ISO 14971 – Application of Risk Management on Medical Device

ISO 14971 – TERMS AND DEFINITIONS

Harm	Physiological injury or damage to the health of people, or damage to property or the environment
Hazard	Potential source of harm
Hazard situation	Circumstance in which people, property, or the environment are exposed to one or more hazard(s)
Severity	Measure of the possible consequences or impact of a hazard. Severity is one component of risk.
Safety	Freedom from unacceptable risk

RISK FOR ISO 14971

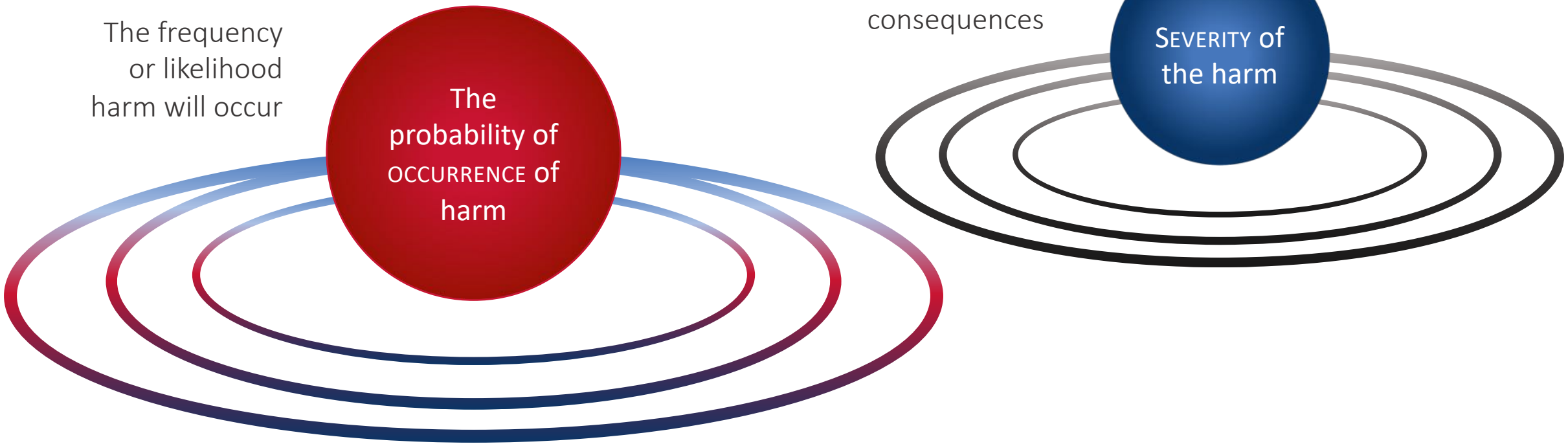
RISK IS DEFINED AS THE COMBINATION OF....

The frequency or likelihood harm will occur

The probability of OCCURRENCE of harm

The extent of its impact or consequences

SEVERITY of the harm



WHAT YOU WILL GAIN FORM THIS GUIDE

ISO 14971 provides a thorough explanation of relevant terms and definitions. And the standard defines a RISK MANAGEMENT process.

In addition to ISO 14971, there are several other key medical device industry standards requiring risk management:

The partial list includes:

- IEC 60601 - is a series of technical standards for the safety and essential performance of medical electrical equipment.
- IEC 62366 - Application of usability engineering to medical devices
- ISO 10993 - series of standards for evaluating the biocompatibility of medical devices
- ISO 13485 - Medical devices - Quality management systems - Requirements for regulatory purposes. It represents the requirements for a comprehensive quality management system for the design and manufacture of medical devices

A BRIEF OVERVIEW OF THE STANDARD & ANNEXES

Today there are two versions of ISO 14971 – both likely to impact you in some way:

