ERNDiM

Quality Assurance in Laboratory Testing for IEM

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Urine Mucopolysaccharides

Centre: The Netherlands

Final Report 2022

prepared by
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Note: This annual report is intended for participants of the ERNDIM Urine MPS scheme. The contents should not be used for any publication without permission of the Scientific Advisor.

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1. Introduction

The ERNDIM Urine Mucopolysaccharide scheme offers (1) urine samples obtained from confirmed MPS patients to enable laboratories to gain or maintain experience to identify MPS patients and (2) proficiency testing for laboratories providing urine screening of mucopolysaccharidoses. The scheme is organized by University Medical Centre Utrecht, the Netherlands in conjunction with SKML, the Dutch organization for quality assurance in medical laboratories (MCA laboratory, Winterswijk, the Netherlands) and CSCQ, the Swiss organization for quality assurance in medical laboratories.

2. Geographical distribution of participants

In 2022 88 laboratories from many different countries have registered for the Urine MPS scheme. The number of participants is relatively stable over the years (2019: 96, 2020: 97, 2021: 87 participants). In 2022 there were no educational participants. Educational participants take part in all aspects of the

[1] If this report is not Version 1 for this scheme year, go to APPENDIX 1 for details of the changes made since the last version of this document.

scheme and receive interim reports with scores, but performance is not indicated on the ERNDIM certificate of performance.

Country	Number of participants
Argentina	2
Australia	4
Austria	1
Belgium	4
Brazil	1
Canada	4
Chili	1
Colombia	1
Croatia	1
Cyprus	1
Czechia	1
Denmark	1
Estonia	1
France	5
Germany	8
Greece	1
Hong Kong	1
Italia	4
Latvia	1
Malaysia	2
Mexico	1

Country	Number of participants
Netherlands	3
New Zealand	2
Norway	1
People's Republic of China	1
Poland	1
Portugal	2
Singapore	1
South Africa	2
Spain	4
Sweden	1
Switzerland	2
Taiwan	1
Turkey	2
United Kingdom	13
United States of America	5
Uruguay	1

3. Design and logistics of the scheme including sample information

The scheme has been designed and planned by Dr. Berthil Prinsen as Scientific Advisor and coordinated by Alessandro Salemma and Nicola Braik (sub-contractors on behalf of CSCQ) and Dr. Eline van der Hagen (sub-contractors on behalf of SKML) as scheme organisers, all appointed by and according to procedures laid down the ERNDIM Board.
SKML prepares lyophilized sample aliquots and dispatches UMPS EQA samples to the scheme participants by courier. CSCQ provides a website for online submission of results and access to scheme reports. Existing Urine MPS scheme participants can log on to the CSCQ results submission website at:
https://cscq.hcuge.ch/cscq/ERNDIM/Initial/Initial.php

2 surveys	Round 1: samples UMPS-NL-2022-A, B and C
	Round 2: samples UMPS-NL-2022-D, E and F

As usual, the samples used in 2022 were authentic human urine samples, four from MPS patients and two from a non-MPS individual. Three samples were from the sample repository at UMC Utrecht, Utrecht, the Netherlands and three samples were from the sample repository at Erasmus MC, Rotterdam, The Netherlands. Samples were selected by the Scientific Advisor and tested for suitability in the Scientific Advisor's laboratory (UMC Utrecht, Utrecht, the Netherlands). Integrity of the samples was checked after preparation of the lyophilized aliquots in the Scientific Advisor's laboratory before shipment to participants. Details regarding stability of (reconstituted) samples are provided in the sample package.

UMPS-NL-2022-A	Male, 9 years	Control
UMPS-NL-2022-B	Male, 5 years	MPS I
UMPS-NL-2022-C	Male, 40 years	MPS II
UMPS-NL-2022-D	Female, 51 years	MPS IV(B)
UMPS-NL-2022-E	Male, 10 years	Control
UMPS-NL-2022-F	Female, 32 years	MPS III(A)

4. Tests

Tests required for participation in the Urine MPS scheme are creatinine analysis and GAG analysis (quantitative total GAG and GAG-fractionation, either qualitative by electrophoresis/TLC or quantitative by LC-MS). Participants are asked to interpret the GAG concentration according to age-matched reference values (i.e normal or increased), interpret GAG subfractions (i.e. normal or increased CS (chondroitin-sulphate), HS (heparan-sulphate), DS (dermatan-sulphate) and KS (keratan-sulphate)) and to give the most likely diagnosis.

5. Schedule of the scheme

- 8 February 2022: sample dispatch
- 21 March 2022: analysis start (survey 1)
- 19 April 2022: website available for result submission (survey 1)
- 16 May 2022: deadline for result submission (survey 1)
- 28 June 2022: interim report of survey 1 available for download
- 25 July 2022: analysis start (survey 2)
- 22 August 2022: website available for result submission (survey 2)
- 19 September 2022: deadline for result submission (survey 2)
- 19 October 2022: interim report of survey 2 available for download
- January, 2023: annual report with final scoring, confirmed by the SAB, available for download

6. Results submitted

81 out of the 88 labs that were registered returned results for both surveys.

