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 Dr Ed Jacobs (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
LEFB2024.01	Control	All enzymes normal	31 May 2024
LEFB2024.02	GM1-gangliosidosis	β-Galactosidase	
LEFB2024.03	Gaucher disease	β-Glucosidase	
LEFB2024.04	MPS 7	β-Glucuronidase	30 August 2024
LEFB2024.05	MPS 3B	α-*N*-acetylglucosaminidase	
LEFB2024.06	β-Mannosidosis	β-Mannosidase	

3. Shipment
One shipment of six samples was dispatched on 6th February 2024, to the 68 laboratories, from 27 countries, which registered for the scheme.

[1] **If this Annual Report is not Version 1 for this scheme year, go to APPENDIX 3 (page 13) for details of the changes made since the last version of this document.**

4. Receipt of results

There were two submission deadlines for the 2024 scheme: (LEFB2024.01, 02 & 03 on 31st May) and (LEFB2024.04, 05 & 06 on 30th 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 (See Table 2 for details). In 2024, the activity as a percentage of sample LEFB 01 was automatically calculated by the results website.

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: Parameters to be measured

Analyte	Parameter 1	Parameter 2 (calculated automatically)
Protein	mg/vial	-
Lysosomal acid lipase	nmol/h/mg protein	% of sample LEFB 01
Palmitoyl protein thioesterase	nmol/h/mg protein	% of sample LEFB 01
α-*N*-acetylglucosaminidase	nmol/h/mg protein	% of sample LEFB 01
α-Galactosidase	nmol/4h/mg protein	% of sample LEFB 01
α-Glucosidase	nmol/h/mg protein	% of sample LEFB 01
α-Mannosidase	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-Glucuronidase	nmol/h/mg protein	% of sample LEFB 01
β-Mannosidase	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 2024 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 2024).

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 this 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 *and* measurement correct was awarded two points

For the protein value a maximum of 2 points could be scored depending on the % recovery. Note that the term recovery is now used instead of CV, as this is the appropriate terminology.

Table 3: Scoring criteria

	Criteria		Score
Protein	**Recovery**	Recovery < 35%	2
		35% ≤ Recovery ≤ 60%	1
		Recovery > 60%	0
Enzymes	**Diagnosis**	Diagnosis correct	2
		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/or incorrect measurement of enzyme activity level.

6.2. Recovery

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

6.3. Appeals

If your laboratory has been sent a performance support letter for the 2024 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-eight laboratories were registered in the 2024 scheme. Sixty-six laboratories (97% of registered laboratories) submitted sufficient results for their performance to be assessed.

One laboratory (1.5% of registered laboratories) did not submit enough results for their performance to be assessed, and one laboratory (1.5% of registered laboratories) did not submit any results.

Table 4: Results returns for the 2024 scheme

	Submission Deadline					
	31st May 2024			30th August, 2024		
Sample Numbers:	**2024.01**	**2024.02**	**2024.03**	**2024.04**	**2024.05**	**2024.06**
No. of labs that submitted results:						
By the submission deadline	65	66	67	66	66	66
Within 7 days of the submission deadline	1	1	1	0	0	0
Within 2 weeks of the submission deadline	0	0	0	0	0	0
Did not submit	2	1	1	2	2	2

The results for each sample were published on the results website 21 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:

- 83% 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.
- **84.8% 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	4
3	4
4	3
5	4
6	3
7	6
8	8
9	16
10	18
Total number of labs	**66**

Table 6: Proficiency per analyte

Analyte	No of returns	Correct interpretation* (diagnostic proficiency)
Protein	66	87.1%
Lysosomal acid lipase	33	100%
Palmitoyl protein thioesterase	35	100%
α-N-acetylglucosaminidase	42	90.5%
α-Galactosidase	62	96.8%
α-Glucosidase	53	100%
α-Mannosidase	54	100%
β-Galactosidase	62	100%
β-Glucosidase	65	100%
β-Glucuronidase	50	97.0%
β-Mannosidase	44	87.5%

