Tissue Typers Meeting, Scandiatransplant, Copenhagen
February 8th 2013 - Minutes

1. **Welcome and presentation of participants:**
   Helle Bruunsgaard (Copenhagen) welcomed participants. All centers were represented as well as the Scandiatransplant administrative office.

2. **Election of meeting chairman and secretary:**
   Helle Bruunsgaard was elected chairmen of the meeting; Copenhagen was also elected to write the minutes of the meeting.

3. **Confirmation of the agenda:** The agenda was accepted without any alterations

4. **Election of a person who will give a report at the meeting of the council of representatives:**
   Christian Naper (Oslo) was elected to give a report at the meeting of the council of representatives.

5. **Changes in the EFI standards:**
   Juha Peräsaari (Finland), who is a member of the Standard and Quality Assurance Committee within the European Federation for Immunogenetics (EFI), informed about proposed changes to EFI standards: v 6.1. Juha Peräsaari focused especially on new guidelines for using a virtual crossmatch instead of a prospective crossmatch before a solid organ transplantation including also selected sensitised patients. Additionally, DNA based methods may be reported as a serological assignment for solid organ. EFI members can submit their thoughts about the proposed modifications until 1st May 2013. During the following discussion the general opinion was that at the moment Scandiatransplant laboratories do not plan to omit a prospective crossmatch for any kidney patient if it can be avoided as it is not considered to be an optimal procedure with regard to safety and especially sensitized patients run a high risk that is not necessary.
   The proposed changes to EFI standards (v 6.1) can be downloaded from http://www.efiweb.eu/index.php?id=102.

6. **Status and experiences in STAMP:**
   Torbjörn Leivestad presented the latest data on STAMP. *The waiting list status 19.11.2012:* A total of 1269 patients are waitlisted; 210 patients have PRA > 80 % and among these people 151 waited > 12 months; 68 patiens are on STAMP including 50 active patients and 18 patients who are temp. off. 2 patients on STAMP have been withdrawn. *Activities in theperiod April 09 – Oct. 2012:* Sinse the beginning there has been 11 positive crossmatches (2009:1; 2010: 4; 2011: 6; 2012: none); 7 STAMP patients have been transplanted due to exhange obligation priority 1; 41 STAMP patients have been transplanted due to exhange obligation priority 3 (STAMP); 16 STAMP patients have been transplanted locally against DSA; There have been 15 obligations without exchange, which could all be acceptably explained. *Conclusions about the STAMP program so far:* Initially there have been too many positive crossmatches but the number is satisfactory at the moment; The centre

compliance is acceptable; The post transplantation graft survival is acceptable (>90% 1 year graft survival); The post transplantation rejections are acceptable (~20%). Torbjörn Leivestad concluded finally that not all patients can be helped by STAMP. However, not all that can be helped by STAMP are on STAMP!
It was discussed if all patients should be put on STAMP despite their calculated chances for having an organ offer. Torbjörn Leivestad thought all patients should have the chance and the hope. Ilse Duus Weinreich (Scandiatransplant administrative Office) commented that she had performed a survey based on Scandiatransplant data, which had shown that highly immunized kidney patients were often transplanted against all odds. Additionally, the calculator in the Scandiatransplant database is still only based on a limited number of transplants.

7. **Proposal concerning exchange obligation 2 and 3 shifting priority:**
The Nordic Kidney Group has decided to propose to the Council of Representatives Meeting May 2013 that exchange obligation 2 and exchange obligation 3 shift positions with regard to priority. Mats Bengtsson (Uppsala) presented that in 2012 there were a total of 421 searches. Of those 65 had one or more exchange obligation (15%) and 51 resulted in kidney exchange: 6 exchanges (12%) were due to priority 1; 4 exchanges (8%) were due to priority 2; 24 exchanges were due to priority 3 (47%); 2 exchanges (4%) were due to priority 4; and 15 exchanges were due to priority 5 (29%). Additionally, in 2012 all searches resulted in a total of 9 exchange obligations with priority 2. Among those none had priority 3 and 5 were not exchanged due to acceptable reasons. In 2011 searches resulted in a total of 6 exchange obligations with priority 2 and among those 3 had also priority 3. Based on these figures Mats Bengtsson suggested that Tissue Typers also propose that exchange obligation 2 and 3 shift priority with the purpose to give highly immunized patients the highest priority within Scandiatransplant. Based on the figures, he concluded that this proposal will not cause major changes it the total exchanges.

