Biobank Research Ethics Committee

Annual report 2020

UMC Utrecht

tcbio.umcutrecht.nl

Content

Preface

With this annual report, the Biobank Research Ethics Committee (BREC, in Dutch: TCBio) reports its contribution to the biobank governance structure in the UMC Utrecht in 2020.

Although the COVID-19 pandemic has likely impacted the number of submissions for review, the Committee was able to contribute to fast review for COVID-19 research, allowing research to start quickly in the early days of the pandemic. Also with adapted timelines for review, medical ethical review remains essential as even in these exceptional circumstances of the COVID-19 pandemic, requirements for good research need to be upheld in order to protect patient's rights and interests.
As noted in last year's annual report, increasing the Committee's meeting frequency has become necessary in order to facilitate an efficient and rapid review procedure. We are grateful for the support from the Board of Directors in making this possible.

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

Summary

The COVID-19 pandemic started in March of the year of this annual report 2020. Although the lockdowns changed the way in which both the Committee and her secretariat worked, from physical meetings to online video conferencing, reviews continued with the same high level standard as before. However, there was some reduction in both the number of release protocol as well as the number of biobank submissions. The COVID-19 pandemic may have played a role in this reduction as the ability to carry out research in the UMC Utrecht was restricted in order to reduce the spread of the SARS-CoV-2 virus. However, the number of opinions granted for release protocols as well as the number of amendments submitted increased slightly compared to 2019. The increase in opinions granted for release protocols may be explained by a carryover effect from the higher number of release protocol submissions in 2019.

The committee aims to complete the review in as short a time as possible. As in previous years, the average number of days needed to review the protocols was more than the committee's time limit. As previously concluded, with the monthly meeting frequency the review time cannot be reduced any further. Therefore in 2020 preparations were started to increase the meeting frequency to bi-weekly in 2021.

1 Competent authority BREC

Biobanks, comprising collections of human biological material and associated data, are increasingly important in medical-scientific research. Typically, the research question for which the human biological material and associated data will be used, is only globally known at the time donors provide their material to the biobank. Also, researchers generally do not know for which specific purpose the material and data will be used and by whom. This allows only general information to be provided to the donor. 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[1] 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 cases where human biological material is collected for yet unspecified purposes from participants during clinical research that is subject to the Medical Research Involving Human subjects Act (WMO), the Committee has requested the MREC Utrecht to perform the review of the establishment of the sub-biobank in parallel with the WMO review in order to avoid that researchers have to deal with two separate ethics committees at the same time.

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

2 Committee members

New Committee members are recruited through the divisions of the UMC Utrecht or proposed by members leaving the Committee. In 2020, there were no changes to the Committee members. A list of the Committee members in 2020 is provided in Attachment 1.

3 Committee secretariat

The Committee is supported by staff from the Department of Research Review (in Dutch: Afdeling Toetsing Onderzoek), part of the Directorate Quality of Care & Patient Safety. This Department also supports the Medical Research Ethics Committee (MREC, in Dutch: METC) Utrecht. Head of Department in 2020 was Mrs. S. de Weerd.

In 2020, the Department of Research Review employed four secretaries, four review procedure coordinators, one administrative employee and one management assistant. One review procedure coordinator was replaced. A list of all employees can be found in Attachment 1.

4 Committee’s operating procedure

In general, the Committee’s operating procedure is comparable to that of an accredited MREC. The Committee’s operating procedures have been laid down in the rules of procedure (in Dutch: huishoudelijk reglement). The most recent version can be found on the Committee’s website: Meer informatie - Toetsingscommissie Biobanken (umcutrecht.nl)

In 2020, the Committee convened 13 times. This included 12 regular meetings (every third Thursday of the month) and 1 meeting dedicated to accelerated assessment of one COVID-19 file (see section 5.1 below).

From March 2020 onwards, due to the measures related to the COVID-19 pandemic, all meetings were held online via video conferencing. As usual, meeting documents were provided via a digital platform (Viadesk).

At the beginning of each meeting, the chair checks whether all required experts are present and whether any members have a conflict of interest with any of the files to be discussed. These issues are documented in the minutes. Members with a conflict of interest leave the meeting for the duration of the discussion of the files concerned.

During the Committee 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. Members do not put their advice in writing ahead of the meeting. In general, decisions are reached unanimously.