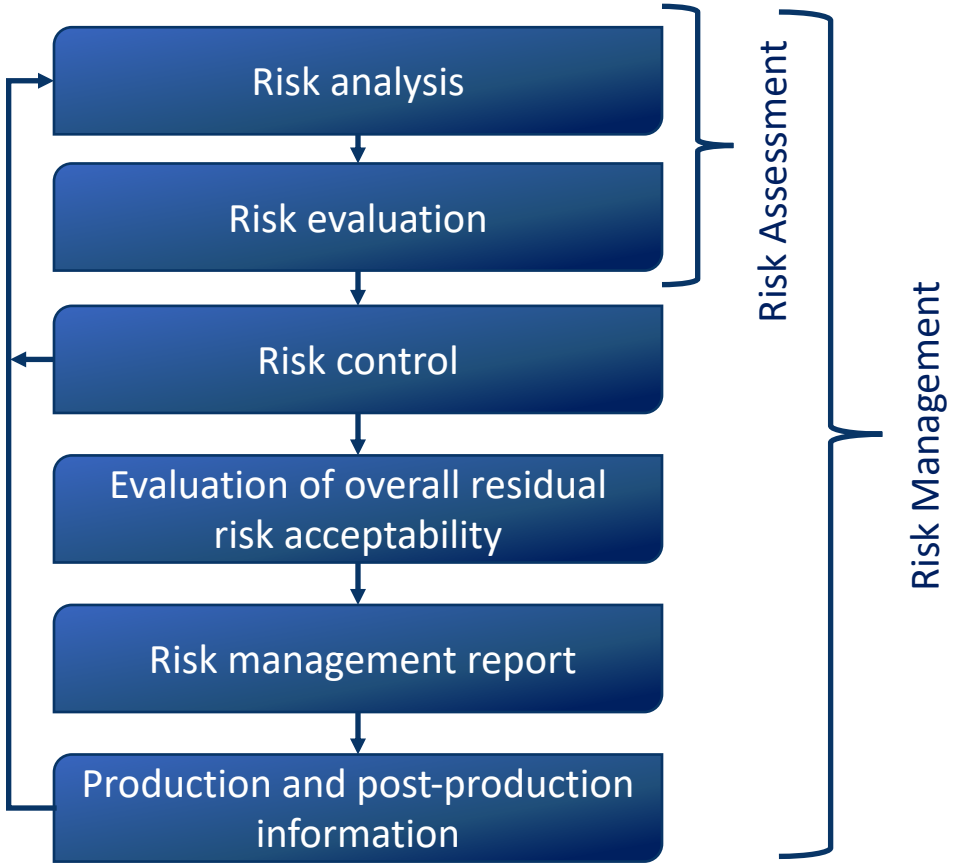
- ISO 14971:2007 and EN ISO 14971:2012

The EN version is applicable if you are selling medical device in Europe.

In both cases, the abstract describing the standard is the same:

"ISO 14971 is a key standard specifying a process for a manufacturer to identify the hazards associated with medical devices, including in vitro diagnostic (IVD) medical devices, to estimate and evaluate the associated risks, to control these risks, and to monitor the effectiveness of the controls. The requirements of this standard are applicable to all stages of the life-cycle of a medical device."

ISO 14971- General requirements for Risk management



The risk Managment steps according to ISO 14971

- Risk analysis
  - Identification of subject (product, process, decision)
  - Identification of characteristics related to safety
  - Identification of hazards
  - Estimation of risk(s) for each hazardous situation
- Risk evaluation
- Risk control
  - Implementation of risk control measure(s)
  - Residual risk evaluation
- Evaluation of overall residual risk acceptability

ISO 14971 – RISK ANALYSIS

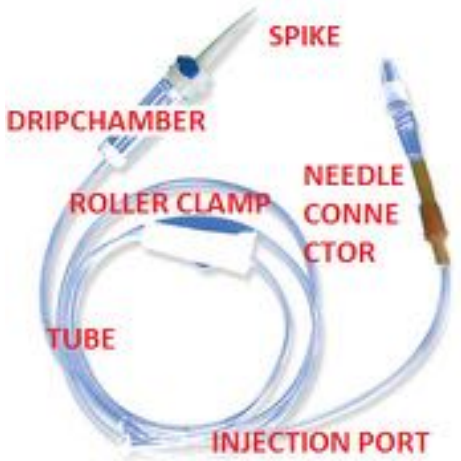
Systematic use of available information to identify hazards and to estimate the risk.

