

# **Amino Acids Interpretation (AAI) Scheme**

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# 2025 First Round Interim Report (DOC5136)

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#### **Please Note:**

- This interim report is intended for participants of the ERNDIM AAI scheme. The contents should not be used for any publication without permission of the Scientific Advisor.
- This is an interim report and it includes provisional scores only. All scores are subject to change following moderation at the Scientific Advisory Board meeting in autumn of this year. For final scores and performance data the ERNDIM AAI Annual Report should be referred to.
- The fact that your laboratory participates in this scheme is not confidential, however, the raw data and
  performance scores are confidential and will only be shared within ERNDIM for the purpose of evaluating your
  laboratories performance, unless ERNDIM is required to disclose performance data by a relevant government
  agency. For details, please see the ERNDIM Privacy Policy on <a href="https://www.erndim.org">www.erndim.org</a>.

#### 1. Results Submission

The deadline for submission of the 2025 first round results was 27<sup>th</sup> May 2025. Participants were able to view the cases and submit their results using the ERNDIM Formdesk website.

148 laboratories registered for the 2025 AAI scheme, of these 142 labs (96%) submitted results for the first round.

### 2. Scoring System

As for the previous circulations, each of the three aspects, analytical findings, diagnosis, and further tests, were scored equally with a maximum of two points for each category. Plasma amino acid concentrations together with the laboratories reference ranges were provided.

The tables (Table 1-3) show scoring to which the evaluators agreed previously. Scoring was done by two blinded evaluators each (the evaluators were blinded to both, the ERN number and to the scores of the second evaluator). If the scores were not concordant the scheme advisor scored in addition. Further close evaluation based on agreed/revised scoring criteria was used to determine on the final score.

Case 1 abnormalities	1	2	7	111	normalities	Case 1 diagnosis	1	2	7	diagnosis	Case 1 further testing recommendations (Is the missing recommendation for ammonia determination a critical error? YES, if not UCD is suspected)	1	2	7	nmendations
Each 1 point: elevated gin and/or ala, low normal arg and/or cit and/or orn, maximum 2 points				4-100	2025.0	OTC deficiency 2 points, proximal urea cycle disorder 2 points, urea cycle disorder 1 point, mitochondrial dysfunction/disorder 1 point, CA-VA 1 point, maximum 2 points				2025.01	each 1 point (maximum 2 points): ammonia, urea in plasma, orotic acid or organic acids in urine, uracil in urine, molecular genetic analysis of OTC gene/UCD genes				2025.01 recor
Elevated concentration of Glutamine, Glutamic acid, Proline, Alanine. Citrulline, Arginine level in the low normal range.	_2	2	<b>2</b>	: :	2	Possible urea cycle disorder. The elevated glutamine and alanine and the low-normal levels of citrulline and arginine may reflect impaired flux through the urea cycle, possibly involving partial enzyme deficiency such as in NAGS deficiency, OTC deficiency, or other proximal defects	2	_2	_2	2	Plasma ammonia measurement (venous blood, processed immediately)     Liver function panel including urea, AST/ALT, lactate and pyruvate     Urine organic acid analysis (GC-MS)     Cenetic testing: NGS panel targeting urea cycle	2	_2	_2	2

**Figure 1:** Example of scoring for case 2025-1.

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<sup>&</sup>lt;sup>1</sup> If this Report is not Version 1 for this scheme year, go to APPENDIX 2 (page 10) for details of the changes made since the last version of this document.



### 3. Results of samples and evaluation of reporting

### 3.1. Case 2025-1: Ornithine transcarbamylase deficiency (OTC deficiency)

#### 3.1.1. Sample Details

The results are from an 18-months-old boy who was admitted to the emergency department due to vomiting and apathy. No previous illness was known. The medical history revealed that the boy had had recurrent episodes of clouding of consciousness for four months. The ammonia concentration was slightly elevated (137  $\mu$ mol/L). The diagnosis was confirmed by molecular genetics (detection of a hemizygous mutation in the *OTC* gene). The therapy consists of a protein-defined diet with substitution of essential amino acids.

