Biobank Research Ethics Committee (TCBio)

Annual Report 2024

UMC Utrecht

tcbio.umcutrecht.nl

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Preface

This annual report describes the results of the reviews by the Biobank Research Ethics Committee (BREC, in Dutch: TCBio) in 2024. As part of the UMC Utrecht's biobank governance structure, the reviews of sub-biobank protocols to collect and store patient's tissue and release protocols using their tissues for medical research, contributes to protect the rights and interests of these patients. In addition, the biobank catalogue constitutes an integral part of the governance structure. The Committee, the Central Biobank and the Biobank Catalogue can be viewed as part of the biobank ecosystem. By providing an overview of the available materials, the catalogue contributes to efficient use of the collected material for purposes for which patients donated their materials. The different parts in this biobank ecosystem are interdependent and could strengthen each other. Further development of this ecosystem, in which researchers as well as patients take part, should be initiated with this ecosystem in mind.

Due to the lack of a national ethical and legal framework for the initiation and the use of biobank collections, review of multicenter protocols for both biobank set up and release protocols is hampered.
This may result in differences in protection of rights of patients taking part in the same biobank in different hospitals and does not facilitate researchers collaborating in multicenter research. Therefore, harmonization of the ethical framework for the collection and use of human tissues in the Netherlands is urgently needed. In the NFU project 'Mutual Recognition', the first steps are taken towards this goal. In previous years, the Committee has been committed to this project. This commitment will continue in 2025.

We thank the Board of directors for their continued support of the Committee. This has resulted in faster review of protocols in recent years. In addition, it has allowed more focus on complex protocols and issues.

Prof. J.J.M. van Delden (MD PhD, chair)

Summary

The reporting year 2024 saw a substantial increase in the number of new release protocols received compared to 2023. The key facts are summarized below.

Review of new sub-biobank submissions comprise a relatively small part of the Committee's review procedures. In 2024, there was an increase in the number of sub-biobank submissions (from 5 submissions in 2023 to 10 in 2024). The number of biobank recommendations to the Board of Directors remained stable (from 6 recommendations in 2023 to 5 in 2024).

Release protocol reviews comprise the majority of the Committee's review procedures. In 2024, the number of release protocol submissions increased (from 54 in 2023 to 90 in 2024), while the number of decisions taken on release protocol submissions remained at the same level (59 in both 2023 and 2024).

The average review time for sub-biobank submissions was 60.5 days (n=5). On average this duration is just above the time limit set by the Committee's Rules of Procedure (56 days). In addition, multicenter biobanks frequently take longer to review due to a lack of national legislation. In order to improve the latter, participation was continued in the project 'Mutual Recognition' for review of multi center biobanks that has been initiated by the NFU (in Dutch: Nederlandse Federatie van Universitair Medische Centra).
Release protocol reviews were on average completed in 43.5 days (n=59). This is just above the time limit set by the Committee 's Rules of Procedure (42 days). A range of factors could together have contributed to delays leading to longer review times for both types of submissions.

Four incidental findings were reported in 2024. The findings originated from the use of material from two biobanks. Although this low number is still worrisome, these reports illustrate that at least a few biobanks are aware of this procedure for the return of results.

1 Competent authority BREC

Collections of human biological material and associated data, also known as biobanks, continue to play an important role in medical-scientific research. The research question for which the human biological material and associated data will be used, is typically only globally known at the time donors provide their material to the biobank. Therefore, only general information can to be provided to the donor as researchers generally also do not know for which specific purpose the material and data will be used and by whom. By giving broad consent at the time of donation to the biobank, donors transfer part of their control rights over the material and data to the biobank. To continue donor support for biobanks now and in the future, donors must be able to rely on their material and data being handled in a responsible manner in the biobank and during the medical-scientific research.

The following principles are important for donor trust:

- protection of confidentiality of the human biological material and associated data,
- type of donor consent,
- handling of findings,
- ownership of the material, and
- transparency on commercial use.

For the UMC Utrecht, these principles are detailed in the UMC Utrecht Biobank Regulations.