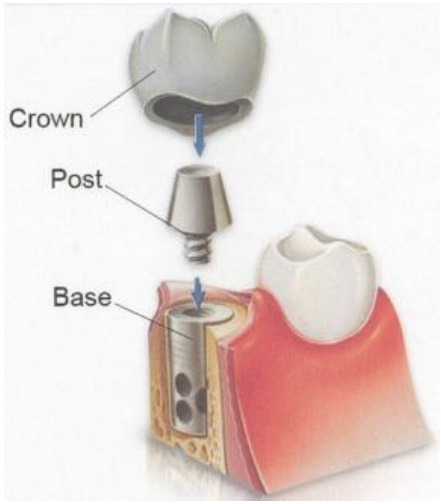
1. Intended use and identification of characteristics elated to the safety of medical device – ANNEX C
2. Identification of hazards - ANNEX E
3. Estimation of the risk(s) for each hazardous situation

PRODUCT DESCRIPTION

Intended use and identification of characteristics related to the safety of medical device – ANNEX C

- description, part number, important subassemblies (functional groups)
- Intended use





ANNEX C - CHECKLIST EXAMPLE

- C.2.1 What is the intended use and how is the medical device to be used?
  - 2.1.1 What is the medical device's role relative to:
    - 2.2.1.1 Diagnosis, prevention, monitoring, treatment or alleviation of disease;
    - 2.2.1.2 Compensation for injury or handicap;
    - 2.2.1.3 Replacement or modification of anatomy, or control of conception?
  - 2.1.2 What are the indications for use (e.g. patient population)?
  - 2.1.3 Does the medical device sustain or support life?
  - 2.1.4 Is special intervention necessary in the case of failure of the medical device?
- C.2.2 Is the medical device intended to be implanted? Factors that should be considered include:
  - 2.2.1 The location of implantation;
  - 2.2.2 The characteristics of the patient population;
  - 2.2.3 Age;
  - 2.2.4 Weight;
  - 2.2.5 Physical acutivity;
  - 2.2.6 The effect of ageing on implant performance;
  - 2.2.7 The expected life time of the implant;
  - 2.2.8 The reversibility of the implantation

IDENTIFICATION OF HAZARDS

Identification of hazards ANNEX E

- WHAT?
  - Known and foreseeable
  - Normal use and first fault condition
  - Technical and user related
- HOW?
  - Use of the checklist in the norm (Appendix E)
  - Review of history
  - Opinion of experts
  - State of the art
  - Test (challenging tests)
  - Non compliance to (harmonised) standards

Examples of energy hazards	Examples of biological and chemical hazards	Examples of operational hazards	Examples of information hazards
Electromagnetic energy Line voltage Leakage current — enclosure leakage current — earth leakage current — patient leakage current Electric fields Magnetic fields **Radiation energy** Ionizing radiation Non-ionizing radiation **Thermal energy** High temperature Low temperature **Mechanical energy** Gravity — falling — suspended masses Vibration Stored energy Moving parts Torsion, shear and tensile force Moving and positioning of patient Acoustic energy — ultrasonic energy — infrasound energy — sound High pressure fluid injection	**Biological** Bacteria Viruses Other agents (e.g. prions) Re- or cross-infection **Chemical** Exposure of airway, tissues, environment or property, e.g. to foreign materials: — acids or alkalis — residues — contaminates — additives or processing aids — cleaning, disinfecting or testing agents — degradation products — medical gasses — anaesthetic products **Biocompatibility** Toxicity of chemical constituents, e.g.: — allergenicity/ irritancy — pyrogenicity	**Function** Incorrect or inappropriate output or functionality Incorrect measurement Erroneous data transfer Loss or deterioration of function **Use error** Attentional failure Memory failure Rule-based failure Knowledge-based failure Routine violation	**Labelling** Incomplete instructions for use Inadequate description of performance characteristics Inadequate specification of intended use Inadequate disclosure of limitations **Operating instructions** Inadequate specification of accessories to be used with the medical device Inadequate specification of pre-use checks Over-complicated operating instructions **Warnings** Of side effects Of hazards likely with re-use of single-use medical devices **Specification of service and maintenance**

Hazard	Foreseeable sequence of events	Hazardous situation	Harm
Electromagnetic energy (Line voltage)	(1) Electrode cable unintentionally plugged into power line receptacle	Line voltage appears on electrodes	Serious burns Heart fibrillation Death
Chemical (Volatile solvent)	(1) Incomplete cleaning of volatile solvent used in manufacturing (2) Solvent residue converts to gas at body temperature	Development of gas bubbles in the blood stream during dialysis	Gas embolisms Brain damage Death
Biological (Microbial contamination)	(1) Inadequate instructions provided for decontaminating re-used anaesthesia tubing (2) Contaminated tubing used during anaesthesia	Bacteria released into airway of patient during anaesthesia	Bacterial infection Death
Electromagnetic energy (ESD)	(1) Electrostatically charged patient touches infusion pump (2) ESD causes pump and pump alarms to fail (3) Insulin not delivered to patient	Failure to deliver insulin unknown to patient with elevated blood glucose level	Minor organ damage Decreased consciousness Coma, death
Function (No output)	(1) Implantable defibrillator battery reaches the end of its useful life (2) Inappropriately long interval between clinical follow-up visits	Device cannot deliver defibrillation shock when an arrhythmia occurs	Death

ESTIMATION OF THE RISKS

Estimation of the risk(s) for each hazardous situation

The concept of risk is the combination of the following two components:

- the probability of **occurrence** of harm;
- the consequences of that harm, i.e., how **severe** it might be.