	Survey 1	**Survey 2**
Receipt of results	85	83
No report	3	5

7. Website reporting

Website reporting system is compulsory for all participants. Please note, the website includes a section to specify methods. Method specification is required for correct evaluation of the quantitative results (method specific statistics for DMB, harmine, Alcian Blue, CPC and LC-MS/MS test results). Unfortunately, not all participants have specified their methods.

In 2017 an evaluation program made by dr Albe from CSCQ was used for the first time to evaluate and score results submitted by participants. The use of this software enabled production of customised interim reports and the annual report, i.e. including scores, for each individual participant.

8. Scoring and evaluation of results

Information regarding procedures for establishment of assigned values, statistical analysis, interpretation of statistical analysis can be found in generic documents on the ERNDIM website.
The scoring system has been established by the Scientific Advisory Board of ERNDIM. Scores are allocated to different elements of the results reported. Two aspects are evaluated: 1) analytical performance, 2) interpretative proficiency. The total score is calculated as a sum of these two aspects. Similar to other qualitative (proficiency testing) ERNDIM schemes, the maximum score for a sample is 4 points. The scores were calculated only for laboratories submitting results.

A	Analytical performance	Correct results of the appropriate tests	2
		Partially correct or missing results	1
		Unsatisfactory or misleading	0
I	Interpretative proficiency	Correct (differential) diagnosis was established	2
		Helpful, but (partially) incorrect	1
		Misleading or wrong diagnosis	0

The specific criteria applied to score the results of the samples included in the 2022 scheme are given under item 9. These criteria have been set by the Scientific Advisor, approved by the Scientific Advisory Board, and have been devised on the basis of (1) for each sample: the type of MPS, (2) current possibilities of routine MPS testing, and (3) actual achievable results for a particular sample.

The final decision about scoring was made in the Scientific Advisory Board (SAB) during the autumn meeting (November 24-25, 2022 for the 2022 scheme).

A note on scoring of diagnostic proficiency and the use of check boxes and the comment box:
To indicate the most likely diagnosis check boxes must be used to facilitate evaluation of results. The use of the 'comments' box in the website form is recommended to explain your interpretation of results. Comments will be taken into account to score interpretation.
For example, we have noted in previous surveys that it may be hard to distinguish MPS I and VI. In the case of increased DS with normal or undetectable HS, checking just the MPS VI box may result in lower than maximum marks if this actually was a MPS I sample. In this case we advise to check the MPS VI box and explain in the comments box that MPS I (and perhaps II) cannot be excluded on the basis of the results. Or alternatively the boxes for MPS I, II and VI could be checked with a comment entered explaining that MPS VI is more likely.
It is important to realize, when no diagnosis is selected a comment or recommendation is mandatory that needs to explain why the diagnosis 'no diagnosis' is selected. This information is essential for correct scoring of your samples.

The concept of critical error was introduced in 2014. A critical error is defined as an error resulting from seriously misleading analytical findings and/or interpretations with serious clinical consequences for the patient. Thus labs failing to make a correct diagnosis of a sample considered as eligible for this category will be deemed not to have reached a satisfactory performance even if their total points for the year exceed the limit set at the SAB. For 2022, the SAB decided that samples UMPS-NL-2022-B, UMPS-NL-2022-C and UMPS-NL-2021-F were eligible for critical error. UMPS-NL-2022-D was decided to be educational (details provided under item 9).

Score required for satisfactory performance: at least 14 points from the maximum of 20 (70%).

From the 87 regular (non-educational) participants 81 participants (93%) submitted results for two rounds of which 73 achieved satisfactory performance (2 reports submitted, score ≥14, no critical error). Fifteen participants did not accomplish satisfactory performance, including 7 due to incomplete submission of results (e.g. no results submitted or 1 survey submitted instead of two reports submitted). A certificate of participation, including a statement on performance (satisfactory yes/no) will be issued for participation. In addition, performance support letters will be sent out if the performance is evaluated as unsatisfactory. Eight performance support letters were sent by the Scheme Advisor for 2022. Any partial submitters or non-submitters will receive a letter from the ERNDIM office.

9. Results of the samples and evaluation of reporting

9.1. Creatinine and total GAG results of all samples

Quantitative results of creatinine and total GAG were summarised in the two interim reports. Quantitative GAG results were evaluated separately for most methods (DMB, Alcian Blue, Harmine/carbazole, CPC/turbidity). Most participants use DMB (approx. 70%) for quantitative total GAG analysis. The number of participants using other GAG screening methods is smaller.

