Lysosomal Enzymes in fibroblasts

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Note: This annual report is intended for participants of the ERNDIM Lysosomal Enzymes in fibroblasts scheme. The contents should not be used for any publication without permission of the Scientific Advisor.

The fact that your laboratory participates in ERNDIM schemes is not confidential. However, the raw data and performance scores are confidential and will only be shared within ERNDIM for the purpose of evaluating performance of your laboratory, unless ERNDIM is required to disclose performance data by a relevant government agency. For details, please see the terms and conditions in the EQA Schemes Catalogue and Participant Guide and the ERNDIM Privacy Policy on www.erndim.org.

1. Scheme Design

The scheme has been designed, planned and coordinated by Ms Marie Jackson (as Scientific Advisor) and Dr. C.W. Weykamp as Scheme Organiser (sub-contractor on behalf of MCA Laboratory); both appointed by and according to procedures laid down by the ERNDIM Board.

1.1. Sub-contracted activities:

The fibroblasts used as the EQA materials were cultured by Centre de Biotechnologie Cellulaire, CHU de Lyon. The fibroblasts were prepared and aliquoted by MCA Laboratory, Netherlands, which also hosts and manages the results submission website (www.erndimqa.nl) on behalf of ERNDIM.

2. Samples

All EQA materials are lyophilised samples of human fibroblasts. All samples were obtained following local ethical and consent guidelines.

Table 1: Samples included in the EQA scheme

Sample	Disorder	Enzyme Defect	Reporting deadline
LEFB2023.01	Control	All enzymes normal	26 May 2023
LEFB2023.02	MPS 3A	Heparan-N-sulphatase	
LEFB2023.03	Fabry disease	α-Galactosidase	
LEFB2023.04	Pompe disease	α-Glucosidase	25 August 2023
LEFB2023.05	Control	All enzymes normal	
LEFB2023.06	MPS 4A	Galactose-6-sulphatase	

[1] **If this Annual Report is not Version 1 for this scheme year, go to APPENDIX 2 (page 12) for details of the changes made since the last version of this document.**

3. Shipment

One shipment of six samples was dispatched on 7th February 2023, to the 69 laboratories, from 28 countries, which registered for the scheme.

4. Receipt of results

There were two submission deadlines for the 2023 scheme: (LEFB2023.01, 02 & 03 on 26th May) and (LEFB2023.04, 05 & 06 on 25th August).

Laboratories were asked to submit results for each EQA sample by the relevant submission deadline using the results website www.erndimqa.nl. All submitted results are treated as confidential information and are only shared with ERNDIM approved persons for the purposes of evaluation and reporting.

Laboratories were asked to report the total protein in mg/vial and the activities for 10 enzymes in:

- Absolute units
- As the percentage of activity in sample *LEFB 01*.

See Table 2 for details. Laboratories could submit results for as many, or as few, of these 10 enzymes as they wished and were asked to select an 'interpretation' of the results from a dropdown list on the results website.

Table 2: Analytes to be measured

Analyte	Parameter 1	Parameter 2
Protein	mg/vial	-
Arylsulphatase A	nmol/h/mg protein	% of sample LEFB 01
Galactose-6-sulphatase	nmol/h/mg protein	% of sample LEFB 01
Heparan-N-sulphatase	nmol/h/mg protein	% of sample LEFB 01
Iduronate sulphatase	nmol/4h/mg protein	% of sample LEFB 01
α-Galactosidase	nmol/h/mg protein	% of sample LEFB 01
α-Glucosidase	nmol/h/mg protein	% of sample LEFB 01
α-Iduronidase	nmol/h/mg protein	% of sample LEFB 01
β-Galactosidase	nmol/h/mg protein	% of sample LEFB 01
β-Glucosidase	nmol/h/mg protein	% of sample LEFB 01
β-Hexosaminidase (A+B)	nmol/h/mg protein	% of sample LEFB 01

5. Reports

All data-transfer, the submission of data as well as request and viewing of reports is via the interactive website www.erndimqa.nl which can also be reached through the ERNDIM website (www.erndim.org). The results of each laboratory are confidential and only accessible by password protected laboratory accounts. The anonymised mean results of all labs are accessible to all participants. Statistics of the respective reports are explained in the general information section of the website.

Short-term reports on the six individual specimens are available three weeks after the submission deadline and provide up-to-date information on analytical performance. Although it is technically possible to produce reports immediately there is a delay of 21 days to enable the Scientific Advisor to inspect the results and add comments to the report when appropriate.

