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Critical Errors in the 2022 Qualitative EQA schemes

All critical errors for the 2022 schemes were agreed at the SAB online meeting held on 24th and 25th November 2022.

EQA scheme							
Scheme Name[1]	**Sample Number**	**Scheme Year**	**Diagnosis**	**Critical Error**	**Number of Labs**	**No of participants[2]**	**% CE**
ACDB Heidelberg	2022-A	2022	3-Hydroxy-3-methy-glutaryl-CoA lyase deficiency (HMG CLD)	Detection of C5DC and C18:1 carnitines as elevated and interpreted as indicative for glutaric aciduria type 1.	1	36	2.8%
	2022-B	2022	Glutaryl-CoA dehydrogenase deficiency (glutaric aciduria type 1)	Failed to report C5DC but found elevated C14:1-based ratios and diagnosed VLCAD.	1	36	2.8%
	2022-D	2022	3-Hydroxy-3-methy-glutaryl-CoA lyase deficiency (HMG CLD)	One lab detected elevated C5DC carnitine and reported MAD deficiency as the primary diagnosis, another lab detected elevated free carnitine, decreased C2 carnitine and reported CPT1a deficiency.	2	36	5.6%
ACDB London	2022-A	2022	3-Hydroxy-3-methy-glutaryl-CoA lyase deficiency (HMG)	Reported a normal profile and no further testing recommendations.	1	42	2.4%
ACDB Rome	2022-B	2022	Ethylmalonic encephalopathy (ETHE1)	No diagnosis made. One lab recommended multi-gene panel testing, another lab suggested organic acids in urine neurological evaluation.	2	43	4.7%
	2022-C	2022	Very long Chain Acyl-CoA Dehydrogenase deficiency	Reported a normal profile, recommended further testing for organic acids in urine and also amino acids in urine and plasma.	1	43	2.3%
CDG	2022-A	2022	Normal	An abnormal profile interpretation of this sample, without additional Diagnostic Suggestions	1	58	1.7%
	2022-B	2022	ATP6V0A2-CDG	A normal profile interpretation without additional Diagnostic Suggestions	1	58	1.7%
DPT CH	2022-C	2022	Mucopolysaccharidosis type VI, arylsulfatase B deficiency (OMIM 253200)	Failure to identify a MPS disease and no recommendation for MPS analysis made.	1	20	5.0%
DPT CZ	2022-A	2022	Barth syndrome (3-methylglutaconic aciduria type II)	Failure to recognize abnormal excretion of 3-methylglutaconic acid.	1	18	5.6%
DPT FR	2022-A	2022	Barth syndrome (3-methylglutaconic aciduria type II)	Failure to recognize abnormal excretion of 3-methylglutaconic acid.	2	20	10.0%
	2022-B	2022	Propionic acidemia due to propionyl-CoA carboxylase deficiency	Propionic acidaemia is a treatable disorder, as such failure to make this diagnosis is considered a critical error.	1	20	5.0%
	2022-E	2022	3-methylcrotonyl-CoA carboxylase deficiency (3-methylcrotonylglycinuria)	Failure to identify an increase of 3-hydroxyisovaleric acid, and misdiagnosis 3-methylcrotonylglycine as tiglylglycine.	1	20	5.0%
	2022-F	2022	Aromatic L-aminoacid decarboxylase (AADC) deficiency	Failure to identify vanillactic in the urine sample.	1	20	5.0%
DPT NL	2022-C	2022	Hyperprolinemia type II due to delta- 1-pyrroline-5-carboxylate (P5C) dehydrogenase (OMIM 239510)	Failure to detect an increase of proline in this sample, patients with this disorder can be treated with B6.	1	17	5.9%
DPT NL	2022-E	2022	MCAD deficiency (OMIM 201450)	Failure to make the correct diagnosis, this was a straight forward sample that has previously been circulated in 2016 (sample E) with a proficiency of 96%.	1	17	5.9%
DPT UK	2022-C	2022	Thymidine phosphorylase deficiency aka Mitochondrial neuro-gastro intestinal encephalopathy (MNGIE)	Provided an incorrect diagnosis and did not perform purine and pyrimidine analysis.	1	20	5.0%
QLOU Barcelona	2022-A	2022	Multiple acyl-CoA dehydrogenases deficiency	Reported a normal profile and made no recommendaitons for further testing.	2	71	2.8%
	2022-F	2022	Glutathione synthetase deficiency	No abnormality detected.	2	71	2.8%
QLOU Heidelberg	2022-B	2022	5-Oxoprolinuria due to glutathione synthetase deficiency (GSS)	No abnormal diagnosis was given, failure to detect 5-oxoproline, elevated lactate reported.	1	71	1.4%
	2022-D	2022	Mevalonic aciduria due to mevalonate kinase (MVK) deficiency	Incorrectly diagnosed as malonic aciduria with a high level of malonic acid reported.	1	71	1.4%
QLOU Sheffield	2022-C	2022	Citrullinaemia Type 1 caused by deficient activity of Argininosuccinate Synthase due to mutations in the ASS gene	If a urea cycle was not considered and/or appropriate follow up tests requested.	1	71	1.4%
UMPS	2022-C	2022	MPS-II	Reporting a normal profile/no diagnosis.	1	81	1.2%
	2022-F	2022	MPS-III(A)	Reporting a normal profile as the most likely diagnosis.	3	81	3.7%
				Totals	**31**	**568**	**5.5%**

Notes

1. ACDB = Acylcarnitines in DBS; CDG = Congenital Disorders of Glycoslylation; DPT = Diagnostic Proficiency Testing; CH = Switzerland; CZ = Czech Republic; FR = France; NL = Netherlands; UK = United Kingdom; QLOU = Qualitative Organic Acid; UMPS = Urine Mucopolysaccharides

2. Number of participants = number of registered labs minus any Educational participants, non- or partial submitters and any labs that withdrew from the scheme