# COPE Annual Meeting 2015
# Meeting Minutes

**Date** 17th of March to 18th of March 2015 from 13:30 – 13.00

**Location** Target Discovery Institute

**Attendees**

## Agenda 17th March

**1. Introduction session**
- Opening and welcome
- Outline and focus of meeting ahead Updates from the COPE project office

**2. COPE clinical trials' sessions**
- POMP Trial (WP3)
- COMPARE Trial (WP4)
- Liver Trial (WP2)

**3. COPE experimental work programme**

**4. Summary of 1st day**

## Agenda 18th March

1. **Introduction Session**
2. **COPE bio-bank**
   - Overview of current sample status
   - Sample handling in COPE
   - Planned research based on approved proposals
3. **COPE Work Package 8**
   - Overview of WP8 methodology
   - Data Monitoring Committee
   - COPE literature review and systematic review
   - Statistics and health economics analysis
4. **Steps ahead, summary and closing**

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# COPE - 3rd Annual Meeting

## Meeting Minutes

*March 17-18, 2015*

## Tuesday, 17th of March 2015

### 1. Introduction Session

Rutger Ploeg (RP) opened the COPE annual meeting 2015 and welcomed all participants to Oxford. He outlined the meeting agenda and asked if the attendees would like to make changes or additions to the agenda. This was not the case. RP then outlined the meeting's purpose to review the COPE activities of the last year and highlight the upcoming steps for 2015. He furthermore stressed that the meeting should provide ample opportunity for all attendees to discuss recent COPE developments and provide their input and valued observations. RP gave the word to Margaux Laspeyres (ML) for an update from the COPE project office.

ML informed the attendees of the overall budget situation in COPE outlining the costs until June 2014 as reported to the EU Commission in the 1st COPE interim report and the costs until December 2014 gathered internally in the monitoring report. In June 2014, the total budget absorption in COPE was 23% while in December 2014; the absorption had risen to 34.5%. This constitutes an increase of 10% of budget absorption within just six months' time and clearly shows the important logistical activities that took place in the second semester of 2014 such as hiring Transplant Technicians and purchasing trial consumables. In relation to the elapsed time, ML pointed out that while 45% of the project duration had passed (as of December 2014, total of 24 months), only 33.5% of the total budget had been spent. ML concluded that the rate of spending was slower than the time passing which mirrored the delays in trial start and which gave a promising outlook unto a possible no-cost extension. ML elaborated the budget perspectives further by looking more closely at the spending rates in staff costs and the spending rates in other direct costs. She furthermore highlighted some observations for specific partners such as high staff costs that needed a close monitoring in the future or the reporting of cost lines that had not initially been budgeted. She invited all partners to get in touch with her if they had specific questions about their individual budget situation. For details of the staff cost and other direct cost budget absorption, please see Annex II.

ML continued with a status update on the achievement of milestones and deliverables as outlined in the Technical Annex of the EU grant. For the timeframe until month 27 (March 2015), a total of 22 milestones and deliverables had been listed. ML emphasised that while the achievement of milestones was indeed delayed, it was nevertheless important to note that all 22 milestones and deliverables had been fulfilled by March 2015. The delays were mainly to be found in the trial-related milestones such as the finalisation of study protocols, the ethical approvals per study and per site as well as the recruitment of first trial patients. She outlined that these milestones were strongly interconnected and that the delay in one automatically meant delay in the other. Peter Morris (PM) asked if the EU Commission was aware of these delays. ML answered that the EU Commission had been fully informed throughout the last year and had already received extensive justification of any delay in the first interim report in the summer of 2014. ML confirmed that no critical questions had been received from the EU Commission and that COPE was now able to report all milestones (list until March 2015) as fulfilled. For the full list of milestones, their planned as well as their actual achievement date, see Annex II.

In the final section, ML informed the attendees of upcoming dates and deadlines such as the next milestones relevant for 2015 and early 2016, the internal report for the first semester of 2015 and the 2nd official interim report covering July 2014 – December 2015 to the EU Commission. She then gave an overview of the communication activities in COPE including the regular newsletter issued monthly since March 2014 to a group of over 100 recipients, the created COPE flyer and roller banner for event communication, the EU "project success story" article as well as COPE presence on the ESOT website and at different recent events (World Transplant congress 2014 and British Transplant Society congress 2015). Based on PM's question, she highlighted that ESOT held the communication budget and was indeed responsible for financing the outlined communication activities and materials.

