OPERATING PROCEDURES OF THE NATIONAL COMMITTEE ON MEDICAL RESEARCH ETHICS (clinical trials on medicinal products under the EU Clinical Trial Regulation 536/2014 and the biobank activities)

1. Legal framework of Tukija's operations

Act on Clinical Trials on Medicinal Products (983/2021)
Medical Research Act (488/1999, as amended 295/2004, 794/2010, 143/2015 and 984/2021)
Biobank Act (688/2012)
Government Decree on the Biobank Consent Document (643/2013)
Decree of the Ministry of Social Affairs and Health on Biobank Notifications (649/2013)
Act on the Medical Use of Human Organs and Tissues (101/2001)
Medical Devices Act (719/2021)
Act on Certain Medical Devices Specified in EU Directives (629/2010)
Decree of the Ministry of Social Affairs and Health on Fees Charged Regarding Clinical Trials on Medicinal Products (103/2022)
Decree of the Ministry of Social Affairs and Health on Fees Charged for Statements of Regional Ethics Committees and of the National Committee on Medical Research Ethics (1171/2020)
Finnish Medicines Agency Fimea's Administrative Regulation (1/2022): Clinical Studies on Medical Devices

Regulation (EU) No 536/2014 of the European Parliament and of the Council of 16 April 2014, on Clinical Trials on Medicinal Products for Human Use, and Repealing Directive 2001/20/EC (Clinical Trials Regulation)
Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on Medical Devices, Amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC)
No 1223/2009 and Repealing Council Directives 90/385/EEC and 93/42/EEC (MD Regulation)
Regulation (EU) 2017/746 of the European Parliament and of the Council of 5 April 2017 on in Vitro Diagnostic Medical Devices and Repealing Directive 98/79/EC and Commission Decision 2010/227/EU (IVD Regulation)

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The formation of Tukija and the expertise of its members are stated in the Government Decision of appointment (27 January 2022, STM/2022/21).

1.1 Meeting schedule

The Committee shall meet regularly, at least every other week. The meeting timetable shall be published on the Tukija website.

There are timelines for assessing an application for clinical trials submitted through the EU portal (Clinical Trials Information System, CTIS), determined in the Clinical Trials Regulation (536/2014). There are no due dates for these applications such that they would be dealt with at the meeting corresponding with the due date (cf. applications submitted under the Directive 2001/20/EC during the transition period).

2. Duties of Tukija

The duties of Tukija are specified by law. Its duties are:

- to issue opinions on clinical trials on medicinal products for human use and on modifications thereto (including combined pharmaceutical and medical device trials and clinical trials using biobank samples);
- to issue opinion on the establishment of and modifications to a biobank;
- to issue opinion on the medical use of human organs, tissues and cells when the aim is to use them in clinical trials;
- to serve as an expert on research ethics in clinical trials on medicinal products, to collaborate with the authorities and to promote public debate on clinical trials.

Tukija is thus responsible for the ethical assessment of clinical trials on medicinal products. Between 31 January 2022 and 31 January 2023, sponsors of clinical trials may choose whether to submit their clinical trial applications in accordance with the procedure for submitting national applications under the Clinical Trials Directive (2001/20/EC) or through the CTIS under the Clinical Trials Regulation (536/2014).

As of 31 January 2023, all new clinical trials applications in the EU and in the EEA must be submitted through the CTIS under the Clinical Trials Regulation. As of 31 January 2025, clinical

trials approved under the Clinical Trials Directive which are still ongoing must begin to comply with the Clinical Trials Regulation, and they must be transferred to the CTIS.

The present operating procedures are valid to the procedure under the Regulation. The EU Clinical Trials Regulation distinguishes between ‘clinical study’, ‘clinical trial’ and ‘low-intervention clinical trial’.

In the case of applications for clinical trials under the Regulation that Fimea has rejected, the applicant may file a claim for a revised decision as per the Administrative Procedure Act (434/2003).

A decision issued on a claim for a revised decision may be appealed to an administrative court as per the Administrative Judicial Procedure Act (808/2019). Directions for appeal will be appended to the national permit decision.

The duties of Tukija also include issuing opinions on any plan to establish a biobank before that biobank is entered in the national biobank registered maintained by the Finnish Medicines Agency (Fimea).

3. Application for a clinical trial

3.1 Procedure under the Regulation

All applications for clinical trials under the Regulation must be submitted through the EU portal and database.

