Ethical review

Etikprövnings myndigheten

Gabriela Spulber
Scientific secretary Stockholm

Mathilda Wåhlander
Administrator EPM

Research ethics

- Ethical standards for the responsible conduct of research
- Regulated in both legislation and ethical guidelines

Main purposes of research ethics

- Protect the research subjects
- Safeguard and uphold the trust and confidence in research
- Help and support to researchers when in conflict of interest and other delicate assessments of risks and benefits

The tools of research ethics

- Informed consent
- Assessment of risk *vs.* benefit
- Choice of research subjects

Laws and regulations

- THE ACT CONCERNING THE ETHICAL REVIEW OF RESEARCH INVOLVING HUMANS
  Etikprövningslagen: Lag (2003:460) om etikprövning av forskning som avser människor

- THE REGULATION CONCERNING THE ETHICAL REVIEW OF RESEARCH INVOLVING HUMANS
  Etikprövningsförordningen: Förordning (2003:615) om etikprövning av forskning som avser människor

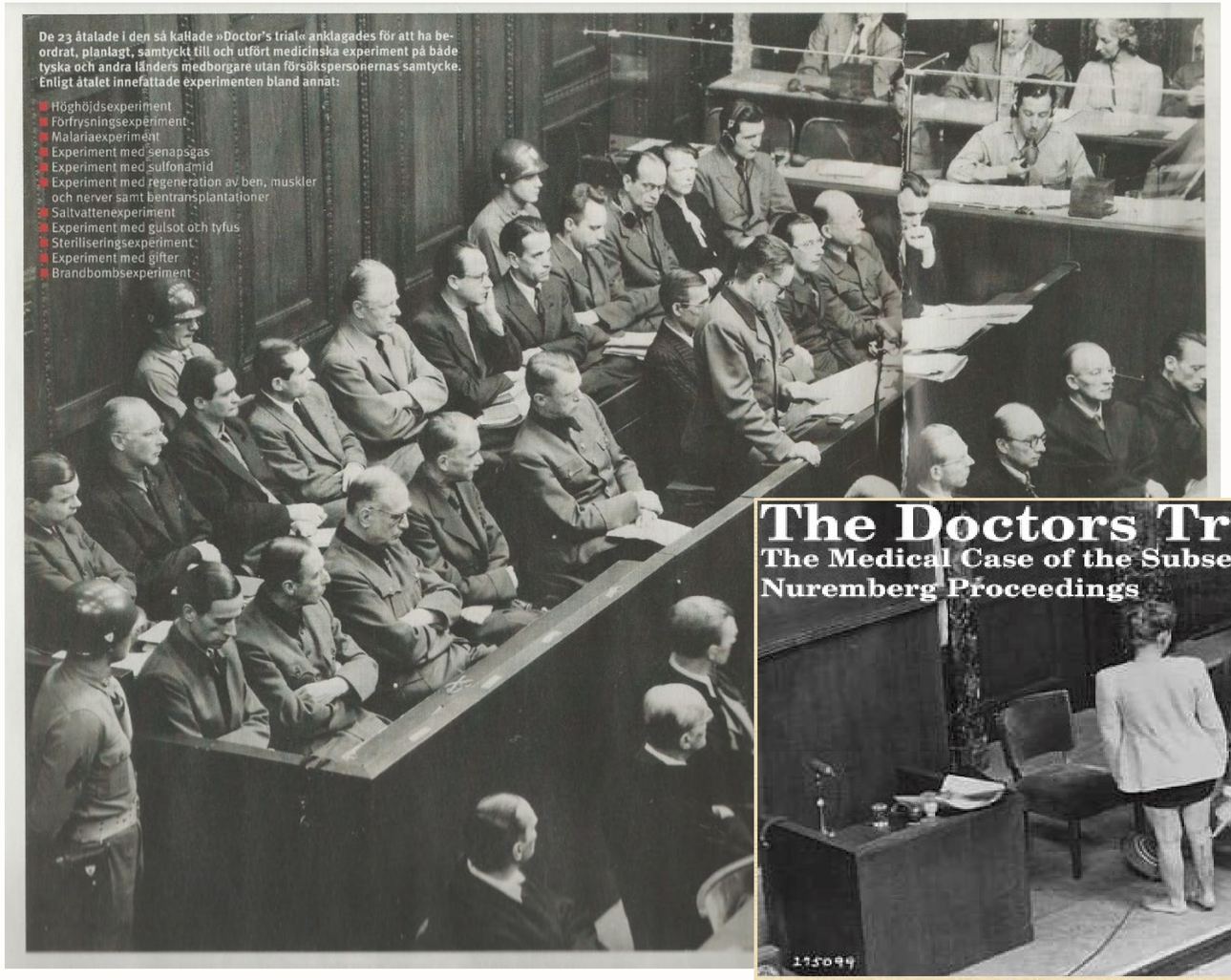
- EU Data Protection Regulation (GDPR)
  EU:s dataskyddsförordning

