



Quality Assurance in Laboratory Testing for IEM

Introduction to the Lipids in Serum (LIS) scheme

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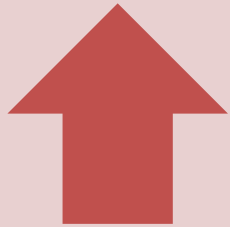
Erndim Workshop 2025 Madrid: October 10

A little bit of history

- In 2020 George reached out to Amsterdam to ask for help in organising a new lipids scheme
- Busy busy busy.....
- Middle 2022 Marie and I teamed up to make a plan..



Why a new Erndim scheme?



Special Assays in Serum (SAS) scheme is expanding: poses challenges for solubility

2002: 15 analytes

2025: 28 analytes



New lipid markers are introduced in clinical practice

PPCS for NPC

C26:0-lysoPC for ALD

Etc...

How did we start?

Started as a pilot scheme in 2024

- Labs submitting results for “specialized lipids” were contacted
- Free of charge

Set of lipids was coordinated with Scientific advisory Board (SAB)

- Set of samples to cover reference values and disease values

Lipids already in SAS were offered in the two schemes

Lipid (n=13)	Disease	Disease group	SAS/New
Lyso-sphingomyelin (Lyso-SM)	Niemann Pick Disease type A/B	Sphingolipidoses	SAS
Lyso-globotriaosylceramide (Lyso-Gb3)	Fabry Disease	Sphingolipidoses	SAS
Glucosylsphingosine	Gaucher Disease	Sphingolipidoses	SAS
N-palmitoyl-O-phosphocholineserine (PPCS)	For PPCS we also asked the question: Is the value within, below or above your reference range? (hybrid scheme)	Sphingolipidoses	New*
Lyso-monosialoganglioside 1 (Lyso-GM1)		Sphingolipidoses	New*
Lyso-monosialoganglioside 2 (Lyso-GM2)		Sphingolipidoses	New*
Cholestane-3β,5α,6β-triol		Sphingolipidoses	SAS
7-ketocholesterol (7-KC)		Sphingolipidoses	SAS
C26:0-lysophosphatidylcholine (C26:0-lysoPC)	ALD, DBP, Zellweger syndrome	Peroxisomal Disorders	SAS: pilot 2023
Cholesterol	Cerebrotendinous Xanthomatosis (CTX)	Bile acid disorders	SAS
7-dehydrocholesterol (7-DHC)	Smith Lemli Opitz Syndrome (SLO)	Sterol biogenesis disorders	SAS
Desmosterol	Desmosterolosis	Sterol biogenesis disorders	New*
Sitosterol	Sitosterolemia	Sterol transport disorders	New*

Statistics from LIS pilot year 2024

N=44 participants overall

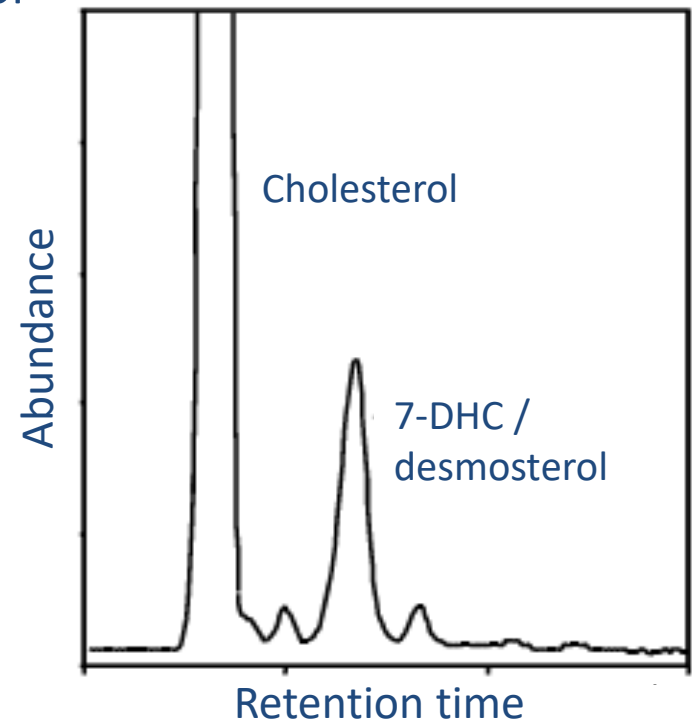
Participants per metabolite range from – to:

- 7 for 7-ketocholesterol
- 43 for 7-dehydrocholesterol

Some “new lipids” already quite popular:
sitosterol: N=26

Experiences from LIS pilot year 2024

- First sample: adjustments to the units
- Some remarks regarding lipemic samples, hard to handle
- Question about PPCS was often not understood. Pro: values quite well harmonized
- Many labs (both GC and GC-MS) experience difficulties discriminating 7-dehydrocholesterol (7-DHC) and desmosterol



Desmosterol

- Increased in the sterol biogenesis disorder desmosterolosis
 - 9 patients reported thus far
 - Clinical picture: psychomotor developmental delay, failure to thrive, dysgenesis of the corpus callosum, cerebral white matter atrophy, spasticity and dysmorphic features
- Can be secondarily increased due to amiodaron use (antiarrhythmic drug)

Figure 1

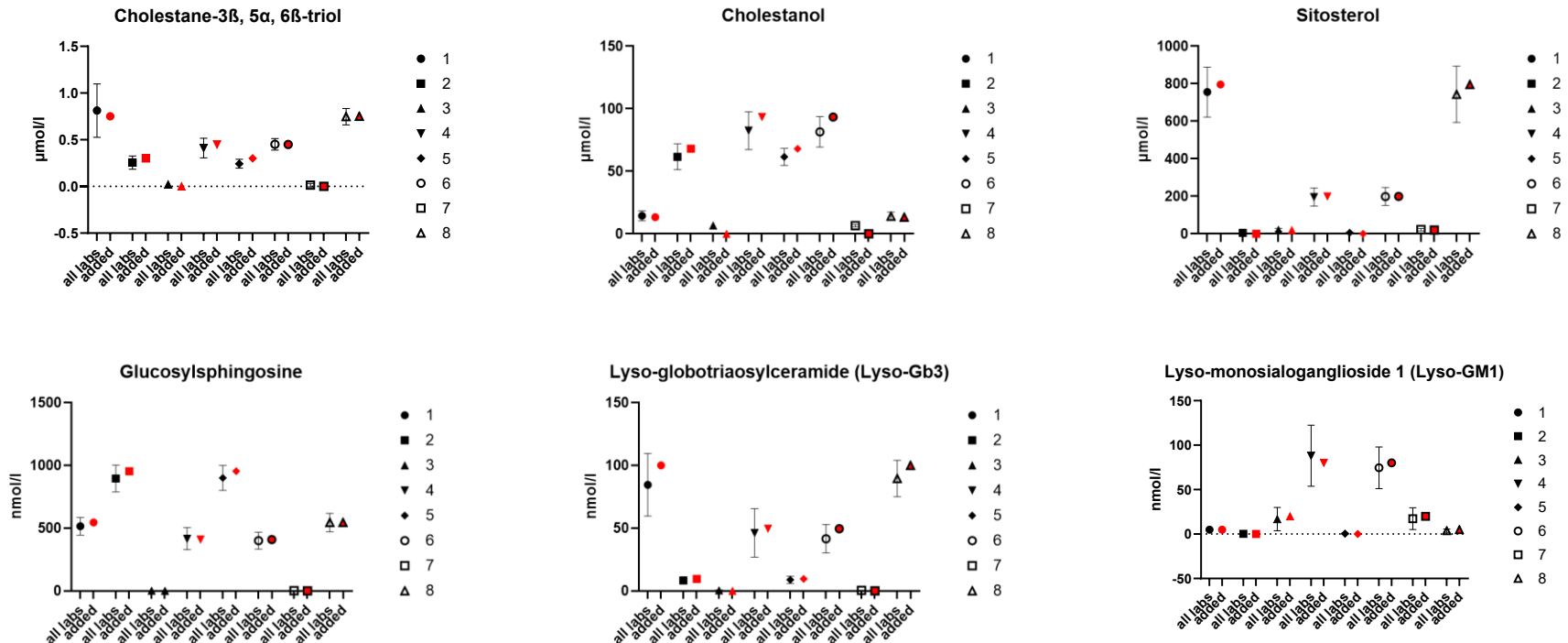


Left: Scaphocephaly, tall forehead with bitemporal narrowing, short palpebral fissures, long nose, hypoplastic nasal alae, prominent columella, low-set posteriorly rotated ears and camptodactyly of the pink.

Right: white matter volume loss, dilated ventricles, thin corpus callosum

Desmosterolosis: an illustration of diagnostic ambiguity of cholesterol synthesis disorders. Orphanet Journal of Rare Diseases volume 9, Article number: 94 (2014)

Quantitative analysis LIS pilot 2024



Close inspection of all lipids: good correlation between spiked amount (red) and median all labs (for 7-DHC and desmosterol wide distribution)

2025: 2nd pilot year

- Addition of CoQ10 (already in SAS) and lathosterol (new)
- Spiking with either 7-DHC OR desmosterol
- Total spike of lipids more evenly distributed
- Removed the question for PPCS: only quantitative results

Interim analysis (after 4 samples):