*** = 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%	0	0.0%
10% – 19%	0	0.0%
20% – 29%	0	0.0%
30% –39%	0	0.0%
40% – 49%	0	0.0%
50% –59%	1	1.5%
60% –69%	1	1.5%
70% –79%	2	3.0%
80% –89%	6	9.1%
90% –99%	10	15.2%
100%	46	69.7%
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	9	9
2	6	6
3	7	7
4	6	6
5	10	10
6	8	8
7	9	9
8	10	10
9	4	4
10	9	9
11	4	4
12	9	9
13	7	6
14	3	3
15	10	10
16	4	4
17	10	10
18	10	10
19	10	10
20	2	2
21	5	5
22	10	10
23	9	9
24	8	8
25	5	5
26	7	7
27	10	8
28	0	0
29	5	4
30	8	8
31	9	9
32	9	9
33	10	9
34	9	9
35	2	2

Anon Lab No.	No of enzymes for which:	
	results were submitted by lab	lab had satisfactory performance
36	9	9
37	5	5
38	10	10
39	2	2
40	9	9
41	10	10
42	10	10
43	8	8
44	7	6
45	8	8
46	8	7
47	9	9
48	2	1
49	6	5
50	9	9
51	10	9
52	9	8
53	3	3
54	9	9
55	3	3
56	3	3
57	8	8
58	10	10
59	9	8
60	7	7
61	7	7
62	10	9
63	10	10
64	10	10
65	9	9
66	10	10
67	8	7
68	0	0

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 2024 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 (LEFB 02 to LEFB 05) had clear enzyme deficiencies confirming the specific disorder in each case.

- One cell line (LEFB 06) had a clear enzyme deficiency, but the value was outside the range of patients. See below for more details
- 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.

LEFB 02 was a patient with GM1-gangliosidosis. The correct interpretation for this sample was β-galactosidase deficiency. Proficiency for this enzyme was 100%. Sixty-two participants submitted data for this enzyme. The historical proficiency since 2015 is 95% (2015; normal); 94% (2016; deficient); 98% (2017; normal); 99% (2018; normal); 96% (2019; deficient); 98.4% (2020; normal); 90.6% (2021; deficient); 98.3% (2022; normal) and 91.9% (2023; normal).

LEFB 03 was a patient with Gaucher disease. The correct interpretation for this sample was β-glucosidase deficiency. Proficiency for this enzyme was 100%. Sixty-five participants submitted data for this enzyme. The historical proficiency since 2015 is 85% (2015; normal); 92% (2016; deficient); 95% (2017; normal); 85% (2018; deficient); 97% (2019; normal); 98.4% (2020; deficient); 92.3% (2021; normal); 100% (2022; normal) and 95.4% (2023; normal).

LEFB 04 was a patient affected with MPS 7. The correct interpretation for this sample was β-glucuronidase deficiency. Proficiency for this enzyme was 97.0%. Fifty participants submitted data for this enzyme. One participant missed the diagnosis (critical error) because an activity of 123% was submitted (mean of all participants was 2%). One participant submitted 4% activity and selected mucolipidosis II/III and wrote in the comments section that all enzymes are low in activity, but that MPS VII is also possible. We disagree that all other enzymes are low in activity and awarded this participant with 1 point. The historical proficiency since 2018 is 100% (2020; normal).

LEFB 05 was a patient affected with MPS 3B. The correct interpretation for this sample was α-*N*-acetylglucosaminidase deficiency. Proficiency for this enzyme was 90.5%. Forty-two participants submitted data for this enzyme. Four participants missed the diagnosis (critical error) because activities of 48%, 52%, 61% and 113% were submitted (mean of all participants was 5%). The historical proficiency since 2018 is 100% (2020; normal).

LEFB 06 was a patient affected with β-mannosidosis. The correct interpretation for this sample was β-mannosidase deficiency. Proficiency for this enzyme was 87.5%. This was the first time this enzyme was included in the LEFB scheme. Forty-four participants submitted data for this enzyme. Five participants missed the diagnosis because activities of 45%, 49%, 55%, 55% and 67% were submitted (mean of all participants 16%). One participant submitted an activity of 16%, but did not select the diagnosis β-mannosidosis. A remark was made that the activity is very high for β-mannosidosis.