#### 3.1.2. Scoring details

Table 1: Scoring details for case 2025-1.

-	interpretation		scores (points)				
findings abnormalities	elevated	gln, ala	1				
findings, abnormalities,	elevated	glu, pro, gly, met	0				
maximum 2 points	(low) normal	arg, cit, orn	1				
	ornithine transcarbam	ylase deficiency	2				
	proximal urea cycle dis	sorder	2				
diagnosis, maximum 2 points	urea cycle disorder		1				
diagnosis, maximum 2 points	mitochondrial dysfunc	tion/disorder	1				
	carbonic anhydrase VA	deficiency	1				
	lysinuric protein intole	erance	0				
further tests (if molecular	orotic acid in urine (or	1					
further tests (if molecular	uracil in urine		1				
genetic recommended specify	ammonia in plasma, ur	rea in plasma/serum	1				
the gene), maximum 2 points	genetic analysis of OTO	1					
comments	The clinical symptoms often the case in every		-				
	If the participant does not recommend the ammonia						
critical error	determination and does not have a suspected						
Circical Ciro	diagnosis of an urea cycle defect, this is considered a						
	critical error.						

Scores for participating laboratories are in APPENDIX 1 on page 7.

### 3.1.3. Comments on overall performance

Overall proficiency was 87%. The proficiency for abnormalities was lowest at 83%. The most common reason for a point deduction was the lack of indication that the concentrations of arginine and/or citrulline and/or ornithine were low normal.

This is a difficult case from everyday life, some points made the diagnosis difficult:

- The age of the child, as non-neonatal OTC deficiency is very rare.
- **It is also important to describe the low concentrations!** Therefore, in some cases there was only one point.
- An increased glutamine concentration should in any case lead to the determination of ammonia. Therefore, it was discussed whether the missing recommendation to determine the ammonia concentration is seen as a critical error. In the event that the diagnosis of a urea cycle defect was made, the lack of recommendation to determine the ammonia concentration was not considered a critical error.
- The specified quotients may be helpful in daily life.



### 3.1.4. Best interpretation (scored with 2 points each)

- **Findings (\*47):** Markedly increased glutamine, glutamic acid, proline, alanine and lysine. Slightly increased methionine. Low-normal levels of citrulline and arginine. Normal ornithine.
- **Diagnosis (\*2)**: A urea cycle defect would need to excluded: OTC (male patient), CPS1/NAGS, CAVA. Orn:Cit=9.5, Cit:Arg=0.6 (ref. <0.36), Cit:Phe=0.15 (ref <0.1), Gln:Cit=130 (ref. <104).
- Further tests (\*135): Urgent plasma ammonia measurement. Urinary orotic acid quantification to distinguish OTC from CPS1 deficiency. Sequence *OTC* gene; consider full urea cycle gene panel if negative. Initiate ammonia-lowering therapy (eg. sodium benzoate, arginine), protein restriction, IV glucose, and dialysis if needed.

### 3.2. Case 2025-2: 'Classical' homocystinuria due to a cystathionine-ß-synthase deficiency

#### 3.2.1. Sample details

This sample is from a 5-year-old boy, who was referred to the general paediatric consultation due to new onset of strabism, neurological deterioration and dizziness.

Based on the results of the plasma amino acid concentrations and the increased concentration of homocysteine, a classic homocystinuria was suspected. This diagnosis was confirmed by molecular genetic analysis of *CBS* gene. Treatment with vitamin B6 reduced the homocysteine concentration to below 50 µmol/l. The patient therefore received treatment with vitamin B6, folic acid and vitamin B12. Nutritional therapy or betaine is not administered.

### 3.2.2. Scoring details

**Table 2:** Scoring details for case 2025-2.

	interpretation		scores (points)				
findings, abnormalities,	elevated	met, hcys	1				
maximum 2 points	decreased	cys	1				
diagnosis, maximum 2 points	"classical" homocystin deficiency	uria due to CBS	2				
<b>further tests</b> (if molecular genetic recommended specify	MMA, folic acid, vitam (each 1 point)	in B12, SAM/SAH	1				
the gene), maximum 2 points	molecular genetic ana	1					
comments	This constellation of findings appears quite clear and indicative of a 'classic' homocystinuria.						
critical error	A critical error is when the participant overlooks the constellation of conspicuous findings and assesses th result as normal.						