RP thanked ML and summarised the session by highlighting the extensive COPE achievements made so far. These included the successful amendment process and 1st interim report, the delivery of all milestones as of March 2015, the visibility of COPE through its communication activities and the opportunity for new partnerships with a broader network of recipient sites and the multitude of received ancillary research proposals. However, he also highlighted risks observed in the last year including the already mentioned delays in the trials' start dates due

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to prolonged regulatory requirements as well as the need for adjustment in the experimental work programmes of WP5 and WP6. He invited all attendees to discuss these risks openly in the following sessions.

## 2. COPE clinical trials' sessions

*Material from slide presentations has not been duplicated in the minutes, and confidential material has been redacted.*

Ally Bradley (AB) gave an introduction to the COPE trials' sessions by outlining the work done over the past months to get the COPE trials up and running. She reviewed the change in sponsorship and the further steps derived from this change such as a review of the trial protocols by the Clinical Trial and Research Governance Unit and the need for sponsorship contracts to be issued by Oxford. She highlighted that in total, 18 different contracts had so far been negotiated and finalised within COPE covering all trials, all site constellations as well as the equipment agreements with Organ Ox and Organ Assist. AB furthermore explained that the different regulatory requirements per country also contributed to lengthy processes as national regulations differed and had to be taken into account when drafting the sponsorship agreements, the ethics approval submission documents as well as any additional approval steps needed such as R&D in British hospital trusts and local ethical approvals in the Netherlands. Various attendees agreed that regulatory requirements had increased significantly in lengthiness and had caused important delays in the project despite everyone's best efforts and the smooth management of the project and its trials. RP agreed that regulations and approvals have become more numerous and cumbersome than in previous trial experiences (e.g. the European MP trial) and informed the attendees that he and the core COPE management group planned to outline the multitude of regulatory approvals and their detrimental impact on science and research to the EU Commission as well as to other appropriate national and local institutions. He encouraged all attendees – particularly those partners involved in the trials – to provide input to this process and to also contact their respective bodies once the information letter had been gathered.

She continued with reviewing the logistical arrangements made in parallel to achieving regulatory approvals. These arrangements included hiring a UK and a continental team of Transplant Technicians, arranging a transport scheme (COPE cars on the continent, taxi transport scheme in the UK), creating the trial databases and purchasing laptops for data collection as well as the WP7 consumables and the preparation and distribution of sample collection boxes for the three trials. Furthermore, the trial devices and their respective disposables had been delivered to all sites and staff had been trained for the machine use. AB finished with an outlook to future steps such as the need for site monitoring visits, the finalisation of WP4 approvals, the ongoing database improvement and the observation of recruitment rates.

a) POMP trial (WP3)

AB then shortly introduced the status of WP3 with its total of nine randomised kidneys (as of 17/03/2015) and gave the word to Peri Kocabayoglu (PK) for a more detailed perspective. PK reviewed the recruitment rates in WP3 so far highlighting the slow progress in recruitment leading to an average of only three kidneys per month. PK outlined that a rate of eleven kidneys per month was needed in average to reach the target inclusion of 262 within 24 months. To allow for such a speedy inclusion, PK suggested including more recruitment centres such as Cardiff for the UK and Maastricht for the Netherland, which have already been approached by RP and Henri Leuvenink (HL), respectively. HL added that Amsterdam would be another option and that he was currently reviewing the possibility of an additional Kidney Assist machine for Amsterdam with the partner Organ Assist. RP agreed that more sites were needed and encouraged the WP3 partners to engage in these additions swiftly. Ina Jochmans (IJ) commented that it was also important to observe in every partner's centre whether inclusions were missed for instance through transplant coordinators not aware of the trial criteria. She mentioned that this had already been the case in Leuven and that swift action was taken to avoid a repetition in the future. PK agreed that the information flow was important and that local teams needed to be well aware of the trial criteria. She added that competing trials in the same centre could also explain a lack of recruitment and needed to be investigated by the WP3 partners.