In the laboratory where all enzymes in the vials are tested before they are distributed (Erasmus MC, Rotterdam), a normal range for β-mannosidase in fibroblasts of 38-184 nmol/h/mg (median 78 nmol/h/mg) is used. The patient range, based on three patients, is 0-1 nmol/h/mg. The activity in the vials was measured twice: 8.7 and 9.2 nmol/h/mg. This activity of 9 nmol/h/mg is above the patient range, but far below the normal range. Moreover, when expressed as percentage of the median, an activity of 11% is found, which is close to the rule of thumb that inborn metabolic disorders have 10% or less residual activity. Moreover, CHU in Lyon, the facility where the fibroblasts for LEFB are stored and cultured, reported that in 1997 an activity of 3.8 nmol/h/mg with a normal average of 51.7 nmol/h/mg in fibroblasts was found and an activity of 2.7 nmol/h/mg (normal range 20-57 nmol/h/mg) in leucocytes of this patient. In the historical records no results of DNA analyses were mentioned.

During the Autumn meeting of the Scientific Advisory Board it was decided that for this enzyme no critical errors would be issued because of the atypical activity pattern in sample LEFB 06. The five participants

which submitted high activities received zero points, the participant which submitted a low activity and made the remark about the atypical activity was awarded one point.

Remaining enzymes: For lysosomal acid lipase, α-glucosidase, α-mannosidase and palmitoyl protein thioesterase the proficiency was 100%. For α-galactosidase the proficiency was 96.8%. Once participant submitted 20% activity for this enzyme (mean of all participants was 75%) and selected α-galactosidase deficiency in LEFB 05 (correct diagnosis α-*N*-acetylglucosaminidase deficiency). Once participant submitted 49% activity for this enzyme (mean of all participants was 60%) and selected α-galactosidase deficiency in sample LEFB 04 (correct diagnosis β-glucuronidase deficiency) and submitted 62% activity for this enzyme (mean of all participants was 75%) and selected α-galactosidase deficiency in sample LEFB 05 (correct diagnosis α-*N*-acetylglucosaminidase deficiency). Both participants received zero points for this enzyme.

Poor performers: There were two participants classified as poor performer because they received less than 70% of the maximum points that could be obtained. One participant submitted data for two enzymes and received all points, but zero points were awarded because of a recovery of 66473% whereas the mean of all participants was 20%. One participant submitted data for two enzymes but received zero points for α-galactosidase and only one point for the recovery of the protein.

10. Preview of the scheme in 2025.

a) Dr Magali Pettazzoni (CHU Lyon, France) is taking over from Marie Jackson as Deputy Scientific Advisor. We would like to thank Marie for her role as Scientific Advisor in previous years in which she has made some important changes in the LEFB Scheme.

b) There will be two submission deadlines for the 2025 scheme:
   - Samples 01, 02 & 03 to be submitted by 30th May 2025
   - Samples 04, 05 & 06 to be submitted by 29th August 2025

c) Introduced in the 2024 LEFB Scheme, the following will be continued:
   - 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 2025.01 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.

d) Some changes have been made to the enzymes included in the 2025 LEFB scheme. See Table 9 for the list of enzymes in the 2025 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, a survey was sent out to learn which enzymes should be in the LEFB scheme. 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, a survey will be combined with the one mentioned in the previous section.

Table 9: Analytes to be measured in 2025

Analyte	2018	2019	2020	2021	2022	2023	2024	2025
Protein	✓	✓	✓	✓	✓	✓	✓	✓
Acetyl-CoA-glucosamine acetyltransferase								✓
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, Dr Ed Jacobs, (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.