As a result of the UMC Utrecht Biobank Regulations adopted by the Board of Directors in 2013, the Biobank Research Ethics Committee (BREC, in Dutch: Toetsingscommissie Biobanken – TCBio, hereafter: the Committee) was appointed by the UMC Utrecht Board of Directors. The Committee operates independently from the Central Biobank UMC Utrecht. The latter is responsible for the monitoring of the quality, the registration and the storage of the human biological material as sub-biobanks.

With the Biobank Regulations the UMC Utrecht aims to build a high-quality infrastructure for medical-scientific research for all UMC Utrecht researchers and their partners. To reach this goal, the Committee reviews whether the human biological material and associated data are collected and stored as sub-biobanks in the Central Biobank UMC Utrecht in accordance with the criteria laid down in the UMC Utrecht Biobank Regulations. Similarly, the Committee reviews whether the human biological material and associated data will be used in a responsible way in medical-scientific research. This governance model does not solely serve the interests of the donor but also those of the researcher and society as a whole ensuring that (scarce) material will be used for the right purposes. Donors must be able to rely on their material and data being used for relevant medical-scientific research only.

In addition to reviews by the Committee, the MREC NedMec has been requested by the Committee to perform the review of the establishment of the sub-biobank in parallel with the Medical Research Involving Human subjects Act (WMO) review when human biological material is collected for yet unspecified purposes from participants during clinical research that is subject to the WMO. This prevents that researchers have to deal with two separate ethics committees for parallel or sequential review procedures and ensures that the collective burden on the donors will be taken into account.

* For details on the UMC Utrecht Biobank Regulations, refer to Biobanks UMC Utrecht - Toetsingscommissie Biobanken.

2 Committee members

In 2024, two Committee members left for various reasons. Two new Committee members were proposed by UMC Utrecht divisions and appointed by the Board of Directors. In addition, UMC Utrecht privacy officer Mrs. E. Kruisselbrink is available for ad hoc advice at the request of the Committee.

The chair, prof. dr. J.J.M. van Delden, was replaced by the deputy chair, dr. K. Tesselaar, during his leave of absence in May-June 2024.

A complete list of the Committee members in 2024 is provided in Attachment 1.

3 Committee secretariat

The Committee is supported by the staff of the Department of Research Review (in Dutch: Afdeling Toetsing Onderzoek). The Department is part of the UMC Utrecht Directorate Quality of Care & Patient Safety.

The Department's staff also supports the Medical Research Ethics Committee (MREC, in Dutch: METC) NedMec that is facilitated by the UMC Utrecht, the Princess Maxima Center of Pediatric Oncology and the Foundation Netherlands Cancer Institute – Antoni van Leeuwenhoek Ziekenhuis (in Dutch: Stichting Nederlands Kankerinstituut - Antoni van Leeuwenhoek Ziekenhuis). Staff members work on location or from home. Most members of staff support either the MREC or the Committee, while others support both committees.

In 2024, there were several changes in members of staff. A list of staff members is provided in Attachment 1.

4 Committee’s operating procedure

The Committee operates analogous to an accredited MREC. The Committee’s operating procedures have been laid down in the rules of procedure (in Dutch: huishoudelijk reglement). For the most recent version refer to the Committee’s website here. Committee meetings take place every two weeks on Mondays. Meetings are held alternating online and on location in the UMC Utrecht. In 2024, twenty-five Committee meetings were held.

Committee members download the meeting documents from a password protected digital platform. The chair checks at the start of each Committee meeting that all required experts are present. Members present who have a conflict of interest with any of the files leave the meeting for the duration of the discussion of that specific file. These issues are noted in the minutes of the meeting. For each file, the relevant review criteria are discussed in a point-by-point fashion. For each review criterion, committee members offer their advice when relevant. In general, decisions are reached unanimously.

5 Results of 2024 and aims for 2025

5.1 Results of 2024

In addition to the review of biobank and release proposals, each year the Committee aims to improve the governance of the collection and use of human biological material in the UMC Utrecht.

