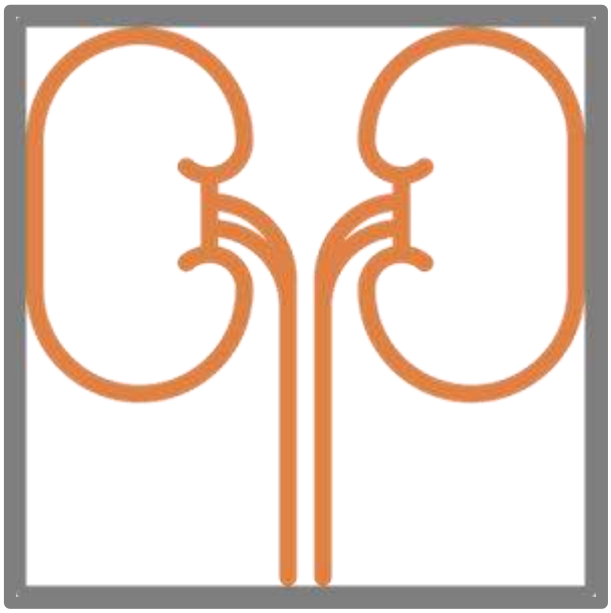

# BILAGA 3

## TILL SLUTRAPPORT DCD-PROJEKTET

DCD-pilotens Data Monitoring Committee

2020-02-13

# DCD-pilotens Data Monitoring Committee
## Slutrapport 2020-01-23

### Bakgrund
DCD-projektet innebär införande av en ny process för organdonation från avlidna i svensk sjukvård. Inom projektet bedrivs 3 vetenskapliga studier med forskningsetiska tillstånd. Till pilotprojektet har knutits en Data Monitoring Committee (DMC) med uppgift att följa patientsäkerhetsdata i projektet.

DMC har arbetat utifrån en utförlig DMC Charter (bilaga 1) med information om donatorer i akutfasen och med individuella uppföljningar av mottagare med uppgifter från akutfasen och vid uppföljning 2 veckor och 3 och 12 månader efter transplantationen.

### DMC:s sammansättning
- Kjell Asplund, Stockholm, professor emeritus i medicin, Stockholm, ordförande
- Styrbjörn Friman, professor emeritus i transplantationskirurgi, Göteborg
- Leif Eriksson, överläkare i lungmedicin, Lund
- Bengt von Zur-Mühlen, överläkare i transplantationskirurgi, specialist njurmedicin, Uppsala
- Thomas Nolin, överläkare i anestesi och intensivvård, Kristianstad

### Allmänt om DMC-arbetet
DMC har uteslutande arbetat via e-postkommunikation och telefonkontakter. Genomgående har gruppen varit eniga i sina bedömningar.

Efter vissa igångsättningssvårigheter av teknisk natur har rapporteringssystemet fungerat helt tillfredsställande. Den tekniska supporten från wTx Systems har varit till mycket god hjälp. DMC har noterat att inrapporteringen från deltagande centra har varit exemplarisk.

DMC har rapporterat till projektets styrgrupp med svar på två enkla frågor: Finns patientsäkerhetsinformation som gör att piloten bör avbrytas? Eller bör pilotprotokollet ändras?

### Inkluderade donationsprocesser
Under pilotprojektet bedömde DMC 21 inledda donationsprocesser där donatorerna avlidit under perioden 2018-02-06–2018-12-10. Av dessa ledde 10 till transplantation till sammanlagt 17 mottagare av njurar och 1 mottagare av lungor. Samtliga mottagare följdes under 12 månader.

### Huvudslutsats
Under DCD-piloten observerades inga kliniska händelser som föranledde att pilotprojektet skulle behöva avbrytas eller pilotprotokollet modifieras. Utifrån de uppgifter DMC haft tillgängliga inträffade inte heller några andra ohanterbara kliniska händelser.

