In considering alternatives to and benefits of plutonium-powered pacemakers, the FES principally compares plutonium-powered pacemakers with pacemakers powered by mercury batteries since at that time there was limited experience with other types of chemical batteries. Recently, lithium batteries have been used extensively in pacemakers and their availability has prompted the staff to update the FES information on alternatives to nuclear-powered pacemakers. This updating includes consideration of the present extent of pacemaker use and the makeup of the patient population.

PATIENTS

At the present time, the United States has an estimated 225,000 persons with implanted cardiac pacemakers.[2] An analysis of patients with pacemakers implanted at a major medical institution by age and sex is shown in Figure 1.[3] This analysis shows that 40% of all patients implanted with pacemakers are initially implanted with them between the age of 70 to 80 years. Age 60 to 70 accounts for about 21% and age 80 to 90 for 25 to 30%. The analysis shows that 3.8% are under 50 years of age and that 2.6% are over 90 years of age. At each age, more men are implanted with pacemakers than women.

Although permanent electrical cardiac pacing is an established method of therapy for selected infants, children, and adolescents, long-term evaluation is relatively limited. Interest in prolonged pulse-generator longevity is of far less importance in children than in adults because in children the major problems requiring resolution are pacemaker size and the child's growth. In view of the problems induced by growth and the need for introducing greater electrode length, prolonged generator longevity is not necessarily an asset. In fact, pulse generator replacement can readily be accomplished at the time of modification of electrode position or length.[4,5]

An analysis of patients receiving pacemakers at one large medical center shows that within 5 years of implantation, about 45% of all pacemaker patients will have died.[6] Less than 25% of the patients will survive for 10 to 15 years (Figure 2).

PACEMAKER REPLACEMENTS

Patient welfare requires continued observation for pacemaker system failure. Until recently, the average longevity of implanted pulse generators was short and the spread of failure wide so that patient follow-up by periodic clinic visits and telephone transmission has been necessary. For the mercury-zinc cell pulse generators, the recommended monitoring schedule is weekly from the time of implant until one-month after implant in order to detect failure of the electrical connection between the pulse generator and the heart. If no failure occurs in the first month, the frequency is decreased until 30 months when weekly monitoring is begun in anticipation of battery depletion. The failure pattern of mercury-zinc cell pulse generators removed at a large medical center in 1976 is shown in Figure 3.[7] The failure pattern for lithium-powered pulse generators is substantially different because of the longer life lithium cell (Figure 4).[6]

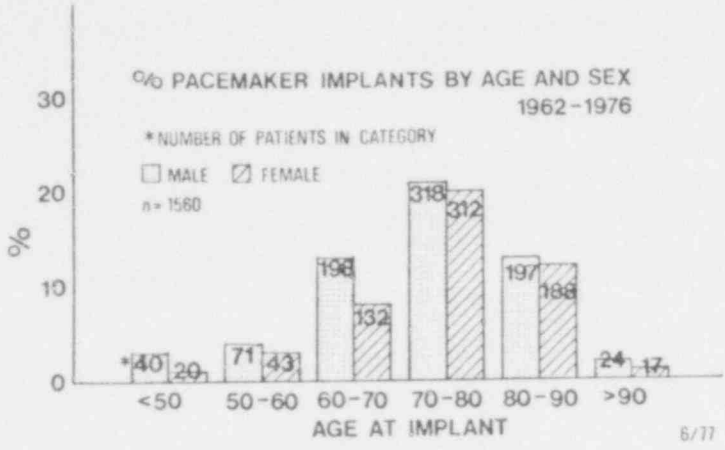

Figure 1. The ratio of pacer implants by age and sex. A plurality of patients is between 70 and 80 years of age (Reference 3).