The system is a centralised repository for data on clinical trials. There is no need for a separate application for an opinion from Tukija, as Tukija will deal with the application in the portal. Any requests for information, responses to those requests and the national decision on a clinical trial shall be delivered via the portal. Sponsors of clinical trials who wish to obtain authorisation from the authorities for a clinical trial in one or more EU or EEA Member State shall only submit one application form and dossier of supporting material through the CTIS for each clinical trial. Submitting an application form and dossier of supporting material for authorisation of a clinical trial also causes the clinical trial to be publicly registered.

The application process and its timeline are laid out in the Clinical Trials Regulation. Part one of the application shall be reviewed by all the Member States concerned, coordinated by the Reporting Member State (RMS). Part two of any application involving Finland shall be reviewed nationally by Tukija and Fimea.

The documents to be included in the application are specified in Annex I of the Regulation; the mandatory attachments are also listed in the course of the application process in the CTIS. The European Commission has issued further instructions and form templates in respect of the documents specified in Annexes I and II. Further instructions on their use are provided on the Tukija website.

The national authorisation decision shall be made and directions for appeal issued by Fimea, and these shall be delivered to the sponsor through the portal.

A user must have an EMA account to use the CTIS. If the user already has an EMA account, for instance in the Eudravigilance database or the substances, products, organisations and referentials database (SPOR), then no new account need be created. Users that do not have an EMA account may register through the EMA account management service:
https://register.ema.europa.eu/identityiq/home.html

Organisations may have to go through further registration stages, depending on what level of user administration in the CTIS they select. The organisation-based approach allows a single administrator to handle user administration at the organisation level (instead of administration of an individual study). This is meant for organisations that frequently submit applications for clinical trials through the CTIS. Organisations that opt for the organisation-based approach shall register in the EMA Organisation Management System (OMS). They shall also register their senior administrator for the CTIS through EMA accounts management.

In Finland, the national contact point as referred to in the Clinical Trials Regulation is Fimea: clinicaltrials(at)fimea.fi

CTIS Handbook for Sponsors: https://www.ema.europa.eu/en/human-regulatory/research-development/clinical-trials/clinicaltrials-information-system-training-support#handbook-for-clinical-trial-sponsors-section

Further information on the Clinical Trials Regulation can be found in the publication Eudralex 10 – Clinical trials guidelines:
https://ec.europa.eu/health/documents/eudralex/vol-10_en

Further information on the CTIS can be found on the website of the European Medicines Agency:
https://www.ema.europa.eu/en/human-regulatory/research-development/clinical-trials/clinicaltrials-regulation

Questions about how the CTIS works can be submitted through the Service Desk of the European Medicines Agency.

3.2 Processing of applications at Tukija under the Regulation

Tukija members shall be provided with a meeting agenda, the relevant clinical trial application documents and other meeting documents no later than one week before the Tukija meeting.

Any and all communication with the sponsor regarding processing of the application shall be managed in the CTIS. Opinions or minutes of Committee meetings shall not be delivered to sponsors. Requests for information (RFI) shall be delivered to sponsors via the portal. Tukija opinions shall be delivered to Fimea, as per the Act on Clinical Trials on Medicinal Products. The national authorisation decision shall be made by Fimea. The national authorisation decision shall be made within 50 days of receiving the validation notification in the CTIS system. If Requests for Information are sent out regarding the application, then the original period shall be extended, but by no more than 31 days. The clock on the authorisation decision does not stop for the duration of delivering any responses to Requests for Information.

The period may be extended by 50 days in the case of an advanced therapy investigational medicinal product.

Tukija may also request a statement on the application from an outside expert specialist.

Note that the time periods for responding to Requests for Information (RFI) in both validation and review are also binding on the sponsor. If the time periods are not complied with, the application will lapse.

A fee shall be charged for trials or modifications thereto as per the Decree of the Ministry of Social Affairs and Health (103/2022). Further information on fee payment is available from Fimea.

3.3 Modifications to protocols under the Regulation

All applications for modifications to clinical trials under the Regulation must be submitted in the CTIS. There is no need for a separate application for an opinion from Tukija, as Tukija will deal with the application in the CTIS. Any requests for information, responses to those requests and the authorisation decision shall be delivered via the portal.

The time periods are specified in the Regulation. The national authorisation decision shall be made within 43 days of receiving the validation notification in the CTIS system. (If a substantial modification only applies to part II of the application, the authorisation decision shall be made within 38 days of the validation notification.) If Requests for Information are sent out regarding the application, then the original period shall be extended, but by no more than 31 days. The clock on the authorisation decision does not stop for the duration of delivering any responses to Requests for Information. The mandated attachments to a modification application are specified in Annex II of the Regulation, which lists the documents required for a substantial modification.

