• Bone marrow (useful, not mandatory): May show foam cells (filipin + if tested for this stain)
• If a liver biopsy is performed for cholestatic liver disease, fixation for EM study is essential
• Serum chitotriosidase: useful, not mandatory; generally (not always) elevated activity
• Isolated (hepato)splenomegaly: enzymatic exclusion of Gaucher and Niemann-Pick B = prerequisite
• Provide the laboratory with sufficient clinical data (essential for correct interpretation of the results)

SKIN BIOPSY
- If local situation permits: fixation and EM study
- Fibroblast culture (mandatory)

FILIPIN TEST
(cell biology) (done twice)

Highly positive « classical »
(85% of NP-C patients)

Moderately positive with pure LDL, « variant »
(15% of NP-C patients)

Difficult Interpretation*
(3-5% of NP-C patients)

Clearly negative

Nearly sure NP-C**

Probable “variant” NP-C***

Kinetics of LDL-induced cholesteryl ester formation

Re-assess clinical features
Reference Centre Complementary investigations
If likely diagnosis, gene sequencing

Sequencing of NPC1 and NPC2 genes
- Depending on countries, study first NPC1 p.I1061T or other most prevalent common mutation
- Conclude quickly on NPC2 if child < 8-10 months
- NPC1: numerous polymorphisms!!! – check allele segregation from parental study
- often need to study both gDNA and cDNA