



**External Quality Assessment  
Enzyme Analysis for Lysosomal Storage Diseases**



**Pilots "large scale"**

**2006 (36)**

**2007 (46)**

**2008 (55)**

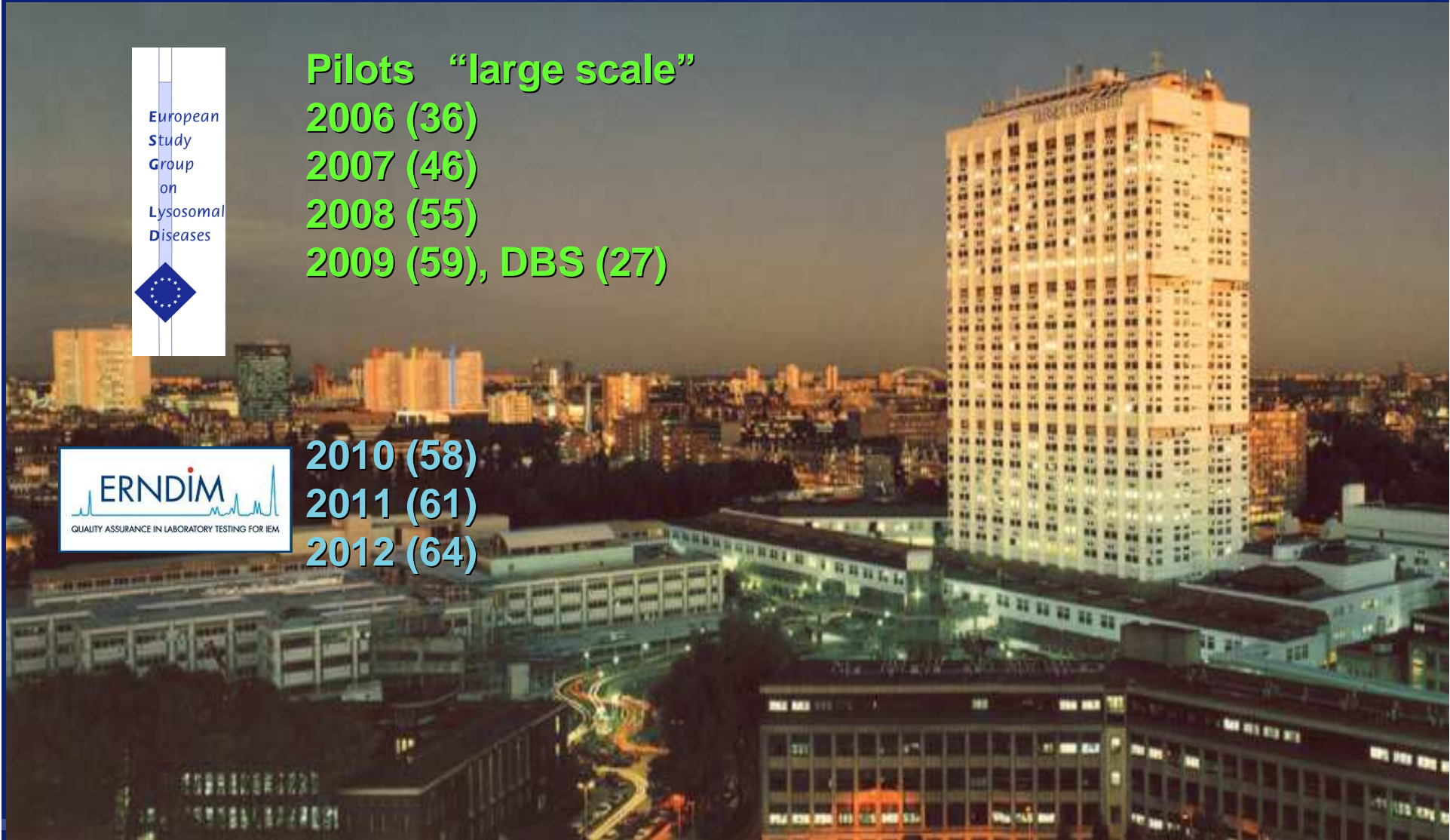
**2009 (59), DBS (27)**



**2010 (58)**

**2011 (61)**

**2012 (64)**



# ENZYMES 2012 PROFICIENCY TESTING FIBROBLASTS

**Hurler/Scheie** (MPS I)  $\alpha$ -L-iduronidase **LF4**

**Krabbe** Galactocerebrosidase

**Niemann Pick A/B** Sphingomyelinase

**Fabry**  $\alpha$ -galactosidase **LF3**

**Gaucher**  $\beta$ -Glucosidase **LF6**

**Hunter** iduronate sulphatase

**MPS VI**, Arylsulphatase B **LF5**

**GM<sub>1</sub>** (Morquio B)  $\beta$ -Galactosidase

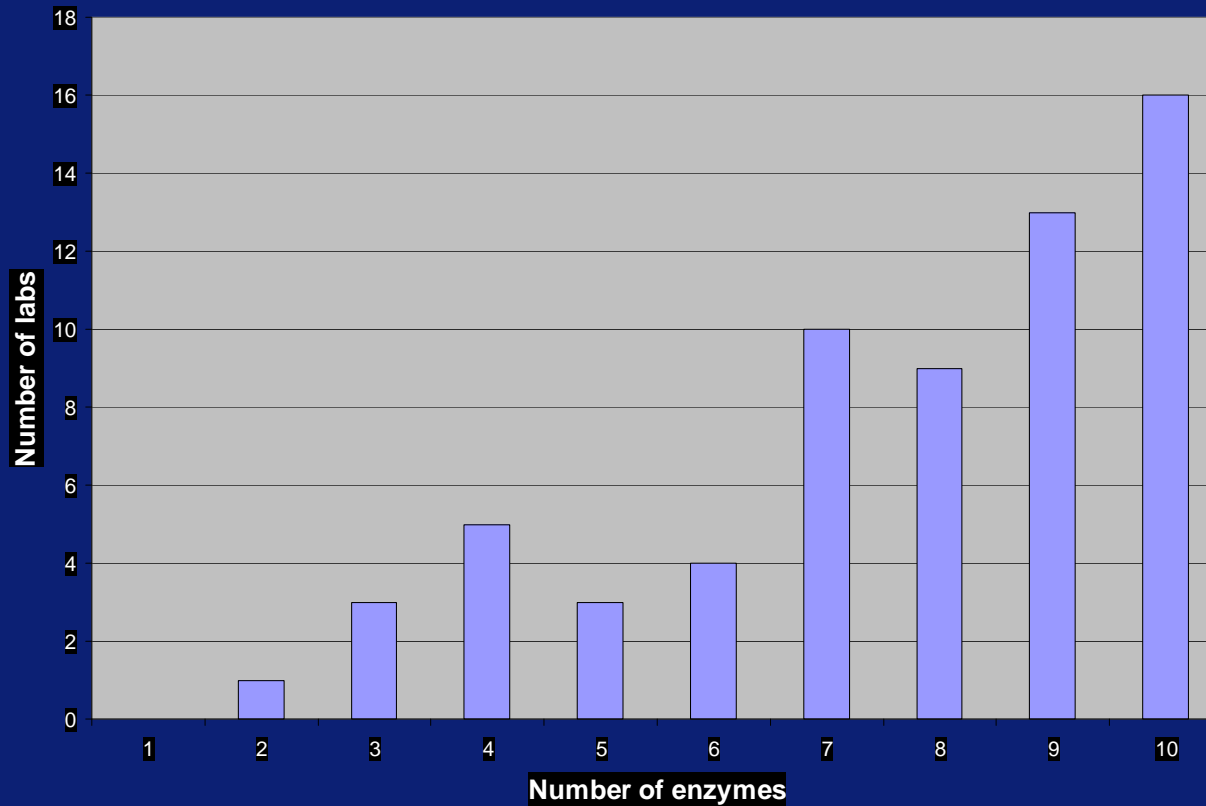
**GM<sub>2</sub>**  $\beta$ -Hexosaminidase A+B

**Pompe**  $\alpha$ -Glucosidase

**LF 1 + 2** control Fibroblasts used for determination CV

# RESULTS 2012

## NUMBER OF ENZYMES MEASURED



# Reproducibility of protein/vial 2012 duplicate samples Fibroblasts

1	15
2	5
3	14
4	3
5	0
6	0
7	0
8	24
9	9
10	8
11	3
12	0
13	1
14	17
15	0
16	10
17	11
18	0
19	4

20	0
21	2
22	0
23	0
24	11
25	0
26	4
27	9
28	3
29	2
30	-
31	0
32	3
33	15
34	0
35	0
36	0
37	3
38	4
39	6

40	3
41	
42	3
43	7