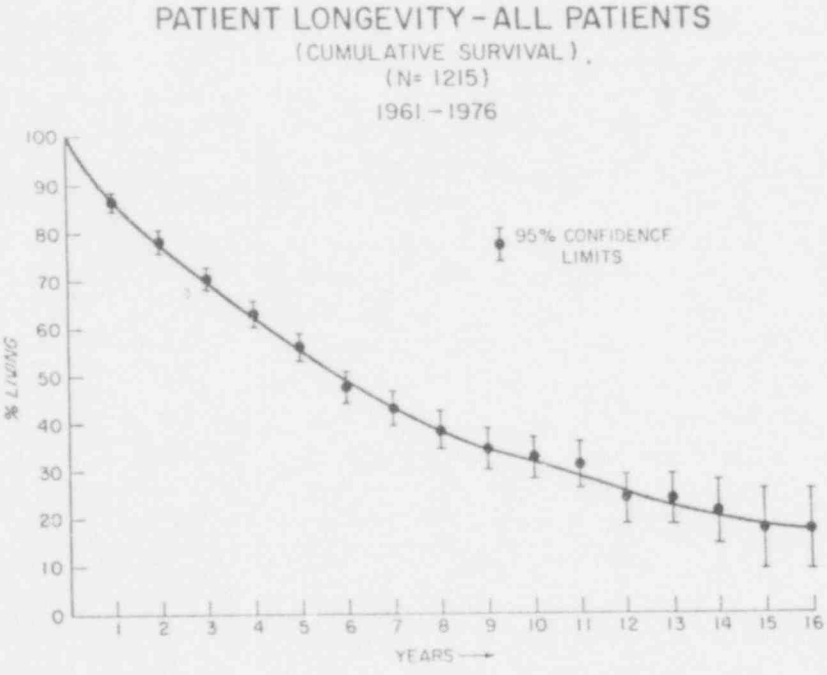

Figure 2. Cumulative survival curve of patients with implanted pacemakers treated at a large medical center (Reference 6).

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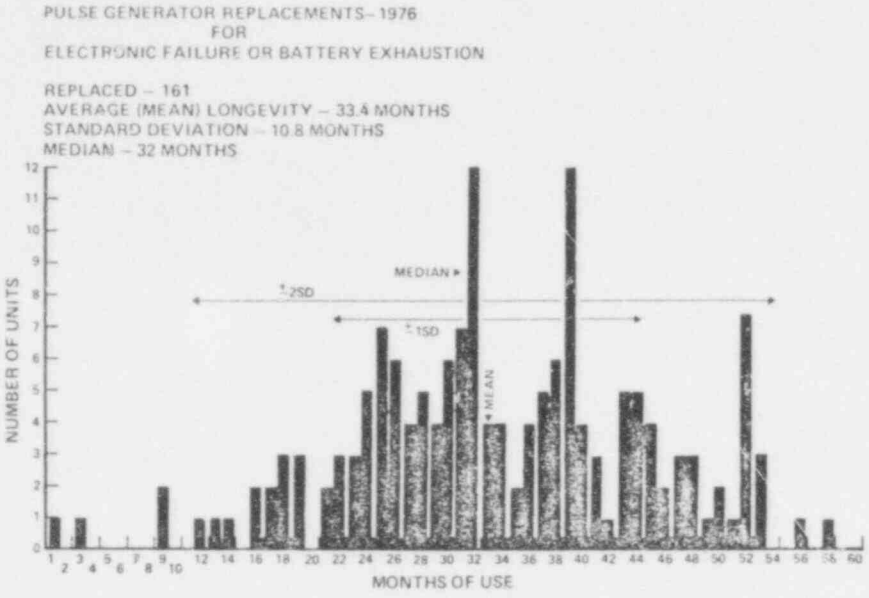

Figure 3. Pulse generators removed for electronic failure or battery depletion during 1976 approximated a normal distribution of longevity with a mean at 33.4 months and a standard deviation of 10.8 months (Reference 7).

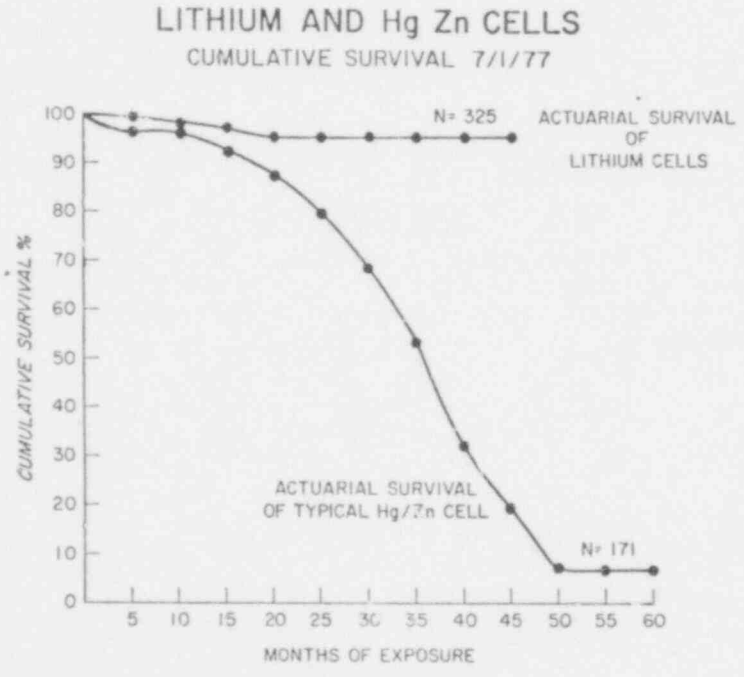

Figure 4. Cumulative survival of all lithium-powered pulse generators implanted at the Newark Beth Israel Medical Center since January 1973, compared to a typical mercury-zinc cell. At 45 months, more than 95% of implants are still in service (Reference 6).