PK then reviewed initial database issues that had been resolved after the first procedure and updated on the sampling changes made such as the shift to dry ice instead of RNAlater. She passed the word to Arjan van der Plaats (AvdP) for an update on the Kidney Assist trial device. AvdP explained that a total of 13 trial devices were

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spread across WP3 and WP4 in the different participating sites with a total of 124 disposable sets distributed and a further 150 sets currently in production. He added that the training videos were available online and that the first batch of double-artery patches had also been delivered. Furthermore, AvdP addressed two device issues observed in the procedures so far namely the “level low message” and “flow high message” and gave guidance on how they were resolved. For more details, please see Annex II. PK closed the WP3 session by concluding that the database was finalised, the SOPs and other logistical arrangements were in place and the equipment had proven safe in its first nine procedures. She underlined that the main focus was to swiftly add further sites to increase recruitment rates.

b) COMPARE trial (WP4)

AB shortly introduced the status of WP4 with two randomisations (one kidney pair) just before the annual meeting. She highlighted that WP4 experienced technical issues with the trial database and resorted back to a paper version at the last minute to bridge the time until the database was rebuilt and fully functioning. She then gave the word to IJ for a more detailed perspective of the trial. IJ updated the attendees of the achievements of WP4 over the last year. Due to the many centres involved and strict regulatory issues, unforeseen but unavoidable delays in start of the trial have been encountered. She then updated the attendees of the status at the different WP4 sites highlighting that Leuven was recruiting since 23rd of February 2015 with its first inclusion done on 15th of March, that the Netherlands were in the final stretch of R&D approvals before being able to recruit and that in the UK Oxford as a recipient centre was up and running with the further hospital trusts to be added once all site visits were completed. She expressed her concerns in the delays caused and the slow recruitment rates even after live-go in the UK and in Belgium and urged all WP4 partners to ensure that the relevant retrieval teams were fully aware of the trial, its inclusion criteria and the steps needed for randomisation. Sijbrand Hofker (SH) gave a detailed outline of the status in the Netherlands explaining the different layers of approvals between the central ethical committee, the local ethical committees as well as the management boards of participating hospital sites. SH explained that these formalities could not be sped up and that he was doing all in his power to achieve full approvals as soon as possible, however, an expected date of final approval and as such start of the trial in the Netherlands could not be given. AB outlined that Oxford was up and running, however, as it is a paired trial and kidneys from Oxford donors will be allocated to other sites, it might make sense to wait for all site visits to have taken place before rolling out the other trial sites in the UK. She explained that this simultaneous roll-out seemed more practical as there might otherwise be cases where one kidney was sent to a partner site while the other was sent to a non-affiliated site.

With the latest data from ET and NHSBT regarding potential donors fulfilling inclusion criteria and keeping into account drop-out for several reasons, assuming the Netherlands and UK would be up and running by May 2015, inclusion will take between 12 and 18 months. As such, patient inclusion will most likely fall within the duration of the FP7 grant. However, as the primary endpoint lies 1year after inclusion, analysis of the endpoint and reporting will fall outside of the trial. It was stressed again that an extension of the grant is possible, however, without additional money from the EU.

IJ then reviewed the logistical arrangements in place in the UK and on the continent and gave the word to Marian Thijssen-Grotten (MTG) from Med-Assist. MTG explained the information and transport flows within WP4 on the continent and outlined the achievements made by Med-Assist including a pop-up notice in the Eurotransplant donor reporting software as soon as a donor matched the trial criteria as well as the training arrangements for the large team of Transplant Technicians on the continent. IJ continued with a SWOT analysis for WP4 which can be viewed in detail in Annex II. She furthermore engaged in a discussion with the meeting attendees on how best to report (Serious) Adverse Events (SAE) in the trial. Susan Dutton (SD) explained that these events where usually predefined in the protocol and that there were therefore clear lists of which incidents needed to be reported. IJ agreed that this was most often the case, but that the WP4 protocol did not encompass a very detailed (S)AE listing, i.e. protocol defined events. She therefore suggested reporting SAEs in accordance with EU law but to gather Adverse Events for a joint reporting at the end of the trial to reduce the ongoing workload. RP furthermore suggested streamlining the process of SAE / AE reporting across the three trials to ensure consistency in the project. He called upon WP8 to support this process in its role of joint methodological frame.

