ECRIN
EUROPEAN CLINICAL RESEARCH INFRASTRUCTURES NETWORK
IA-Integrating Activity

Regulatory and ethical requirements in medical devices studies

Serbia

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

SECTIONS

A.Type of research

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C. Insurance

D. Sponsor

E. Investigators

F. Competent Authority

G. Ethics Committee

H. Data Protection

I. Healthy volunteers/Patients

J. Specific requirements

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

SECTIONS

A.Type of research

B. Definitions/Legal basis

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F. Competent Authority

G. Ethics Committee

H. Data Protection

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J. Specific requirements

B. Definitions/Legal basis

Definitions in Serbian law

• The 8 types of research with medical device are define in Serbia.

• The definitions can be found at the following adress:

http://www.alims.gov.rs/eng/medical-devices/clinical-trials/

B. Definitions/Legal basis

Conventions/guideline/laws to apply

- Declaration of Helsinki
- ICH Guideline of EMA
- European Directive 2001/20/EC

B. Definitions/Legal basis

Acts to apply

- Hospital act
- Data protection act
- Genetical engineering act
- Medical device act
- Drug Act

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

C. Insurance

• For all the type of studies an insurance must be contracted. It has to cover:

- Patients ***(Except for observational studies)***

- Healthy volunteers

- Investigators ***(Except for observational studies)***

The sum covered by the Insurance depends on the contract

There is no compensation sums per participant and/or per trial covered by the insurance

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

D. Sponsor

It is mandatory to have a sponsor or legal representative in Serbia for any of the 8 types of studies

Co-sponsorship is allowed for all the study types

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

E. Investigators

• In Serbia, to participate in a trial investigator are required to have a certificate from the Section for Clinical pharmacology Serbian Medical Society (SCPSMS) accredited by Serbian Medical Chamber for Continuous Medical Education: Good Clinical Practice in clinical investigation

• The Investigator have to be a a doctor of medicine or doctor of dentistry and have to be directly involved and responsible for the treatment and care for patients or participants in the trial

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

F. Competent Authority

Serbian Competent Authority:

Medicines and Medical Devices Agency of Serbia
Zorica Vucinic, MD and Aleksandra Vujacic,pharm
458, Vojvode Stepe Street
Belgrade 11221
Republic of Serbia
Tel.: +381 11 3951-158; +381 11 3951-199
Fax +381 11 3951-158
hygia@alims.gov.rs

F. Competent Authority

A. Type of research
B. Definitions/Legal basis
C. Insurance
D. Sponsor
E. Investigators
F. Competent Authority
G. Ethics Committee
H. Data Ptotection
I. Healthy volunteers/Patients
J. Specific requirements

	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	
Registries	x	

F. Competent Authority – Initial submission

- When a submission is required, the sponsor, the PI or the academic institution is responsible of it
- The submission to the Serbian Competent Authority is national: you only have to submit one dossier to the national competent authority
- The submission have to be by paper
- English documents are accepted
- A submission fee have to be paid
  - 200 € for phase I to III study
  - 60 € for phase IV study

F. Competent Authority – Initial submission

- In general, it take 60 days after the submission to obtain approval
- No deadlines for submission, you can submit anytime
- You need to have some kind of representative or a legal entity in Serbia to submit an application to the Competent Authority. It can be:
  - CRO
  - Sponsor
  - PI
  - Academia (for ECRIN it is SMS)

F. Competant Authority – Initial submission

Main documents required for submission (1/2):

- Submission letter
- Clinical Trial application form
- Clinical Investigation Plan/Protocol signed
- Clinical Investigation Plan/Protocol summary
- CRF draft
- Inform consent form and subject information leaflet
- General practitioner information letter
- Copies of advertisement materials for research participants
- Investigator’s brochure or CE certificate
- Instruction for use/Technical manual
- Performance evaluation