Parameter/Method	UMPS-NL-2022-A	UMPS-NL-2022-B	UMPS-NL-2022-C	UMPS-NL-2022-D	UMPS-NL-2022-E	UMPS-NL-2022-F
Creatinine (mmol/L)						
Average	5,03	2,26	4,22	4,13	4,72	3,70
SD	0,63	0,30	0,37	0,39	0,33	0,50
Median	5,13	2,26	4,22	4,12	4,80	3,70
N	83	81	83	82	82	82
GAG quantitative (mg/mmol creat) DMB colorimetric method						
Average	5,8	40,9	23,0	7,0	6,4	16,8
SD	2,1	11,6	5,9	2,6	2,4	5,9
Median	5,6	39,3	22,8	6,9	6,1	17,0
N	60	59	60	57	57	57

Parameter/Method	UMPS-NL-2022-A	UMPS-NL-2022-B	UMPS-NL-2022-C	UMPS-NL-2022-D	UMPS-NL-2022-E	UMPS-NL-2022-F
GAG quantitative (mg/mmol creat) Alcian blue colorimetric tests						
Average	6,6	45,6	24,9	7,5	7,8	15,2
SD	1,8	14,5	9,1	2,0	1,2	4,9
Median	6,2	45,2	28,1	7,5	7,8	15,2
N	3	3	3	2	2	2
GAG quantitative (mg/mmol creat) CPC turbidity method						
Average	7,6	73,8	47,9	29,6	4,8	20,4
SD	3,7	46,4	21,0	9,3	1,2	9,1
Median	7,6	73,8	47,9	29,6	4,8	20,4
N	2	2	2	2	2	2
GAG quantitative (mg/mmol creat) Uronic acids - carbazole/harmine method						
Average	1,5	10,0	3,3	2,3	2,5	6,7
SD	0,5	3,2	2,2	0,7	1,2	3,2
Median	1,3	9,8	2,5	2,3	3,0	5,0
N	3	3	3	3	3	3
GAG quantitative (mg/mmol creat) LC-MS/MS GAG fragments (Saville method)						
Average	--	--	--	8,9	6,6	51,0
SD	--	--	--	0,0	0,0	0,0
Median	--	--	--	8,9	6,6	51,0
N	--	--	--	1	1	1

9.2. Sample UMPS-NL-2022-A; Normal Profile

Patient details
This urine sample was obtained from a healthy boy of 9 years old.

Analytical performance
Most of the participants (84/85, 99%) reported a normal quantitative GAG screening test. However, 1 participant reported an abnormal quantitative GAG and concluded that this sample was of a patient with MPS-VII. Most participants indeed reported normal GAG-subtyping results by GAG-electrophoresis, TLC or mass-spectrometry. One lab reported elevated HS in combination with elevated DS and CS and one lab reported elevated DS and CS by GAG-subtyping. The analytical performance of this sample was 98%.

Diagnosis / Interpretative proficiency
As is usual for normal samples, most participants (80/84, 95%) correctly conclude that this was not a sample of a patient with a mucopolysaccharidosis. One laboratory concluded that this sample was of a patient with MPS III, 2 participants concluded that this sample was obtained from a patient with either MPS I/II/VI/(VII) and 1 participant concluded that this samples was obtained from a patient with MPS VII. The diagnostic performance was 95% and the overall proficiency of this sample was 97%.

Diagnosis	N	%
Normal	76	90,5
No Diagnosis/Normal	2	2,4
No Diagnosis	2	2,4
MPS I/MPS II/MPS VI	1	1,2
MPS VII	1	1,2
MPS I/MPS II/MPS VI/MPS VII	1	1,2
MPS III	1	1,2
N results	84	100
N non-submitters	5	
N registered	89	

Scoring
- Analytical results: Normal quantitative GAGs and normal GAG-subtyping were each scored 1 mark.
- Interpretation: A normal profile and other combinations with normal profile/no diagnosis were scored 2 marks.
- Critical error: The sample was not considered eligible for critical error.

9.3. Sample UMPS-NL-2022-B; MPS-I

Patient details
This sample was obtained from a 5 years old male with MPS-I. Diagnosis was confirmed by enzyme testing and DNA sequencing of the IDUA gene.

Analytical performance
All participants reported an abnormal GAG-screening test (e.g. DMB-test). An elevated DS was reported by 79/82 (96%) participants and 50/82 (61%) participants noticed an elevated HS. The analytical performance of this sample was 98%.

Diagnosis / Interpretative proficiency
Six participants (7%) concluded that this sample was of a patient with MPS I. In total 70 participants (83%) reported a differential diagnosis including MPS I in various combinations with MPS II, VI and VII. Five participants, that reported both an abnormal GAG-screening test and abnormal GAG-subtype analysis, lost points with the interpretation. The diagnostic performance of this sample was 90% and total performance was 94%.

Diagnosis	N	%
MPS I/MPS II/MPS VI/MPS VII	25	29,8
MPS I/MPS II	16	19,0
MPS I/MPS II/MPS VII	15	17,9
MPS I/MPS II/MPS VI	8	9,5
MPS I	6	7,1
MPS VI	6	7,1
MPS III	3	3,6
MPS VII	2	2,4
No Diagnosis	1	1,2
MPS II/MPS VII	1	1,2
MPS VI/MPS VII	1	1,2
N results	84	100
N non-submitters	5	
N registered	89	

Scoring
- Analytical results: Elevated total GAG: 1 mark, elevated DS: 1 mark.
- Interpretation: MPS I mentioned in the differential diagnosis (based on elevated DS): 2 marks. Combinations of MPS II, VI or VII based on elevated DS: 1 mark.
- Critical error: Reporting a normal profile was considered as a critical error (CE) for this sample.

