



External Quality Assessment
Enzyme Analysis for Lysosomal Storage Diseases

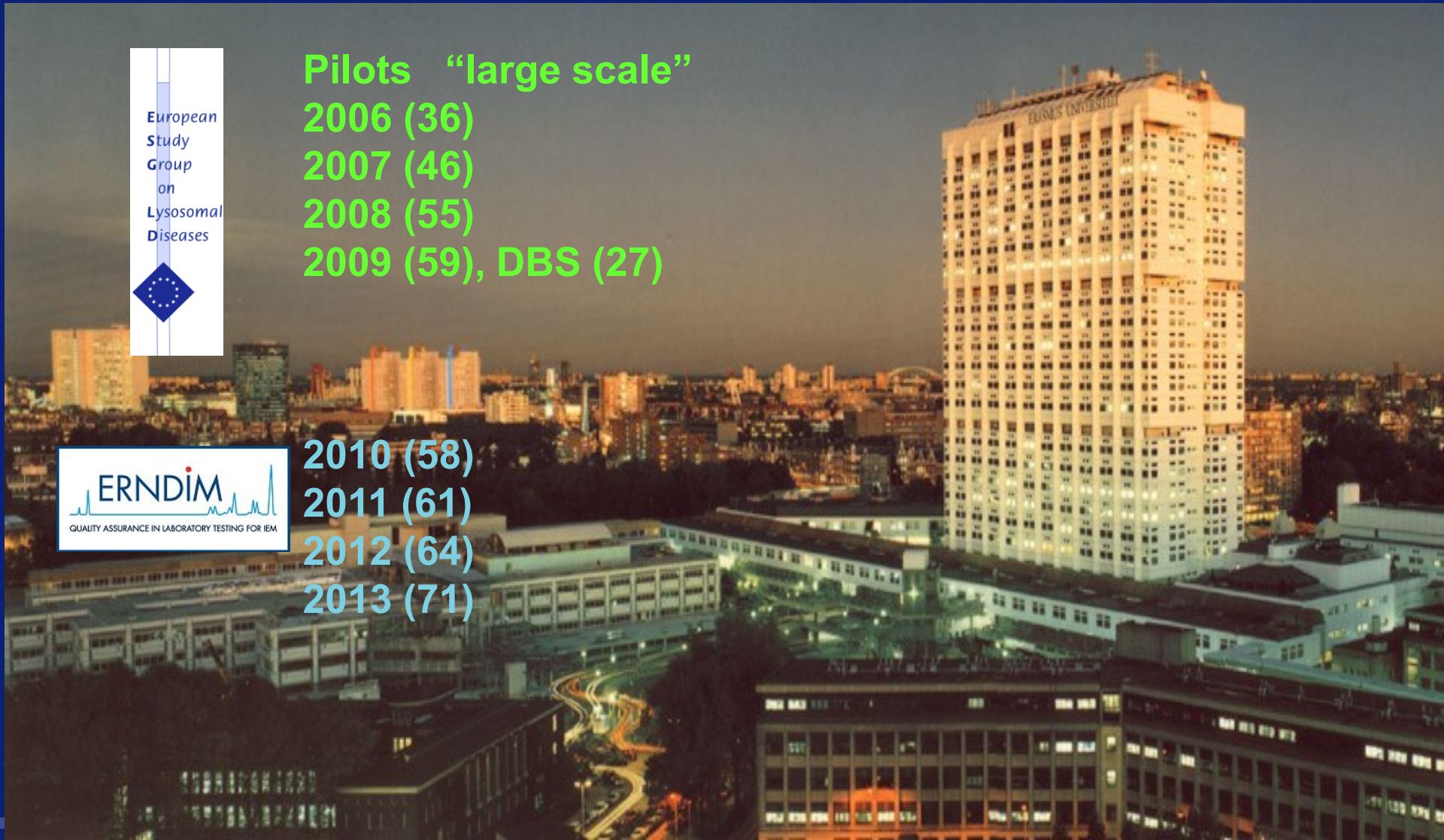


Pilots "large scale"