   Conclusion: All laboratories accepted the proposal

8. **Exchange obligation 1: What do we think about the problem with the lacking control of antibodies directed towards splits, HLA-C and/or HLA-DQ before shipment?**
Several HLA laboratories have experienced that kidney exchanges take place due to exchange obligation 1 without a control of antibodies directed towards splits of HLA-A, B, DR or antibodies against HLA-C and/or HLA-DQ before the shipment. This procedure results in a high risk of a positive crossmatch in the recipient's center. Different strategies were discussed to prevent this. However, procedures and the organization in the centers are very different, and accordingly, there is no easy way to solve this problem. It was suggested that all laboratories discuss with their colleagues local solutions to handle this problem and the size of the problem should be addressed at future meetings.

9. **HLA-C typing on donors (decided at Tissue Typers meeting 2012):** Regarding deceased donors all laboratories use PCR-SSP for HLA-C typing except Copenhagen, which uses still serology. Copenhagen plan also to implement PCR-SSP for HLA-C typing during the next few months.

10. **Flow-based crossmatch for detection of complement-binding antibodies:** Mats Alheim, Stockholm presented data of a flow cytometric assay for detection of complement fixing and

non-fixing antibodies as an alternative method to CDC and FCXM. The assay included PBMC or pre-sorted B cells or pre-sorted T cells that were incubated with serum and rabbit complement. Binding of antibodies were detected by anti-human IgG FITCH and viability of cells were detected by 7-AAD in a flow-based XM. The assay is easy to perform as it only includes two FL parameters and no compensation. It detects cytotoxicity and antibody binding in one assay and results are comparable with CDC and FCXM but with reduced assay time, low variation and low subjectivity.

11. **Discussion of how laboratories define acceptable mismatches in Scandiatransplant Centres**: Helle Bruunsgaard had performed a survey including 8 questions and 2 cases to illustrate how laboratories in Scandiatransplant perform antibody testing before acceptable mismatches are defined and to investigate if laboratories report the same acceptable mismatches. Eight laboratories had responded to the questions but one of these laboratories does not participate in STAMP and one laboratory had not answered to the cases. It was concluded that the laboratories use almost the same assays, with the same cut offs, and the same troubleshooting strategies. Differences in reports of acceptable mismatches were found across laboratories in the presence of allele specific antibodies, DRB3/DRB4/DRB5 antibodies and DQA antibodies. Members of the Steering Committee commented that a patient with antibodies directed against common occurring HLA-DP antigens should not be put on STAMP due to a considerable and unpredictable risk of a positive crossmatch. Helle Bruunsgaard asked if the steering committee of STAMP would consider if a more detailed SOP could be made to guide laboratories in the definition of acceptable mismatches.

12. **The Scandiatransplant Office:** Ilse Duus Weinreich presented Scandiatransplant data concerning the following main topics:
    a. Donor search broad vs. narrow HLA specificities: Most centers have decreased their proportion of searches including one or more broad HLA antigens. Copenhagen has increased their proportion of donor searches that include one or more broad HLA antigens due to problems with HLA-DQ splits. Helle Bruunsgaard informed that Copenhagen was aware of the problem and was working hard on a solution to the problem.

    b. Compliance to kidney exchange rules: In 2012 a total 421 searches have been performed. Among these there have been 65 exchange obligations (15% of all searches). Only in 4,6 % of the cases exchange rules were not followed (3 out of 65).

13. **Additional issues/comments and discussions:**
    Regarding the status for a potential collaboration between Estonia and Scandiatransplant Kaj Anker Jørgensen (medical director of Scandiatransplant) informed that Estonia has been recognized as an official exchange organization at the Council of representatives meeting May 9, 2012. At the same meeting it has been decided to form a working group with the purpose to evaluate the question if Estonia should become a member of Scandiatransplant or not.
    Mats Bengtsson suggested that organizers of the Tissue Typers' Meeting 2014 should consider also to invite representatives of Estonia to participate in the next meeting.
    More detailed information about Estonia and Scandiatransplant is found on http://www.scandiatransplant.org/organ-allocation/agreements/agreement-on-organ-exchange-estonia and

http://www.scandiatransplant.org/about-scandiatransplant/scandiatransplant-representatives/Minutes_rep_2012_2.pdf

Applauses were given to Frank Pedersen (System administrator, Scandiatransplant) for his many years of dedicated work with the Scanditransplant database system.

Gunilla Martinez-Riqué (Lund) informed that the economical crisis had affected resources allocated to solid organ transplantation in the Southern part of Sweden.

Helle Bruunsgaard asked if laboratories were interested in a working group with the aim to discuss and exchange experience and knowledge with regard to strategies for handling ambiguities in high resolution HLA typing. So far there was only a limited interest.

14. **Next meeting:** Oslo will host the next meeting on January 31th 2014