A second important characteristic of the website is the different levels of detail of results which allows individual laboratories the choice of fully detailed and/or summarised reports.

The "Analyte in Detail" is the most detailed report and shows the results of a specific analyte in a specific sample. Thus, for the 10 enzymes in the year 2023 cycle, 6 x 10 (60) such Analyte-in-Detail-reports can be requested.

The "Cycle Review" summarises the performance for all enzymes in a specific sample (6 such Cycle Reviews can be requested in 2023).

6. Scoring scheme and Poor performance policy

If the interpretation of a result is incorrect (such that a deficiency is missed) for a specific enzyme and is designated as a critical error, a performance support letter will be issued. This is to initiate a dialogue between us, the EQA scheme advisor/organiser and you, the participating laboratory, to solve any particular analytical problems and to help you improve performance. If a participant scores less than 70% of the maximum number of points that can be obtained, they will be classed as a poor performer and a letter will be sent to that participant.

***Comments box*:** Participant comments may be taken into account by the Scientific Advisor. Please use this box to note any issues noted regarding the sample or assay, or to note further relevant information.

The **diagnostic proficiency** was scored for each enzyme: i.e., is the interpretation correct or incorrect. One point was awarded for a correct diagnosis.

For the protein value a maximum of 2 points could be scored depending on the %CV.

Table 3: Scoring criteria

	Criteria		Score
Protein	**CV**	CV<35%	2
		CV= 35%<CV<60%	1
		CV>60%	0
Enzymes	**Diagnosis**	Diagnosis correct	1
		Diagnosis incorrect	0

Laboratories could participate in as many of the ten enzymes offered in the scheme, plus the protein assay as required. Each enzyme is assessed individually, the emphasis being on the correct interpretation of the result. Making the correct interpretation / diagnosis for each enzyme/ sample is the priority: i.e., identifying a deficiency in an affected patient and reporting normal activity in unaffected samples.

6.1. Diagnosis

The participants must select an interpretation from the dropdown list on the results website.

Diagnosis correct: correct interpretation and correct measurement of enzyme activity level.

Diagnosis incorrect: incorrect interpretation and incorrect enzyme activity level.

6.2. Coefficient of variation

Only the CV for protein contributes to scoring: this is calculated from median results for all labs.

6.3. Appeals

If your laboratory has been sent a performance support letter for the 2023 scheme and you wish to appeal against this classification please complete the online appeal form (see below) within one month of the date of the relevant Performance Support Letter. Full details of the reason for the appeal should be included. Initial appeals will be considered by the relevant Scientific Advisor and a decision sent within 21 days of receipt of the appeal.

Appeal form: **https://www.formdesk.com/erndim/Poor_Performance_Appeals_Form** [please note this form will only be accessible for one month after the performance support letters have been sent].

7. Results

Sixty-nine laboratories were registered in the 2023 scheme. Sixty-six laboratories (96% of registered laboratories) submitted sufficient results for their performance to be assessed.

Three laboratories (4% of registered laboratories) did not submit enough results for their performance to be assessed.

Table 4: Results returns for the 2023 scheme

	Submission Deadline					
	26th May 2023			25th August, 2023		
Sample Numbers:	**2023.01**	**2023.02**	**2023.03**	**2023.04**	**2023.05**	**2023.06**
No. of labs that submitted results:						
By the submission deadline	68	67	67	66	67	67
Within 7 days of the submission deadline	0	0	0	0	0	0
Within 2 weeks of the submission deadline	0	0	0	2	1	1
Did not submit	1	2	2	1	1	1

The results for each sample were published on the results website 14 days after the relevant submission deadline.

Full details of the results for each participant's results (for labs that submitted results) are given in Appendix 1 but summaries are presented here:

- 91% of participating laboratories submitted results for 5 or more enzymes, see Table 5.
- The proficiency per analyte is given in Table 6.
- The majority of participants made the correct interpretation.