9.4. Sample UMPS-NL-2022-C; MPS-II

Patient details
This sample was obtained from an adult patient with MPS II not receiving ERT treatment.

Analytical performance
Most of the participants (84/85, 99%) reported an elevated GAG screening test and found an abnormal GAG-subtyping as well. One participant reported a normal GAG screening test, while GAG-subtyping was abnormal. Nearly all participants (77/81, 95%) reported elevated DS and 61/82 (74%) participants reported an increased HS.

Four participants did not notice the clearly elevated DS by GAG-subtyping. For diagnosis of MPS I/II DS is more aberrant than HS. Analytical performance was 96%. Reporting a normal profile/no diagnosis was considered as a critical error (CE) for this sample.

Diagnosis / Interpretative proficiency
The majority of participants reported a combination of MPS I/II as the most likely diagnosis (22/84, 26%). In total 73/84 (87%) participants mentioned MPS II among the correct possible diagnoses. Diagnostic performance was 91% and total performance was 94%.

Diagnosis	N	%
MPS I/MPS II	22	26,2
MPS I/MPS II/MPS VI/MPS VII	21	25,0
MPS I/MPS II/MPS VII	12	14,3
MPS I/MPS II/MPS VI	11	13,1
MPS II	6	7,1
MPS III	3	3,6
MPS VI	3	3,6
No Diagnosis	2	2,4
MPS I	1	1,2
MPS I/MPS II/MPS III	1	1,2
MPS I/MPS VI	1	1,2
MPS IV	1	1,2
N results	84	100
N non-submitters	5	
N registered	89	

Scoring
- Analytical results: Elevated (total) GAG and elevated DS were each scored 1 mark.
- Interpretation: MPS II with MPS I, VI or VII in various combinations were scored 2 marks.
- Critical error: Reporting a normal profile/no diagnosis was considered as a critical error (CE) for this sample (n=1).

9.5. Sample UMPS-NL-2022-D; MPS-IV(B)

Patient details
This sample was obtained from a female subject of 51 years old with MPS IVB (mild type). Diagnosis was confirmed by enzyme testing.

Analytical performance
Abnormal GAG-screening was reported by 53 participants (53/77, 69%), while 24 participants (24/77, 31%) reported a normal GAG-screening result for this sample. Thirty-four participants submitted a result for KS (34/71, 48%) and only 17/71 participants (24%) reported an increased amount of CS. Eigtheen participants (18/80, 22%) reported a normal GAG-screening and a normal GAG-subtyping. Remarkably 12/73 participants (16%) and 10/73 participants (14%) reported an elevated DS or HS. The analytical performance of this sample was low (62%).

Diagnosis / Interpretative proficiency
MPS IV was reported as the most likely diagnosis by only 36/80 participants (45%). Four participants (4/80, 5%) reported MPS IV in combination with MPS IV/normal diagnosis. Fifteen participants (15/80, 19%) reported other combinations of MPS. Twenty-five participants (25/80, 31%) concluded that this sample was a normal sample/no diagnosis. Diagnostic proficiency of this sample was 51% and the overall proficiency of this sample was 57%. To conclude, this urine sample of this mild patient with MPS-IV(B) was difficult to diagnose. Therefore, the SAB decided that this sample will not be scored and will be educational.

Diagnosis	N	%
MPS IV	36	45,0
Normal	18	22,5
No Diagnosis	7	8,8
MPS I/MPS II/MPS VI/MPS VII	5	6,3
MPS VI	3	3,8
MPS IV/No Diagnosis	1	1,3
MPS I/MPS II/MPS VII	1	1,3
MPS IV/MPS VI/MPS VII	1	1,3
MPS IV/MPS VII/Normal	1	1,3
MPS IV/No Diagnosis/Normal	1	1,3
MPS III/Normal	1	1,3
MPS IV/Normal	1	1,3
MPS I/MPS II/MPS III/MPS VI/MPS VII	1	1,3
MPS VII	1	1,3
MPS I/MPS II/MPS III	1	1,3
MPS I/MPS II/MPS VI	1	1,3
N results	80	100
N non-submitters	9	
N registered	89	

Scoring
- Analytical results and interpretation are not scored.
- Critical error: The sample was not considered eligible for critical error.

9.6. Sample UMPS-NL-2022-E; Normal Profile

Patient details
This urine sample was obtained from a healthy boy of 10 years old.

Analytical performance
Most of the participants (79/80, 99%) reported a normal quantitative GAG screening test. However, 1 participant found an increased GAG concentration and reported that this urine sample was obtained from a patient with MPS-IV. Most participants (77/80, 96%) reported normal GAG-subtyping results by GAG-electrophoresis, TLC or mass-spectrometry. One participant reported and increased DS and one participant reported and increased DS in combination with increased HS and CS. The analytical performance of this sample was 92%.