Scores for participating laboratories are in APPENDIX 1 on page 7.

### 3.2.3. Comments on overall performance

Overall proficiency was 98%. The case was very clear, so there was a high overall proficiency.

- For two points in the assessment of laboratory abnormalities, it was necessary to also describe the low cystine concentration. Eleven participants therefore had one point deducted.
- The term 'classical' was not necessary to receive two points in the diagnosis section.
- Recommendations for therapy could not be assessed (although they are very important), as this scheme is a diagnostic scheme.
- In the further testing recommendations part, it is important for us to recommend not only molecular genetic analysis (although this of course confirms the diagnosis), but also metabolite diagnostics.



### 3.2.4. Best interpretation (scored with 2 points each)

- **Findings** (\*52): Strongly elevated homocysteine concentration and strongly elevated methionine concentration in plasma. Cystine is undetectable.
- **Diagnosis (\*52):** The combination of strongly elevated tHcy and Met points to cystathionine beta-synthase deficiency (classical homocystinuria). Low cystine in plasma also fits with this diagnosis. Based on the extent of the tHcy elevation SAHH, MATI/III, GNMT, and ADK deficiency are unlikely.
- Further tests (\*134): The diagnosis CBS deficiency should be confirmed by the identification of biallelic pathogenic variants in the CBS gene. We would request to repeat AAs in plasma, B12, folate, complete blood count, kidney function, methylmalonic acid (in plasma or urine).

### 3.3. Case 2025-3: 2-Aminoadipic acid semialdehyde synthase (AASS) deficiency

#### 3.3.1. Sample details

The results are from a 14 year-old boy with psychomotor retardation and behavioural disorder, without other symptoms. The patient was confirmed to have a 2-aminoadipic acid semialdehyde synthase deficiency (detection of homozygous pathogenic variant in AASS gene).

#### 3.3.2. Scoring details

Table 3: Scoring details for case 2025-3.

	interpretation		scores (points)					
	elevated (plasma/urine)	lys	1					
findings, abnormalities,	elevated (plasma)	pipicolic acid	1					
maximum 2 points	elevated (urine)	cys, orn, arg, cit	no add. points					
		-						
	hyperlysinemia due to 2-	-AASS deficiency	2					
diagnosis, maximum 2 points	hyperlysinemia (without	further specification)	1					
	lysinuric protein intolera	0						
further tests (if molecular	saccharopine	1						
genetic recommended specify	2-aminoadipic acid semia	1						
the gene), maximum 2 points	molecular genetic analys	2						
the gene), maximum 2 points	lactic acid, ammonia (sec	1						
	2-Aminoadipic acid semialdehyde synthase deficiency as form							
	of primary hyperlysinemia is considered as a non-disease.							
comments	Primary hyperlysinaemia	n must be differentiated	d from					
	secondary forms, includi	ng pyruvate carboxylase	e deficiency and					
	mitochondrial NADP(H)	due to NADK2 mutation	ıs.					
critical error	none							

Scores for participating laboratories are in APPENDIX 1 on page 7.

### 3.3.3. Comments on overall performance

Overall proficiency in this case was 95 %. The concentrations of amino acids were clearly conspicuous.

• For two points in the assessment of laboratory abnormalities, it was also necessary to assess the increased pipecolic acid concentration. Nine participants were therefore deducted one point.

### 3.3.4. Best interpretation (scored with 2 points each)

- **Findings (\*59):** The plasma AA profile shows significantly elevated levels of lysine and pipecolic acid. In the urine sample, the concentration of lysine remains significantly elevated, with an increase in the levels of cysteine and arginine. Slight increase in ornithine, citrulline and leucine.
- Diagnosis (\*31): Hyperlysinemia due to alpha-amino adipic semialdehyde synthase deficiency.