Laws and regulations

- Regulation (EU) 2017/745 on medical devices MDR (EU-förordning 2017/745 om medicintekniska produkter)
- Regulation (EU) 2017/746 on in vitro diagnostic for medical devices, IVDR (EU-förordning 2017/746 om medicintekniska produkter för in-vitro diagnostik)
- Regulation (EU) 536/2014 on clinical trials on medicinal products for human use, CTR (EU-förordning 536/2014 om kliniska prövningar av humanläkemedel)
- Biobanks in Medical Care Act (Biobankslagen)
- Autopsy Act (Obduktionslagen)
- Transplantation Act (Transplantionslagen)
- Medicinal Products Act (Läkemedelslagen)
- Radiation Protection Regulation (Strålskyddsförordningen)
- Public Access to Information and Secrecy Act (Offentlighets- och sekretesslagen)

Why the need for ethical review?

The Nuremberg Trials



During testimony at the Doctors Trial, American medical expert Dr. Leo Alexander points to scars on Jadwiga Dzido's leg. Dzido was a victim of medical experiments at the Ravensbrueck concentration camp. Nuremberg, Germany, December 22, 1946. NARA

Nuremberg Code 1947

- Informed consent
- The research should yield fruitful results for the good of society
- The degree of risk for the participants should be at a minimum
- Right for the human subject to bring the experiment to an end

Declaration of Helsinki

Adopted by the 18th WMA General Assembly, Helsinki, Finland, June 1964
Ethical Principles for Medical Reasearch Involving Human subjects

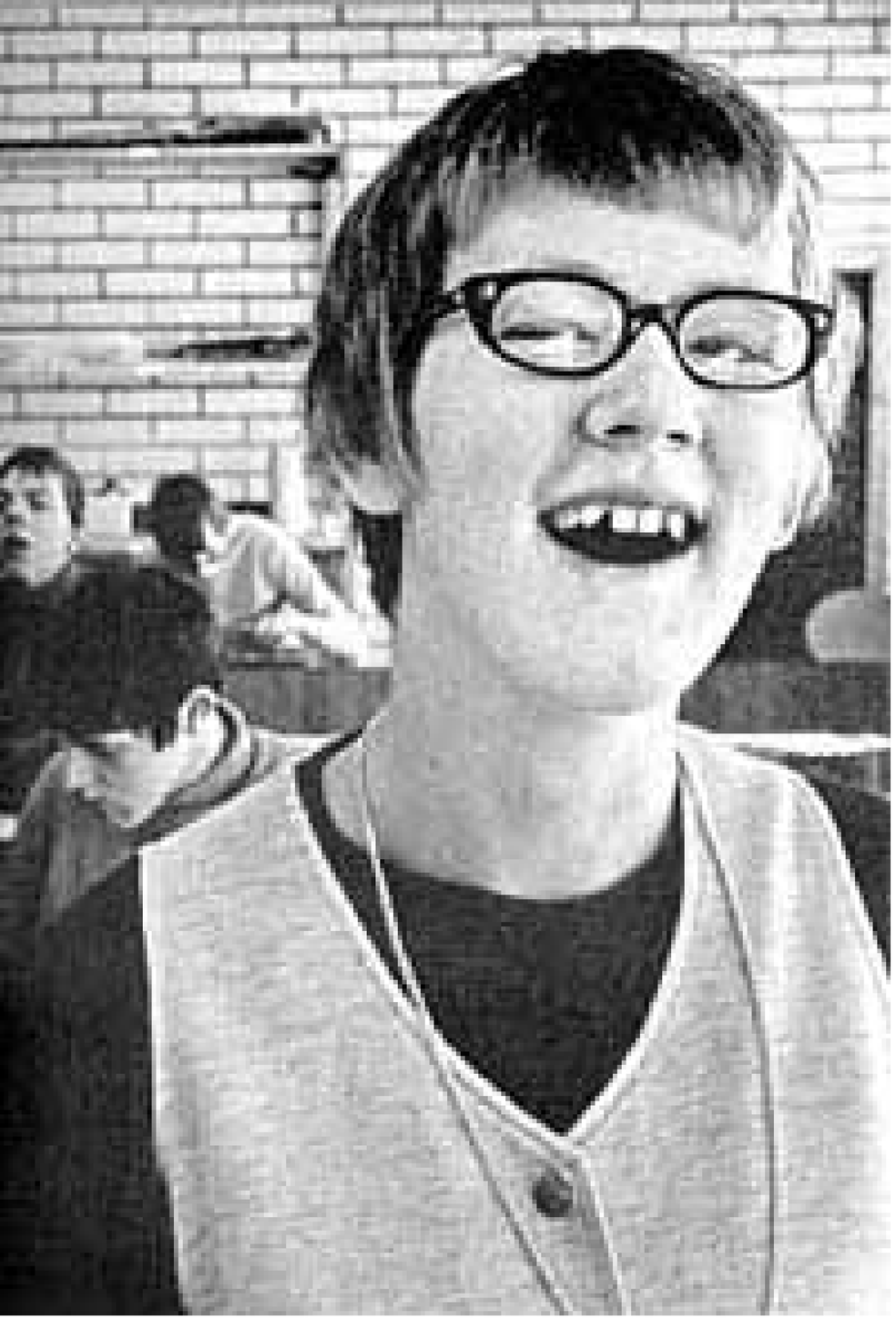
- The competence of the researcher
- Research must be based on careful assessment of risks and benefits
- Information to the research subjects
- The research subject's welfare must always take precedence over the interests of science and society
- The researcher's responsibility for using correct data and for its interpretation