In 2024 the following were achieved:

A) The Committee continued to provide input in the NFU project Mutual Recognition of the review of multicenter biobanks by participating in pilot reviews of fake protocols. With this project, the NFU (in Dutch: Nederlandse Federatie van Universitair Medische Centra) aims to harmonize the review of multicenter biobanks within The Netherlands. Due to a lack of a national legal framework, criteria and procedures for setting up a biobank involving multiple medical centers vary across the country. Similarly, every medical center has its own review procedures and criteria for use of the human biological material collected in the biobanks. As a result of harmonization, multiple parallel or sequential procedures may become no longer necessary.

As part of the project, templates for biobankprotocol, biobank information leaflet and release protocol have been developed and tested in two pilot reviews in late 2023 (biobank protocol review) and early 2024 (release protocol review).

B) In 2024, the Dutch Ministry of Health published an amended version of the draft legal framework for public control on the use of human tissue (Dutch: Wet Zeggenschap Lichaamsmateriaal - Wzl). The committee provided a reaction on key points via the public consultation that can be downloaded here.

C) Although they operate independently, the Committee and the Central Biobank, are part of the same biobank infra-structure of the UMC Utrecht. To further strengthen the infrastructure, actions were initiated to improve the cohesion between the different parts. As an example, the coordination of sample release after approval by the Committee was improved.

5.2 Aims for 2025

A) The NFU project Mutual Recognition of the review of multicenter biobank is expected to move into the next phase in 2025: the implementation of the review of multicenter biobanks by mutual recognition of the review of the primary review committee. The Committee and her secretariat are committed to continue to support the project.

B) Given the development of NFU templates (see 5.1), it is preferable to align the Committee's sub-biobank template protocol with the national NFU template where possible. The Committee's template would therefore be suitable for both mono and multicenter biobanks. The updated version should provide an improved lay-out, and include clear questions on privacy aspects. In addition to the NFU template, questions on e-consent and patient participation will be included.

6 Review of sub-biobanks and release protocols

To comply with the UMC Utrecht Biobank Regulations, two types of protocols may be submitted: sub biobank protocols (in Dutch: deelbiobankprotocol) and release protocols (in Dutch: uitgifteprotocol).

6.1 Sub-biobank submissions

6.1.1 Number of new sub-biobanks submitted

As laid down in the UMC Utrecht Biobank Regulations, all new sub-biobank protocols collecting human biological material for as yet unspecified research questions are reviewed by the Committee. However, as described in section 1, the MREC NedMec reviews sub-biobanks that are established in conjunction with clinical studies.

As explained above, the total number of new UMC Utrecht sub-biobanks submissions in 2024 is reflected by the sum of sub-biobank submissions received for review by either the Committee or the MREC NedMec.

The total number of sub-biobank submissions increased in 2024 compared to 2023 (Figure 1). Ten out of fifteen sub-biobanks were received by the Committee while the remaining five sub-biobank protocols were submitted by UMC Utrecht departments to the MREC NedMec in parallel with clinical research that was subject to the WMO (see section 1).

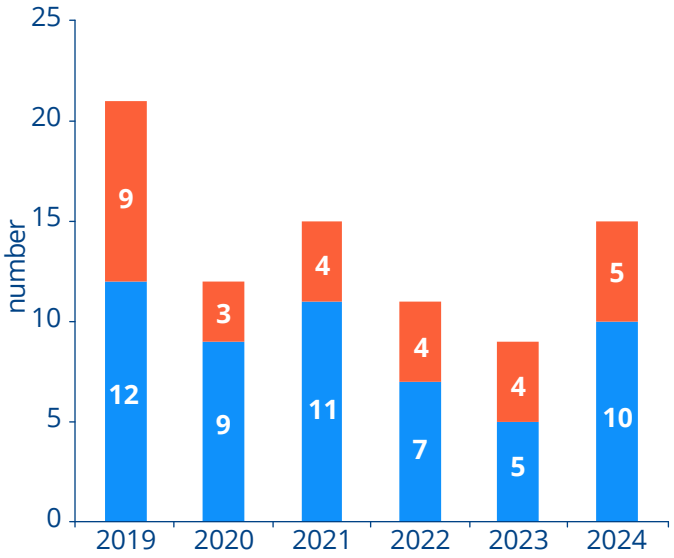

Figure 1: Number of sub-biobank protocols submitted to the Committee (blue) and the MREC (orange) in 2024 compared to 2019-2023.

