International Standard 5841/2

INTERNATIONAL ORGANIZATION FOR STANDARDIZATION•МЕЖДУНАРОДНАЯ ОРГАНИЗАЦИЯ ПО СТАНДАРТИЗАЦИИ•ORGANISATION INTERNATIONALE DE NORMALISATION

Implants for surgery — Cardiac pacemakers — Part 2: Reporting of the clinical performance of populations of pulse generators

Implants chirurgicaux — Stimulateurs cardiaques — Partie 2: Instructions pour l'établissement d'un rapport concernant le fonctionnement clinique de populations de générateurs d'impulsions

First edition — 1986-11-01

UDC 615.46 : 616.12-008.31 : 616-089.28 **Ref. No. ISO 5841/2-1986 (E)**

Descriptors : medical equipment, surgical implants, pacemakers, utilization, data representation.

Price based on 16 pages

Foreword

ISO (the International Organization for Standardization) is a worldwide federation of national standards bodies (ISO member bodies). The work of preparing International Standards is normally carried out through ISO technical committees. Each member body interested in a subject for which a technical committee has been established has the right to be represented on that committee. International organizations, governmental and non-governmental, in liaison with ISO, also take part in the work.

Draft International Standards adopted by the technical committees are circulated to the member bodies for approval before their acceptance as International Standards by the ISO Council. They are approved in accordance with ISO procedures requiring at least 75 % approval by the member bodies voting.

International Standard ISO 5841/2 was prepared by Technical Committee ISO/TC 150, *Implants for surgery.*

Users should note that all International Standards undergo revision from time to time and that any reference made herein to any other International Standard implies its latest edition, unless otherwise stated.

Printed in Switzerland

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Implants for surgery — Cardiac pacemakers — Part 2 : Reporting of the clinical performance of populations of pulse generators

0 Introduction

ISO 5841/1 requires the clinician's manual to contain a statement of nominal pulse generator service life. Expectations of available power source energy are not always fulfilled and changes in pacemaker components and assemblies have resulted in actual service life different from the nominal service life. Defined production groups of pulse generators have required closer follow-up or replacement due to changes in performance exhibited in clinical use.

This experience shows the value of maintaining an accurate and discriminating view of clinical performance of a population of pulse generators so as to aid patient management. In order to do this, it is necessary to collect implant and explant information. ISO 5841/1 specifies the content of forms to report implant and explant information.

The primary purpose of this part of ISO 5841 is to describe the reporting responsibilities in sharing clinical performance information for patient management. When clinical performance reports discriminate by production group and focus on recent experience, they are of value in patient management.

This part of ISO 5841 concerns the clinical performance of pacemakers, not the clinical reasons for their use. It is realized that reasons for use can be a guide in the design of future products.

At present, reporting parties give cumulative clinical experience information based on a variety of assumptions and statistical techniques. This part of ISO 5841 gives, in annexes, a method for categorizing pacemakers, guidelines to the statistical techniques that should be used to obtain the most benefit from the data and a statement of the rationale for this part of ISO 5841.

Clinicians have emphasized that a pulse generator the performance of which has changed, either expectedly or unexpectedly, is sometimes left implanted due to other medical considerations. Instances exist where the performance of an implanted pulse generator has changed to stable but out-of-specification performance which is considered safe and effective by the attending clinician. This is an important reason why the term "failure" is avoided throughout the classification.

"Failure" is not sufficiently specific to express the significance of a change in performance. In addition, "failure" implies a negative connotation for pulse generators which meet all longevity claims and cease functioning due to normal power source depletion.

1 Scope and field of application

This part of ISO 5841 specifies requirements for reports on the clinical performance in humans of population samples of pulse generators. It includes general requirements for all reports and supplementary requirements for reports on recent experience and cumulative experience, including specific statistical expressions based on an adaptation of actuarial analysis.