c) Liver trial (WP2)

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AB shortly introduced the status of WP2 with a total of 84 randomisations since June 2014 (as of 17/03/2015). She outlined that the randomisation rate was good, but that the higher level of discards or withdrawals than anticipated meant that the inclusion rate was lower than required for successful completion of the trial by June 2016. She gave the word to David Nasralla (DN) who updated the attendees in more detail. DN explained that there were a larger number of organ withdrawals in the NMP compared to SCS arm (11 Vs 5). DN reviewed the different reasons for this such as in non-retrievable livers or non-proceeding DCDs in the withdrawals. He added that there had also been a few cases where a last minute change to a non-consented recipient had to be made also leading to a withdrawal of the liver from the trial. A more detailed breakdown of discards and withdrawals can be found in Annex II. Meanwhile there is a lower organ discard rate in the NMP arm compared to SCS (4 Vs 8). He stressed that the recruitment rate had to be increased to reach the inclusion target within the set timeframe. Peter Friend (PF) strongly underlined this point expressing his hope that the recruitment would increase once the continental sites were able to join with more randomisations. He expanded that in the UK a majority of the patients on the waiting list were now consented and that ongoing close communication with the liver centres was crucial to keep randomisation rates high. DN added that it was also important to overcome the impression that the trial was linked to one specific surgeon within the centre and explained that he actively aimed at reaching out to all surgeons on the team to engage them with the trial.

Following a question asked by Andreas Paul (AP) concerning the discards due to cannulation issues, DN confirmed that additional training had been provided immediately after these issues had been observed and that the concerned trial site did not recruit anymore until the additional training had been completed and all felt confident that the cannulation techniques were optimal. PF added that it was in part the nature of a trial that the staff experience was only just being built up. DN showed a video demonstrating how the vena cava collapsed, then gradually re-filled before collapsing again due to sub-optimal cannulation. PF explained that the machine detected this issue and automatically adjusted the perfusion parameters. However, DN added that in one case of sub-optimal cannulation, the machine was not able to counter-balance the collapsing vena cava and that this situation had come about in the mentioned case.

DN continued reviewing operational and logistical arrangements set up since the beginning of the trial including the developed machine training videos, the fully trained team of Transplant Technicians for the cold storage arm of the trial as well as the availability of two normothermic machines in Oxford for simultaneous randomisations. DN also added that the machine alarms and other machine information transmitted via the display or the new mobile app function had proven very accurate and that all surgical teams should pay close attention to machine messages. DN and PF then presented two SAE cases in more detail and discussed them with the meeting attendees. For more detail on these two cases, please see Annex II. Based on a question by AP, DN explained that in the first case of SAE, the death was not to be attributed to the machine perfusion. DN stated that different assessments had been made by different clinicians involved and that there was no definitive way of asserting or entirely ruling out a machine relationship. No questions were asked in the second presented SAE. Based on a further inquiry, DN confirmed that SAEs occurred in the cold stored arm of the trial, but had not resulted in death.

### 3. COPE experimental work programmes (WP5 and WP6)

The experimental WP's reported on their last findings. After a general description of the aim of the WP's by HL (WP6), Thomas Minor (TM, WP5) reported on the experiments performed in Bonn with the oxygenated Cold Storage concept in which pre-oxygenated Aqix-RSI with addition of M101 was tested in a rat model. Reperfusion was tested in the isolated perfused liver set-up. As additional controls, traditional preservation solutions (UW and HTK) were tested as well.

HL reported on the latest experiments in which AQIX-RSI and M101 were investigated as short term rewarming and normothermic perfusion combinations. The results showed an increase in ATP (cellular energy) after reperfusion in both groups. The general discussion after the presentation focused on the potential bias of the model used (isolated perfused rat organ). Suggestions to further investigate in larger animals will be followed up (budget calculations). HL will initiate a separate meeting for this discussion in Poitiers.