- 2006 (36)**
- 2007 (46)**
- 2008 (55)**
- 2009 (59), DBS (27)**



- 2010 (58)**
- 2011 (61)**
- 2012 (64)**
- 2013 (71)**



ENZYMES 2013 PROFICIENCY TESTING FIBROBLASTS

Hurler/Scheie (MPS I) α -L-iduronidase

Krabbe Galactocerebrosidase **LF2**

Niemann Pick A/B Sphingomyelinase **LF4**

Fabry α -galactosidase

Gaucher β -Glucosidase

Sanfilippo A Heparansulphate sulphamidase **LF6**

MPS VI, Arylsulphatase B

GM₁ (Morquio B) β -Galactosidase

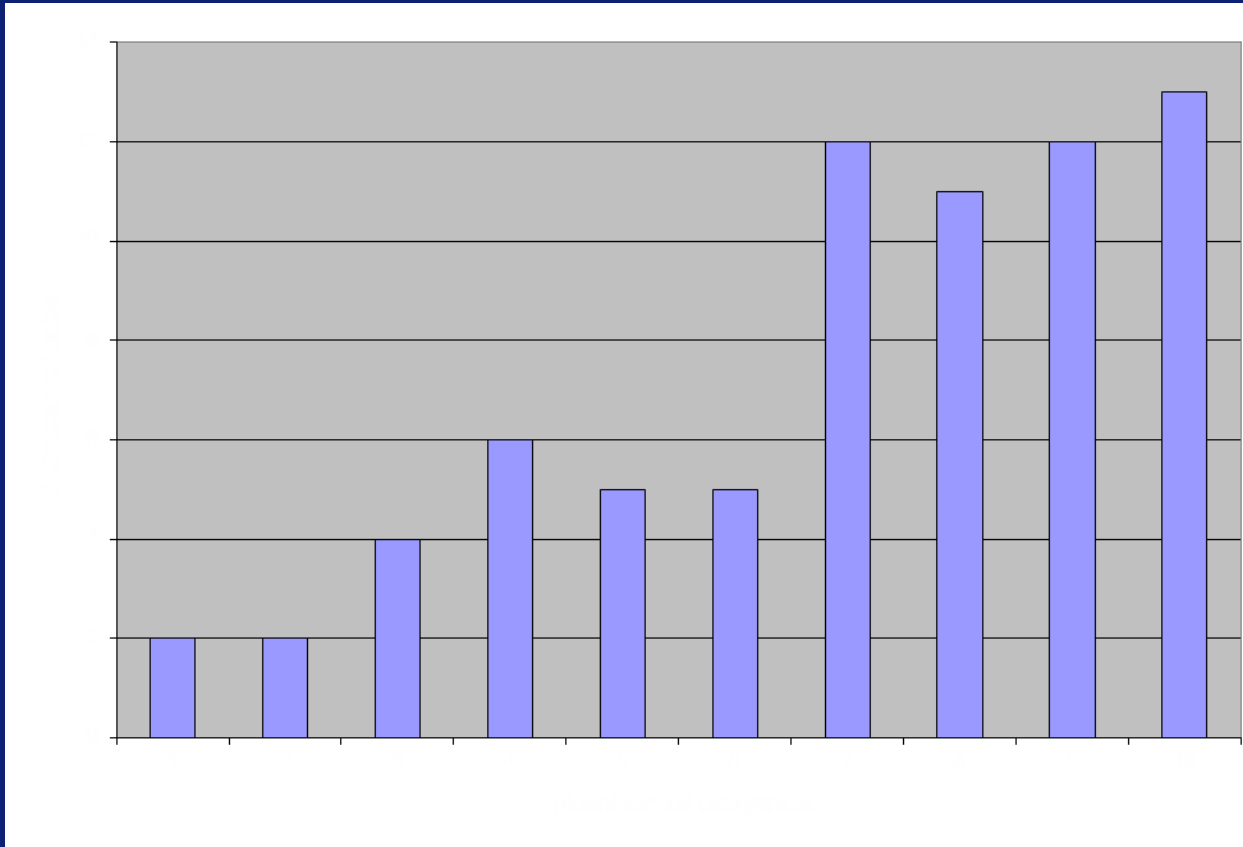
GM₂ β -Hexosaminidase A+B **LF1**

Pompe α -Glucosidase

LF 3 + 5 control Fibroblasts used for determination CV

RESULTS 2013

NUMBER OF ENZYMES MEASURED



Reproducibility of protein/vial 2013 duplicate samples Fibroblasts

1	0
2	178
3	3
4	7
5	10
6	4
7	16
8	12
9	15
10	0
11	0
12	2
13	15
14	25
15	3
16	0
17	15
18	6
19	8

20	1
21	1
22	-
23	38
24	16
25	3
26	0
27	7
28	35
29	16
30	19
31	0
32	-
33	3
34	-
35	13
36	13
37	7
38	3
39	13

40	20
41	11
42	-
43	3
44	7
45	4
46	29
47	1
48	18
49	11
50	1
51	3
52	3
53	-

54	13
55	14
56	4
57	37
58	7
59	1
60	0
61	99
62	5
63	26
64	4
65	10
66	4
67	6
68	-
69	26
70	8
71	95