Diagnosis / Interpretative proficiency
As is usual for normal samples, most participants (77/80, 96%) correctly conclude that this was not a sample of a patient with a mucopolysaccharidosis. One participant concluded that this sample was of a patient with MPS IV and 2 participant reported that this sample was obtained from a patient with MPS I/II/VI/VII. The diagnostic performance was 95% and the overall proficiency of this sample was 94%.

Diagnosis	N	%
Normal	73	91,3
No Diagnosis	3	3,8
MPS I/MPS II/MPS VI/MPS VII	2	2,5
No Diagnosis/Normal	1	1,3
MPS IV	1	1,3
N results	80	100
N non-submitters	9	
N registered	89	

Scoring
- Analytical results: Normal quantitative GAGs and normal GAG-subtyping were each scored 1 mark.

- Interpretation: A normal profile and other combinations with normal profile/no diagnosis were scored 2 marks.
- Critical error: The sample was not considered eligible for critical error.

9.7. Sample UMPS-NL-2022-F; MPS-III(A)

Patient details
This sample was obtained from an adult patient with MPS-IIIA.

Analytical performance
In this sample 96% of the participants (74/77) reported increased total quantitative GAGs. Two participants reported a normal quantitative GAGs (3%). One participant found increased total quantitative GAGs, but reported no abnormalities by GAG-subtyping. The majority of the participants reported elevated HS. The analytical performance of this sample was 94%.

Diagnosis / Interpretative proficiency
In total 67/79 participants reported that this urine specimen was of a patient with MPS III, while 12 participants did not report the correct diagnosis. For this sample reporting a normal profile was considered to be a critical error. The diagnostic performance of this sample was 85% and the overall performance was 90%. This urine sample was also circulated in 2018 and 2021. The overall performance was 89% for both years and is similar to the overall performance of 2022.

Diagnosis	N	%
MPS III	65	82,3
No Diagnosis	5	6,3
Normal	3	3,8
MPS VI	1	1,3
MPS I/MPS II/MPS VI/MPS VII	1	1,3
MPS II	1	1,3
MPS II/MPS III/MPS VII	1	1,3
MPS I/MPS VI/MPS VII	1	1,3
MPS I/MPS II/MPS III	1	1,3
N results	79	100
N non-submitters	10	
N registered	89	

Scoring
- Analytical results: Elevated (total) GAG and elevated HS were each scored 1 mark.
- Interpretation: MPS III was scored 2 marks.
- Critical error: Reporting a normal profile as the most likely diagnosis was considered as a critical error (CE) in this sample (n=3).

10. Scores of participants

All data transfer, i.e. the submission of data as well as viewing and downloading of reports proceed via the CSCQ results website. The results of your laboratory are confidential and only accessible to you (with your username and password).The anonymous scores of all laboratories are accessible to all participants and only in your version of the annual report (available from https://cscq.hcuge.ch/cscq/ERNDIM/Initial/Initial.php) is your laboratory highlighted in the leftmost column.

10.1. Detailed scores – Round 1

Lab n°	Sample 1 Control subject			Sample 2 MPS-I			Sample 3 MPS-II			Round 1 Total
	A	I	Total	A	I	Total	A	I	Total	
1	2	2	4	2	2	4	2	2	4	12
2	2	2	4	2	1	3	2	2	4	11
3	2	2	4	2	2	4	2	2	4	12
4	2	2	4	2	2	4	2	2	4	12
5	2	2	4	2	2	4	2	2	4	12
6	2	2	4	2	2	4	2	2	4	12
7	2	2	4	2	2	4	2	2	4	12
8	2	2	4	2	1	3	2	2	4	11
9	--	--	--	--	--	--	--	--	--	0
10	2	2	4	1	0	1	0	0	0	5
11	2	2	4	2	2	4	2	2	4	12
12	2	2	4	2	2	4	2	2	4	12
13	2	2	4	2	2	4	2	2	4	12
14	2	0	2	2	2	4	2	2	4	10
15	2	2	4	2	2	4	2	2	4	12
16	2	2	4	2	2	4	2	2	4	12
17	2	2	4	2	2	4	2	2	4	12
18	2	2	4	1	0	1	2	2	4	9
19	2	2	4	2	2	4	2	2	4	12
20	2	2	4	2	1	3	2	2	4	11
21	2	2	4	2	2	4	2	2	4	12
22	2	2	4	2	1	3	1	0	1	8
23	2	2	4	2	2	4	2	2	4	12
24	2	2	4	2	2	4	2	2	4	12
25	1	0	1	2	2	4	2	2	4	9
26	2	2	4	2	2	4	2	2	4	12
27	2	2	4	2	2	4	2	2	4	12
28	2	2	4	2	2	4	2	2	4	12
29	2	2	4	2	2	4	2	2	4	12

