ECRIN
EUROPEAN CLINICAL RESEARCH INFRASTRUCTURE NETWORK

Regulatory and ethical requirements in medical devices studies

Italy

SECTIONS

A.Type of research

B. Definitions/Legal basis

C. Insurance

D. Sponsor

E. Investigators

F. Competent Authority

G. Ethics Committee

H. Data Protection

I. Healthy volunteers/Patients

J. Specific requirements

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A. Type of research

We have differentiated 8 types of research:

- Medical device alone with CE mark use within label
- Medical device alone with CE mark use outside label
- Medical device alone without CE mark
- Medical device combined with medicinal product with CE mark use within label
- Medical device combined with medicinal product with CE mark use outside label
- Medical device combined with medicinal product without CE mark
- Observational studies with medical device
- Registries

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Definitions in Italian law

• Except for « Registries»,for which there is no Italian definition, the other type of research are define in legislative decrees 46/97 and 507/92 modified by legislative decree 37/10 and 332/2000.

B. Definitions/Legal basis

Conventions/guideline/laws to apply

- Declaration of Helsinki
- ISO 14155:2011
- European Directive 2011/20/EC ***(Except for studies with MD alone and observational studies)***
- Ministerial Decree 2, 2005. Official Journal n°210 September 9, 2005 ***(Only for studies with MD alone)***
- Legislative Decree December 14, 1992, n°507 ***(Only for studies with MD alone)***
- Legislative Decree February 24, 1997, n°46 ***(Only for studies with MD alone)***
- Legislative Decree, 2000, n°332 ***(Only for studies on in vitro diagnostic MD)***
- Legislative Decree, 2010, n°37

B. Definitions/Legal basis

Acts to apply

- Data protection act

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C. Insurance

- For all the type of studies in exception of registries and observational study, an insurance must be contracted. It has to cover:
  - Patients and /or healthy volunteers
- The information need for an insurance for sponsors, Investigators and manufacturers is not known
- There need to be a compensation sum coverage per paticipant for the following type of study:
  - Medical device alone with CE mark use outside label
  - Medical device alone without CE mark
  - Medical device combined with medicinal product with CE mark use outside label
  - Medical device combined with medicinal product without CE mark

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D. Sponsor

- It is mandatory to have a sponsor for all type of study except the registries
- Co-sponsorship is not allowed

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E. Investigators

- No Italian specific requirements/regulations for GCP training of the investigators

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F. Competent Authority

Italian Competent Authority:

Ministero della Salute

Direzione Generale dei dispositive medici Offico
VI sperimenzione clinica dei dispositive medici
Vialle Giorgio Ribotta, 5
00144 Roma
+39 0659942525
a.parisi@sanita.it

F. Competent Authority

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	Approval	
	Yes	No
Medical device alone with CE mark use within label		X
Medical device alone with CE mark use outside label	X	
Medical device alone without CE mark	X	
Medical device combined with medicinal product with CE mark use within label		X
Medical device combined with medicinal product with CE mark use outside label	X	
Medical device combined with medicinal product without CE mark	X	
Observational studies with medical device		X

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	Registration	
	Yes	No
Medical device alone with CE mark use within label	X	
Medical device alone with CE mark use outside label	X	
Medical device alone without CE mark	X	
Medical device combined with medicinal product with CE mark use within label	X	
Medical device combined with medicinal product with CE mark use outside label	X	
Medical device combined with medicinal product without CE mark	X	
Observational studies with medical device	X	

F. Competent Authority – Initial submission

• When a submission is required, the sponsor or his authorized representative are reponsible for it

• The submission to the Italian Competent Authority is national: you only have to submit one dossier to the national competent authority

• The submission have to be:

- by paper

- or by email (dgfdm@postacert.sanita.it)or CD-Rom

• English documents are accepted

• The submission fee cost 2 160,45 € for study without medicinal product

F. Competent Authority – Initial submission

- In general, 60 days maximum to obtain approval
- Implicit approval after 60 days without questions with EC favourable opinion
- No deadlines for submission, you can submit anytime

F. Competant Authority – Initial submission

Main documents required for submission:

- Submission letter
- Clinical Trial application form
- Clinical Investigation Plan/Protocol signed
- Clinical Investigation Plan/Protocol summary
- Informed consent form
- Subject Information leaflet
- Investigator’s brochure or CE certificate
- Instruction for use/Technical manual
- Performance evaluation
- Pre-clinical evaluation
- Product training of Investigators
- Proof of payment of submission fees

F. Competent Authority – Initial submission

• Standard application form available on the Ministero della Salute's website:

Carta intestata della Società

Ministero della Salute
Direzione Generale dei dispositivi medici,
del servizio farmaceutico e della sicurezza delle cure
Ufficio VI-Sperimentazione clinica dei dispositivi medici
Viale Giorgio Ribotta, 5
00144 Roma

Oggetto: **IC-PREM** - Notifica di indagine clinica.

- ☐ Indagine clinica con dispositivo medico di classe III, dispositivo impiantabile o invasivo a lungo termine appartenente alla classe IIa o IIb (D. Lgs. 46/97 s.m.i.)
- ☐ Indagine clinica con dispositivo medico di classe I, dispositivo medico di classe IIa o IIb non impiantabile né invasivo a lungo termine (D. Lgs. 46/97 s.m.i.)
- ☐ Indagine clinica con dispositivo medico impiantabile attivo (D. Lgs. 507/92 s.m.i.)[1]

Si trasmette la notifica di indagine clinica del dispositivo medico di seguito indicato, come previsto dall'art.1 del D.M. 2/8/05 e dalla circolare 2 agosto 2011.

1) Denominazione ed indirizzo del fabbricante [2]:
.....
Nome e cognome del legale rappresentante
.....