• Further tests (\*99): Analysis of saccharopine in urine, analysis of NH<sub>3</sub> (because lysine inhibits arginase and leads to diminished ornithine urea cycle could theoretically be affected), molecular genetic analysis of AASS gene

### 3.4. Comments on the whole of the first circulation results 2025

We hope that we have once again succeeded in presenting three interesting and instructive cases to the participants this year. The aim should be to describe the laboratory changes, the diagnosis and the further recommendations in such a way that it is also easy to understand for the doctors looking after the patient. In this year's cases, it was also important to describe the low concentrations of certain amino acids (cases 1 and 2) or the presence of particular metabolites (case 3).

The overall competence was good with 93%.

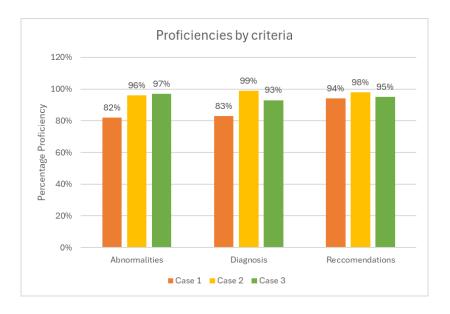


Figure 2: Proficiencies by criteria.

The common methods used by the participants for amino acid analysis are LC-MS/MS with a share of 43% and HPLC with ninhydrin detection with a share of 38%.

**Table 4:** Laboratory methods for the analysis of amino acids used by the participants (141/148 participants completed this question)

Method	No of responses
LC-MS/MS	61
Ion-exchange chrom Ninhydrin 1/2 Int. Std	46
Reverse phase HPLC/UPLC with non MS detection	14
LC-MS	9
Ion-exchange chrom Ninhydrin 0 Int. Std	6
GC-FID and/or Reverse phase HPLC with Fluorimetric detection	1
HPLC-FLD Detection	1
Ion exchange and reverse phase HPLC	1
Ion-exchange chrom Ninhydrin 1 Int. Std	1
Ultraperformance liquid chromatography/Ultraviolet detection	1
Total	141



Table 5: Overall scores for the first circulation in the Amino Acid Interpretation scheme

		2025.01					5.02			2025.01 - .03			
	Α	D	R	Sum	Α	D	R	Sum	Α	D	R	Sum	Totals
Total Points	234	236	268	738	273	282	279	834	275	264	269	808	2380
% proficiency	82%	83%	94%	87%	96%	99%	98%	98%	97%	93%	95%	95%	93%

#### Key

A = Findings, abnormalities

D = Diagnosis

R = Recommendations for further testing

We encourage participants to send us comments and suggestions regarding this scheme and do not hesitate to contact us if you question any of our scoring.

Date: 4th August 2025

The Scientific Evaluators

Sabine Scholl-Bürgi, Scientific Advisor

Scheme Assessors: Apolline Imbard, Olivier Braissant, Rachel Carling, Alistair Horman, Daniela Karall, and Anke Schumann

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## APPENDIX 1. Detailed scores for submitting laboratories