Lab n°	Sample 1 Control subject			Sample 2 MPS-I			Sample 3 MPS-II			Round 1 Total
	A	I	Total	A	I	Total	A	I	Total	
30	2	2	4	2	2	4	2	2	4	12
31	2	2	4	2	2	4	2	2	4	12
32	2	2	4	2	2	4	2	2	4	12
33	2	2	4	2	1	3	2	2	4	11
34	2	2	4	2	2	4	2	2	4	12
35	2	2	4	2	2	4	2	2	4	12
36	2	2	4	2	2	4	2	2	4	12
37	2	2	4	2	2	4	2	2	4	12
38	2	2	4	2	2	4	2	2	4	12
39	2	2	4	2	2	4	2	2	4	12
40	2	2	4	2	2	4	2	2	4	12
41	2	2	4	2	2	4	2	2	4	12
42	2	2	4	2	2	4	2	2	4	12
43	2	2	4	2	2	4	2	2	4	12
44	2	2	4	2	2	4	2	2	4	12
45	2	2	4	2	2	4	2	2	4	12
46	2	2	4	2	2	4	2	2	4	12
47	2	2	4	2	2	4	2	2	4	12
48	2	2	4	2	2	4	2	2	4	12
49	2	2	4	2	2	4	2	2	4	12
50	2	2	4	2	2	4	2	2	4	12
51	2	2	4	2	2	4	1	0	1	9
52	2	2	4	2	2	4	2	2	4	12
53	2	2	4	2	2	4	2	2	4	12
54	2	2	4	2	2	4	2	2	4	12
55	2	2	4	2	2	4	2	2	4	12
56	2	2	4	2	2	4	2	2	4	12
57	2	2	4	2	1	3	2	2	4	11
58	2	2	4	2	2	4	2	2	4	12
59	2	2	4	2	2	4	2	2	4	12
60	1	0	1	2	2	4	2	2	4	9
61	2	2	4	2	2	4	2	2	4	12
62	2	2	4	2	2	4	2	2	4	12
63	2	2	4	2	2	4	2	1	3	11
64	2	2	4	2	2	4	2	2	4	12

Lab n°	Sample 1 Control subject			Sample 2 MPS-I			Sample 3 MPS-II			Round 1 Total
	A	I	Total	A	I	Total	A	I	Total	
65	2	2	4	2	2	4	2	2	4	12
66	2	2	4	2	1	3	2	2	4	11
67	2	2	4	2	2	4	2	2	4	12
68	2	2	4	2	2	4	2	2	4	12
69	2	2	4	2	1	3	2	2	4	11
70	2	2	4	2	2	4	2	2	4	12
71	2	2	4	2	2	4	1	0	1	9
72	2	2	4	1	0	1	1	0	1	6
73	2	2	4	2	2	4	1	0	1	9
74	2	2	4	2	2	4	2	2	4	12
75	2	2	4	2	2	4	2	2	4	12
76	2	2	4	2	2	4	2	2	4	12
77	2	2	4	2	2	4	2	2	4	12
78	1	0	1	1	0	1	2	2	4	6
79	2	2	4	2	2	4	2	1	3	11
80	2	2	4	2	2	4	2	2	4	12
81	2	2	4	2	2	4	2	2	4	12
82	2	2	4	2	2	4	2	2	4	12
83	2	2	4	2	2	4	2	2	4	12
84	2	2	4	2	2	4	2	2	4	12
85	--	--	--	--	--	--	--	--	--	0
86	2	2	4	2	1	3	2	1	3	10
87	0	0	0	1	0	1	1	0	1	2
88	--	--	--	--	--	--	--	--	--	0

10.2. Detailed scores – Round 2

Lab n°	Sample 4 MPS-IV(B)			Sample 5 Control subject			Sample 6 MPS-III(A)			Round 2 Total
	A	I	Total	A	I	Total	A	I	Total	
1	--	--	--	2	2	4	2	2	4	8
2	--	--	--	0	0	0	2	2	4	4
3	--	--	--	2	2	4	2	2	4	8
4	--	--	--	2	2	4	2	2	4	8
5	--	--	--	2	2	4	2	2	4	8
6	--	--	--	2	2	4	2	2	4	8
7	--	--	--	2	2	4	2	2	4	8
8	--	--	--	2	2	4	2	2	4	8
9	--	--	--	0	2	2	2	2	4	6
10	--	--	--	2	2	4	1	2	3	7
11	--	--	--	2	2	4	2	2	4	8
12	--	--	--	2	2	4	2	2	4	8
13	--	--	--	2	2	4	2	2	4	8
14	--	--	--	2	2	4	2	2	4	8
15	--	--	--	2	2	4	2	2	4	8
16	--	--	--	2	2	4	2	2	4	8
17	--	--	--	2	2	4	2	2	4	8
18	--	--	--	2	2	4	2	2	4	8
19	--	--	--	1	2	3	2	0	2	5
20	--	--	--	2	2	4	2	2	4	8
21	--	--	--	2	2	4	2	2	4	8
22	--	--	--	2	2	4	2	2	4	8
23	--	--	--	1	0	1	1	0	1	2
24	--	--	--	2	2	4	2	2	4	8
25	--	--	--	--	--	--	--	--	--	0
26	--	--	--	2	2	4	2	2	4	8
27	--	--	--	2	2	4	2	2	4	8
28	--	--	--	2	2	4	2	2	4	8
29	--	--	--	1	0	1	2	2	4	5
30	--	--	--	2	2	4	2	2	4	8
31	--	--	--	2	2	4	1	0	1	5
32	--	--	--	2	2	4	2	2	4	8
33	--	--	--	2	2	4	2	2	4	8