Annex A provides requirements for categorizing pulse generators. Annex B provides guidelines for statistics, including a discussion on application of the results obtained. As with other statistical methods, the benefit of the analytical methods in this part of ISO 5841 is limited by the size of population under consideration. Annex C gives the rationale for this part of ISO 5841.

2 Reference

ISO 5841/1, *Implants for surgery — Cardiac pacemakers — Part 1: Implantable ventricular pacemakers.*

3 Definitions

For the purposes of this part of ISO 5841, the definitions given in ISO 5841/1 and the following definitions apply.

3.1 advisory notification: In respect of a device, any action taken to inform the clinicians concerned by a manufacturer who has become aware that the pulse generator may fail to conform to any claims made relating to effectiveness, benefits, performance characteristics or safety.

3.2 clinical performance period: A calendar period, defined by the reporting party, during which the clinical performance of a specific population sample of pulse generators is assessed.

3.3 damaged: Term used to describe a device the characteristics of which have changed outside the limits stated by the manufacturer due to some external agency.

3.4 dysfunction: Term used to describe a device having some characteristic outside the limits recommended by the manufacturer for clinical use, except changes due to the expected battery condition.

3.5 follow-up centre: A medical centre, hospital, clinic or individual responsible for the care of a patient after the implantation of a pacemaker.

3.6 in service: Term used to describe a device that is functioning in such a manner as to provide potential medical benefits to the patient although the pulse generator may be out of specification (see 3.10).

3.7 in specification: Term used to describe a device having characteristics within the limits recommended by the manufacturer for clinical use.

3.8 medical reasons: Reasons unrelated to the pulse generator or its operation (e.g. infection, extrusion, high threshold, etc.).

3.9 out of service: Term used to describe a device not providing a medical benefit to the patient. The pulse generator is not necessarily out of specification (see 3.10) or explanted.

3.10 out of specification: Term used to describe a device having one or more characteristics outside the limits recommended by the manufacturer for clinical use.

3.11 population sample: A group of pulse generators designated for the purpose of reporting performance experience that it assumed to be representative of the population.

3.12 production group: A particular population sample of pulse generators designated by the manufacturer on the basis of, for example, time or place of manufacture or a change in the manufacturing process or components.

3.13 prophylactic explantation: Explantation for reasons based on expected performance of the pulse generator.

3.14 recommended replacement condition: Condition in which the pulse generator has exhibited the maximum allowable changes in the battery condition indicators stated by the manufacturer.

3.15 registered explant: A registered implant for which the date of explantation is known by the reporting party.

3.16 registered implant: An implanted pulse generator for which the date of implantation is known by the reporting party.

3.17 registered implant month: One month of operation by a registered implant.

3.18 reporting party: An individual or organization publishing clinical pacemaker data or the analysis thereof.

4 General requirements (see also annex C)

4.1 The report shall indicate the sources of the data and the methods used to collect them.

4.2 The report shall specify the sample size and how the population and population sample are defined.

4.3 The criteria for including and excluding data shall be given.

4.4 The time period over which the data were acquired shall be given.

4.5 The units of time of the data shall be given.

4.6 Each report shall explain the presentation of the information and any methods of analysis used to calculate numerical expressions of performance. It shall be stated in the report that it has been prepared in accordance with this part of ISO 5841.

4.7 The report shall explain methods used to adjust for any sources of bias known to be present (see annex B).

4.8 Any generalizations or inferences from data shall be qualified as to assumptions, limitations and associated confidence levels.

4.9 Pulse generators referred to in an advisory notification shall be identified by means of the serial numbers of the devices.

4.10 The report shall state the basis for adjusting registered implant months to compensate for unreported mortality and unreported explants.

4.11 Pulse generators shall be assigned the appropriate category in accordance with annex A.

NOTES ON CLAUSE 4

1 Reports applicable to any number of production groups or population samples may be included in one document. However, they should be arranged in an easily distinguishable manner.

2 It is recommended that supplementary information be included in the report, for instance lower confidence limits (see annex B).