2) Denominazione ed indirizzo del mandatario [3] (in caso di fabbricante extra Unione Europea):

F. Competent Authority - Vigilance

- SAE definition:

Adverse event that

- led to a death,
- led to a serious deterioration in health that either:
  - resulted in a life-threatening illness or injury,
  - resulted in a permanent impairment of a body structure or a body function
  - required in-patient hospitalization or prolongation of existing hospitalization,
  - resulted in medical or surgical intervention to prevent life threatening illness or injury or permanent impairment to a body structure or a body function
- led to fetal distress, fetal death or a congenital abnormality or birth defect.

F. Competent Authority - Vigilance

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• The Sponsor is responsible for the declaration to the Competent Autority.

• There is no deadline for the declaration

•There declaration should be done using the reporting form-Meddev 2.7/3

•The sponsor don’t have to declare events to the Competent Authorities in the specific countries

• The annual safety is not required but the CA could require it for device without CE mark or used off-label

F. Competent Authority - Vigilance

Events mandatory to declare to the Competent Authority:

	AE	ADE	SADE	SAE
Medical device alone with CE mark use within label		X	X	X
Medical device alone with CE mark use outside label			X	X
Medical device alone without CE mark			X	X
Medical device combined with medicinal product with CE mark use within label		X	X	X
Medical device combined with medicinal product with CE mark use outside label			X	X
Medical device combined with medicinal product without CE mark			X	X
Observational studies with medical device		X	X	X

AE: Adverse Event (Non device related)
ADE: Adverse Device Effect (Device or procedure related)
SADE: Serious adverse Device Effect (Device or procedure related)
SAE: Serious Adverse Event (Non device related)

F. Competent Authority - Notification

- It is mandatory to notify the first patient enrolled to the Competent Authority

F. Competent Authority – Substantial amendment

• There is no specific procedure for submitting a substantial amendment to the Competent Authority

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G. Ethics Committee

- The Italian Ethic committees are locals
- There are 84 certified EC, the list is available at the following address : http://www.comitatietici.it/elenco/

G. Ethics Committee

	Positive opinion required	
	Yes	**No**
Medical device alone with CE mark use within label	x	
Medical device alone with CE mark use outside label	x	
Medical device alone without CE mark	x	
Medical device combined with medicinal product with CE mark use within label	x	
Medical device combined with medicinal product with CE mark use outside label	x	
Medical device combined with medicinal product without CE mark	x	
Observational studies with medical device	x	

G. Ethics Committee – Initial submission

• When a submission is required, the sponsor is responsible of it

• The submission to the Ethics Committee is local (to all reference ECs of the participating clinial sites)

• The submission have to be by paper and in italian

•A submission fee have to be paid (between 2000 and 4000 €)

G. Ethics Committee – Initial submission

- No implicit approval
- No deadlines for submissions
- When both Competent Authority approval and Ethics Committee positive opinion are required, it is possible to request the 2 (authorization and approval) in parallel
- There needs to be some kind of representative or a legal entity in Italy to submit an application to the Competent Authority or Ethics Committee if you are from the EU
- A standard application form have to be used

G. Ethics Committee – Initial submission

Main documents required for submission:

Submission letter

- Clinical Trial application form
- Clinical Investigation Plan/Protocol signed
- Clinical Investigation Plan/Protocol summary
- Inform Consent Form and subject Information leaflet
- CV of PIs
- Insurance certificate
- Proof of payment of submission fees

G. Ethics Committee - Vigilance

- There is no deadline for the declaration of an AE to the ethic committee

- The sponsor don’t have to declare events to the Ethics Committee in the specific countries

G. Ethics Committee - Vigilance

Events mandatory to declare to the competent authority:

	AE	ADE	SADE	SAE
Medical device alone with CE mark use within label			x	x
Medical device alone with CE mark use outside label			x	x
Medical device alone without CE mark			x	x
Medical device combined with medicinal product with CE mark use within label			x	x
Medical device combined with medicinal product with CE mark use outside label			x	x
Medical device combined with medicinal product without CE mark			x	x
Observational studies with medical device				

AE: Adverse Event (Non device related)
ADE: Adverse Device Effect (Device or procedure related)
SADE: Serious adverse Device Effect (Device or procedure related)
SAE: Serious Adverse Event (Non device related)

G. Ethics Committee - Vigilance

- The sponsor is responsible for the declaration to the Ethics Committee
- No special form for the declaration of AE,

G. Ethics Committee - Notification

G. Ethics Committee – Substantial amendment

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H. Data Protection

Italian Data Protection:

Garante per la protezione dei dati personali
Piazza di Monte Citorio,
121 – 00186 Roma
Phone: +39 06 6967 71;
Fax: +39 06 6967 73785 ;
email: rp@gpdp.it

H. Data Protection

	Notification required	
	Yes	No
Medical device alone with CE mark use within label		
Medical device alone with CE mark use outside label		
Medical device alone without CE mark		
Medical device combined with medicinal product with CE mark use within label		
Medical device combined with medicinal product with CE mark use outside label		
Medical device combined with medicinal product without CE mark		
Observational studies with medical device		

H. Data Protection

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I. Healthy volunteers/Patients

• No specific requirements/regulations for specific population

• No specific requirements regarding compensation fees for subjects

•No national registry for Healthy volunteer

•No obligation to inform the subject of the outcome of the study

I. Healthy volunteers/Patients

• Healthy volunteers participating in clinical research have to be compensated (not mandatory for patients, but possible)

• National healthy volunteers registry: VRB

• Obligation to inform the healthy volunteers/patients on the outcomes of the study if she/he asks

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J. Specific requirements

J. Specific requirements

- No specific requirements for data management
- No specific strategies for monitoring
- Accreditation process for research centres