5 Results of goals for 2020 and aims for 2021

5.1 Results in 2020

In the annual report 2019, two goals were set for 2020 to enhance the Committee's performance:
a) to prepare to increase the meeting frequency in order to decrease the review time in 2021, and
b) to improve the information for researchers by setting up a new website.

a) Although many factors affecting the review time had been optimized, such as increasing the duration of the meetings to allow more files to be discussed, improvements of the templates to reduce the number of rounds of question's and allowing the chair to review non-substantial amendments reducing the number of items discussed in the monthly meetings, the average review period could not be reduced further to within the limit set by the committee's rules of procedure. The monthly frequency of the Committee meetings is likely the last contributing factor in the longer review periods.

   In order for the secretariat to handle the increased total workload of the past few years and in addition to be able to increase the meeting frequency to every other week, an increase in the staff supporting the committee was necessary. In addition, for the increased demands on the time and expertise of the Committee members, financial compensation was deemed appropriate. Therefore, funds for both extra staff and compensation for members of the Committee were applied for and in November 2020, the board of directors decided to award the extra funds. As a result, preparations started to recruit both a new secretary and a review procedure coordinator in early 2021. Both positions were filled in early 2021 allowing the increased meeting frequency to commence as of April 1, 2021.

   With the pressure on faster review already especially high during 2020 for COVID-19 research, given that in 2020 the Committee still met once a month, the Committee allowed a fast track review procedure for research that needs to start immediately and for which the monthly frequency would seriously hamper the possibility to start the research on time. The researchers needed to give arguments why a fast track procedure should be granted based on scientific and societal impact and was allowed in exceptional circumstances only. As noted in section 4, in one case, the Committee convened specifically for this purpose in between two regular monthly meetings.

b) The Committee's website has until now only been available on the UMC Utrecht intranet website Connect and could therefore not be accessed by external partners. While the UMC Utrecht Biobank Regulations demand that a file can only be submitted by UMC Utrecht employee's, this lack of accessibility sometimes hampers collaborations with external partners. In addition, the information was due for an update and improvement on the lay-out of the information to increase the ease of finding the right information on e.g. submission instructions. Therefore, in 2020 a new website was built as a subsite of the new UMC Utrecht corporate website, the Dutch version of which went live in January 2021: Home - Toetsingscommissie Biobanken (umcutrecht.nl). In addition, in 2021, the English version of the website was completed and became operational in August 2021.

5.2 Aims for 2021

a) In 2021 we will continue to strengthen the organization of the Committee's review process by further optimization of procedures in order to reach the goal to reduce the average review time to within the time limit.

   In 2021 we aim to address this with the following points:

   - Providing additional explanation on various aspects of the biobank review procedures in a frequently asked questions (FAQ) format on the website. This should help researchers to further clarify the UMC Utrecht biobank review system and guide them through the information on the website.
   - Improving the information required for review of privacy aspects.
     Privacy aspects e.g. concerning linking of human material to medical data, frequently lead to committee questions resulting in prolonging the procedure. By improving the information for researchers, e.g. in a FAQ (see a)) or in the template protocols, the number of questions and or review rounds could perhaps be reduced further.

b) In 2021, we will strengthen our network with biobank committees in other academic hospitals. To this end, we will share our experience and procedures with our counterparts in other academic hospitals and contribute in initiatives to harmonize procedures for multicenter biobanks.