Of the ten sub-biobank protocols received by the Committee, one concerned a request of an external organization not associated with the UMC Utrecht. Also in this situation, the protocol was reviewed according to the UMC Utrecht Biobank Regulations even though this external organization does not formally fall within the scope of the UMC Utrecht Biobank Regulations.

6.1.2 Number of recommendations to the Board of Directors issued on sub-biobanks

For all sub-biobank review procedures completed in 2024, the Committee/MREC recommended the Board of Directors to approve the sub-biobank (Figure 2). There were no recommendations for rejection. Compared to 2023, the total number of recommendations for approval decreased slightly in 2024 (Figure 2).

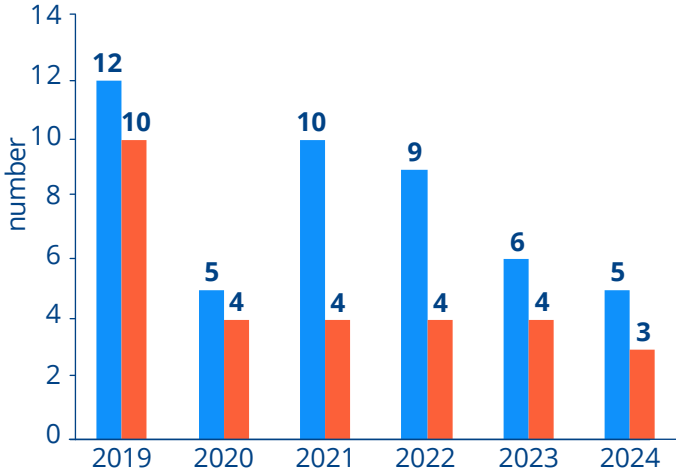

Figure 2: Number of sub-biobanks recommended by the Committee (blue) and MREC (orange) for approval by the Board of Directors in 2024 compared to 2019-2023.

Note: Review procedures may extend into the next calendar year. Therefore, the sum of both committees' recommendations (for either approval or rejection) within a calendar year may differ from the total number of submissions in that year shown in Figure 1.

6.2 Release protocols

6.2.1 Number of new release protocols submitted

There was a substantial increase in the total number of new release protocol submissions in 2024 compared to 2023 (Figure 3). Of the total number of submissions (90), the majority of release protocol submissions (55) originated from UMC Utrecht researchers or from institutions that store their biobank material in the UMC Utrecht Central Biobank. This is an increase compared to the number of UMC Utrecht submissions in 2023 (42).

The remaining increase in new release protocol submissions, resulted from an increase in submissions from the Foundation Hubrecht Organoid Biobank (hereafter: the Foundation[+]). Until 2021, a substantial number of release protocol submissions originated from the Foundation and its predecessor Foundation HUB Organoids Technology. In both 2022 and 2023, the number of submissions submitted by the Foundation was reduced, with the lowest number in 2023 (12). In 2024 the number of release protocols submitted by the Foundation increased again substantially to a total of 35 release protocols.

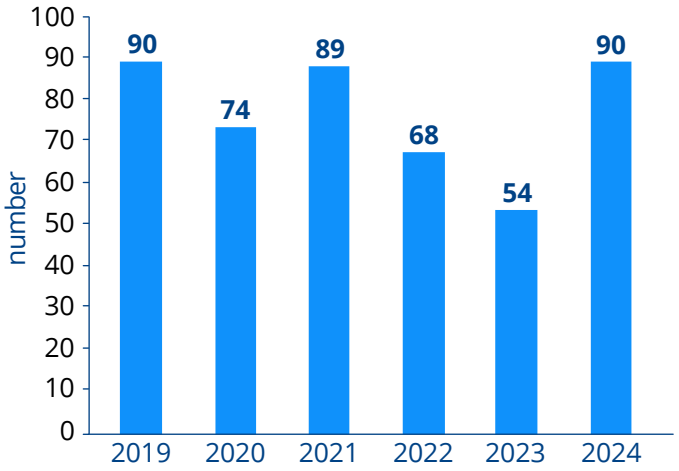

Figure 3: Number of new release protocols submitted in 2024 compared to 2019-2023