### <u>Key</u>

A = Findings,  $\underline{A}$ bnormalities

D = <u>D</u>iagnosis

R = Recommendations for further testing

DNS = did not submit any results

Anon.		202	25.01			202	25.02			202	25.03		2025.0103
lab number	Α	D	R	Sum	Α	D	R	Sum	Α	D	R	Sum	Total Score
1	1.0	1.0	2.0	4.0	2.0	2.0	0.0	4.0	2.0	2.0	2.0	6.0	14.0
2	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	18.0
3	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	18.0
4	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	18.0
5	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	18.0
6	1.0	2.0	1.0	4.0	1.0	2.0	2.0	5.0	2.0	2.0	2.0	6.0	15.0
7	1.0	2.0	1.0	4.0	1.0	2.0	2.0	3.0	2.0	2.0	2.0	0.0	DNS
8	2.0	1.0	2.0	5.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	17.0
9	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	18.0
10	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	18.0
11	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	18.0
12	1.0	2.0	2.0	5.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	17.0
13	2.0	1.0	2.0	5.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	17.0
14	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	18.0
15	1.0	1.0	2.0	4.0	1.0	2.0	2.0	5.0	2.0	2.0	2.0	6.0	15.0
16	2.0	2.0	2.0	6.0	1.0	2.0	2.0	5.0	2.0	2.0	2.0	6.0	17.0
17	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	18.0
18	1.0	2.0	2.0	5.0	1.0	2.0	2.0	5.0	1.0	1.0	1.0	3.0	13.0
19	1.0	2.0	2.0	5.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	17.0
20	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	18.0
21	1.0	1.0	2.0	4.0	2.0	2.0	2.0	6.0	2.0	1.0	2.0	5.0	15.0
22	1.0	1.0	1.0	3.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	15.0
23	2.0	2.0	2.0	6.0	1.0	2.0	2.0	5.0	2.0	2.0	2.0	6.0	17.0
24	1.0	1.0	2.0	4.0	2.0	2.0	2.0	6.0	1.0	1.0	2.0	4.0	14.0
25	1.0	1.0	2.0	4.0	2.0	2.0	2.0	6.0	2.0	2.0	1.0	5.0	15.0
26	2.0	0.0	2.0	4.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	16.0
27	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	18.0
28	1.0	1.0	2.0	4.0	1.0	2.0	2.0	5.0	2.0	2.0	2.0	6.0	15.0
29	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	18.0
30	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	18.0
31	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	18.0
32	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	18.0
33	1.0	1.0	1.0	3.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	15.0
34	2.0	2.0	2.0	6.0	1.0	2.0	2.0	5.0	2.0	2.0	2.0	6.0	17.0
35	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	18.0
36	2.0	1.0	2.0	5.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	17.0
37	2.0	2.0	2.0	6.0	1.0	2.0	2.0	5.0	2.0	2.0	0.0	4.0	15.0
38	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	18.0

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Anon.		202	25.01			202	25.02			202	25.03		2025.0103
lab number	Α	D	R	Sum	Α	D	R	Sum	Α	D	R	Sum	Total Score
39	2.0	1.0	1.0	4.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	16.0
40	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	18.0
41	2.0	1.0	2.0	5.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	17.0
42	1.0	2.0	2.0	5.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	17.0
43	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	18.0
44	2.0	1.0	2.0	5.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	17.0
45	1.0	2.0	2.0	5.0	2.0	2.0	2.0	6.0	2.0	1.0	1.0	4.0	15.0
46	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	1.0	0.0	1.0	2.0	14.0
47	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	18.0
48	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	18.0
49	2.0	1.0	2.0	5.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	17.0
50	2.0	1.0	2.0	5.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	17.0
51	1.0	2.0	2.0	5.0	2.0	2.0	2.0	6.0	2.0	1.0	2.0	5.0	16.0
52	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	18.0
53	1.0	1.0	2.0	4.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	16.0
54	1.0	2.0	2.0	5.0	2.0	2.0	2.0	6.0	1.0	2.0	2.0	5.0	16.0
55	1.0	1.0	2.0	4.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	16.0
56 57	1.0	0.0	0.0	6.0 1.0	2.0	2.0	0.0	6.0 4.0	2.0	2.0	2.0	5.0 6.0	17.0 11.0
58	2.0	1.0	2.0	5.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	17.0
59	1.0	2.0	2.0	5.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	17.0
60	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	18.0
61	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	18.0
62	1.0	1.0	2.0	4.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	16.0
63	1.0	1.0	1.0	3.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	15.0
64	1.0	1.0	2.0	4.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	16.0
65	1.0	1.0	1.0	3.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	15.0
66	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	18.0
67	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	18.0
68	2.0	1.0	2.0	5.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	17.0
69	1.0	1.0	2.0	4.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	16.0
70	2.0	1.0	2.0	5.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	17.0
71	1.0	2.0	2.0	5.0	2.0	2.0	2.0	6.0	1.0	2.0	2.0	5.0	16.0
72	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	18.0
73	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	18.0
74	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	18.0
75	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	18.0
76	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	18.0
77	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	18.0
78	1.0	2.0	2.0	5.0	2.0	2.0	2.0	6.0	1.0	2.0	2.0	5.0	16.0
79 80	1.0	2.0	2.0	3.0 5.0	2.0	2.0	2.0	3.0	2.0	1.0	2.0	5.0	11.0
81	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	2.0	1.0	2.0	5.0	16.0 17.0
81	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	18.0
83	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	18.0
03	2.0	2.0	2.0	0.0	2.0	2.0	2.0	0.0	2.0	2.0	∠.∪	0.0	10.0