Risk = Occurrence x Severity

Risk estimation should examine, for example:

- the initiating event or circumstance (see E.3);
- the sequence of events that could lead to a hazardous situation occurring;
- the likelihood of such a situation arising;
- the likelihood that the hazardous situation leads to harm;
- the nature of the harm that could result.

Assessment of Severity (S) and Occurrence (O)

Annex D

- Method:
  - Qualitative
  - Semi-quantitive
- Focus:
  - Systematic faults, first faults
  - Events

EXAMPLE OF OCCURRENCE ESTIMATION

Qualitative

Probability of occurrence O	Description of hazard/failure occurrence	Index
Very high	The event is almost sure	5
High	Many cases in the evaluated period	4
Moderate	Some cases in the evaluated period	3
Low	A few cases in the evaluated period	2
Remote	Potential hazard or failure, no known cases	1

Quantitative

Probability of occurrence O	Range of occurrence	Index
Frequent	≥ 10-3	5
Probable	<10-3 and ≥ 10-4	4
Occasional	<10-4 and ≥ 10-5	3
Remote	<10-5 and ≥ 10-6	2
Improbable	<10-6	1

EXAMPLE OF OCCURRENCE ESTIMATION

Qualitative: gives a description of probability range

- Index associated to each range to simplify Risk Index evaluation
- Based on historical data, evaluated by field experts
- Past production information – State of the art, literature

Quantitative: gives estimated ranges

- Index associated to each range to simplify Risk Index evaluation:
- Based on data from:
  - Modellization
  - Production data
  - Evaluation of statistics on past defect data

SEVERITY OF THE HARM

Measure of the possible outcome and consequences of a hazard

- Estimating the severity:
  - estimating consequences of a failure,
  - the nature of harm that may arise
  - the involvement of all stakeholders, in order of criticality

EXAMPLE OF SEVERITY LEVEL

Qualitative

Severity S	Description of harm	Index
Catastrophe	Results in patient death	5
Critical	Results in permanent impairment or life-threatening injury	4
Serious	Results in injury or impairment requiring professional medical intervention	3
Minor	Results in temporary injury or impairment not requiring professional medical intervention	2
Negligible	Inconvenience or temporary discomfort	1

ISO 14971 – Qualitative Risk matrix

Probability of Occurance		Severity				
		Negligible	Minor	Serious	Critical	Catastrophic
		1	2	3	4	5
Very high	5	5	10	15	20	25
High	4	4	8	12	16	20
Moderate	3	3	6	9	12	15
Low	2	2	4	6	8	10
Remote	1	1	2	3	4	5

ISO 14971 – Semi-quantitative Risk matrix

Probability of Occurance		Severity				
		Negligible	Minor	Serious	Critical	Catastrophic
		1	2	3	4	5
Frequent	5	5	10	15	20	25
Probable	4	4	8	12	16	20
Occasional	3	3	6	9	12	15
Remote	2	2	4	6	8	10
Improbable	1	1	2	3	4	5

ISO 14971 - TABLE

Hazard	Hazard situation	Harm	Occurance	Severity	Ri (SxO)
					R1=…
					R2=…
					R3=…
					R4=…

ISO 14971 – Risk matrix

Qualitative probability levels	Qualitative severity levels: Negligible	Moderate	Significant
High	R_1	R_2	
Medium		R_4	R_5, R_6
Low		R_3	

Figure D.2 — Example of a qualitative 3 x 3 risk matrix

Semi-quantitative probability levels	Qualitative severity levels: Negligible	Minor	Serious	Critical	Catastrophic
Frequent					
Probable	R_1	R_2			
Occasional		R_4		R_5	R_6
Remote					
Improbable			R_3		