6.2.2 Number of decisions regarding release protocols

In contrast to the increased number of release protocol submissions, the number of decisions in 2024 was comparable to 2023 (Figure 4). This difference may be due to a number of factors. For example, no decision can be reached if the researcher does not respond to Committee's questions. Procedures are terminated if no response is received within one month and the researcher does not respond to reminders for a response.

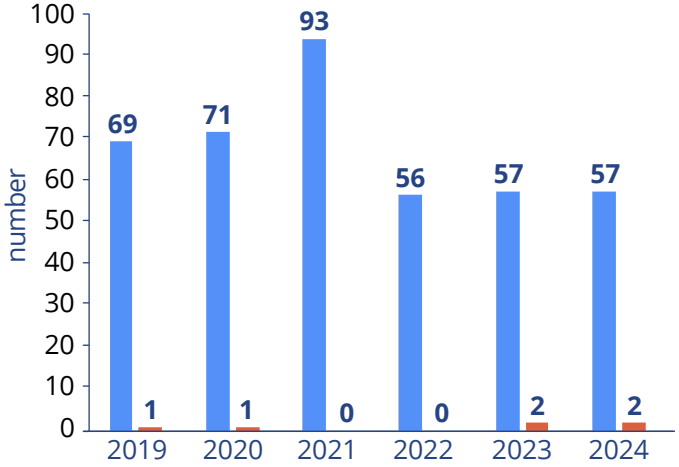

Figure 4: Number of release protocols approved (blue) and rejected (orange) in 2024 compared to 2019 2023.

Note: Review procedures may extend into the next calendar year. Therefore, the sum of the approvals and rejections within a calendar year may differ from the total number of submissions in that year shown in Figure 3.

[+]Founded by Hubrecht Institute, UMC Utrecht and Royal Academy of Arts and Sciences (KNAW), the Foundation aims to refine organoid development and foster organoid adoption globally . The Foundation manages the organoid sub-biobanks in cooperation with the UMC Utrecht Central Biobank. As for all UMC Utrecht sub-biobanks, release requests from the Foundation's sub-biobanks are reviewed by the Committee. The Foundation facilitates release protocol submissions from the Foundation's sub-biobanks. These submissions therefore also include a small number of release protocols for studies by UMC Utrecht researchers although the vast majority of the Foundation's release protocols concern requests not directly related to UMC Utrecht research.
Link to the Foundation's website: Foundation Hubrecht Organoid Biobank

6.3 Review time

The average total time the committee needed for protocol reviews in 2024 is shown in Table 1. Compared to 2023, the average number of days for both types of protocols exceeded the committee's time limits of 56 and 42 days.

Year	Sub-biobank	Release protocol
2019	54,9 (n=12)	48,3 (n=70)
2020	67,6 (n=5)	51,5 (n=72)
2021	66,5 (n=10)	46,5 (n=93)
2022	65,9 (n=9)	37,4 (n=56)
2023	64,5 (n=6)	36,4 (n=59)
2024	60,4 (n=5)	43,5 (n=59)

Table 1: Average duration of committee review (in calendar days) for the recommendations and decisions on release protocols given in 2024 compared to 2019-2023. The review time limit according to the Committee's rules of procedure are 56 days for sub-biobanks and 42 days for release protocols.

Factors that may have contributed to longer review time could include:

- Full meeting agenda's. This may result in insufficient time to discuss all protocols on the agenda leading to deferral of protocols to the next meeting adding to the review time.
- Changes in office staff during 2024.
- Delays due to review of legal agreements when researchers collaborate with parties outside the UMC Utrecht.

6.4 Amendments

The committee has delegated the review of non-substantial amendments to the chair. Only changes that affect the criteria for approval of a biobank or release protocol are reviewed in the Committee meeting. Amendments for which no review by the Committee is required are reported to the Committee in the subsequent meeting as weekly listings.