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# COPE - 3rd Annual Meeting

## Meeting Minutes

*March 17-18, 2015*

## Wednesday, 18th of March 2015

### 1. Introduction Session

RP welcomed all attendees back to the second day of the COPE annual meeting and gave a quick review and summary of the contents discussed the day before. He then handed the word to Bhumika Patel (BP) – the COPE Senior Biobank Coordinator – for an update on the Work Package 7 arrangements.

### 2. COPE biobank

a) Overview of current sample status

BP updated all attendees that in total 880 samples had already been collected in COPE (figure as of 13/03/2015) and detailed that WP2 had naturally the biggest share in these with 502 NMP samples and 324 SCS samples collected since end of June 2014. In WP3, a total of 53 samples had been collected with 38 in HMP and 15 in SCS (figures as of 13/03/2015). In the sample graphs created, BP also outlined how these samples were distributed per sample type, for more detail please see Annex II.

b) Sample handling in COPE

She then reviewed the sample handling in COPE explaining that formalin fixed biopsies were being transferred to ethanol as outlined in the specific SOP created and distributed by her. Furthermore, these formalin fixed samples, transferred into ethanol would then be embedded into paraffin blocks - a process that had already started in Oxford. She added that an archive of all formalin fixed paraffin embedded samples will have matched H&E slides, which will be scanned and the images will be available to share.

BP continued with outlining the transport arrangements and requirements to bring continental samples from the participating centres to Oxford. She highlighted that all shipments needed to conform to the applicable packaging and shipment regulations and that the necessary materials for this would be provided by Oxford. She explained that samples would need to be “checked into” the WP7 database when they are being placed in the -80 freezer / in ethanol respectively. Once they are checked into the WP7 database, shipment lists can be created directly in the database and can be printed out to be added to the correctly labelled and prepared packages. Once the samples had been received in Oxford, BP would update the shipment information in the database and enter each sample’s new storage location.

BP added that for the sample collection and transport, a rotating system had been devised using the disposable distribution route of Med-Assist. Every 9-10 weeks, Med-Assist would bring disposables to the different participating centres and would use this occasion to pick up any samples that needed to be shipped. These would first be gathered centrally in Groningen and would then be brought over to Oxford approximately every three months. BP finished stating that any question with regards to the ethanol transfer, the sample “check in” for the WP7 database or the sample packaging and transport arrangements could be directed to her at any time.

c) Planned research in COPE

Zeeshan Akhtar (ZA) started by thanking all attendees involved in the trial for the efforts in collecting the samples in such a precise and meticulous way. He highlighted that the sample collection was at the heart of any research in COPE and it was therefore a crucial effort to make. ZA reviewed the underlying principles of research collaboration and publications within COPE. He explained that a joint approach was very much at the heart of the consortium involving all work package contributors into whose area a research proposal might reach. He furthermore outlined that two stages of proposal development had now been set in place with the preliminary proposal giving a short one-page overview of the research idea and the definitive application developing this idea further. The definitive application was particularly important to gain insights into the exact sample needs and ensure that the sample volume in WP7 would allow for the research to be carried out. ZA updated the attendees that so far 24 research proposals had been submitted in COPE with ten on WP2, seven on WP3 and seven on WP4 which led to a

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distribution of ten research proposals on the liver and 14 on the kidney. He continued that 15 were core proposals and nine ancillaries and that a total of six had an external collaboration. He added that only two proposals did not require any WP7 samples as they focused on the perfusion parameters of the trial devices.

This multitude of already submitted research proposals showed how valuable the samples were and ZA underlined that close monitoring was needed to ensure that all sample needs could be met. He continued presenting sample volume graphs that very clearly showed the estimated sample collection. ZA explained that two scenarios had been chosen: the target of 100% sample collection and the more realistic estimate of 75% of sample collection. The sample volume graphs (see Annex II. for more detail) showed that the WP7 core proposals' sample needs could be covered even in the scenario of a reduced sample collection at 75%. However, the KT1 biopsy of WP4 was in that case down to zero and therefore used up for the WP4 core research. For the sample needs of ancillary proposals, the sample volume graphs (see Annex II.) showed a more diverse picture. In WP2, in the scenario of a 100% sample collection, all current ancillary proposals could be covered. However, in the more realistic 75% of sample collection, the sample volume would become tighter. Particularly the LT2 biopsy showed as a potential bottleneck. For WP3, the sample volume was again without problems in a collection scenario of 100% while the biopsies would become tight in the 75% collection scenario. However, ZA added that as WP3 was carried out "in house", a high level of collection could be expected. For WP4, the graphs had already shown that the KT1 biopsy would be used up for the WP7 core research and would therefore not cover the WP7 ancillary studies in WP4.