5 Reporting of recent clinical performance of implanted pulse generators for patient management

5.1 A report of this type shall comply with the qualifications and limitations given in 5.2 to 5.5. (See also annex C.)

5.2 The basis of the report on a specific registered implant shall be the clinical performance of that production group to which it belongs.

5.3 The clinical performance period shall fall completely within a specified 12 calendar month period. The date of the report shall be within six months of the end of the specified period.

5.4 For the production group and clinical performance period, the report shall compare the number of registered implant months with the number of pulse generators categorized, in accordance with annex A, as being out of specification (including sub-categories). As a minimum, monthly survival rate and population sample size shall be given.

NOTE — Examples of data sets and analyses are given in annex B.

5.5 The manufacturer of the pulse generator shall provide a report on the production group at least once a year for as long as there are devices known to be in service. This report shall be made available to the implanting and follow-up centres at their request.

6 Reporting of cumulative experience with implanted pulse generators

6.1 A report of this type shall comply with the qualifications and limitations given in 6.2 to 6.5. (See also annex C.)

6.2 For a given population sample, the report shall compare the total number of registered implant months with the total number of pulse generators categorized, in accordance with annex A, as being out of specification (including sub-categories). As a minimum, the cumulative survival probability for the population sample and population sample size shall be given.

NOTE — Examples of data sets and analyses are given in annex B.

6.3 The report shall state that it is based on cumulative analysis and, as such, may not reflect changes in recent implant performance nor reflect differences in performance between production groups.

6.4 The report shall direct attention to recent experience reports suitable for patient management purposes.

6.5 The manufacturer shall provide a report on each model at least once a year for as long as there are devices known to be in service. This report shall be made available to the implanting and follow-up centres at their request.

Annex A

Method for categorizing pulse generators

(This annex forms an integral part of the standard.)

The pulse generator shall be assigned the appropriate category in accordance with figure 1 and according to the evidence available to the reporting party.

A pulse generator shall be classified in that category which best describes its status, use being made of the best information available. The reporting party should detail the composition of the categories A, B and C, with special attention given to distinguishing units in categories C_1 and C_2.

A general category (A, B or C) shall be assigned to the generator, in accordance with the following criteria:

- Category A: Pulse generator that is in service and, as far as can be verified, in specification.
- Category B: Pulse generator removed from service for reasons not related to the functioning of the device.
- Category C: Pulse generator that is out of specification.