The little Albert experiment by John B. Watson, the father of behaviorism 1920

..“On the whole he was balanced and passive.” “We had a sense that the experiments would cause him comparably little damage.”

When Albert was 8 months old Watson hit a hammer in an iron bar behind the child. “By the third hit the children had a screaming attack”. When Albert was 11 months old, Watson taught him to be afraid of a white rat by connecting the hammer hitting to the rat. Five days later Watson was able to prove that Albert was also afraid of a rabbit, a dog, a seal skin coat and of wadding, hair and a Santa Claus face mask.

When Watson published the results, he wrote that ”these reactions will probably remain forever, unless somenone by coincidence finds a method to eliminate them.”



The Vipeholm Study
1945-1955

- Research subjects: Intelectually disabled patients Vipeholm hospital Lund, Sweden.
- Aim: Use of a special toffee (Vipeholm Toffee) to provoke dental caries.
- Some of the research subjects had to eat it almost every day for 4 years.
- Many of the subjects' teeth were completely ruined after this study.
- *Research performed without informed consent*

Later examples

- The Neurosedyne Catastrophe (1951)
- The Milgram experiment on obedience to authority figures (1965)
- The Stanford Prison Experiment (1971)
- The Macchiarini Scandal (2014)

Ethical review in Sweden

Ethical review in Sweden

In the past

- The first Ethics Committee in the late sixties
- Voluntary evaluation
- A service for the researcher

2004

- The Act concerning the ethical review of research involving humans (The Swedish Code of Statutes (SFS), 2003:460)
- 6 Regional Ethical Review Boards

2019

- Swedish Ethical Review Authority

Swedish Ethical Review Authority

- 6 operating regions
- 23 employees
- 72 people working for emolument
- 18 departments with 450 members
- 198 department meetings
- 7 000 digital applications

www.etikprovning.se

Our mission

To protect the individual and to ensure the respect for human dignity in research

- *Co-workers and members of the review with high ethical competence.*
- *An efficient and legally secure review.*
- *Well functioning collaboration and communication with the surrounding world.*

A multimodal team for each department

Entity responsible for the research

Chief investigator

Research subject

Chairperson (judge)

Administrators

Scientific secretary

Members representing the public

Members with scientific competence

The Ethical Review

Section 1 - Purpose

The purpose of the Act is to protect the individual-and the respect for human dignity in research.

- The research subject shall be protected against the risk of being hurt physically or mentally or for having his or her individual integrity compromised.
- The public shall be able to monitor and influence the research ethical review.
- The research subjects as well as the researchers shall be treated in compliance with the rule of law.

Section 2 - The definition of research

Research: Scientifically experimental or theoretical work intended to result in new knowledge and development outcomes on a scientific basis, excluding work that is performed within the framework of higher education on the basic or advanced level.

- Scientific hypothesis or method
- Performed by a person with scientific competence
- Intention to publish the results in scientific journals
- The Act does not apply to student work

Section 3 - When does the law apply?