Figure D.3 — Example of a semi-quantitative risk matrix

ISO 14971 - Risk evaluation and risk acceptability

$$Ri = S \times O$$

Following the examples above

- Ri≤4 acceptable
- 5≤ Ri ≤12 requires further evaluation
- Ri≥13 not acceptable

ISO 14971 – Qualitative Risk evaluation

Probability of Occurance		Severity				
		Negligible	Minor	Serious	Critical	Catastrophic
		1	2	3	4	5
Very high	5	5	10	15	20	25
High	4	4	8	12	16	20
Moderate	3	3	6	9	12	15
Low	2	2	4	6	8	10
Remote	1	1	2	3	4	5

ISO 14971 – Semi-quantitative Risk evaluation

Probability of Occurance		Severity				
		Negligible	Minor	Serious	Critical	Catastrophic
		1	2	3	4	5
Frequent	5	5	10	15	20	25
Probable	4	4	8	12	16	20
Occasional	3	3	6	9	12	15
Remote	2	2	4	6	8	10
Improbable	1	1	2	3	4	5

ISO 14971 - TABLE

Hazard	Hazard situation	Harm	Occurance	Severity	Ri (SxO)
					R1=…
					R2=…
					R3=…
					R4=…

ISO 14971 - RISK CONTROL

The manufacturer must apply the following principles in the following order:

- eliminate or reduce risks as far as possible (inherently safe design and construction),
- where appropriate take adequate protection measures including alarms if necessary, in relation to risks that cannot be eliminated,
- inform users of the residual risks due to any shortcomings of the protection measures adopted.

Identification of Risk control measures

Used to reduce risk (either occurrence or severity or both)

Risk control methods, in the preferred order of:

- Safe design
- Alarms and protections
- Advertences and warnings

Implementation of RCM

Measure of RCM impact on lowering the Occurrence and/or Severity of any harm

In the design

- Inherent design for safety – Design of protection measures

In the manufacturing or quality control

- Process control
- Additional/ dedicated testing

In the final user training

EXAMPLE OF RMC

Product/ process	Example devices	Hazard	Inherent safe design	Protective measure	Information for safety
Single use medical device	Catheter	Bio-(cross)-contamination	Self-destruction after use	Obvious indication after first use	Warning against re-use and of the adverse consequence(s) that could arise from any such re-use
Active implant	Pacemaker	Electric fields	Use of non-electric drives and controls	Use of differential amplifiers and additional filter algorithms	Warning for commonly encountered hazardous situations
IVD medical device	Blood analyser	Incorrect result due to method bias	Implement traceable calibrators	Provide traceable trueness controls	Inform users of unacceptable deviation from assigned values
Software	Patient data management	Erroneous data	High integrity software	Use of checksums	Warnings on screen for user
Steam sterilization	Biopsy device, operation forceps	High temperature (material degradation)	Use of material that is compatible with high temperatures	Pressure and temperature monitoring and recording	Packaging and loading instructions

Figure D.6 — Some examples of risk control measures

EXAMPLE OF RMC INDEX TABLE

RCM Index R	Description	Index
Negligible	Design: no control during design; harm not detected during manufacturing steps Alarms and protections: not activated; harm not detectable during a routine check Warning: no warnings foreseen in label	1
Very low	Design: no control during design; harm may be detected by a 100% control Alarms and protections: not activated; harm is detectable during a routine check Warning: no warnings foreseen in label	0.8
Low	Design: no control during design; harm easily detected by a 100% control Alarms and protections: not activated; harm is surely detected during a routine check Warning: general warning foreseen in label	0.6
Normal	Design: QC test designed for harm detection at manufacturing steps; or characteristic is rendered less risky during design; harm may be detected by a sampling plan control Alarms and protections: activated after a certain amount of time Warning: normed warnings and symbols foreseen in label	0.4
High	Design: characteristic is rendered safe at design step (design solution or process validaton) Alarms and protections: activated immediately Warning: detailed, evident warnings and symbols foreseen in label	0.2

RISK AFTER RCM

Measures level of risk after the RCM is implemented and verified

$$Riafter=RixR$$

Keep same levels for acceptability, for easiness of use (RCM Index is a fraction when effective)

If risk is higher,

- new RCM may be required and/or
- the RCM under evaluation may be discarded as not feasible

FINAL TABLE

Hazard	Hazard situation	Harm	Occurance	Severity	Ri (SxO)	RMC	RMC index	Ri after
					R1=…			
					R2=…			
					R3=…			
					R4=…			

ISO 14971 - Overall evaluation and risk approval

- Set acceptable percentage of yellow risk in the analysis
- NO red risk should be accepted before the overall risk-benefit evaluation