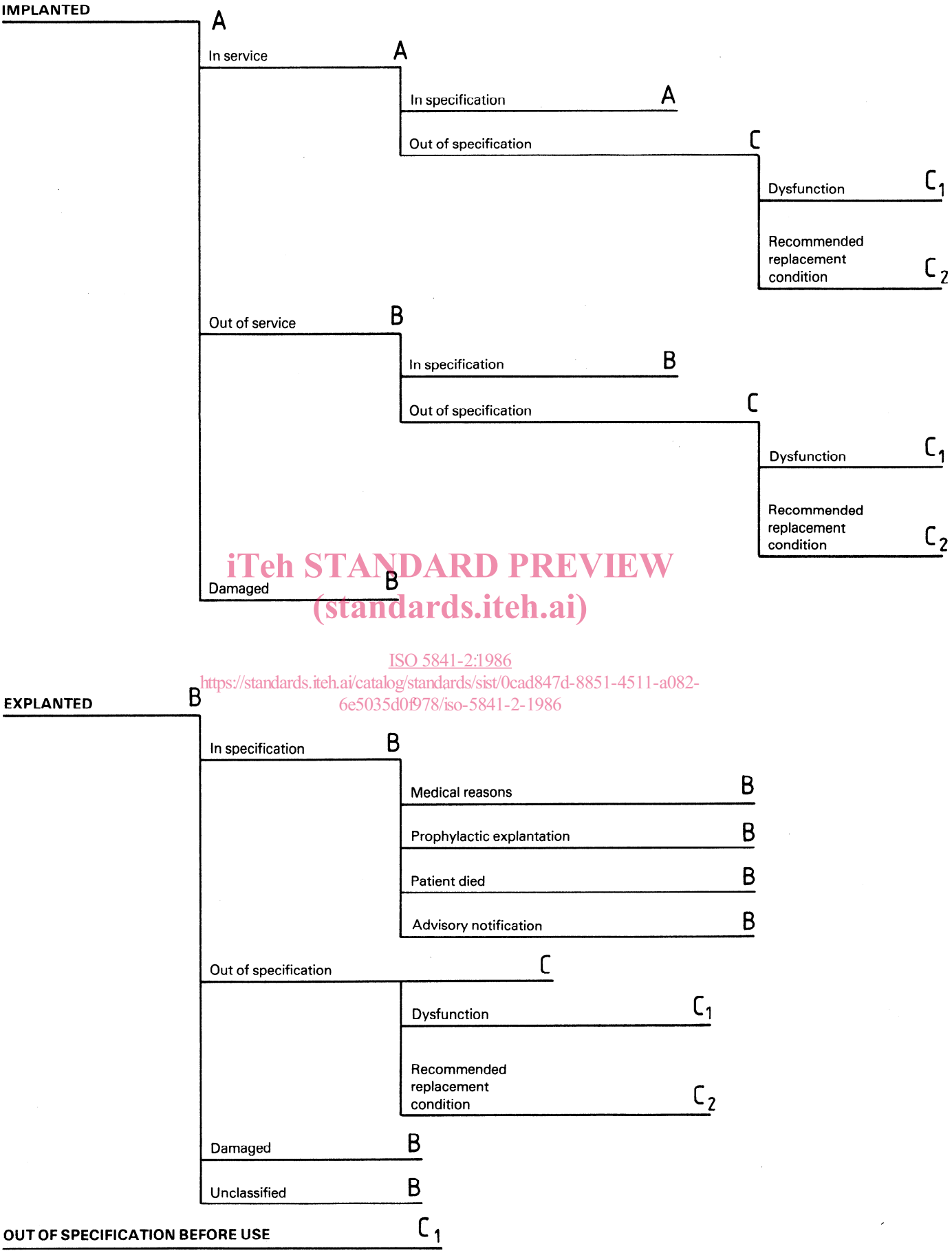

Figure 1 — Assignment of category and general category to pulse generators

Annex B

Statistical guidelines and discussion of the application of the results obtained

(This annex does not form an integral part of the standard.)

B.1 Introduction

This annex illustrates the application of actuarial analysis to obtaining the expressions of clinical performance for population samples of pulse generators. It is intended only as an introduction to this type of analysis for users of this part of ISO 5841 unfamiliar with such statistical tools and their application to clinical experience with pulse generators. For a further understanding of the assumptions, methods and use of actuarial techniques, the reader is encouraged to refer to the more comprehensive discussions contained in the bibliography listed in clause B.4.

The main advantage of actuarial methods is that no underlying statistical distribution of the data needs to be assumed. As such, actuarial techniques are suitable for use with a wide variety of the kinds of data arising from clinical experience with pulse generators. It is because of this wide applicability in the analysis of pulse generator data that this annex presents an outline of these methods. Nothing in this annex is intended to preclude the use of additional analytical techniques, which may be appropriate for specific data sets and other reporting objectives.

This part of ISO 5841 is aimed at all individuals or organizations who publish reports of clinical experience with pulse generators. For a manufacturer to be in compliance with this part of ISO 5841, there are additional requirements for reporting (as discussed in clauses 5 and 6). Analysis techniques and actuarial displays are illustrated in this annex. Additional or more detailed analyses of such clinical data are, of course, not precluded.

This annex will demonstrate the use of actuarial methods on a hypothetical set of implanted pulse generator data. It will be assumed that complete information is available on the classification status and on the important dates associated with each unit.

B.2 Statistical guidelines

B.2.1 Organizing the data

In accordance with annex A, the letters A, B or C are assigned to general categories to facilitate analysis of the population sample.