Anon.		202	25.01			202	25.02			202	25.03		2025.0103
lab number	Α	D	R	Sum	Α	D	R	Sum	Α	D	R	Sum	Total Score
84	1.0	1.0	1.0	3.0	1.0	2.0	2.0	5.0	2.0	2.0	2.0	6.0	14.0
85	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	18.0
86	1.0	2.0	2.0	5.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	17.0
87	2.0	2.0	2.0	6.0	1.0	2.0	2.0	5.0	2.0	2.0	2.0	6.0	17.0
88	1.0	2.0	2.0	5.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	17.0
89	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	18.0
90	1.0	1.0	2.0	4.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	16.0
91													DNS
92	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	18.0
93	2.0	1.0	1.0	4.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	16.0
94	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	2.0	2.0	1.0	5.0	17.0
95													DNS
96	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	18.0
97	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	18.0
98	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	18.0
99	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	18.0
100	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	18.0
101													DNS
102	1.0	0.0	2.0	3.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	15.0
103	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	18.0
104	1.0	1.0	2.0	4.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	16.0
105													DNS
106	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	18.0
107	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	18.0
108	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	18.0
109	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	18.0
110	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	18.0
111	1.0	1.0	2.0	4.0	2.0	2.0	2.0	6.0	1.0	0.0	1.0	2.0	12.0
112	1.0	2.0	1.0	4.0	2.0	2.0	2.0	6.0	2.0	2.0	1.0	5.0	15.0
113	2.0	2.0	1.0	5.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	17.0
114	1.0	1.0	2.0	4.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	16.0
115	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	18.0
116	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	18.0
117	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	18.0
118 119	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	18.0
120	2.0	2.0	2.0	5.0 6.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0 4.0	17.0 16.0
121	1.0	0.0	1.0	2.0	2.0	2.0	2.0	6.0	2.0	0.0	0.0	2.0	10.0
122	1.0	2.0	2.0	5.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	17.0
123	1.0	2.0	2.0	5.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	17.0
124	1.0	2.0	2.0	5.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	17.0
125	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	18.0
126	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	18.0
127	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	18.0
128	1.0	1.0	1.0	3.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	15.0
120	1.0	1.0	1.0	3.0	2.0	2.0	0	0.0	2.0	2.0	2.0	0.0	15.0



Anon.		202	25.01			202	25.02			202	25.03		2025.0103
lab number	Α	D	R	Sum	Α	D	R	Sum	Α	D	R	Sum	Total Score
129	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	18.0
130	2.0	1.0	2.0	5.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	17.0
131	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	18.0
132	1.0	2.0	2.0	5.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	17.0
133													DNS
134	1.0	2.0	2.0	5.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	17.0
135	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	18.0
136	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	18.0
137	2.0	1.0	2.0	5.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	17.0
138	1.0	0.0	1.0	2.0	2.0	2.0	2.0	6.0	2.0	1.0	1.0	4.0	12.0
139	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	18.0
140	1.0	2.0	2.0	5.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	17.0
141	1.0	2.0	2.0	5.0	2.0	2.0	2.0	6.0	1.0	2.0	2.0	5.0	16.0
142	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	18.0
143	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	18.0
144	1.0	1.0	2.0	4.0	2.0	2.0	2.0	6.0	2.0	1.0	2.0	5.0	15.0
145	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	18.0
146	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	1.0	2.0	2.0	5.0	17.0
147	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	2.0	2.0	2.0	6.0	18.0
148	2.0	2.0	1.0	5.0	1.0	2.0	2.0	5.0	2.0	0.0	0.0	2.0	12.0

## APPENDIX 2. Change log (changes since the last version)

Version Number	Published	Amendments
1	04 August 2025	2025 first round interim report published

### **END OF REPORT**