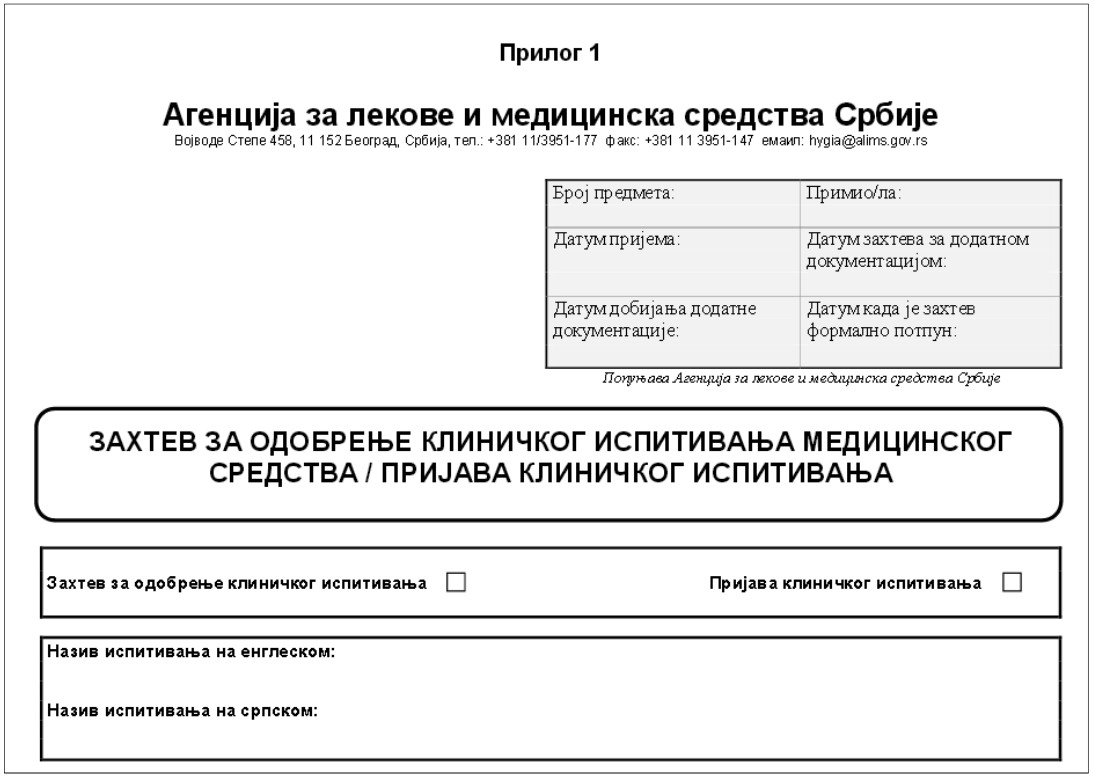
F. Competant Authority – Initial submission

Main documents required for submission (2/2):

- Insurance Certificate
- Signed and dated CV of investigators
- Investigator agreement
- GCP training certificate of investigators
- Product training of investigators
- Qualification certificate of investigators
- Conflict of interest statement from the investigator
- Financial disclosure
- Study approval from administration department
- Agreement between sponsor and CRO specifying responsibilities
- Proof of payment of submission fees

F. Competent Authority – Initial submission

• Standard application form available on the Serbian Competent authority website:



Прилог 1

Агенција за лекове и медицинска средства Србије

Војводе Степе 458, 11 152 Београд, Србија, тел.: +381 11/3951-177 факс: +381 11 3951-147 емаил: hygia@alims.gov.rs

Број предмета:	Примио/ла:
Датум пријема:	Датум захтева за додатном документацијом:
Датум добијања додатне документације:	Датум када је захтев формално потпун:

Попуњава Агенција за лекове и медицинска средства Србије

ЗАХТЕВ ЗА ОДОБРЕЊЕ КЛИНИЧКОГ ИСПИТИВАЊА МЕДИЦИНСКОГ СРЕДСТВА / ПРИЈАВА КЛИНИЧКОГ ИСПИТИВАЊА

Захтев за одобрење клиничког испитивања ☐ **Пријава клиничког испитивања** ☐

Назив испитивања на енглеском:

Назив испитивања на српском:

F. Competent Authority - Vigilance

• SAE definition:
Serious adverse event is every adverse event having a consequence:

- Death
- Life vulnerability
- Permanently or serious damage/disability,
- Hospital treatment or prolonged present hospital treatment
- Congenital anomalies or baby defect detected after birth
- Other medical significant state

• SADE (Serious adverse Device Effect) declaration by the sponsor:

- If life in danger: 7 days
- Other case: 15 days

• The sponsor has to declare events to the Competent Authorities in the specific countries

• The sponsor needs to provide to the Competent Authority an annual safety report

F. Competent Authority - Vigilance

A. Type of research
B. Definitions/Legal basis
C. Insurance
D. Sponsor
E. Investigators
F. Competent Authority
G. Ethics Committee
H. Data Ptotection
I. Healthy volunteers/Patients
J. Specific requirements

Events mandatory to declare to the Competent Authority:

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

• The sponsor, PI or Academic institution are responsible for the declaration to the Competent Authority

• Special form for the declaration of AE available at the following address

http://www.alims.gov.rs/ciril/prijava-nezeljene-reakcije-na-medicinsko-sredstvo/

F. Competent Authority - Notification

- No specific requirement to notify the first patient enrolled to the Competent Authority