Mean CV 15.5±27.7 %

N=71	2012	2013
No data	13%	8%
CV<25	91%	79%
CV>25	3%	13%

Reproducibility of Arylsulfatase B 2013

duplicate samples Fibroblasts

1	46
2	3
4	16
5	3
6	35
7	13
8	40
10	117
13	83
14	51
18	8
19	-
20	6
22	-
23	67
24	63
27	62

30	42
31	90
32	-
33	65
34	-
35	42
36	14
37	22
39	10
40	D+
41	114
44	27
45	7
46	42
47	33
48	1
50	33;D+
51	7

54	16:D+
56	20
58	34
59	8
60	1
61	2
64	12
65	34
66	1
68	-
69	2;D+
71	159

D+ enzyme activity
other samples < 20
% control
Fibroblasts

Mean CV 35 ± 36 %

D incorrect 2%

N=47	2012	2013
No data	16%	13%
CV<25	66%	43%
CV>25	27%	45%

Reproducibility of α -Galactosidase 2013

duplicate samples Fibroblasts

1	24
2	6
3	14
5	9
6	7
7	19
8	13
17	104
10	13
11	0
12	11
13	10
14	19
15	7
18	48
19	31

20	1
23	23
24	14
25	1
27	2
28	47
29	7
30	21
31	2
32	-
33	5
34	-
35	74
36	10
37	5
38	193
39	12
41	99
42	-
44	6
45	32

46	24
47	16
48	24
49	1
50	12
51	5
54	9
55	28
56	15
57	10
58	1
59	5
60	0
61	7
63	51
64	1
65	32
66	14
67	9
68	-
69	25
70	93
71	24

N=60	2012	2013
No data	18%	7%
CV<25	76%	73%
CV>25	11%	20%

Mean CV $16 \pm 15\%$
D incorrect 0%

Reproducibility of β -Galactosidase 2013 duplicate samples Fibroblasts

1	36
2	2
3	19
4	7
5	7
6	9
7	94
8	11
10	43
11	14
12	4
13	8
14	19
15	30
16	4
17	27
18	35
19	23
20	11
21	4
22	-
23	54
24	10

25	6
27	36
28	30
29	92
30	49
31	0
32	-
33	16
34	-
35	8
36	2
37	0
38	7
39	88
40	19
41	85
42	-
43	3
44	7
45	40
46	22
47	8
48	13

49	27
50	6
51	11
52	2
53	-
54	12
55	41
56	194;D+
57	8
58	24
59	45
60	11
61	0
62	21
63	106
64	4
65	37
66	36
67	D+
68	-
69	24
70	43
71	140

N=69	2012	2013
No data	19%	10%
CV<25	83%	57%
CV>25	8%	33%

D+ enzyme activity
other Fibroblast < 20 %
control Fibroblast

Mean CV 29 ± 36 %
D incorrect 3%

Reproducibility of α -Glucosidase 2013 duplicate samples Fibroblasts

5	3
6	16
7	64
8	11
10	17
13	38
14	50
15	8
18	40
19	27
20	3
22	-
23	4
24	4

25	4
29	19
30	8
31	86
32	-
34	-
35	56
36	3
37	46
39	63
44	19
45	25
46	49;D+
47	13
48	32

49	30
50	0
51	6
54	2
58	3
59	6
60	7
61	10
63	66
64	3
65	15
66	20
68	-
69	127
71	64

N=44	2012	2013
No data	24%	9%
CV<25	81%	57%
CV>25	10%	34%

D+ enzyme activity
other Fibroblast < 20 %
control Fibroblast

Mean CV 27 ± 28 %
D incorrect 5 %

Reproducibility of β -Glucosidase 2013 duplicate samples Fibroblasts

1	22
2	17
3	4
4	10
5	6
6	11
7	8
8	23
10	12
11	51
13	6
14	19
16	1
17	46
18	6
19	7
20	0
21	40
22	-
23	13
24	2

25	9
27	0
28	23
29	9
30	53
31	15
32	-
33	96
34	-
35	12
36	4
37	6
38	-
39	103
40	65
42	-
44	111
45	75
46	44
47	2
48	15
49	30

50	6
51	19
52	8
53	-
54	8
55	9
56	7
57	34
58	61
59	25
60	3
61	4
63	52
64	6
65	61
66	29
68	-
69	43
70	62
71	117