### Övriga observationer
Under pilotprojektets gång gjorde DMC-medlemmarna vissa observationer som inte har direkt med patientsäkerheten att göra men som redovisas här som information för fortsatt DCD-verksamhet: Två sjukhus har stått för merparten av inledda donationsprocesser (Västerås och SÖS, vardera 7/21). Dessa sjukhus kan tjäna som föredömen när DCD-processer utformas.

- Genomgående förefaller logistiken ha varit mycket god beträffande tid från död till spolning (median 7 min, spann 5-11 min för njurtransplanterade) och kall ischemitid fram till påsläpp (median 7 tim 16 min, spann 5 tim 30 min - 9 tim 49 min).

- Det är önskvärt med information om potentiella DCD-givare där donationsprocess överhuvudtaget inte inletts eller där donation av olika anledningar inte kunnat genomföras, detta som underlag för att optimera donationsprocesserna och för att kunna bedöma möjlig framtida omfattning av DCD.
- Även fortsättningsvis är det önskvärt att följa och beakta internationella erfarenheter.

## DMC:s bedömningar

- De 10 donationsprocesserna i DCD-piloten räcker för att bedöma att DCD fungerar med
- tillräcklig säkerhet vid de svenska sjukhus som deltagit i projektet
- Ur patientsäkerhetssynpunkt har DMC inte observerat något som hindrar stegvis implementering av DCD i Sverige.
- De legala förutsättningarna för DCD bör vara tydliga för samtliga aktörer i verksamheterna.
- Implementering av DCD i Sverige bör ske stegvis.
- Nya centra utan tidigare erfarenhet av DCD bör kvalitetsbedömas var för sig: Kompetens?
- Förutsättningarna för god logistik? Utbildningar bör innefatta också lärdomar från centra som deltagit i den nu avslutade DCD-piloten.
- Vid implementering av DCD bör donationsprocessernas kvalitet följas av projekt-/arbets-/säkerhetsgrupp.

# The DCD Project

# Independent Data Monitoring Committee (DMC)

# CHARTER

### Study Identifiers

| | |
|---|---|
| Responsible Organisation | Vävnadsrådet i Sveriges Kommuner och Landsting<br>Representative for Responsible Organisartion: Jan Forslid |
| Funder | Vävnadsrådet |
| Chair of the Steering Committee | Jan Forslid, Region Örebro Län, jan.forslid@regionorebrolan.se |
| Principle Investigator | Markus Gäbel, Sahlgrenska Universitetssjukhuset |
| Approval of Regional Ethical Committee: | Date: January 25, 2018-01-25<br>Registration No: Regionala etikprövningsnämnden i Göteborg 1051-17 |
| ISRCTN Number | To be completed |
| Version of DMC Charter | Version 3, date: February 15, 2018 |
| DCD Project Protocol | Date: January 15, 2018 |

DMC Members:

- Professor em Kjell Asplund, chair
- Professor em Styrbjörn Friman, University of Gothenburg, member
- Dr Leif Eriksson, University of Lund and Skånes Universitetssjukhus. member
- Överläkare Bengt von Zür-Mühlen, University of Uppsala and Akademiska Sjukhuset, Uppsala, member
- Överläkare Thomas Nolin, Centralsjukhuset i Kristianstad, member

Contact details are available in Appendix 1.

DMC Coordinators: Kerstin Karud, SUS Malmö, kerstin.karud@skane.se

Kerstin Engman, Acando/CGI Business Consulting, Stockholm,

kerstin.engman@acando.com

### Approval signatures

The following individuals, by providing their signatures, indicate their understanding of and willingness to comply with the roles and responsibilities assigned to them in this Charter.

| | Expertise | Date | Signature |
|---|---|---|---|
| Kjell Asplund | Chair, DMC | | |
| Styrbjörn Friman | Transplantation surgery | | |
| Leif Eriksson | Pulmonary medicine | | |
| Bengt von Zür-Mühlen | Nephrology | | |
| Thomas Nolin | Intensive care | | |

## I Scope of the DMC Charter

The Data Monitoring Committee (DMC) will independently monitor patient safety information in The DCD Project, and study conduct, during the period of the project.