ZA outlined three possible solutions to alleviate the sample bottlenecks: firstly, to perform close and ongoing monitoring of sample collection performance at all sites to ensure a collection rate closer to 100% than 75%; secondly, to provide final figures on the exact sample needs for all submitted studies and thirdly, to evaluate more closely the amount of biopsies needed in the WP7 core research. He passed the word to Maria Kaisar (MK) to review the outcomes of the so-called "biopsy reduction working group" investigating how to reduce biopsy needs in the core research.

MK summarised that in the mentioned working group, different approaches had been chosen: firstly, to optimise protein extraction in parallel to RNA and micro RNA; secondly, to use biopsy samples from the forerunning trial on the continent to address the question of power calculation and thirdly, to resort back to biopsy tissues from DCD pig model O2 vs -O2 for validation studies. She continued explaining the scientific rationale of assessing pre-analytical variability of plasma samples for proteomics profiling and biomarker discovery. For more details on the scientific background, please see Annex II.

## 3. COPE Work Package 8

a) Overview of WP8 methodology

Sir Peter Morris outlined the role of WP8 within COPE naming the design of high quality clinical trials and the systematic reviews to validate the rationale and methodology as its main responsibilities alongside ensuring patient safety, providing statistical support and carrying out the health economic evaluation and cost effectiveness of the proposed novel technologies. He listed the team involved in WP8 with their COPE-specific role and responsibility including members from the Centre for Evidence in Transplantation, the Health Economic Research Centre and the Surgical Intervention Trials Unit.

b) Data Monitoring Committee

PM continued with highlighting that WP8 had also established the COPE Data Monitoring Committee (DMC) consisting of five members chaired by Chris Watson (Cambridge). He added that the 1st DMC meeting took place in person in June 2014 in London, while the 2nd and 3rd meetings were held as a conference calls in December 2014 and upcoming in June 2015.

c) COPE literature review and systematic review

Liset Pengel (LP) and Simon Knight (SK) gave an overview of the systematic review performed for W3 and WP4 in a combined paper and the literature review performed for WP2. After outlining the scope and methodology used, LP concluded that the evidence available for these techniques investigated in WP3 and WP4 was poor and

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presented conflicting results across both human and animal studies, although some results showed oxygenated hypothermic machine perfusion to potentially be beneficial for kidneys which have undergone a period of warm ischemia. She added that the poster of the WP3 / WP4 systematic review was presented at the World Transplant Congress in San Francisco in July 2014 where it received a distinction award. SK summarised the WP2 literature review which was used to inform the study protocol design and the outcome selection. He added that it included all aspects relevant to the design of the WP2 trial such as its background, rationale, perfusion technologies or early human studies/pilot data. ML added that both reviews had been submitted to the EU Commission as official deliverables of the grant.

d) Statistics and health economics analysis

Virginia Chiocchia (VC) from the Surgical Intervention Trials Unit reviewed the statistical support given to COPE and started by explaining that a variable block size randomisation had been chosen stratified by donor type and centre for WP2, by centre for WP3 and by country for WP4 minimising allocation bias and making the groups similar.

For WP3 and WP4, not many procedures could yet be observed as the inclusions as per 17th March 2015 had been low. However, VC noted that in WP3 performance bias needs to be avoided while in WP4 the double-blinding of the trial requires very close observation of protocol procedures. She furthermore recommended sharing as little information divided by trial arm as possible to avoid the risk of bias. PF and AP commented that this might indeed be important in a theoretical setting, but the health and safety decisions in surgery depended on sharing surgically relevant information also with regards to the machine handling and its clinical techniques. RP agreed that knowledge transfer within the surgical team was important and concluded that trial-arm specific information should be kept within a small confidential core group of the project.