18th Feb 2025

Ed Jacobs
Scientific Advisor

APPENDIX 1. Results per laboratory (part 1)

(see page 12 for key)

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

Anon Lab No.	Score					
	Protein/vial	LAL	α-Galactosidase	α-Glucosidase	α-Mannosidase	α-N-Acetylglucosaminidase
43	2	2	2	2	2	2
44	2		2	2	2	
45	2		2	2	2	2
46	2		2	2	2	0
47	2		2	2	2	2
48	1		0			
49	0		2	2	2	
50	2		2	2	2	2
51	2	2	2	2	2	2
52	1		2	2	2	0
53	2		2			
54	2	2	2	2	2	2
55	2		2			
56	2		2	2		
57	2		2	2	2	2
58	0	2	2	2	2	2
59	1	2	2	2	2	2
60	2	2	2	2	2	
61	2		2	2	2	2
62	2	2	2	2	2	2
63	2	2	2	2	2	2
64	2	2	2	2	2	2
65	2	2	2	2	2	
66	2	2	2	2	2	2
67	1		2	2	2	
68						

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

(see page 12 for key)

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

Anon Lab No.	Score				
	β-Galactosidase	β-Glucosidase	β-Glucuronidase	β-Mannosidase	Palmitoyl protein thioesterase
43	2	2	2		
44	2	2	2	1	
45	2	2	2	2	
46	2	2	2	2	
47	2	2	2	2	2
48		2			
49	2	2	0		
50	2	2	2	2	2
51	2	2	2	0	2
52	2	2	2	2	2
53	2	2			
54	2	2	2	2	
55	2	2			
56		2			
57	2	2	2	2	
58	2	2	2	2	2
59	2	2	2	0	
60	2	2		2	
61	2	2	2		
62	2	2	2	0	2
63	2	2	2	2	2
64	2	2	2	2	2
65	2	2	2	2	2
66	2	2	2	2	2
67	2	2	2	0	2
68					

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)
- incorrect interpretation and/or incorrect measurement: deficient enzyme assigned as normal (0 pts but no CE)
- no diagnoses submitted
- not enough data submitted for this enzyme
- partial submitter

APPENDIX 2. Overall scores per laboratory

Key

N = Poor performer for score only

CE = Poor performer for critical error only

P = Partial submitter

D = Did not submit any results

Anon lab no.	Total points scored	Maximum points	% score	Performance code
1	20	20	100.0%	
2	14	14	100.0%	
3	16	16	100.0%	
4	14	14	100.0%	
5	21	22	95.5%	
6	18	18	100.0%	
7	20	20	100.0%	
8	22	22	100.0%	
9	10	10	100.0%	
10	20	20	100.0%	
11	10	10	100.0%	
12	20	20	100.0%	
13	14	16	87.5%	CE
14	8	8	100.0%	
15	22	22	100.0%	
16	10	10	100.0%	
17	22	22	100.0%	
18	22	22	100.0%	
19	22	22	100.0%	
20	6	6	100.0%	
21	12	12	100.0%	
22	22	22	100.0%	
23	20	20	100.0%	
24	18	18	100.0%	
25	12	12	100.0%	
26	16	16	100.0%	
27	19	22	86.4%	
28				P
29	9	12	75.0%	
30	18	18	100.0%	
31	19	20	95.0%	
32	20	20	100.0%	
33	20	22	90.9%	CE
34	20	20	100.0%	
35	4	6	66.7%	N

Anon lab no.	Total points scored	Maximum points	% score	Performance code
36	20	20	100.0%	
37	11	12	91.7%	
38	22	22	100.0%	
39	6	6	100.0%	
40	18	20	90.0%	
41	22	22	100.0%	
42	21	22	95.5%	
43	18	18	100.0%	
44	15	16	93.8%	
45	18	18	100.0%	
46	16	18	88.9%	CE
47	20	20	100.0%	
48	3	6	50.0%	N
49	10	14	71.4%	CE
50	20	20	100.0%	
51	20	22	90.9%	
52	17	20	85.0%	CE
53	8	8	100.0%	
54	20	20	100.0%	
55	8	8	100.0%	
56	8	8	100.0%	
57	18	18	100.0%	
58	20	22	90.9%	
59	17	20	85.0%	
60	16	16	100.0%	
61	16	16	100.0%	
62	20	22	90.9%	
63	22	22	100.0%	
64	22	22	100.0%	
65	20	20	100.0%	
66	22	22	100.0%	
67	15	18	83.3%	
68				D

APPENDIX 3. Change log (changes since the last version)

Version Number	Published	Amendments
1	18 February 2025	• 2024 annual report published

END OF REPORT