MLD screening from the laboratory's perspective

The integration of metachromatic leukodystrophy (MLD) into newborn screening represents significant progress in the early detection of this rare, genetic metabolic disease, which leads to severe disabilities and premature death if left untreated. Despite promising results from pilot studies that demonstrate reliable and safe diagnostics in screening, there are difficulties in the development and validation of the analytical algorithm in the laboratory.
Key challenges include the selection and standardisation of sensitive and specific test methods, particularly for measuring the activity of arylsulfatase-A and the mass spectrometric detection of the corresponding sulfatides.
The differentiation of pseudodeficiencies and rare genetic variants requires additional genetic analyses and complex decision trees in the algorithm. Laboratory validation is further complicated by the rarity of the disease, limited sample availability and the need to minimise false-positive and false-negative findings.
Overall, the establishment of a robust screening algorithm for MLD is associated with high methodological and organisational demands that require close cooperation between the laboratory, clinic and science in order to ensure reliable and efficient early detection.