BELGIAN GUIDELINES FOR MANAGING INCIDENTAL FINDINGS DETECTED BY NIPT

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NIPT by means of whole genome sequencing may result in incidental findings such as whole chromosome aneuploidies other than trisomy 13, 18 or 21 or sub-chromosomal abnormalities. Such incidental finding should be managed according to the guidelines outlined below. In case of uncertainty, the responsible clinical geneticist takes the decision after consulting the ad hoc committee. If no consensus can be reached, the responsible clinical geneticist decides and communicates his decision to the ad hoc committee.
For all reported incidental findings, referral for genetic counselling is required.

Fetal incidental findings

1. **Fetal autosomal aneuploidies** other than trisomy 13, 18 or 21 will be communicated, stating the possibility of confined placental mosaicism in the report. Follow-up amniocentesis can be offered to exclude fetal mosaicism and, if applicable, uniparental disomy (chromosome 7, 11, 14, 15 and 16).
2. **Fetal sub-chromosomal abnormalities** will be communicated when they are considered technically valid and are in concordance with the Belgian invasive prenatal testing guidelines. Follow-up amniocentesis is indicated to confirm the finding.

Maternal incidental findings

Five groups of maternal incidental findings can be distinguished. Follow-up amniocentesis can be indicated, since NIPT cannot confirm or exclude the presence of the detected aberration in the fetus.

1. Copy number variations (CNVs) causing highly penetrant disorders with validated evidence on the phenotype associated with the deletion or duplication. These are considered clinically relevant and will be reported.
2. CNVs proven to be risk factors for developmental disorders with reduced penetrance and/or variable expression. The predictability of the future phenotype resulting from such CNVs remains very poor. Therefore, these susceptibility CNVs will not be reported.
3. CNVs causing late-onset genetic disorders that are still asymptomatic in the mother. Disorders with clinical utility, typically cancer caused by the deletion of a tumor suppressor gene, will be reported according to the guidelines from the ACMG (2013), as undeniable health benefit can be expected for the mother and/or relatives when communicated.
4. CNVs that have no consequence for the mother but, if inherited, are potentially harmful for the fetus in the current or in a future pregnancy:
    a. Carriership for autosomal recessive disorders will not be communicated, unless the disorder is frequent, i.e. carrier frequency is >1/50 and testing is available in Belgium (CFTR, SMA and Connexin 26).
    b. Carriership for X-linked recessive disorders will be communicated, irrespective of the sex of the fetus.
    c. Carriership of a mosaic CNV will be communicated if it poses a high risk for developmental disorders in the fetus.
5. NIPT may lead to the incidental finding of a malignancy in the mother. This will be communicated.