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IMPROVED PACEMAKER TECHNOLOGY

Over the past 5 years, there have been striking improvements in pacemaker power sources, electronics, and encapsulation.[6] Each technology is so closely interrelated with the others that it is virtually impossible to discuss one independently of the others. In addressing the merits of a pacer, it is incorrect, therefore, to speak of a "lithium pacer" as if the power source completely defined the characteristics of the pacer because such a unit incorporates within it many associated technical developments. However, it is common practice to speak of "mercury," "lithium," "rechargeable," or "nuclear" pacers. This practice is followed in the FES and in this updating of its presentation on alternative power sources.

Pacemakers Powered by Mercury Batteries

For many years the mercury-zinc cell was the workhorse of the cardiac pacemaker industry and is still an acceptable power source.[8] Its use has decreased relative to other power sources because of its irregular failure modes, the significant internal losses, the generation of gas that must be absorbed by a "getter" or vented to the outside, and the availability of lithium batteries at a comparable price.

A large part of the published experience on pacemaker longevity has been related to the mercury-zinc cell. Up until a few years ago the average survival of these batteries was 18 to 22 months, and then improved versions began to last closer to 3 years. There is a theoretical potential of a mercury-zinc cell lasting as long as 8 years, although this prediction has never been achieved in fact. The longest survivals on record have been 65 and 72 months.[6]

Rechargeable Cells

A pulse generator with a single rechargeable NiCad battery has been manufactured and distributed by Pacesetters, Inc. for several years. The battery contained in the implanted pacemaker is recharged by a device that is external to the patient's body. Recharging frequencies and intervals are either once per week for about an hour or once a month for about 4 hours. The first rechargeable pacemakers made by Pacesetters were implanted in February 1973, and there are about 3,500 in use. To date, no indication of wear-out or premature generic type failure has been observed, and achievement of a pacemaker life in excess of 30 years still appears likely.[9]

The FES reported that in 1975 the Milton S. Hershey Medical Center, Pennsylvania State University, was developing a pacemaker that used a silver-mercury-zinc battery that required recharging about every 4 years. That pacemaker has not become available for clinical use.[9]

Lithium Pacemakers

The FES notes that use of lithium-powered cardiac pacemakers began in 1972 and that in 1975, after 3 years of clinical use, a major battery manufacturer conservatively estimated a 6-year battery life. In June 1978, after 6 years of clinical experience, the manufacturer indicated a battery life of 10 years with 6 to 10 years for smaller batteries and the technology for 20-year life batteries.[10] The manufacturer further stated there is no indication of a premature battery failure mechanism in 200,000 lithium batteries.

Cardiac pacemakers powered by lithium batteries are now manufactured by every pacemaker company.[8] Experience at a large medical center suggests that within a few years lithium-powered cells will replace the older mercury-zinc units entirely. As indicated in Figure 4, cumulative survival curves over a 4-year period show the lithium units outlast the mercury units.

An article in American Heart Journal, October 1977,[8] reports no battery failures in 20,000 lithium implants during a 5-year period and other component failures occurring at a rate of less than 0.3% per year. This reported experience is comparable to that summarized in FDA's 36-month report on its registry for implanted cardiac pacemakers[2] and represents a definite improvement over the pacemakers of the previous generation. As mentioned earlier, the improved performance of these pacemakers relates not only to the power sources but also to the associated advances in other technologies that are involved with the construction of these units.

Plutonium-Powered Pacemakers

From April 1970 through December 1976, more than 2,358 nuclear pacemakers were implanted throughout the world (Table 1). There has not been a single known battery failure. About 4% of the units are out of service for other reasons (exclusive of deaths) such as those shown in Table 2.[8] A May 1978 count showed 1161 plutonium-238 pacemakers in use in the U.S.[11] FDA's 36-month report of its registry for pacemakers includes coverage of 101 nuclear-powered units. It shows 0% battery depletion and 1% component failure for the nuclear units.