The objective of the DMC Charter is to outline the specific purposes and functions of the DMC and those supporting its activities, and the procedures for data abstraction and data delivery to and from the DMC members for review purposes.

## II Composition of the DMC

The DMC will comprise five members. The DMC members will include expertise in DMC work, transplantation surgery, pulmonary medicine, renal medicine and intensive care. Vävnadsrådet (through its representative), the Principle Investigator and the Steering Committee will approve all DMC members.

DMC members will not be involved as investigators in the DCD Project. In addition, DMC members must not have a conflict of interest that would bias their review of trial data (e.g. DMC members must not have a financial interest that could be substantially affected by the outcome of the study, strong views on the relative merits of the intervention, relationships with individuals in trial leadership positions that could be considered reasonably likely to affect their objectivity, or involvement in any potential competing trial).

All DMC members are expected to serve from study start until the project is completed. Should it be necessary for a member to resign, the member must submit the effective date of resignation in writing to the Steering Committee Chair, DMC Chair, and Principle Investigator. In the event a member resigns, the Steering Committee Chair, DMC Chairman and Principle Investigator, will initiate the process to identify a replacement member.

## III DMC Contacts and *ad hoc* Consultants

The Principle Investigator will serve as a primary contact person for the DMC.

The Principle Investigator will assign a DMC Coordinator who will provide administrative, logistical, and coordinating services to the DMC. The DMC Coordinator will serve as the primary administrative point of contact for communications with the DMC members and DMC-related issues and will liaise with the Steering Committee and the operational leads on the project team, as appropriate.

The DMC may contact and involve selected expert consultants who may, in strict confidence, provide additional, relevant insight or expertise to the DMC, regarding any specific issues that may arise. DMC contacts and *ad hoc* consultants are not considered to be members of the DMC.

As a rule, DMC contacts and consultants must not attend closed sessions of DMC Data Review Meetings.

## IV DMC responsibilities

The DMC is an independent expert advisory group commissioned and charged with the responsibility of evaluating cumulative clinical data. As such, the primary objective of the DMC is to monitor the safety of the subjects in The DCD Project.

At intervals determined by the number of subjects accrued, the DMC Chair will provide the official DMC recommendation to the Principle Investigator and the Chair of the Steering Committee regarding the appropriateness of continuing the project from a safety perspective, as well as any other recommendations relevant to project conduct and/or patient safety.

Specifically, the DMC members are authorised and expected to perform the following functions:

- Safeguard the interests of trial participants by monitoring the safety of the procedures and taking into account information from external sources.

- Ensure the confidentiality of all information received relating to the project.

- Participate in and vote on DMC recommendations bearing in mind the fact that ethical considerations are of prime importance.

- Make clear recommendations to the Steering Committee Chair and the Principle Investigator.

The DMC will review safety outcomes, including serious adverse events. For the first 10 patients in the project, evaluations will be based on individual assessment of each case. Thereafter, the DMC will decide whether or not accumulated data may be used for DMC evaluations (but still based on individual assessments). A formal report of safety data will be compiled after 10, 20, 30 and 50 cases, thereafter at intervals that the DMC decides. No formal statistical boundaries will be used for terminating the study for safety reasons but clear and consistent evidence of net harm that overrides any benefit should be apparent.

Throughout the project, the DMC Chair will take responsibility for the Committee's operation and will be authorised and charged with the following responsibilities:

- Chair DMC Data Review meetings, that may be performed as face-to-face meetings, teleconferences or e-mail correspondence meetings.

- Ensure that all relevant data have been reviewed by the DMC members and that all issues have been addressed.

- Ensure that only the members of the DMC are present during DMC deliberations and when DMC recommendations are discussed.

- Ensure the generation of confidential, written minutes of all closed sessions of any DMC Meetings and maintain these minutes as confidential to DMC members only, until the end of the project.

- Communicate, author, sign, and provide the official recommendations of the DMC according to the specifications outlined in this charter. If the DMC is divided in opinion on any major issue affecting the DMC's recommendations, the DMC Chair is responsible for assembling and presenting the majority and dissenting opinions for all recommendations considered.