- **75.8% of participating laboratories achieved >90% of their maximum possible score (i.e., of enzymes plus proteins). See Table 7 which shows the percentage of the maximum possible score for the laboratories that submitted results.**

Table 5: Number of enzymes for which laboratories submitted results (excluding non/partial submitters)

Number of Enzymes for which results were submitted	Number of laboratories
0	0
1	0
2	2
3	1
4	3
5	6
6	4
7	6
8	4
9	10
10	30
Total number of labs	**66**

Table 6: Proficiency per analyte

Analyte	No of returns	Correct interpretation* (diagnostic proficiency)
Protein	66	93.2%
Arylsulphatase A	60	91.7%
Galactose-6-sulphatase	43	88.4%
Heparan-N-sulphatase	36	86.1%
Iduronate sulphatase	45	93.3%
α-Galactosidase	61	78.7%
α-Glucosidase	54	88.9%
α-Iduronidase	52	94.2%
β-Galactosidase	62	91.9%
β-Glucosidase	65	95.4%
β-Hexosaminidase (A+B)	59	93.2%

*** = percentage of maximum possible score (for laboratories that submitted results)**

Table 7: Percentage of maximum possible scores for laboratories that submitted results (excluding partial submitters)

%age of maximum possible score	No of submitting labs	%age of submitting labs
0% – 9%	1	1.5%
10% – 19%	2	3.0%
20% – 29%	0	0.0%
30% –39%	0	0.0%
40% – 49%	1	1.5%
50% –59%	0	0.0%
60% –69%	2	3.0%
70% –79%	0	0.0%
80% –89%	10	15.2%
90% –99%	10	15.2%
100%	40	60.6%
Total	**66**	**100%**

Table 8: Number of enzymes for which laboratories had satisfactory performance

Anon Lab No.	No of enzymes for which:	
	results were submitted by lab	lab had satisfactory performance
1	10	10
2	9	9
3	6	6
4	10	10
5	6	6
6	7	7
7	9	5
8	5	4
9	10	10
10	10	10
11	10	10
12	10	10
13	2	2
14	10	10
15	9	9
16	10	10
17	10	0
18	7	7
19	5	5
20	9	9
21	0	0
22	5	4
23	6	6
24	10	10
25	8	7
26	2	2
27	5	3
28	10	10
29	10	10
30	10	8
31	8	8
32	9	9
33	10	10
34	9	8
35	10	9
36	5	5
37	3	3
38	10	10
39	10	10
40	4	3
41	9	8
42	7	0
43	4	3
44	10	9
45	9	8
46	4	3
47	10	10
48	9	9
49	9	9
50	8	8
51	7	0

Anon Lab No.	No of enzymes for which:	
	results were submitted by lab	lab had satisfactory performance
52	7	7
53	10	10
54	8	8
55	10	10
56	10	8
57	10	10
58	10	10
59	5	5
60	10	10
61	10	10
62	0	0
63	10	9
64	10	4
65	10	10
66	6	6
67	0	0
68	7	7
69	10	10

8. Certificates of Participation

As for other ERNDIM schemes, the performance for this scheme is summarised in the annual Certificate of Participation. The certificate lists the total number of enzymes in the scheme, the number for which results have been submitted and the number for which satisfactory performance has been achieved. It is important to bear in mind that the certificate must be backed up by the laboratory's individual on-line reports in the case of internal or external auditing.

9. Comments on Overall Scheme Performance.

All ten enzymes included in the 2023 scheme were assayed in all six samples prior to distribution for validation.

- One cell line (LEFB 01) had no enzyme deficiency confirming no disorder in respect to the enzymes to be tested and was classified as Control.
- Four affected cell lines had clear enzyme deficiencies confirming the specific disorder in each case.
- One cell line (LEFB 05) was expected to have an enzyme deficiency, but no deficiencies in either of the 10 enzymes were found and the cell line was classified as Control. Because there was no time to culture another cell line, the scheme went ahead with 4 instead of 5 affected cell lines.
- The remaining enzymes in all six samples included in the scheme had confirmed normal levels of enzyme activity.

The majority of participants made the correct interpretation: that is, the correct enzyme deficiency was observed in the samples from affected patients and normal activity was observed in the unaffected samples.

LEFB 01 was included as a control to enable an improved comparison of overall results from all participants, and to provide a control to participants that do not use fibroblasts.

Participants were asked to express enzyme results as a percentage of sample LEFB 01: all participants must enter this data correctly in order to be able to evaluate the proficiency correctly.

LEFB 02 was a patient with MPS 3A. The correct interpretation for this sample was heparan-N-sulphatase deficiency. Proficiency for this enzyme was 86.1%. Thirty-six participants submitted data for this enzyme; two participants missed the diagnosis (critical error). Since 2018, this enzyme was only in 2023 included in the LEFB scheme.

