Respect for people and test animals involved in scientific research

In addition to the aforementioned principles, respect for each individual and for the rights of each participant, regardless of his or her level of involvement in the study, is an absolute requirement in any kind of scientific research. This applies particularly to the right to protection of physical and mental integrity of individuals involved in research and their right to protection of privacy. Research with human subjects can only take on voluntary cooperation after they are fully informed about the research. In addition to humans, animals can also be the subjects of scientific research. Animal testing for research purposes is only allowed if there are no suitable alternatives available.

3. Involvement of human subjects in scientific research

In scientific research a general distinction can be made between three types of research involving people (human subjects):

- Scientific research with human participants that is subject to the Medical Research Involving Human Subjects Act (WMO)
- Scientific research using human biological materials (non-WMO)
- Scientific research using personal information (non-WMO)

For each of these three types of research, more details are given below about the following three aspects:

- whether a medical ethics review is mandatory,
- the most important substantive rules, and
- other available sources of information.

3.1. Scientific research with human participants that is subject to the Medical Research Involving Human Subjects Act (WMO)

Research involving human subjects that is subject to the WMO must undergo a medical ethics review. This is the case if the following two criteria are met:

1. medical-scientific research is to be conducted,
2. the research will involve subjecting people to treatments or requiring them to engage in specific behavior.
WMO-research can only be conducted if a Medical Ethics Review Committee (METC) that is recognized by the Central Committee on Research Involving Human Subjects (CCMO) has approved the research protocol. Maastricht UMC+ has its own recognized, independent METC, the METC azM/UM. For a scientific study to be conducted within Maastricht UMC+, the Executive Board Maastricht UMC+ must have approved the scientific research proposal beforehand. The Clinical Trial Center Maastricht (CTCM) coordinates the applications and the central registration of these reviews on behalf of the Executive Board Maastricht UMC+. In addition to approval of the research by a METC, the subject has to be fully informed about the research and a written ‘informed consent’ needs to be obtained from each trial subject who has been asked to participate in the research. For research involving human subjects, clinical trials insurance must be taken out. The METC will check whether this has been done (or may grant an insurance exemption at the written request of the researchers) and whether liability insurance is applicable.

In some cases, additional guidelines may need to be followed when applying for WMO-research:
- research in which human subjects are exposed to sources of ionizing radiation does not only need to be reviewed and approved by the METC azM/UM, but also by the general coordinating radiation expert.
- if the research involves gene therapy or genetically modified organisms (GMOs), the review can only be carried out by the CCMO, together with the Environmental Safety Officer (MVF).
- drug research not only requires a positive review by the METC azM/UM, but also a declaration of no objection from the authorized organization (CCMO). In addition, the WMO stipulates additional requirements for drug research, as a result of the implementation of the Guideline Good Clinical Practice (GCP) in 2006.

The CCMO website offers a step-by-step guide to find out how a particular research study needs to be reviewed. Research conducted by Maastricht UMC+ researchers in Europe or in developing countries is the responsibility of the METC in the country where the research takes place. Also in these kinds of studies,

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4 For more information regarding the Medical Ethics Committee METC azM/UM: http://www.azm.nl/info/azMorganisatie/MEC/
5 The ministry of Health, Welfare and Sport, in cooperation with the CCMO and the recognized METCs, has set up a brochure containing general information about participating in scientific research. See http://www.rijksoverheid.nl/documenten-en-publicaties/brochures/2008/10/02/medisch-wetenschappelijk-onderzoek.html
6 The Radiation Protection Unit (SBE) is part of CRISP. See http://crispmaastricht.nl/
7 The biological safety unit is part of CRISP. See http://crispmaastricht.nl/
8 http://www.ccmo-online.nl/main.asp
human subjects must give written consent for participation in the research study by ways of 'informed consent'.

**GCP**

For all WMO research that takes place within Maastricht UMC+ the clinical researcher must have the national GCP certificate or acquire it within 6 months after the study has commenced. The CTCM frequently organizes so-called BROK (legislation and organization for clinical researchers) courses. This course covers the GCP, laws and regulations, ethics and practices of the CCMO and METCs.

**Local feasibility of multicenter research**

Multicenter research, which is research that is conducted at a number of locations in The Netherlands, can only commence once it has received a positive recommendation from one of the METCs. The Executive Board of each of the other centers participating in the multicenter research must inform the reviewing METC that they are able and willing to participate in the research study by means of a local feasibility declaration. Within Maastricht UMC+, advice on local feasibility is coordinated by the CTCM. As from March 1st 2012, the local feasibility does not have to be part of the researchfile anymore. The revising METC will include in the revision of multicenter research the new “research declaration”. This research declaration has to been given by the head of the department or the division where the local researcher is working.

Figure 1 shows a summary of the procedures a researcher will come across in each phase of research involving human subjects that is subject to the WMO:

![Research Procedures Diagram](image)

Figure 2: procedures during each phase of research that is subject to the WMO.