6 Review of sub-biobanks and release protocols

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

6.1 Sub-biobank submissions

6.1.1 Number of new sub-biobanks submitted

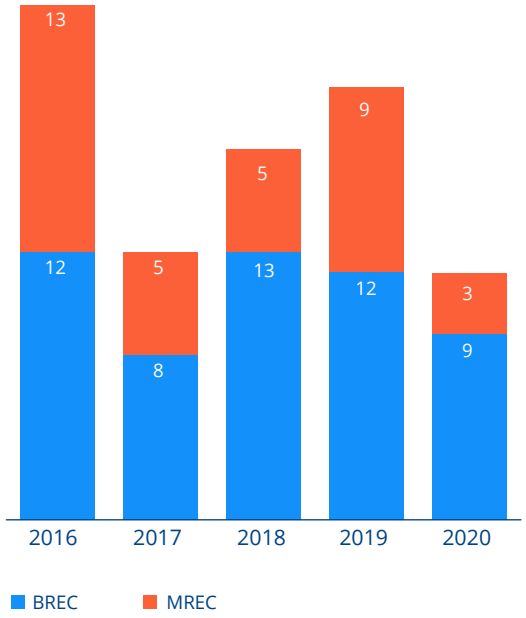
As laid down in the UMC Utrecht Biobank Regulations, all new sub-biobank protocols collecting human biological material for as yet unspecified research questions are reviewed by the Committee. However, as described in section one, the MREC Utrecht reviews sub-biobanks that are established when human biological material for storage for later, not yet specified use is also collected from subjects taking part in clinical research subjected to WMO review by the MREC. Given the above, the total number of new UMC Utrecht sub-biobanks that were intended to be set up in 2020 is therefore reflected by the sum of sub-biobank submissions received for review by either the Committee or the MREC.

The total number of sub-biobank submissions decreased in 2020 to around the level of 2017 of which the majority (9 out of 12) were reviewed by the Committee (Figure 1). The decrease may (in part) be explained by the restrictions as a result of the COVID-19 pandemic to carry out research in the UMC Utrecht.

Alternatively, it may be that for most patient populations sub-biobanks have now been established, reducing the necessity for new sub-biobanks.

Figure 1

Number of sub-biobank protocols submitted to the Committee (blue) and the MREC (orange) in 2020 compared to 2016-2019.

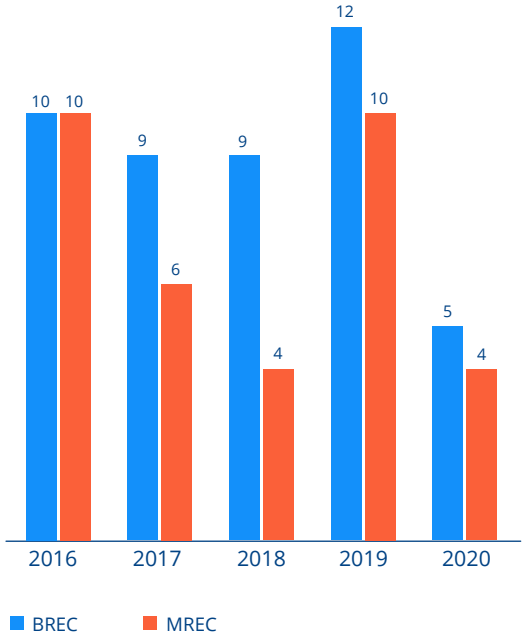


6.1.2 Number of recommendations to the Board of Directors issued on sub-biobanks

For all nine sub-biobank review procedures completed in 2020, the Committee/MREC recommended the Board of Directors to approve the sub-biobank (Figure 2). There were no recommendations for rejection. Similarly to the reduced number of sub-biobank submissions in 2020 (Figure 1), the total number of recommendations for approval was also reduced in 2020 (Figure 2).

Figure 2

Number of sub-biobanks recommended by the Committee (blue) and MREC (orange) for approval by the Board of Directors in 2020 compared to 2016-2019.



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.

6.1.3 Sub-biobanks submitted by UMC Utrecht Divisions

Of the nine sub-biobank protocols submitted by UMC Utrecht divisions to the Committee (Figure 1), two protocols were submitted by the divisions Internal Medicine & Dermatology, Surgical Specialties and Brain. The divisions Women & Babies, Images & Oncology and Laboratories, Pharmacy & Biomedical Genetics submitted one sub-biobank protocol each. The Committee received no sub-biobank protocols from the divisions Julius Center, Heart & Lung, Children and Vital Functions.

In addition, the MREC received three sub-biobank protocols for review in parallel with a WMO review (Figure 1), which were submitted by the divisions Images & Oncology (2) and Children (1).