LEFB 03 was a patient with Fabry disease. The correct interpretation for this sample was α-galactosidase deficiency. Proficiency for this enzyme was 78.7%. Sixty-one participants submitted data for this enzyme; two participants missed the diagnosis (critical error); six participants assigned, incorrectly, another sample as α-galactosidase deficient. The historical proficiency since 2018 is 77% (2018; affected), 93% (2018; normal), 90.3% (affected; 2020); 86.5% (affected; 2021) and 89.8% (2022; affected). The proficiency of 78.7% was the lowest of all enzymes in 2023. This may be a reflection of the difficulties of measuring α-galactosidase in cultured fibroblasts. This assay is rarely performed in cultured fibroblasts by the majority of participants as testing is more commonly offered in plasma, leucocytes and /or dried blood spots.

LEFB 04 was a patient affected with Pompe disease. The correct interpretation for this sample was: α-glucosidase deficiency. Proficiency for this enzyme was 88.9%. Fifty-four participants submitted data for this enzyme; two participants missed the diagnosis (critical error). The historical proficiency since 2018 is 90% (2018; normal), 88% (2019; affected), 100% (2020; normal), 91.1% (2021; normal) and 94% (2022; affected).

LEFB 05 should have been from a patient with multiple sulphatase deficiency. However, when the lyophilized sample was tested, there was no enzymatic evidence for this disorder. As the distribution deadline was close, it was not possible to culture another cell line and it was decided to consider this sample as control or normal. Indeed, all measured enzymes had normal activities. To prevent this in future, selected cell lines are now first tested by the reference lab in an early phase, well before the vials will be prepared.

Interestingly, 20 participants assigned an arylsulphatase deficiency to this sample, with an average activity of 35 ± 3% as compared to control sample LEFB 01 whereas 35 participants choose no obvious enzyme

deficiency with an average activity of 59 ± 7% as compared to control sample LEFB 01, with a large overlap between the individual values. It cannot be excluded that there is overinterpretation of the results, maybe participants expected an affected sample (in the last years only LEFB 01 has been normal) and did not want to miss a diagnosis and therefore choose MLD or pseudodeficiency for this enzyme. Moreover, the majority of wrong diagnoses involving heparan-N-sulphatase and iduronate sulphatase are related to LEFB 05, despite that the reported enzyme activity levels are not consistent with those expected in diagnostic samples of these two diseases. Therefore, it may be that these diagnoses were also selected due to overinterpretation.

Although the reference lab as well as the majority of participants detected normal levels (normal or not in the patient range) of arylsulphatase, heparan-N-sulphatase and iduronate sulphatase, it is interesting to see that all three enzymes are sulphatases, whereas the cell line was selected as being multiple sulphatase deficient.

Because of the uncertainty about the diagnosis as well as the high number of wrong diagnoses, it was decided to not include LEFB 05 in the evaluation and to assign it as an educational sample.

LEFB 06 was a patient affected with MPS 4A. The correct interpretation for this sample was: galactose-6-sulphatase (or galactose-6-sulphate sulphatase) deficiency. Proficiency for this enzyme was 88.4%. Forty-three participants submitted data for this enzyme; two participants missed the diagnosis (critical error). The historical proficiency since 2018 is 90% (2018; normal).

10. Preview of the scheme in 2024.

a) Dr Ed Jacobs is taking over as Scientific Advisor with Marie Jackson stepping back to deputy Scientific Advisor.

b) There will be two submission deadlines for the 2024 scheme:
   - Samples 01, 02 & 03 to be submitted by 31st May 2024
   - Samples 04, 05 & 06 to be submitted by 30th August 2024

c) Some changes have been made for the 2024 LEFB scheme:
   - Age, gender and clinical symptoms will be provided to facilitate the interpretation of the enzyme testing results, especially in case of late onset disorders.
   - The CV has been renamed recovery, as this is the appropriate term.
   - All values as % activity in sample 2024.01 will be automatically calculated by the results website.
   - An interpretation/diagnosis must be submitted for each sample. If at least one of the offered interpretations/diagnoses is not selected for each sample, it is not possible to evaluate the results of any of the enzymes for which values are submitted. Therefore, if at least one interpretation/diagnosis is not selected for **every** sample, zero points will be given for **each** of the submitted enzymes. In case no deficiency is found in one or more of the measured enzymes, whether or not all 10 enzymes have been measured, “No obvious deficiency (according to the enzymes tested)” has to be selected.
   - The interpretation/diagnosis selection list has been extended with the options “Multiple sulphatase deficiency” and “Mucolipidosis II or III”.