The national authorisation decision shall be made and directions for appeal issued by Fimea, and these shall be delivered through the portal. Note that the time periods for responding to Requests for Information (RFI) in both validation and review are also binding on the sponsor. If the time periods are not complied with, the application will lapse.

A fee shall be charged for trials or modifications thereto as per the Decree of the Ministry of Social Affairs and Health. Further information on fee payment is available from Fimea.

3.4 Transition of a clinical trial authorised under the Directive

If the sponsor considers that substantial modifications need to be done to the clinical trial to make it compliant with the Regulation and/or if the protocols of a clinical study employed in different countries are being harmonised to one protocol, these changes shall be made in the procedure specified in the Directive to Tukija. This is not dependent on which committee (TUKIJA/Tukija or a regional ethics committee) has given favourable opinion for the clinical trial. After receiving a favourable opinion on the modification, the clinical trial shall be entered in the EU portal as a new clinical trial, using the simplified authorisation procedure. (See the European Commission

harmonisation guidance for clinical trials: https://ec.europa.eu/health/system/files/2020-11/harmonisation_guidance_en_0.pdf)

A fee is charged for modification applications (Decree 1171/2020).

4. Applying for ethics reviews on the conditions for establishing a biobank

4.1 Establishing a biobank

A favorable opinion by Tukija is a precondition on the establishment of a biobank. Tukija must issue its opinion within 60 days of receiving a valid request for ethical evaluation. For its opinion, Tukija must determine whether the activities of the biobank meet the conditions concerning the protection of privacy and self-determination laid down in the Biobank Act and in other regulations and present a justifiable view on the ethics of the activities.

Applications submitted to Tukija must also include the following documents:

1. Signed cover letter;
2. Application form issued by TUKIJA;
3. Name or another identifier of the biobank;
4. Owner of the biobank, business name of the owner and main financiers of the biobank;
5. Locations and methods of storing the samples and information associated with them and an account of arranging the management of information in the registers;
6. Description of the biobank's area(s) of research, and an account of the principles and terms to be applied in the collection of samples, in granting access to the samples for the purposes of biobank research, and in processing of samples, and an account of the information associated with the samples, and of the restrictions concerning the use of the samples;
7. The informed consent form used, and an example of the written document to be presented when requesting consent, or information on the contents of the written document and a description on how this document will be presented;
8. An account of, whether the biobank stores samples and related information other than those based on consent;
9. An account of whether samples and related information other than those owned by the biobank will be stored in the biobank and, if necessary, information on the owner of the samples;

10. An operational plan that outlines the scale planned for the biobanking activities, the plan for organizing the activities and for the division of responsibilities;
11. Statement on the ethics of the activities of the biobank, especially the objectives and the planning of the biobank, as well as on the pre-evaluation of the risks and benefits of the biobank;
12. Statement on the realization of the protection of privacy and self-determination of the donors.

The signed application with attachments should be submitted using the online form on Tukija's website (www.tukija.fi). The form template is also available as a PDF document on the Tukija website; this may be filled in and sent to hakemukset[at]tukija.fi.

4.2 Changes in the information provided to the biobank register

Any substantial changes in the information provided to the national biobank register must be submitted to Tukija for an ethical evaluation. Finnish Medicines Agency Fimea shall estimate the need for ethical evaluation. As a rule, changes must be submitted to Tukija in case the changes relate to the information referred to in section 6 of the Biobank Act.

5. Fees

5.1 Clinical trials under the EU Regulation

The processing fee for applications submitted through the EU portal shall be collected by the Fimea in accordance with the Decree of the Ministry of Social Affairs and Health. Fimea shall collect fees according to the kind of processing at hand. Tukija shall not collect a separate fee. Fimea shall issue instructions in respect of collecting fees.

5.2 Applications for biobank establishment and modification of operations

Tukija shall collect the processing fee for applications for biobank establishment and modification of biobank operations in accordance with the Decree of the Ministry of Social Affairs and Health on fees charged for statements of Regional Ethics Committees and of the National Committee on Medical Research Ethics (1171/2020). The payment decision shall apply to all decisions that require consideration by and a statement from Tukija.

The statement application shall include the invoicing address and business ID of the company for the purposes of fee collection.

6. Contact information

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Further information: info(at)tukija.fi
Applications for opinions in respect of biobanks, notifications and responses to requests for information and to requests for rectification shall be submitted via electronic forms that are available on Tukija's website:
www.tukija.fi

Version history

Date	Modification
11.2.2022	First version in Finnish
5.4.2022	Ch. 3.4, Tukija's meeting frequency changed