It is important to note that categories are assigned on the basis of the best information available to the reporting party. For some pulse generators, the reporting party may have information that they are functioning in specification (or out of specification). If all that is known is that a pulse generator has been implanted, then the general category A is assigned. Clause B.3 describes how the bias which arises from this assumption can be compensated for in part.

There are three pieces of data about a pulse generator that are needed to proceed with an actuarial analysis:

a) the date of implantation;

b) the assignment of the category (see annex A);

c) the date associated with the assignment.

The date associated with the assignment is the date on which a category is assigned to a pulse generator. This would be, for example, the date on which a unit was explanted for reasons not related to its function (a "B") or that date (implanted or not) a unit went out of specification (a "C"). For units still in service and in specification (an "A"), it is the date on which the clinical performance period described by a particular report ends.

Special consideration is required for those patients with pulse generators who lose contact with the follow-up centre. In an "active" data system, the units are effectively withdrawn from the population at the moment continuing contact with the patient is broken. If the pulse generator was performing in specification up until the time, a classification of "B" can reasonably be assigned. This would be the case, for example, if a patient changes address without notification. Assignment of a "B" category makes the assumption that the reason contact was lost was unrelated to the functioning of the generator. If the follow-up centre re-establishes contact with a lost patient, information about the pulse generator condition can once again be determined. That unit could resume its place with other units in the population sample being monitored.

B.2.2 Cumulative experience reports

B.2.2.1 Actuarial analysis

This sub-clause presents the steps involved in performing an actuarial analysis for the purpose of preparing a report on cumulative experience. Figure 2 shows the implant lifetime, according to calendar time, of a hypothetical group of 24 pulse generators. A group of units would, in practice, be selected on the basis of some common characteristic, making it suitable to report on their collective performance. The conclusion of the clinical reporting period is taken to be at the end of year 4.

Figure 3 shows the implant lifetime of the sample data set on a scale measuring the length of implant for each pulse generator. The notation remains the same as that defined for figure 2.

The focus of this discussion will be the actuarial data presented in table 1. The sample data set shown in figures 2 and 3 is given numerically in the table in columns N, A, B and C. These variables and the other calculated quantities shown are described below. Each of the variables is actually a function of time. Thus, for example, the quantity N can be represented as $N(t)$. The selection of a time interval of three months was arbitrary.

Number entering (N): The number of pulse generators entering any given time interval with the classification "A".

Incomplete lifetime (A): The number of units in a general category "A" the implant time of which at the end of the clinical reporting period falls within the given interval.

Withdrawn in specification (B): Number of units classified as "B" within the given interval.

Withdrawn out of specification (C): Number of units classified as "C" within the given interval.

Units at risk (U): The effective number of units in service which are subject to a change in category during the given interval:

$$U(t) = N(t) - \frac{[A(t) + B(t)]}{2}$$

Registered implant months (M): The number of months of effective pacing during the given interval:

$$M = U(t) \times n$$

where n is the number of months in the given interval.

(Approximation applicable to large data set; more accurate method is to count implant months.)

Monthly survival rate (R): The monthly survival rate during the given interval:

$$R(t) = 1 - \frac{C(t)}{M(t)}$$

Survival fraction (P): The estimated probability of a unit entering the interval operating normally throughout the given interval:

$$P(t) = [R(t)]^n$$

where n is the number of months in the given interval.

Cumulative survival (S): The estimated probability of a unit surviving from the time of implant throughout the given interval:

$$S(t) = P(t)\,P(t-1)\ldots P(1)$$

i.e. the product of the survival fractions $P(1)$ . . . to $P(t)$.

The information in column (S) of table 1 is presented in graphical form, see figure 4.

B.2.2.2 Lower confidence limit

Those parties reporting cumulative survival statistics are encouraged to present additional information to that in column (S). The effective sample size data for each interval, column (U), or lower confidence limits (90 %, 95 %) would aid greatly in interpreting the data. For the statistical techniques involved in preparing such confidence limits, the reader is referred to the bibliography in clause B.4.