d) Some changes have been made to the enzymes included in the 2024 LEFB scheme. See Table 9 for the list of enzymes in the 2024 scheme.

e) For purposes of laboratory accreditation there is an increasing demand for the inclusion of further and different enzymes in the scheme. In order to address this requirement, it is intended that ERNDIM continue to provide regular rotation of the enzymes included each year. In addition, ERNDIM is in the process of investigating if the scheme can be extended to different enzymes as well as to a higher frequency of rotation. To this end, last year a survey was sent out to learn which enzymes should be in the LEFB scheme. The results of the assay will be disseminated in the coming months. As the number of respondents was low, a new, altered survey will be sent out as well.

f) Furthermore, ERNDIM is in the process of investigating whether it is possible to initiate a Lysosomal Enzymes in Dried Blot Spot (LEDB) pilot scheme. To learn the wishes of the participants, another survey will be sent out as well.

Table 9: Analytes to be measured in 2024

Analyte	2018	2019	2020	2021	2022	2023	2024
Protein	✓	✓	✓	✓	✓	✓	✓
Arylsulphatase A	×	✓	✓	×	✓	✓	×
Arylsulphatase B	×	×	×	✓	×	×	×
Aspartylglucosaminidase	×	×	×	×	✓	×	×
Galactose-6-sulphate sulphatase	✓	×	×	×	×	✓	×
Galactosylceramidase	✓	✓	✓	×	✓	×	×
Heparan-N-sulphatase	×	×	×	×	×	✓	×
Iduronate-sulphatase	×	✓	×	×	×	✓	×
Lysosomal acid lipase (LAL/acid/esterase)	×	✓	✓	×	×	×	✓
Palmitoyl protein thioesterase	×	✓	✓	×	×	×	✓
Sphingomyelinase	✓	×	×	✓	✓	×	×
Tripeptidyl peptidase	×	✓	×	×	×	×	×
α-Fucosidase	×	×	×	✓	×	×	×
α-Galactosidase	✓	✓	✓	✓	✓	✓	✓
α-Glucosidase	✓	✓	✓	✓	✓	✓	✓
α-Iduronidase	✓	×	×	×	×	✓	×
α-Mannosidase	×	×	×	✓	×	×	✓
α-N-Ac-glucosaminidase	×	×	✓	×	×	×	✓
β-Galactosidase	✓	✓	✓	✓	✓	✓	✓
β-Glucosidase	✓	✓	✓	✓	✓	✓	✓
β-Glucuronidase	×	×	✓	×	×	×	✓
β-Hexosaminidase A	✓	×	×	✓	✓	×	×
β-Hexosaminidase A+B	✓	×	×	✓	✓	✓	×
β-Mannosidase	×	×	×	×	×	×	✓

11. Questions, Comments and Suggestions

If you have any questions, comments or suggestions in addition to specific user comments please address these to the either the ERNDIM Administration Office (admin@erndim.org), the scientific advisor of the scheme, Ms Marie Jackson, (admin@erndim.org) or the scheme organiser Dr. C.W. Weykamp (mca.office@skbwinterswijk.nl).

12. Confidentiality Statement

This annual report is intended for participants of the ERNDIM Lysosomal Enzymes in fibroblasts scheme. The contents should not be used for any publication without the permission of the Scientific Advisor and Administration Office.

Marie Jackson
Scientific Advisor

Ed Jacobs
Deputy Scientific Advisor

APPENDIX 1. **Results per laboratory (part 1)**

(see page 12 for key)

Anon Lab No.	Protein/vial		Score				
	CV	Score	ASA	α-Galactosidase	β-Galactosidase	α-Glucosidase	β-Glucosidase
1	11	2	2	2	2	2	2
2	7	2	2	2	2	2	2
3	40	1	2	2	2		2
4	8	2	2	2	2	2	2
5	7	2	2	2	2	2	2
6	8	2	2	2	2	2	2
7	5	2	0	0	2	2	2
8	7	2	2	2	2	0	2
9	22	2	2	2	2	2	2
10	13	2	2	2	2	2	2
11	23	2	2	2	2	2	2
12	23	2	2	2	2	2	2
13	28	2		2			2
14	39	1	2	2	2	2	2
15	7	2	2	2	2	2	2
16	28	2	2	2	2	2	2
17	4	2	0	0	0	0	0
18	33	2	2	2	2		2
19	14	2	2		2		2
20	14	2	2	2	2	2	2
21							
22	14	2		0	2	2	2
23	57	1	2		2	2	2
24	6	2	2	2	2	2	2
25	3	2	2	0	2	2	2
26	24	2				2	2
27	34	2	0	0	2		2
28	12	2	2	2	2	2	2
29	24	2	2	2	2	2	2
30	32	2	2	0	2	2	2
31	33	2	2	2	2	2	2
32	16	2	2	2	2	2	2
33	20	2	2	2	2	2	2
34	8	2	2	0	2	2	2
35	29	2	2	0	2	2	2
36	11	2	2	2	2		2
37	10	2	2				2
38	30	2	2	2	2	2	2
39	11	2	2	2	2	2	2
40	15	2		0		2	2
41	7	2	2	0	2	2	2
42	33	2		0	0	0	0