- Arrange for consultation(s) and/or request additional data, as deemed necessary.

- Maintain a secure central file of all data outputs received for DMC review and all minutes of all sessions of DMC meetings. Provide a copy of this file to the Principle Investigator at the end of the project.

## V Steering Committee responsibilities

The Steering Committee (in which the Principle investigator is a member, and in which the Principle investigator concurrently also represents Vävnadsrådet) will have the following responsibilities with respect to the DMC:

- Provide final approval of the DMC Chair and Members to serve on the DMC.
- Assign a DMC Coordinator who will provide administrative, logistical, and coordinating services to the DMC.
- Ensure that relevant external clinical or other safety data are provided to the DCM.
- Ensure that DCM members are informed of project progress and issues at least every 6 months, and ensure that the DCM members then receive a general summary of the status of the trial and any relevant clinical issues.
- Arrange for fair and reasonable reimbursement to DCM members for their data monitoring activities (any study-related travel costs, such as transportation, lodging, and meals).
- Maintain ultimate responsibility for safe study conduct.

## VI DMC Coordinator responsibilities

The DMC Coordinator will provide administrative, logistical and coordinating support to the DMC members. The DMC Coordinator will be charged with the following responsibilities:

- Serve as the primary administrative point of contact for the DMC members and as the main liaison between the project operations teams and the DMC members. (*Kerstin Karud / Kerstin Engman)*
- Coordinate the schedule for preparation and distribution of data to DMC members *(Kerstin Karud)*
- Follow-up to verify that all data required by the DMC is provided according to an agreed timeframe. *(Kerstin Karud)*
- Coordinate arrangements for all data review meetings and DMC ad hoc meetings. *(Kerstin Engman)*
- Receive and arrange payment of DMC member invoices and expense reports, e.g. for travels*.(Kerstin Engman)*

## VII DMC Data Reports

DMC members will receive all DMC Data Reports directly from the project secretariat.*(Via iSMaRT)*

Clinical information on an included case will be provided to the DMC members as soon as the data on an individual patient has been collected. Serious adverse events will be reported immediately to the DMC Chair.

The DMC may request additional information on individual patients, as needed.

In the light of the analyses, the DMC will advise the Chair of the Steering Committee and the the Principle Investigator if, in their view, there are safety concerns strong enough to modify the project protocol or terminate the project

Following a report from the DMC, the Steering Committee will decide whether to modify entry to the project or terminate it.

## VIII DMC Committee meetings

The Committee will convene mainly via telephone conferences or e-mail correspondence meetings at intervals described in section IV. The DMC Coordinator will organize the meetings but not otherwise participate.

The Principle Investigator may be invited to give an update on the trial's status. This will be followed by a closed session attended by DMC members only. Closed minutes and recommendation will be drafted by the DMC Chair and agreed by the DMC members. The DMC Chair will report to the Chair of the Steering Committee and the Principle Investigator at intervals described in section IV.

## IX DMC Data

All assessments of clinical information will be performed in a pseudononymised manner after removing names and dates of birth (but retaining age).

All continuously recorded outcomes, including serious adverse events, must be immediately reported to the Chair of the DMC, who decides if other members of of DMC should be consulted.

To monitor adherence to the project protocol and outcome, all information reported in project protocol appendices 12 and 13-14 will be made available to the DMC for each patient included.

Adjudications using medical records (after pseudonymisation) of a 1:5 sample selected randomly will be performed. The adjudications will be performed by ckecking information in appendices 12 and 13-14 in the project protocol against information in the medical records. Additional adjudications of medical records will be performed as the DMC deems needed. The outcomes of the adjudication will be documented.