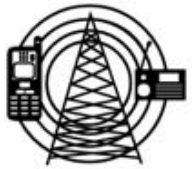
Benefit evaluation

- As compared to state of the art
- As per intended use and expected results
- As compared to the patient clinical state, life expectancy, quality of life
- Usually is difficult to express in quantitative terms, relative to many factors

INFUSION PUMP EXAMPLE

Hazard	Foreseeable Sequence of Events	Hazard situation	Harm	O	S	Ri
Elettromagnetic energy (ESD)	Electrostatically charged patient touches infusion pump	Failure to deliver insulin unknown to patient with elevated blood glucose level	Minor organ damage	2	2	R1=4
	ESD causes pump and pump alarms to fail		Decreased consciousness	3	4	R2=12
	Insulin not delivered to patient		Coma, death	5	5	R3=25

INFORMATION FOR SAFETY



Questa pompa è protetta contro gli effetti derivanti dalle interferenze esterne, comprese le emissioni in radiofrequenza ad alta energia, i campi magnetici e le scariche elettrostatiche (ad esempio quelle generate da apparecchiature elettrochirurgiche e di cauterizzazione, motori di grandi dimensioni, radio portatili, telefoni cellulari, e così via) ed è progettata per garantire la sicurezza in presenza di livelli eccessivi di interferenza.

In alcuni casi la pompa può essere esposta a scariche elettrostatiche pari o superiori a 15 kv o a radiazioni in radiofrequenza pari o superiori a 10 v/m. Se esposta a queste interferenze esterne, la pompa imposta la modalità di sicurezza, arresta prontamente l'infusione e avverte l'utente con una serie di allarmi visivi e acustici. Se la condizione di allarme persiste anche dopo l'intervento dell'utente, è consigliabile sostituire la pompa e isolarla in modo che possa essere ispezionata da personale tecnico qualificato. Per ulteriori informazioni, consultare il manuale tecnico di servizio.

Non aprire la copertura di protezione dell'interfaccia RS232/Chiamata Infermiere quando non è in uso. Adottare tutte le misure necessarie per prevenire le scariche elettrostatiche al momento del collegamento dell'interfaccia RS232/Chiamata Infermiere. Il contatto con i pin dei connettori può rendere nulla la protezione contro le scariche elettrostatiche. È consigliabile far eseguire tutte le operazioni da personale debitamente qualificato.

INFUSION PUMP EXAMPLE

Hazard	Foreseeable Sequence of Events	Hazard situation	Harm	O	S	Ri	RMC	RMC index	Rafter
Elettromagnetic energy (ESD)	Electrostatically charged patient touches infusion pump	Failure to deliver insulin unknown to patient with elevated blood glucose level	Minor organ damage	2	2	R1=4	Information for safety – Electrostatic discharge alarms and warnings	0.2	0.4
	ESD causes pump and pump alarms to fail		Decreased consciousness	3	4	R2=12			2,4
	Insulin not delivered to patient		Coma, death	3	5	R3=15			5

Hazards for infusion Pump

Hazardous or potentially harmful situations for the generic infusion pump can be classified under the following categories

1. Operational Hazards
2. Environmental Hazards
3. Electrical Hazards
4. Hardware Hazards
5. Software Hazards
6. Mechanical Hazards (Physical Hazards)
7. Biological and Chemical Hazards
8. Use Hazards

Hazards for infusion Pump

Hazardous or potentially harmful situations for the generic infusion pump can be classified under the following categories

1. Operational Hazards
    1. Overinfusion - Programmed flow rate too high
    2. Underinfusion - Programmed flow rate too low
2. Environmental Hazards
    1. Failure to operate/ Pump malfunction - Temperature /Humidity/ Air pressure too high or too low
    2. Failure to attend alarm - Background noise (may cause alarms not being heard by medic)
3. Electrical Hazards
    1. Charge Error - Battery could not be charged
    2. Electric shock - Leakage Current too high (pump could be source of electric shock)
4. Hardware Hazards
    1. Failure alarm - Sensor failure

Hazards for infusion Pump

5. Software Hazards
    1. Incorrect version - Software updates not installed; Incorrect version installed
6. Mechanical Hazards (Physical Hazards)
    1. Injury to medic/patient - Sharp edges
7. Biological and Chemical Hazards
    1. Biological / Chemical Hazard - Device contaminated during use; Device contaminated by blood- /leaking fluid
8. Use Hazards
    1. Incorrect dose settings - Key pressed too long

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