The number of amendments to sub-biobank or release protocols increased in 2024 (Figure 5). This added to the already increased workload for both Committee and supporting staff due to the increase in new sub-biobank and release protocol submissions.

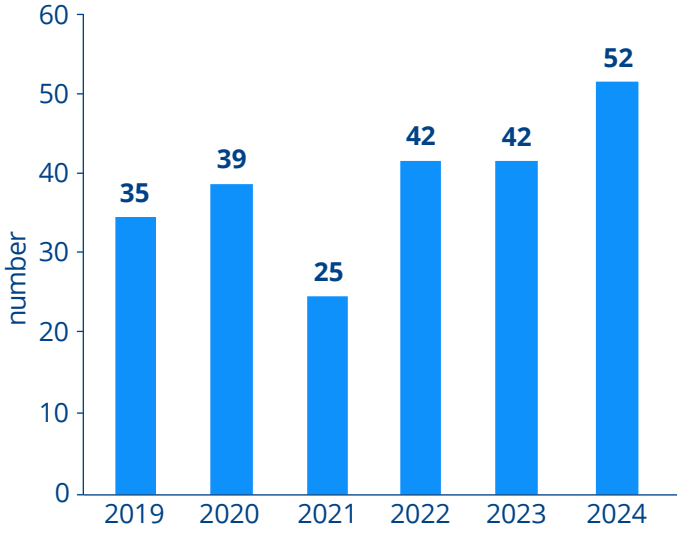

Figure 5: Number of sub-biobank and release protocols amended at least once in 2024 compared to 2019 2023.

6.5 Incidental findings

The term "incidental findings" refers to unforeseen individual donor results that raise issues regarding the obligation to return the results to the donor. Per the Committee's Standard Operating Procedure Reporting of Findings published on the Committee's website here, all reports of incidental findings are subject to review, in order to provide guidance on the return of the results to the donor. Despite the availability of a clear procedure on the reporting and review of incidental findings and in line with previous years, only a few reports of incidental findings were received, in 2024. This low number of reports is unexpected and worrisome.

In total, 4 incidental findings were reported. The findings originated from the use of material from two biobanks. Three reports originated from one biobank. The single report from one biobank did not directly involve DNA diagnostics. In the other three cases, clinically relevant germline DNA mutations were found during the course of characterization of the cells as part of the establishment of the biobank. In all four cases the Committee's advice took into account possible consequences for the donor and/or their family members.

These cases illustrate the need to have a review procedure in place to handle incidental findings. The Committee's review provides researchers with an independent advice on whether or not to report the finding to the donor and by whom. However, the low number of findings reported continues to be worrisome.

6.6 Final reports

After approval of their release protocol, researchers are asked to report results within one year of completion of the study. Similar to previous years, only a few final reports were received in 2024. There has been no active follow-up by the Committee to ascertain study results, as it is considered the responsibility of the researcher to submit the final report.

6.7 Submission procedures

Information on the background of the UMC Utrecht Central Biobank and the role of the committee's review of sub-biobank and release protocols are provided on the Committee's website*. In addition, forms and templates for researchers as well as instructions for submissions are provided there. The templates facilitate the Committee's review per UMC Utrecht Biobank Regulations.

The information on the website is provided in both Dutch and English. The website is accessible from outside the UMC Utrecht systems and can therefore be reached by both UMC Utrecht researchers and external parties wishing to collaborate with the UMC Utrecht.

The employees of the Department of Research Review can be contacted daily by e-mail for questions and advice on review procedures and requirements. When necessary, researcher are re-contacted by telephone or given the opportunity for video consultations.

* Home - Toetsingscommissie Biobanken (umcutrecht.nl)

7 Appeal against committee decisions

No formal appeals were received.

8 Other review activities

Besides the reviews under the UMC Utrecht Biobank Regulation reported above there are no other review activities to report for 2024.

9 Requests for information under the Freedom of Information Act

As in previous years, no requests for information under the Open Government Act (in Dutch: Wet Open Overheid, WOO) were received in 2024.