The DMC will monitor outcome of organ recipients by using information collected within TheDCD Project, as described in the project protocol, appendices 12, and 13-14:

*Kidney transplants*

Continuously:
- Loss of transplant; cause
- Primary Non Function (PNF)
- Serious adverse events as defined in the project protocol (event causing transfer of contagious disease, death, life-threatening condition, serious functional impairment, prolonged disease or need for hospital care),

At 2 weeks:
- DG-38
    - Number of dialysis occasions
    - Time point for start of function
- Surgical complications
- Acute rejections

At 3 and 12 months:
- Renal function; s-creatinine, eGFR
- Acute rejections
- Survival (not stated in the project protocol)

*Lung transplants*

Continuously:
- Loss of transplant; cause
- Primary Non Function (PNF)
- Serious adverse events as defined in the project protocol (event causing transfer of contagious disease, death, life-threatening condition, serious functional impairment, prolonged disease or need for hospital care),

At 2 weeks:
- PGD (primary graft dysfunction)
- Time in respirator
- Surgical complications
- Treated rejection

At 3 och 12 månader:
- Possible signs of acute or chronic rejection (CLAD)

All information on recipient and donor characteristics and on outcome in recipients will be collected in the iSMaRT database, generated by the DCD project. Data will be reported to the DMC as decided separately.

## X Records Retention

The DMC Chair will ensure a copy of the DMC file (i.e., copies of all reports reviewed by the DMC and copies of final minutes of all sessions of any DMC meeting) is sent to the Principle Investigator after the end of the study. It will be the responsibility of the Principle Investigator, on behalf of the Steering Committee, to arrange for long-term archiving.

## XI Indemnification and Liability

The Responsible Organisation (Vävndsrådet) shall indemnify, defend and hold harmless each DMC member (and their employer where their DMC member duties are undertaken in the course of their employment), from and against any and all losses, damages, liabilities, reasonable attorney fees, court costs, and expenses (collectively "Losses") resulting or arising from any third-party claims, actions, proceedings, investigations or litigation relating to or arising from or in connection with the performance of responsibilities by such DMC member contemplated herein, except to the extent any such Losses have resulted from a breach of such DMC member's obligations hereunder or from any wilful or intentional misconduct of the DMC member seeking indemnity hereunder.

**Appendix 1: Contact details**

***DMC members:***

| | |
|---|---|
| Professor em Kjell Asplund (Chair)<br>Reimersholmsgatan 59<br>117 40 Stockholm<br>Tel +46 8 669 5175<br>mobile phone +46 70 573 2281<br>e-mail kjellasplund1@gmail.com | Professor em Styrbjörn Friman<br>Myrbäcksvägen 20 B<br>43642 Askim<br>mobile phone +46 706609963<br>e-mail styrbjorn.friman@surgery.gu.se |
| Dr. Leif Eriksson<br>Rösträttsgatan 24<br>227 60 Lund<br>Mobile phone +46703483515<br>e-mail leif.eriksson@med.lu.se | Dr. Bengt von Zur-Mühlen<br>Västmannagatan 3<br>111 24 Stockholm<br>Tel +46 18 611 31 70<br>mobile phone +46 73 909 9165<br>e-mail bengt.muhlen@medsci.uu.se |
| Dr. Thomas Nolin<br>Sälgvägen 18<br>296 38 Åhus<br>Mob.: +46708242820<br>e-mail: nolin.thomas@gmail.com | |

***DMC Coordinators:***

| | |
|---|---|
| Kerstin Karud<br>Transplantationssekretariatet<br>Inga Marie Nilssons gata 47, plan 5<br>SUS Malmö<br>205 02 Malmö<br>0705-105854, (0761-414121)<br>kerstin.karud@skane.se | Kerstin Engman<br>Vasagatan 38<br>111 20 Stockholm<br>0708- 964 046<br>kerstin.engman@soprasteria.com |

***Responsible Organisation:*** Vävnadsrådet I Sveriges Kommuner och Landsting

***Representative of the Responsible Organisation:***
Jan Forslid (see below)

***Chair of the Steering Committee:***
Jan Forslid
jan.forslid@regionorebrolan.se

***Principle Investigator:***
Markus Gäbel, överläkare
Transplantationscentrum
Sahlgrenska Universitetssjukhuset
413 45 Göteborg
markus.gabel@vgregion.se