6.2 Release protocols

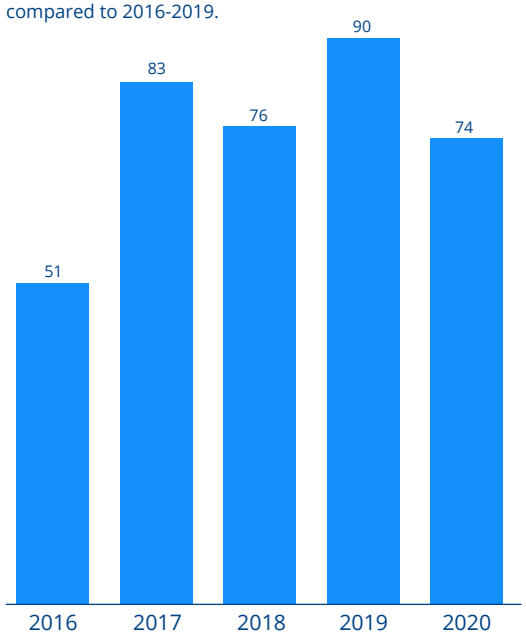
6.2.1 Number of new release protocols submitted

The total number of new release protocol submissions in 2020 decreased slightly to about the level of 2018 (Figure 3).

Each year, a substantial number of release protocol submissions originates from HUB (Hubrecht Organoid Technology). HUB was founded by Hubrecht Institute, UMC Utrecht and Royal Academy of Arts and Sciences (KNAW) to refine organoid development and foster organoid adoption globally[2]. As promised to donors to all UMC Utrecht sub-biobanks, release requests from the HUB sub-biobanks are reviewed by the Committee. HUB facilitates release protocol submissions from the HUB sub-biobanks.

These therefore also include some release requests for studies by UMC Utrecht researchers although the fast majority of submissions concern requests not directly related to UMC Utrecht research and for which HUB bears the responsibility. In 2020, 33 of the total of 74 release protocol submissions were submitted by HUB. This is an increase compared to 2019 when 21 release protocols were submitted by HUB. In contrast, UMC Utrecht release protocol submissions decreased from 69 in 2019 to 41 in 2020. This decrease in submission by UMC Utrecht researchers may (in part) be explained by the restrictions as a result of the COVID-19 pandemic to carry out research. A breakdown of the release protocol submissions by UMC Utrecht division is given in Figure 5.

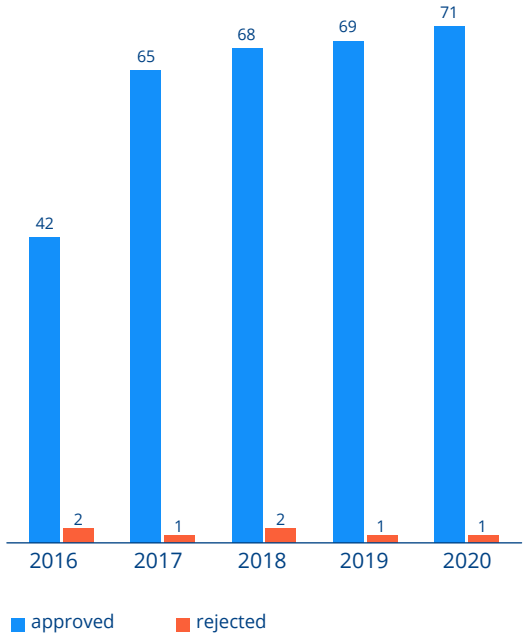
Figure 3
Number of new release protocols submitted in 2020 compared to 2016-2019.



6.2.2 Number of opinions granted

The total number of opinions (in Dutch: besluiten) granted by the Committee in 2020 remained at the same high level as in previous years (Figure 4). In almost all cases, the release protocol was approved. While the number of new release protocol submissions has varied over recent years (Figure 3), the number of opinions granted by the Committee continued to slightly increase (Figure 4). This apparent discrepancy is probably due the large variation in individual protocol review times, resulting in a carry-over effect where protocols submitted in one year may be approved or rejected in the next.

Figure 4
Number of release protocols approved (blue) and rejected (orange) in 2020 compared to 2016-2019.



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.