- Again in general good correlations between spikes and median all labs
- No comments on lipemic samples received
- Still difficulties with 7-DHC/desmosterol, especially labs which only submit for 7-DHC



2026: LIS full scheme

- 7-DHC will be offered both in SAS and LIS (as well as cholestanol)
- No further extensions (list of lipids identical to 2025)

2026 EQA Schemes

1. Introduction
2. EQA Schemes



QTOU	Quantitative Organic Acids (urine).....	5
SADB	Special Assays in dried blood spots.....	6
SAS	Special Assays in Serum.....	6
SAU	Special Assays in Urine.....	6
SAC	Special Assays Combined (serum & urine).....	6
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Lipid (n=15)	Disease	Disease group	SAS/New
Lyso-sphingomyelin (Lyso-SM)	Niemann Pick Disease type A/B	Sphingolipidoses	SAS
Lyso-globotriaosylceramide (Lyso-Gb3)	Fabry Disease	Sphingolipidoses	SAS
Glucosylsphingosine	Gaucher Disease	Sphingolipidoses	SAS
N-palmitoyl-O-phosphocholineserine (PPCS)	Niemann Pick Disease type A/B and C	Sphingolipidoses	New*
Lyso-monosialoganglioside 1 (Lyso-GM1)	GM1 gangliosidosis	Sphingolipidoses	New*
Lyso-monosialoganglioside 2 (Lyso-GM2)	GM2 gangliosidoses (Tay Sachs and Sandhoff disease)	Sphingolipidoses	New*
Cholestane-3β,5α,6β-triol	Niemann Pick Disease type C	Sphingolipidoses	SAS
7-ketocholesterol (7-KC)	Niemann Pick Disease type C	Sphingolipidoses	SAS
C26:0-lysophosphatidylcholine (C26:0-lysoPC)	ALD, DBP, Zellweger syndrome	Peroxisomal Disorders	SAS: pilot 2023
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Desmosterol	Desmosterolosis	Sterol biogenesis disorders	New*
Sitosterol	Sitosterolemia	Sterol transport disorders	New*
Lathosterol	Lathosterolemia	Sterol biogenesis disorders	New*
Coenzyme Q10 (CoQ10)	Primary CoQ10 Deficiency	Mitochondrial Disorders	SAS

Questions?