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10 [http://www.ccmo-online.nl/main.asp](http://www.ccmo-online.nl/main.asp)
3.2. Scientific research using human biological materials (non-WMO)

The use of human biological materials that are already available (taken during diagnosis and/or treatment) ‘for further application’ for the purpose of scientific research is subject to regulations. Research involving human biological materials that is conducted within Maastricht UMC+ must meet all legal requirements as stipulated in the Safety and Quality of Human Tissues Act and the Code for Proper Secondary Use of Human Tissue\textsuperscript{11}, which include rules of conduct for the use of human biological materials (taken during diagnosis and/or treatment) ‘for further application’ for the purpose of scientific research.

The Code for Proper Secondary Use of Human Tissue makes a distinction between:

a. \textit{coded-anonymous human biological materials}: the provider can only trace these materials back to the individual from whom they originated via a code.

b. \textit{identifiable human biological materials}: the researcher can trace these materials back to the individual from whom they originated;

c. \textit{anonymous human biological materials}: it is reasonable to assume that it is impossible to trace these materials back to the individual from whom they originated;

As stated in the Code for Proper Secondary Use of Human Tissue, scientific research with human biological materials has preferably to take place with coded-anonymous human biological materials. \textit{Coded-anonymous human biological materials}, conform Article 467 (1) of the Dutch Civil Code (Burgerlijk Wetboek), may be used for scientific research as long as the patient from whom the material has been taken, does not object and the research is conducted with due care. The researcher must submit the research protocol for this non-WMO research to the medical ethics review committee and explain the recourse to the rule of ‘no objection’. The researcher must also check the patient’s medical records to see whether the patient has objected. Maastricht UMC+ informs patients about the use of human biological materials in medical scientific research via the brochure (in Dutch) “\textit{Medisch-wetenschappelijk onderzoek met uw gegevens en/of lichaamsmateriaal\textsuperscript{12}”\textsuperscript{12}}. This brochure informs patients about the possibility to object to the use of their (anonymous or coded) human biological materials in scientific research.

The use of \textit{identifiable human biological materials} requires written consent (signed informed consent) from the individual from whom the human biological materials originated.

\textsuperscript{11} The ‘Code for Proper Secondary Use of Human Tissue’, latest version May 2011, established by the Dutch federation of Biomedical Scientific Societies (FMWV), is available online: \url{http://www.federa.org/?s=1&m=82}

\textsuperscript{12} This brochure is available via the patient information office of azM or online: \url{http://www.azm.nl/onderbehandeling/meewerkenaanonderzoek1}
This also applies to ‘biobank research’, when extra tissue is taken during diagnosis and/or treatment for the purpose of future, not yet defined research.

3.3. Scientific research using personal data (non-WMO)

This concerns research with data acquired from either patients’ medical records and other sources where data are stored, or from individuals themselves.

Out of the three types of research involving human subjects, data research is in principle the least invasive. This includes research that involves data collection via interviews/surveys as well as research using patient data that are already available to the researcher in his or her role as health care provider. Please note that scientific research comprising interviews or surveys (single or in series) that could pose a burden and/or risk on the participants, may fall under the scope of the WMO. The researcher must submit the research protocol for non-WMO research to the medical ethics review committee.

In addition, when conducting research using personal data the following points must be taken into account:

- The results of data research must not be traceable to the data subjects; direct or indirect traceability in publications is absolutely prohibited.
- The breach of privacy of data subjects must be as limited as possible; which means, for example a) not collecting materials from those involved if sufficient secondary data are available, b) not using identifiable data if the research can be conducted by using anonymous data, and c) using coded data if the latter is not possible.
- In general, data processing for scientific research is subject to the Personal Data Protection Act (WBP)\(^\text{13}\), and to Act on Consent to Medical Treatment (WGBO)\(^\text{14}\) in particular. The latter does not require a patient’s consent for research using data that the researcher collected in his or her role as health care provider. It does, however, stipulate that a patient has given consent before personal data are shared with other researchers (including perusal of the patient’s medical records by others).

4. Animal testing

In Maastricht UMC+ researchers treat animals with respect. The framework of the Animal Testing Act (WOD)\(^\text{15}\) provides guidance on this issue. The purpose of the WOD is to protect animals: it is prohibited to carry out animal testing for purposes that can be achieved by alternative means, by animal testing

\(^{13}\) http://www.cbpweb.nl/Pages/ind_wetten_wbp.aspx
\(^{14}\) http://www.rbng.nl/userfiles/file/wetten/WGBO.pdf
\(^{15}\) The original law from 1977, the changes to the law (2003), the General Administrative Orders (AMvBs) and a number of ministerial regulations can be found at http://wetten.overheid.nl/zoeken/ (search ‘dierproeven’).