Lab n°	Sample 4 MPS-IV(B)			Sample 5 Control subject			Sample 6 MPS-III(A)			Round 2 Total
	A	I	Total	A	I	Total	A	I	Total	
34	--	--	--	1	0	1	1	0	1	2
35	--	--	--	1	2	3	2	0	2	5
36	--	--	--	2	2	4	2	2	4	8
37	--	--	--	2	2	4	2	2	4	8
38	--	--	--	2	2	4	2	2	4	8
39	--	--	--	2	2	4	2	2	4	8
40	--	--	--	2	2	4	2	2	4	8
41	--	--	--	--	--	--	--	--	--	0
42	--	--	--	2	2	4	2	2	4	8
43	--	--	--	2	2	4	2	2	4	8
44	--	--	--	2	2	4	2	2	4	8
45	--	--	--	2	2	4	2	2	4	8
46	--	--	--	--	--	--	--	--	--	0
47	--	--	--	2	2	4	1	0	1	5
48	--	--	--	2	2	4	2	2	4	8
49	--	--	--	2	2	4	2	2	4	8
50	--	--	--	2	2	4	2	2	4	8
51	--	--	--	2	2	4	2	2	4	8
52	--	--	--	2	2	4	2	2	4	8
53	--	--	--	2	2	4	2	2	4	8
54	--	--	--	2	2	4	2	2	4	8
55	--	--	--	2	2	4	2	2	4	8
56	--	--	--	0	2	2	2	2	4	6
57	--	--	--	2	2	4	2	2	4	8
58	--	--	--	2	2	4	2	2	4	8
59	--	--	--	1	0	1	2	2	4	5
60	--	--	--	2	2	4	2	2	4	8
61	--	--	--	2	2	4	2	2	4	8
62	--	--	--	2	2	4	2	2	4	8
63	--	--	--	2	2	4	2	2	4	8
64	--	--	--	2	2	4	2	2	4	8
65	--	--	--	2	2	4	0	0	0	4
66	--	--	--	2	2	4	2	2	4	8
67	--	--	--	1	2	3	2	0	2	5
68	--	--	--	2	2	4	2	2	4	8

Lab n°	Sample 4 MPS-IV(B)			Sample 5 Control subject			Sample 6 MPS-III(A)			Round 2 Total
	A	I	Total	A	I	Total	A	I	Total	
69	--	--	--	2	2	4	2	2	4	8
70	--	--	--	1	2	3	2	2	4	7
71	--	--	--	2	2	4	0	0	0	4
72	--	--	--	2	2	4	1	0	1	5
73	--	--	--	1	2	3	2	2	4	7
74	--	--	--	2	2	4	--	--	--	4
75	--	--	--	2	2	4	2	2	4	8
76	--	--	--	2	2	4	2	2	4	8
77	--	--	--	--	--	--	--	--	--	0
78	--	--	--	2	2	4	1	0	1	5
79	--	--	--	0	0	0	1	0	1	1
80	--	--	--	2	2	4	2	2	4	8
81	--	--	--	2	2	4	2	2	4	8
82	--	--	--	2	2	4	1	0	1	5
83	--	--	--	2	2	4	2	2	4	8
84	--	--	--	2	2	4	2	2	4	8
85	--	--	--	2	2	4	1	0	1	5
86	--	--	--	2	2	4	2	2	4	8
87	--	--	--	1	0	1	1	0	1	2
88	--	--	--	--	--	--	--	--	--	0

10.3. Total scores

Lab n°	1	2	3	4	5	6	Cumulative score	Cumulative score (%)	Critical error
1	4	4	4	--	4	4	20	100	
2	4	3	4	--	0	4	15	75	
3	4	4	4	--	4	4	20	100	
4	4	4	4	--	4	4	20	100	
5	4	4	4	--	4	4	20	100	
6	4	4	4	--	4	4	20	100	
7	4	4	4	--	4	4	20	100	
8	4	3	4	--	4	4	19	95	
9	--	--	--	--	2	4	6	30	
10	4	1	0	--	4	3	12	60	
11	4	4	4	--	4	4	20	100	
12	4	4	4	--	4	4	20	100	
13	4	4	4	--	4	4	20	100	
14	2	4	4	--	4	4	18	90	
15	4	4	4	--	4	4	20	100	
16	4	4	4	--	4	4	20	100	
17	4	4	4	--	4	4	20	100	
18	4	1	4	--	4	4	17	85	
19	4	4	4	--	3	2	17	85	
20	4	3	4	--	4	4	19	95	
21	4	4	4	--	4	4	20	100	
22	4	3	1	--	4	4	16	80	
23	4	4	4	--	1	1	14	70	
24	4	4	4	--	4	4	20	100	
25	1	4	4	--	--	--	9	45	
26	4	4	4	--	4	4	20	100	
27	4	4	4	--	4	4	20	100	
28	4	4	4	--	4	4	20	100	
29	4	4	4	--	1	4	17	85	
30	4	4	4	--	4	4	20	100	
31	4	4	4	--	4	1	17	85	
32	4	4	4	--	4	4	20	100	
33	4	3	4	--	4	4	19	95	
34	4	4	4	--	1	1	14	70	
35	4	4	4	--	3	2	17	85	