If the research entails handling of

1. personal data of the kind listed in Article 9.1 of the EU Data Protection Regulation (GDPR) (sensitive personal data), or

2. personal data regarding legal offences involving crimes, criminal convictions, procedural coercive measures or administrative detention.

Handling of personal data in section 3 is only approved if this is necessary to enable that the research can be carried out.

Sensitive personal data

Personal information concerning

- ethnic origin
- political views
- religious or philosophical convictions
- trade union membership
- health
- sexual orientation or sex life
- genetic data
- biometric data

- *Personal data is any information that refers to an identified or identifiable natural person*
- *Traceability - name or code key or any other way.*

Section 4 - When does the law apply?

If the research

- entails a physical intervention on a living human being or a deceased person
- is conducted according to a method which aims to affect the research subject physically or mentally or entails an obvious risk of harming the research subject physically or mentally
- concerns studies on biological samples taken from a living human being or a deceased person for medical purposes and which are traceable to that individual

Section 5 - Geographical applicability

- The Act is only applicable for research carried out fully or partly in Sweden.

Specific requirements

- An approval from the Swedish Ethical Review Authority has to be given before the research project can start.

- The approved project has to start within two years from the approval.

- Starting or completing a research project that falls within the scope of the Act without approval from an ethics review board is a breach of the law and is punishable with a fine or imprisonment.

Section 7-11
Legal requirements for approval

- A research project can only be approved if it is conducted with ***respect for human dignity***.

- Human rights and fundamental freedoms shall always be considered in ethical review. At the same time regard shall be made to the interest in the developing of new knowledge through research. ***The welfare of human beings should be placed before the needs of society and science.***

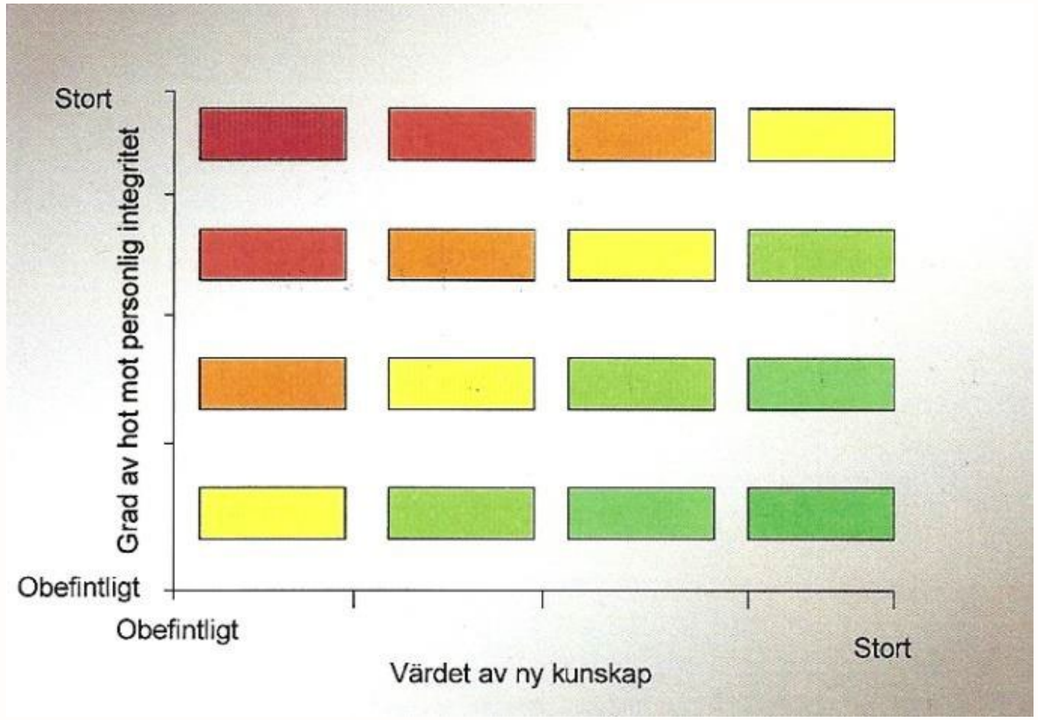
- A research project can only be approved if the ***risks*** that it can cause for the research subject's health, safety and personal integrity are outweighed by the knowledge of the research.

- A research project cannot be approved ***if the expected results can be reached in another way that presents fewer risks*** for the research subject's health, safety and personal integrity.

- A research project can only be approved if it is to be conducted or monitored by ***a researcher that has the required scientific competence***.