N=64	2012	2013
No data	21%	11%
CV<25	81%	61%
CV>25	7%	30%

Mean CV 27 ± 30 %
D incorrect 0%

Reproducibility of β -Hexosaminidase A+B 2013 duplicate samples Fibroblasts

1	35
3	19
5	58
6	10
7	27
8	84
10	17
11	52
12	4
13	1
14	13
15	0
17	35;D0
18	3
19	17
20	2
21	9
22	-
23	36
24	77;D+
25	14;D0D+

27	46
28	44
29	7
30	20
31	7;D+
33	50
34	-
35	27
36	4
37	124
38	127
39	27
40	18;D0
41	109
42	-
43	4
44	9
45	13

Mean CV $28 \pm 33\%$
D incorrect 8%

46	0
47	2
48	9
49	3
50	11
51	20
54	15
55	13
56	11
58	28
59	6;D0
60	0
61	4
62	11
63	8
64	4;D+
66	10
67	-
68	-
69	88;D+
70	71
71	93

N=61	2012	2013
No data	14%	8%
CV<25	86%	59%
CV>25	7%	33%

D+ enzyme activity
other Fibroblast < 20
% control Fibroblast

D0 patient sample not
measured

Reproducibility of α -Iduronidase 2013 duplicate samples Fibroblasts

2	8
4	100
5	1
6	9
7	11;D+
8	97
10	15
13	13
14	24
15	18;D+
16	1
17	41
18	23
20	10
22	-
23	1
24	37

25	3
27	38
28	35
30	40
31	140;D+
32	-
33	49
34	-
35	175;D+
36	2
37	38;D+
38	43
40	-
44	36
45	16
46	18
47	2
48	35

49	19
50	93
51	15
53	-
54	18;D+
55	38
56	13
58	55
59	23
60	3
61	4
62	25
63	15;D+
64	16
65	22
68	-
69	4
71	73

N=53	2012	2013
No data	18%	11%
CV<25	86%	55%
CV>25	8%	34%

D+ enzyme activity
other Fibroblast < 20
% control Fibroblast

Mean CV 30 ± 35 %
D incorrect 2 %

Reproducibility of Heparansulphate sulphamidase 2013 duplicate samples Fibroblasts

5	2
7	154;D-
8	4;D-
10	-
13	64
15	-;D0
20	2
24	1;D-

25	-;D0
28	18
30	-
31	-;D0D+
33	60
35	-;D0
36	6
37	-;D0D+

47	15;D-
48	-;D0
51	2
54	-;D0
62	27;D0
63	21
65	85

N=23	2013
No data	39%
CV<25	39%
CV>25	22%

Mean CV 33 ± 44 %
D incorrect 26%

D- enzyme activity
patient sample > 30%
control Fibroblast

D+ enzyme activity
other Fibroblast < 20 %
control Fibroblast

D0 patient sample not
measured

Reproducibility of Galactocerebrosidase 2013 duplicate samples Fibroblasts

5	7;D-
6	18;D-
7	0
8	24;D-
10	-
13	41;D+
15	59;D-
17	67
19	4
20	6
21	112
23	39;D-

25	38;D+
27	28
28	0
31	8
32	-
33	3
35	27
36	2
37	-;D0
38	D-
40	71;D+
45	115
47	34
48	32;D-

49	21
50	118
51	12
55	62
57	6
58	75
59	23;D+
61	7
62	89
63	23;D0
65	11;D-
68	-;D-
69	54
71	79

N=39	2012	2013
No data	21%	10%
CV<25	71%	46%
CV>25	16%	44%

D- enzyme activity
patient sample > 30%
control Fibroblast

D+ enzyme activity
other Fibroblast < 20
% control Fibroblast

D0 patient sample not
measured

**Mean CV 38± 35 %
D incorrect 33%**

Reproducibility of Sphingomyelinase 2013 duplicate samples Fibroblasts

4	9
5	189;D-
6	4
7	21
8	12
10	-
13	20
15	3
17	194
18	1
19	21
20	3
22	-;D0
23	67

24	1;D-
25	87
27	46
28	26
29	-;D0
31	35
33	14
35	5
36	1
37	14
38	-
40	193;D+D0
44	2

45	188
47	11
49	49
50	29
51	15
57	161
58	82
59	10
61	17;D-
62	10
63	-;D0
65	5
68	-
69	13

N=41	2012	2013
No data	23%	15%
CV<25	92%	54%
CV>25	3%	32%

D- enzyme activity
patient sample > 30%
control Fibroblast

D+ enzyme activity
other Fibroblast < 20
% control Fibroblast

D0 patient sample not
measured

Mean CV 44 ± 63 %
D incorrect 10%

OVERALL PERFORMANCE 2013

10 Participants: 100% score, CV<25%; enzyme patient<30%; enzyme control >20%

44 Participants: no false negative of positive patients