It was reported in the American Heart Journal, October 1977,[8] that the radioisotopic battery was designed to last 10 years with 95% confidence limits. It was further stated that 7 years after the first implant there was every reason to believe that this objective would be achieved and that a pulse generator longevity of 20 to 30 years is a reasonable expectation.

At the time of issuance of the FES, there were five U.S. manufacturers of nuclear-powered pacemakers. In June 1978, there were two. Discussion with a former manufacturer indicated that its decision to discontinue production of nuclear pacemakers was influenced by the availability of lithium batteries, the relatively high cost of nuclear pacemakers, and the effort needed to comply with NRC and Agreement States regulations.[12]

TABLE 1

NUCLEAR PACEMAKERS -- WORLD WIDE EXPERIENCE (12/31/76)* (Reference 8)

Type	Total Implanted	USA	Elsewhere	In Service	Longest Followup (months)
Alcatel-Medtronic	1531	495	1036	1392	81
ARCO	126	124	2	103	45
Biotronik-Betacel	246+	55	(12/31/75) 191 No 1976 data	?	48
Coratomic	261	261	--	243	28
Cordis	94	91	3	93	26
Total	2258+	1026	1232+	1831+	
Devices-- Harwell ≅ Siemens	100(1971) 0 2358+				

*Includes only models available in U.S.

? - Data incomplete.

TABLE 2

NUCLEAR PACERS--2258+ WORLD WIDE*

REASONS FOR OUT OF SERVICE (12/31/76) (Reference 8)

Type	Number Implanted	Out of service	Deaths	Other Reasons
Alcatel-Medtronic	1521	139	67	72-38 infection/erosion 22 lead problems 6 other complications 6 pacemaker failures
ARCO	126	23	7	16-5 infection/erosion 2 competition (VOO) 3 lead problems 1 elective replacement not pacer related 3 component 2 patient required faster rate pacer
Betacel-Biotronik	246?	?	?	?-2 component (U.S.) ? information outside U.S. is unavailable
Coratomic	261	18	6	12-3 component 9 lead problems 7 insufficient R wave amplitude 2 replaced during electrode replacement procedure
Cordis	94	1	1	0
Total	2258+	181+	81+	100+

*Includes only models available in U.S.

? - Data incomplete.

SELECTION OF A PACEMAKER

In an article in the February 1977 edition of the American Journal of Cardiology,[13] it is estimated that 1187 physicians are annually putting in 57,000 pacemakers in 2,000 medical centers. The article further indicated that since 1959 a total of 14 different American manufacturers have marketed 174 different pacemaker models, and at the time of preparation of the article there were 12 companies active and 44 different pulse generators on the market.

Pacemakers currently cost on the order of (1) $1795 to $2500 for lithium-powered units, (2) $2750 for rechargeable units, and (3) $5500 for nuclear-powered units.[9] Mercury-powered units cost slightly less than lithium-powered units. Warranties vary for the various models, but at least one manufacturer distributes a lithium-powered pacemaker with a lifetime guarantee. If the patient receives that model and later needs a replacement, he receives the second unit free. Further, if the initial pacemaker fails because of a defect in materials or workmanship, the manufacturer will reimburse the patient for up to $450 of uninsured medical expenses incurred in connection with the replacement.[14] The manufacturing and marketing of pacemakers has been described as a very competitive business.[15]

The selection of the pacemaker for the patient is usually made by the physician. As suggested by the number of models available to choose from and the large number of published articles on the use of pacemakers, there are variations in the needs of the patients and the physicians' choices for meeting those needs. A model particularly suited to one patient may be less than ideal for another patient.

To select a pacemaker, the physician should take into consideration the anticipated life expectancy of the patient, the expense of the pulse generator, the preferred mode of pacing, and the financial and emotional costs of follow-up care and reoperations.[6] The physician may also consider the regulatory requirements associated with certain pacemakers. The weight given to each of these factors is largely a matter of judgment by the physician. One physician may believe it very important that he select a pacemaker for the patient that will last his entire life. On the other hand, another physician may give greater importance to the lower initial cost that generally accompanies shorter battery life and less importance to possible need for replacement operation(s). The latter may also believe that when a replacement is required, a new generation of pacemakers will be available that will be more effective or flexible.

In considering the relative merits of a nuclear-powered cardiac pacemaker and its alternatives, pacemaker longevity is significant. As indicated in Figure 5,[6] a combination of advances in power sources, electronics, and encapsulation has led to the development of pacemakers that can be expected to last the lifetime of most patients (also, see Figure 2). Although most pulse generators today are powered by lithium batteries, rechargeable or nuclear-powered units may be a physician's choice for a particular patient if the physician places high priority on avoiding replacement operations.