VC continued with a short update on the statistical analysis plans that had been signed off for WP2 and WP3 and needed to be finalised for WP4. She furthermore informed the attendees that the next DMC meeting would take place on 15th of June which led to the need for a data lock in mid-April to allow sufficient time for data analysis. She asked to inform all involved sites and clinicians of the forthcoming data lock to fill any missing data to ensure data entry is as complete as possible at the time of data lock. She then gave the word to Richéal Burns (RB) from the Health Economics Research Centre (HERC)

RB outlined her plans for the cost-effectiveness analysis (CEA) within COPE that will be undertaken for each of the trials. RB explained that the CEA would start at the point of organ storage and would include the cost of the intervention, the device, its consumables, its potential staffing needs, overheads and training, the resource use post-operation as well as the resource use across the follow up period. RB explained that the cost of the intervention and its comparator (e.g. NMP versus SCS) would be estimated using micro-costing techniques which will take place in UK centres and the derived resource use estimates would be circulated to all centres for comment and to identify potential variations in practice. The resource use on the other hand would be gathered based on the resource use log and the inpatient data collected. IJ asked how data accrual could be guaranteed if patients don't fill the resource use log or the quality of life questionnaire used for the utility measure of the proposed novel technologies. RB agreed that this was a risk that could not fully be eliminated as the patient information could not be retrieved otherwise. RB added that she was hoping for enough resource logs flow-back for a statistically robust analysis but that a full data accrual was indeed unlikely to be achieved. RB emphasised the importance of collecting the utility data (EQ-5D-5L questionnaire). RB said while it is anticipated that response rates may be low for the resource use, centres must do their best to ensure EQ-5D-5L questionnaires are collected and more importantly, fully completed. RB explained all five questions in the EQ-5D-5L are used to estimate a single composite score which is needed for the utility estimate and so incomplete questionnaires are not of any real value.

Focusing on the cost analysis for the continental sites, RB explained that the UK costs of care would be used in the basecase analysis and these would be adjusted for purchasing power parity (PPP) and reported in Euro (2015). She added that a costs parameter sheet (representative of the country specific Euro equivalent) would be circulated to the WP lead within the other European countries and that the variation in costs of care across countries relative to the UK costs would be used in the sensitivity analysis.

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RB summarised that health economic analysis were important to be able to influence policies across jurisdictions and that effectiveness of a novel technology was not sufficient – cost-effectiveness needed to be ascertained as well. She added that if lower quality organs were not as optimal for transplant when cold stored compared to normothermically preserved, then it may be possible to build this into the analysis as a benefit.

RP supported to arrange a separate meeting between WP2, WP3 and WP4 respectively with RB to discuss in detail how to proceed with the cost effectiveness analysis. He added that it would be helpful for RB to give her support about relevance and feasibility of certain clinical parameters and follow-up variables including the experience by the consortium members involved in the European MP trial.

RP thanked all attendees for their valuable inputs to the 3rd COPE Annual Meeting and closed the 2nd day session.

## Summary of Actions

- Core COPE management group to outline the multitude of regulatory approvals and their detrimental impact on science and research to the EU Commission as well as to other appropriate national and local institutions. All attendees – particularly those partners involved in the trials – to provide input to this process and to also contact their respective bodies once the information letter had been gathered.;
- In WP3, Oxford and Groningen to swiftly add further sites to increase recruitment rates (i.e. Cardiff & Maastricht);
- WP8 to help streamline the process of SAE / AE reporting across the three trials to ensure consistency in the project;
- WP2 to ensure that all surgeons at all involved sites are fully aware of the trial to ensure high recruitment rates;
- HL to initiate a separate meeting for WP5/WP6 discussions in Poitiers;
- Any sample related question to be brought to BP in order to ensure a correct “checking in” of samples in database and a correct packaging in line with all legal requirements;
- Project office to organise separate meetings between WP2 and WP3/WP4 respectively with RB to discuss in detail how to proceed with the cost effectiveness analysis.

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