Anon Lab No.	Protein/vial		Score				
	CV	Score	ASA	α-Galactosidase	β-Galactosidase	α-Glucosidase	β-Glucosidase
43	15	2	2	0	2		
44	1671	0	2	2	2	2	2
45	5	2	2	2	2	2	2
46	11	2		2	0		2
47	4	2	2	2	2	2	2
48	25	2	2	2	2	2	2
49	52	1	2	2	2	2	2
50	8	2	2	2	2	2	2
51	15	2	0	0	0	0	0
52	27	2	2	2	2		2
53	39	1	2	2	2	2	2
54	11	2	2		2		2
55	29	2	2	2	2	2	2
56	27	2	0	2	2	2	2
57	5	2	2	2	2	2	2
58	7	2	2	2	2	2	2
59	13	2	2	2	2		2
60	6	2	2	2	2	2	2
61	27	2	2	2	2	2	2
62							
63	37	1	2	2	2	0	2
64	29	2	2	2	0	0	2
65	38	1	2	2	2	2	2
66	10	2	2	2	2	2	2
67							
68	12	2	2	2	2	2	2
69	14	2	2	2	2	2	2

APPENDIX 1. **Results per laboratory (part 2)**

(see page 12 for key)

Anon Lab No.	Score				
	β-Hexosaminidase	Iduronate sulphatase	Galactose-6-Sulphatase	Heparan-N-sulphatase	α-iduronidase
1	2	2	2	2	2
2	2	2	2		2
3	2				2
4	2	2	2	2	2
5	2				
6	2				2
7	2		0	0	2
8					
9	2	2	2	2	2
10	2	2	2	2	2
11	2	2	2	2	2
12	2	2	2	2	2
13					
14	2	2	2	2	2
15	2		2	2	2
16	2	2	2	2	2
17	0	0	0	0	0
18	2	2	2		
19	2				2
20		2	2	2	2
21					
22					2
23	2		2		
24	2	2	2	2	2
25	2	2			2
26					
27	2				
28	2	2	2	2	2
29	2	2	2	2	2
30	2	2	2	0	2
31	2	2	2		
32	2	2	2		2
33	2	2	2	2	2
34	2	2	2		2
35	2	2	2	2	2
36	2				
37					2
38	2	2	2	2	2
39	2	2	2	2	2
40					2
41	2	2	2		2

Anon Lab No.	Score				
	β-Hexosaminidase	Iduronate sulphatase	Galactose-6-Sulphatase	Heparan-N-sulphatase	α-iduronidase
42	0	0			0
43	2				
44	2	2	2	0	2
45	2	2	0		2
46	2				
47	2	2	2	2	2
48	2	2	2		2
49	2	2		2	2
50	2	2			2
51	0				0
52	2	2		2	
53	2	2	2	2	2
54	2	2	2	2	2
55	2	2	2	2	2
56	2	2	0	2	2
57	2	2	2	2	2
58	2	2	2	2	2
59	2				
60	2	2	2	2	2
61	2	2	2	2	2
62					
63	2	2	2	2	2
64	0	0	0	0	2
65	2	2	2	2	2
66	2				
67					
68	2				2
69	2	2	2	2	2

Key

= no data submitted for this enzyme
= correct interpretation and correct measurement
= incorrect interpretation and/or incorrect measurement: normal enzyme assigned as deficient (0 pts)
= incorrect interpretation and/or incorrect measurement: deficient enzyme assigned as normal (0 pts and CE)
= no diagnoses submitted
= not enough data submitted for this enzyme
= partial submitter
= assigned arylsulphatase deficiency in (normal) sample *LEFB 05*

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

Version Number	Published	Amendments
1	09 July 2024	• 2023 annual report published

END OF REPORT