Lab n°	1	2	3	4	5	6	Cumulative score	Cumulative score (%)	Critical error
36	4	4	4	--	4	4	20	100	
37	4	4	4	--	4	4	20	100	
38	4	4	4	--	4	4	20	100	
39	4	4	4	--	4	4	20	100	
40	4	4	4	--	4	4	20	100	
41	4	4	4	--	--	--	12	60	
42	4	4	4	--	4	4	20	100	
43	4	4	4	--	4	4	20	100	
44	4	4	4	--	4	4	20	100	
45	4	4	4	--	4	4	20	100	
46	4	4	4	--	--	--	12	60	
47	4	4	4	--	4	1	17	85	
48	4	4	4	--	4	4	20	100	
49	4	4	4	--	4	4	20	100	
50	4	4	4	--	4	4	20	100	
51	4	4	1	--	4	4	17	85	
52	4	4	4	--	4	4	20	100	
53	4	4	4	--	4	4	20	100	
54	4	4	4	--	4	4	20	100	
55	4	4	4	--	4	4	20	100	
56	4	4	4	--	2	4	18	90	
57	4	3	4	--	4	4	19	95	
58	4	4	4	--	4	4	20	100	
59	4	4	4	--	1	4	17	85	
60	1	4	4	--	4	4	17	85	
61	4	4	4	--	4	4	20	100	
62	4	4	4	--	4	4	20	100	
63	4	4	3	--	4	4	19	95	
64	4	4	4	--	4	4	20	100	
65	4	4	4	--	4	0	16	80	CE
66	4	3	4	--	4	4	19	95	
67	4	4	4	--	3	2	17	85	
68	4	4	4	--	4	4	20	100	
69	4	3	4	--	4	4	19	95	
70	4	4	4	--	3	4	19	95	
71	4	4	1	--	4	0	13	65	CE

Lab n°	1	2	3	4	5	6	Cumulative score	Cumulative score (%)	Critical error
72	4	1	1	--	4	1	11	55	
73	4	4	1	--	3	4	16	80	CE
74	4	4	4	--	4	--	16	80	
75	4	4	4	--	4	4	20	100	
76	4	4	4	--	4	4	20	100	
77	4	4	4	--	--	--	12	60	
78	1	1	4	--	4	1	11	55	
79	4	4	3	--	0	1	12	60	CE
80	4	4	4	--	4	4	20	100	
81	4	4	4	--	4	4	20	100	
82	4	4	4	--	4	1	17	85	
83	4	4	4	--	4	4	20	100	
84	4	4	4	--	4	4	20	100	
85	--	--	--	--	4	1	5	25	
86	4	3	3	--	4	4	18	90	
87	0	1	1	--	1	1	4	20	
88	--	--	--	--	--	--	0	0	

10.4. Performance

	Number of labs	% total labs
Satisfactory performers (≥ 70 % of adequate responses)	73	83
Unsatisfactory performers (< 70 % adequate responses and/or critical error)	8	9
Partial and non-submitters	7	8

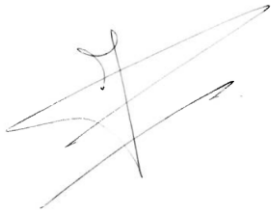
10.5. Overall Proficiency

Sample	Diagnosis	Analytical (%)	Interpretation (%)	Total (%)
UMPS-NL-2022-A	Control subject	97	94	96
UMPS-NL-2022-B	MPS-I	97	89	93
UMPS-NL-2022-C	MPS-II	95	90	93
UMPS-NL-2022-D	MPS-IV(B)	--	--	--
UMPS-NL-2022-E	Control subject	89	92	90
UMPS-NL-2022-F	MPS-III(A)	91	82	86

11. Tentative schedule for 2023

Sample distribution	7 February
Start of analysis of Survey 2023-1. Website open	21 March
Survey 2023-1 - Results submission	17 April
Survey 2023-1 - Reports	June
Start of analysis of Survey 2023-2	17 July
Survey 2023-2 – Results submission	18 September
Survey 2023-2 - Reports	October
Annual Report 2023	December/January

Date of report, 2023-02-06



Dr. H.C.M.T. Prinsen

APPENDIX 1. **Change log (changes since the last version)**

Version Number	Published	Amendments
1	01 March 2023	2022 annual report published

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