Critical moments in ethical review

- Weighing of RISKS *vs.* BENEFITS
- Informed consent



Section 17 - The principle of informed consent

- A research project is only permitted if the research subject has consented to being part of the study.
- Consent is only valid if the research subject has received information regarding the study prior to giving their consent.
- Consent must be voluntary, explicit and specific to the research in question.
- Consent must be documented, normally through a written consent.

Vulnerable groups

Section 18

- Children – consent is aquired from the legal guardians
  Despite the consent of the legal guardians, research may not be performed if a research subject under the age of 15 is able to understand what their participation in the study entails, and the subject does not want to consent.

- Youths between 15 and 18 years of age give their own consent if they can comprehend what their participation in the research project entails.

Section 20

- Research may be carried out without consent if illness, mental disorder, weakened state of health or some other similar circumstance prevents the subject of the research from expressing an opinion.

Sections 21 and 22

- Specific conditions

Section 21-22 - Research without consent

- Knowledge that is not possible to obtain by means of research using informed consent.
- Expected to be of direct benefit to the research subject
- Unless direct benefit
  - purpose to be of benefit to the person who is the subject of the research or someone else who suffers from a similar illness or disorder
  - insignificant risk of injury and insignificant discomfort
- As far as is possible, the research subject must personally be informed about the research.
- Consultation with the closest relatives and/or with a custodian or other legal representative must take place.
- The research may not be carried out if the research subject has indicated in any way that they do not wish to participate, or if anyone that has been consulted is opposed to the undertaking.

Section 16 -Information to the research subject

The subject of the research is to be informed about

- the overall research plan
- the purpose of the research
- the methods that will be used
- the consequences and risks that the research might entail
- the entity responsible for the research
- the fact that participation in the research is voluntary
- the right of the research subject to cease participating at any time

Section 16 -Information to the research subject

14 § If there is interdependence between the research subject and the entity responsible for the research, and/or the chief investigator,

or if the research subject can be assumed to have specific difficulties in mantaining his or her rights, special attention shall be given to questions related to information and consent when the application is examined.

No inappropriate or misleading information!

Responsible for the project

- **Entity responsible for the research (forskningshuvudman)**

A governmental authority or a physical or legal entity under whose auspices the research is conducted. The entity has the overall responsibility of the research project.

- **Authorised representative of the entity responsible for the research (behörig företrädare)**

A person that has the authority to act on behalf of the research entity

- **Chief investigator (ansvarig forskare)**

The contact person and the person guaranteeing the project has the required necessary competency

  - *Should normally have a doctoral degree*

Application

Application for ethical review

- Filled out in Swedish and with a Swedish title
- Understandable for laypeople
- The review starts when the application fee is paid
- Administrative review/validation
- Reviewed at the earliest possible department meeting
- A decision is made available in Ethix, our online application platform, within two weeks after the meeting

- New application - max of 60 days handling time.
- Substantial modification max of 35 days handling time.

Requests for amendements - Common reasons

- Inadequate research ethical considerations
- Annexes are missing
- Inadequacies in the informed consent form

Words that are perceived as coercive
The information is not age appropriate
The language is unclear and difficult to understand
Information regarding how personal data is handled and the registered persons rights according to GDPR are missing
No information regarding the timescale of the project
No information that participation is voluntary and the research subject can cease to participate at any time
No contact information to the chief investigator

It is called pseudonymised, not anonymised or ”avidentifierat”

Which decisions do we take?

- ***Approval***
- ***Approved subject to conditions***

The project is approved if the specified conditions are met. No need to prove that necessary measures have been taken.

- ***Refusal***

If the applicant, despite a formal request, has not amended the application in a sufficient manner.

If the risks outweigh the benefits or, the research otherwise do not meet the criteria laid down in the Act.

- ***Rejection***

The research does not fall within the scope of the Act.

The application does not live up to formal requirements.

- ***Advisory statement*** (+rejection)

If the applicant has requested such a statement.

- ***Removal***

If the applicant recalls the application.

The Ethics Review Appeals Board

- A decision that is not in favour of the applicant can be appealed to the Ethics Review Appeals Board
- The entity responsible for the research is qualified to make the appeal.
- The appeal can be lodged within three weeks from the date when the complainant received the decision.

Substantial modification

- Modifications that change the risk/benefit
- Change of entity responsible for the research or change of the chief investigator
- Addition of research subjects
- New units or locations
- New methods and new analyses

Extensive changes require a completely new application

Questions?

Etikprövnings myndigheten

Thank you!

registrator@etikprovning.se
010-475 08 00
www.etikprovning.se