10 Internal quality assurance and training

In order to support committee members in their review activities, the following training sessions took place in 2024:

10.1 Annual meeting MERC NedMec

In the annual meeting of MREC NedMec, to which members of the Committee are invited, relevant developments regarding research ethics and national and or international regulations are discussed. Attendance facilitates training of the Committee members.

The theme of the 2024 meeting was: 'non-WMO and the review landscape'.

The following presentations on the topic were given:

Non WMO, ethical framework and future
Dr. S. Rebers and E.M. van Heertum

Fourth evaluation of the WMO
Dr. M. Timmers

10.2 Committee's internal training seminar

About once a year, a seminar is organized on a topic relevant to the committee's review. This year's seminar was planned at the end of November 2024. Due to unforeseen circumstances, the session was postponed to early 2025.

10.3 Training of members of Staff

As part of continued education and networking, the following meetings were attended by secretaries of the Committee:

- 10 October 2024: Trusting Forward', conference organized by Health-RI regarding secondary use of health care data.
- 10 December 2024: Working conference on implementation of the Dutch nWMO ethical framework.

11 Attachments

Attachment 1

Committee members and office staff

Committee members in 2024

Prof. J.J.M. (Hans) van Delden MD PhD	Ethicist, chair
Mr. M. (Martin) Bootsma PhD	Epidemiologist
Mrs. B.C. (Claire) Collins LLM	Lawyer
Mr. J.E. (Jan Erik) Freund (from 01-04-2024)	Pathologist
Prof. R. (Roel) Goldschmeding MD PhD (until 01-04-2024)	Pathologist
Mr. I. (Imo) Höfer MD PhD	Physician/scientist
Mrs. H.E. (Titia) van Lier LLM MA	On behalf of donors
Mrs. G.V. (Gaby) Minasian LLM	Lawyer
Mr. M. (Marcel) R. Nelen PhD	Geneticist
Mrs. J.M.L. (Jeanine) Roodhart MD PhD (until 01-01-2024)	Medical Oncologist
Mrs. N.A. (Kiki) Tesselaar PhD	Immunologist
Mr. T. (Terry) Vrijenhoek PhD	Geneticist
Mrs. L. (Lotte) van der Wagen MD PhD (from 01-01-2024)	Clinical Hematologist
Mr. P.M.J. (Paco) Welsing PhD	Epidemiologist

Substitute members in 2024

Mrs. M. (Marieke) Bakker MD	On behalf of donors
Mrs. M. (Marieke) Hollestelle MA	Ethicist

Staff from the Department of Research Review that supported the Committee in 2024

Mrs. A.C. (Anna) Bakker LLM (until 01-07-2024)	Head of Department Research Review
Mr. R.P. (Rutger) Chorus MA	Junior Staff advisor
Mrs. E. (Esther) van Doorn MSc (from 01-02-2024)	Senior review procedure coordinator
Mrs. W.A. (Antoinette) Groenewegen PhD	Official Secretary
Mrs. S. (Sigrid) Heinsbroek PhD (from 01-08-2024)	Official Secretary
Mrs. M. (Mandy) Koppes MSc (until 01-04-2024)	Senior review procedure coordinator
Mrs. A.H.M. (Anita) van den Oetelaar MSc (until 01-08-2024)	Official Secretary
Mrs. A.T. (Arina) Onnink	Secretary
Mr. M. (Michael) de Ridder (until 01-10-2024)	Advisor on information and archive
Mrs. S. (Simone) Timmer (from 01-10-2024)	Advisor on information and archive
Mrs. K. (Kitty) Valk (from 01-07-2024)	Manager Department Research Review a.i.

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Attachment 2: Abbreviations

BREC Biobank Research Ethics Committee
(in Dutch: Toetsingscommissie Biobanken, TCBio)

MREC Medical Research Ethics Committee
(in Dutch: Medisch-Ethische Toetsingscommissie, METC)

UMC University Medical Center

WMO Medical Research Involving Human Subjects Act
(in Dutch: Wet Medisch-Wetenschappelijk Onderzoek met Mensen)

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