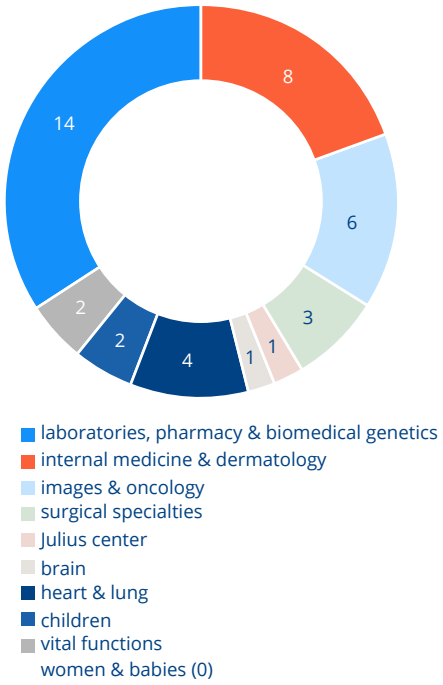
2 Link to HUB website: About | HUB Organoids

Overall, as release protocols comprise the majority of the committee's agenda, these data confirm a continuous increase in the committee's workload from 2017 onwards. Therefore, plans previously initiated to increase the meeting frequency from monthly 2.5 hour meetings to fortnightly 1.5 hour meetings were finalized in 2020 and implemented in 2021 (see section 5).

6.2.3 Release protocols submitted by UMC Utrecht Divisions

The number of release protocol submissions per UMC Utrecht division varied in 2020 from 0 and 14 (Figure 5). The highest numbers of release protocols were submitted by the divisions Laboratories, Pharmacy and Biomedical Genetics (14) and Internal Medicine and Dermatology (8).

Figure 5
Number of release protocols submitted in 2020 by UMC Utrecht divisions.



6.3 Review time

The average total time for sub-biobank and release protocol reviews are shown in Table 1.
In 2020, as in previous years, the average review time exceeded the maximum time limit set by the committee. As already described in section 5, in 2021 the meeting frequency will be increased in order to reduce the average review time.

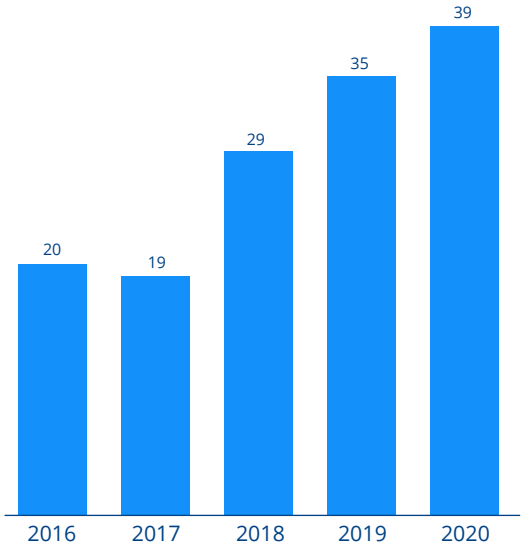
Year	Sub-biobank	Release protocol
2019	54,9 (n=12)	48,3 (n=70)
2020	67,6 (n=5)	51,5 (n=72)

Table 1
Average duration of review (in calendar days) for the recommendations and opinions given in 2020 compared to 2019. The review time limit according to the Committee's rules of procedure are 56 days for sub-bio-banks and 42 days for release protocols.

6.4 Amendments

In 2020, the number of sub-biobank and release protocols that were amended one or more times continued to increase. As the total number of previously approved protocols increases, this is not unexpected. However, it does add to the workload of both the committee and her secretariat. To deal with the increased number of 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 next meeting as weekly listings.

Figure 6
Number of sub-biobank and release protocols amended at least once in 2020 compared to 2016 - 2019.



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 Procedures, all reports of incidental findings are subject to review, in order to provide guidance on the return of the results to the donor. In 2020, no reports of incidental findings were received.

6.6 Final reports

Once their release protocol is approved, researchers are asked to report results within one year of completion of the study. As in previous years, only a handful of final reports were received in 2020. To date, there has been no active follow-up by the Committee to ascertain study results, as this is considered to be the responsibility of the researcher.

6.7 Submission procedures

Background information on the importance of review, current forms and templates to facilitate the Committee's review per UMC Utrecht Biobank Regulations, and instructions for submissions are provided on the Committee's website: Home - Toetsingscommissie Biobanken (umcutrecht.nl)

In 2020, as described in section 5, preparations were undertaken to completely redesign and update the website. The new website went live in January 2021. While previously the website was only available to UMC Utrecht employees, the new website and is accessible from both within the UMC Utrecht as well as from outside the UMC Utrecht systems.

The employees of the Department of Research Review can be contacted daily by e-mail and telephone for questions and advice on review procedures and requirements. Visits for consultation are usually allowed twice a week at scheduled times, but were replaced by telephone or video consultations from March 2020 onwards due to the COVID-19 pandemic.