F. Competent Authority – Substantial amendment

• There is a specific procedure for submitting a substantial amendment to the Competent Authority

(Submission is done by the Ethic Committee)

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

G. Ethics Committee

In Serbia, Each Hospital have an Ethic Committee

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	
Registries	x	

G. Ethics Committee – Initial submission

- When a submission is required, the sponsor, PI or Academic Institution are responsible of it
- The submission to the Ethics Committee is local (submission to the EC of each site involved)
- The submission have to be by paper or electronic format (depending on the EC)
- English documents are accepted
- There is a submission fee (depend on the EC)

G. Ethics Committee – Initial submission

- In general, 60 days maximum to obtain approval
- No deadlines for submission, you can submit anytime
- When both Competent Authority approval and Ethics Committee positive opinion are required, it is not possible to request the 2 (authorization and approval) in parallel
- You need to have some kind of representative or a legal entity in Serbia to submit an application to the Competent Authority. It can be:
  - CRO
  - Sponsor
  - PI
  - Academia (for ECRIN it is SMS)

G. Ethics Committee – Initial submission

Main documents required for submission (1/2):

- Submission letter
- Clinical Trial application form
- Clinical Investigation Plan/Protocol signed
- Clinical Investigation Plan/Protocol summary
- CRF draft
- Inform consent form and subject information leaflet
- General practitioner information letter
- Copies of advertisement materials for research participants
- Investigator’s brochure or CE certificate
- Instruction for use/Technical manual
- Performance evaluation

G. Ethics Committee – Initial submission

Main documents required for submission (2/2):

- Insurance Certificate
- Signed and dated CV of investigators
- Investigator agreement
- GCP training certificate of investigators
- Product training of investigators
- Qualification certificate of investigators
- Conflict of interest statement from the investigator
- Financial disclosure
- Study approval from administration department
- Agreement between sponsor and CRO specifying responsibilities
- Proof of payment of submission fees

G. Ethics committee – Initial submission

- Use the same standard application form that for the Competent Authority
- Standard application form available on:

http://www.alims.gov.rs/ciril/prijava-nezeljene-reakcije-na-medicinsko-sredstvo/

G. Ethics Committee - Vigilance

- SAE declaration by the sponsor:
  - If life in danger: 7 days
  - Other case: 15 days

- The sponsor also has to declare events to the Ethics Committee in the specific countries

- The sponsor don’t needs to provide to the Ethics Committee an annual safety report

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

G. Ethics Committee - Vigilance

- The sponsor, PI or Academic institution are responsible for the declaration to the Ethics Committee
- Special form for the declaration of AE available at the following address

http://www.alims.gov.rs/ciril/prijava-nezeljene-reakcije-na-medicinsko-sredstvo/

G. Ethics Committee - Notification

- There is no specific requirement to notify the first patient enrolled to the Ethics Committee

G. Ethics Committee – Substantial amendment

• There is a specific procedure for submitting a substantial amendment to the Ethics Committee

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

H. Data Protection

Serbian Data Protection:

Commissioner for Information of Public Importance and Personal Data Protection

(in serbian: Poverenik za informacije od javnog značaja i zaštitu podataka o ličnosti)

15, Bulevar kralja Aleksandra str, Belgrade 11000

Tel: +381 11 3408 900

Fax: +381 11 3343 379

office@poverenik.rs

H. Data Protection

	Notification 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	
Registries	x	

• A confidentiality agreement have to be signed between Sponsor and Investigators

H. Data Protection

- English accepted for submission
- Submission fee

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

I. Healthy volunteers/Patients

• In Serbia, there are specific requirements/regulations for specific population:

- Children
- Elderly
- Pregnant women
- Lactating women
- Prisoners and psychiatric patients

I. Healthy volunteers/Patients

• No specific requirements regarding compensation fees for subjects (patients or healthy volunteers) participating in a clinical research

• No national healthy volunteer registry

• Obligation to inform the healthy volunteers/patients on the outcomes of the study

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A.Type of research

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J. Specific requirements

• For sponsored studies it is mandatory to have sponsor permition to publish study results in scientific journal.

• Specific requirements/regulations regarding devices emitting radiation: **medical device class III are regulated by Serbian Law for drugs and medical devices**

•Specific requirements/regulations regarding the ICF: **needs to be written in Serbian**

• Specific requirements/regulations regarding archiving of documentation: **5 years**

• Specific requirements regarding blood/tissue samples (circulation and storage) : **regulated by ministry of science**.

J. Specific requirements

• Specific requirements for data management: have to be done in accordance to GCP

• Specific strategies for monitoring

• Mandatory to register clinical studies in a registry managed by the Competent Authority

• Accreditation process for research centres by Ministry of science