The FES states, "It is expected that plutonium-powered pacemakers would be selected by physicians for only 5 to 10% of all pacemaker patients." In recent discussions with pacemaker manufacturers and with physicians, the staff attempted to ascertain the type of patient that needs a pacemaker with a useful life longer than now expected from a lithium unit (i.e. greater than about 10 years) and the frequency of occurrence of that type of patient. The comments received suggest that the patient would be a young but fully grown adult, typically 21 to 25 years old, who is otherwise in good health. Such individuals would constitute less than 1% of all patients. Accordingly, it now appears the FES estimate that 5 to 10% of all patients may be selected for plutonium pacemakers is high. Similarly, the 10,000 patient population considered in the FES now appears high by a factor of 5 or 10.

During its recent review of the use of pacemakers, the staff discussed the subject with German and Canadian regulatory personnel.[16,17] In Germany, no more nuclear-powered pacemakers are expected to be implanted. If a replacement is needed for a presently implanted nuclear pacemaker, a lithium unit will be used. This use of lithium to the exclusion of nuclear pacemakers reportedly is by the choice of the German medical profession.

In Canada, the provincial governments are involved in payment of medical expenses. The Province of Quebec reportedly will not pay for a nuclear-powered pacemaker because of its high cost. Also, the governmental body that controls medical payments in the Province of Ontario recently gave notice that it would not pay for any more nuclear pacemakers because their costs do not appear justified in view of available lithium units that last 7 to 10 years and cost much less than the nuclear units.

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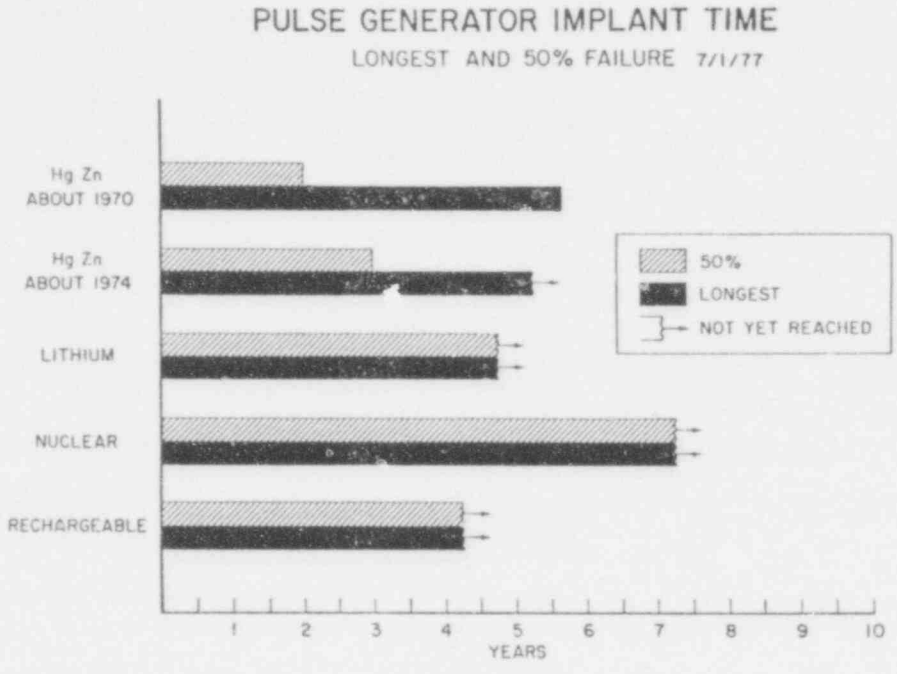

Figure 5. Projected longevity of power sources now in clinical use. Calculations are based on the energy density of the battery, the current required to operate the circuit and to produce a stimulating impulse, and internal cell and circuit losses (Reference 6).

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* Available for inspection and copying for a fee at the NRC Public Document Room, 1717 H Street, N.W., Washington, D.C.

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16. ABSTRACT *(200 words or less)*

The Final Environmental Statement on Routine Use of Plutonium-Powered Cardiac Pacemakers (FES) was issued in July 1976. Supplement 1, prepared in 1978, updates the FES with respect to power sources for pacemakers. Particular attention is given to the non-nuclear lithium batteries as alternatives to Pu-238 power sources in pacemakers. Supplement 1 also considers the current extent of pacemaker use and makeup of the patient population and concludes that the FES' conclusion is still valid that distribution of Pu-238 powered pacemakers for routine use should be authorized subject to specific conditions.

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