7 Appeal against committee decisions

No formal appeals were received.

8 Other committee activities

Besides the reviews under the UMC Utrecht Biobank Regulation reported above there are no other review activities to report for 2020.

9 Requests for information under the Freedom of Information Act

As in previous years, no requests for information under de Freedom of Information Act (in Dutch: Wob-verzoek) were received in 2020.

10 Internal quality assurance and training

About once or twice a year, the Committee's secretary (re)trains UMC Utrecht employees on the UMC Utrecht biobank policy. However, in 2020 no such presentations took place.

In November 2020, the annual meeting of the MREC was again held jointly with members of the Committee. Due to the COVID-19 measures, the meeting was held online using video conferencing. During the annual meeting relevant developments regarding research ethics and national and or international regulations are discussed. Attendance facilitates training of TCBio committee members.

Three speakers were invited to give presentations on the topic "Early Phase Clinical Trials".
The Committee frequently reviews release protocols using organoids. It is expected that organoid systems will become increasingly relevant as a tool in first-in-man assessments in drug development. Therefore knowledge of the discussions regarding early phase clinical trials is also relevant for members of the Committee.

The following presentations were given:

Dr. N.K.A. van Eijkelenburg
(*pediatric oncologist solid tumors, Prinses Máxima Center*):
Clinical Research in pediatric oncology – emphasis on studies.

Dr. J. van der Lugt
(*pediatric (neuro) oncologist, Prinses Máxima Center*):
Clinical Research in pediatric oncology – emphasis on the patient.

Dr. J.B. Reitsma
(Epidemiologist, Julius Center):
Early evaluation studies: considerations and challenges.

There was a large attendance by members of both committees.

11 Attachments

Attachment 1

Committee members and office staff

Committee members in 2020

Prof. J.J.M. (Hans) van Delden MD PhD	Ethicist, chair
Mr. M. (Martin) Bootsma PhD	Epidemiologist
Mrs. B.C. (Claire) Collins LLM	Lawyer
Prof. R. (Roel) Goldschmeding MD PhD	Pathologist
Mrs. D.A.H. (Dennie) Gulikers-Schoonderbeek BSc	Privacy officer
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. F.A.A. (Firdaus) Mohamed Hoesein MD PhD	Radiologist
Prof. J.K. (Hans Kristian) Ploos van Amstel PhD	Geneticist
Mrs. N.A. (Kiki) Tesselaar PhD	Immunologist
Mr. P.M.J. (Paco) Welsing PhD	Epidemiologist

Substitute members in 2020

Prof. A.L. (Annelien) Bredenoord PhD	Ethicist
Mrs. I.E. (Irene) de Bruijne	On behalf of donors
Mrs. A.M. (Alexia) Franse LLM	Lawyer
Mrs. A.M. (Jenny) Zijlmans LLM	On behalf of donors

Office staff Department of Research Review in 2020

Mrs. M. (Marion) Berk-van der Linden	Administrative employee
Mrs. N.M. (Nina) Beusmans LLM	Senior review procedure coordinator
Mr. R.P. (Rutger) Chorus MA	Senior review procedure coordinator
Mrs. A.M. (Annemiek) van den Dries LLM	Senior review procedure coordinator
Mr. G.M. (Guido) Geusebroek MSc	Review procedure coordinator until May 28, 2020
Mrs. W.A. (Antoinette) Groenewegen PhD	Secretary BREC & MREC (nWMO research)
Mrs. R.G. (Rashieda) Jahangier MSc	Secretary MREC (Chamber M)
Mrs. S. (Solange) Levison MSc	Secretary MREC (Chamber D)
Mrs. M.D. (Myriam) van de Loo-Waller MA	Secretary MREC & BREC
Mrs. I. M. (Ingrid) Schut PhD	Review procedure coordinator as of March 23, 2020
Mrs. P.B. (Pauline) de Vries Bed	Management assistant
Mrs. S. (Saskia) de Weerd LLM	Head of Department Research Review

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)

Wob Freedom of Information Act
(in Dutch: Wet Openbaarheid van Bestuur)

Colophon
Text and graphics: R. Chorus
Text and editing: W.A. Groenewegen, A.H.M. van den Oetelaar
Final version: W.A. Groenewegen
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