44	4
45	2
46	4
47	6
48	6
49	24
50	0
51	6
52	3
53	14

54	-
55	0
56	10
57	2
58	-
59	63
60	9
61	0
62	26
63	11
64	4

Mean CV 6.5±9.6 %

N=64	2011	2012
No data	16%	13%
CV<25	68%	91%
CV>25	16%	3%

# Reproducibility of Arylsulfatase B 2012 duplicate samples Fibroblasts

1	97
2	2
3	28;D0
4	9
5	28
6	5
8	23
9	32
11	-
14	139;D+
15	21
16	24
43	1
19	12
20	D0
21	17
24	3
25	18

26	0
28	12
29	24
31	11
32	58
34	73
35	24
38	200;D+
40	13
44	9
45	19
46	7
47	0
48	4
49	21
51	7
52	11;D-

53	58
54	-
56	33;D+D0
57	30
59	26;D-
60	8;D-
61	8;D-D+
62	9
64	10

**D-** enzyme activity  
patient sample >  
30% control  
Fibroblasts

**D+** enzyme activity  
other samples < 20  
% control  
Fibroblasts

**D0** patient sample  
not measured

N=44	2011	2012
No data	25%	16%
CV<25	27%	66%
CV>25	48%	27%

Mean CV  $23 \pm 28$  %

D incorrect 16%

# Reproducibility of $\alpha$ -Galactosidase 2012 duplicate samples Fibroblasts

1	43
2	17
4	4
5	4
6	10
8	4
9	
10	27
11	4
12	2;d-
13	3
14	14
15	0
16	22
17	10
18	6;d-

19	5
20	9
21	2
25	2;d-
43	17
26	9
27	2
28	5
29	2
30	
31	4
32	0
33	22
34	10;d-
35	4;d-
37	
39	
40	10
41	
44	2
45	8

46	8
47	6;d-
48	4
49	37;d-d+
50	5;d-
51	6;d-
52	9
53	4;d0
54	-
56	4
57	8
58	d0
59	70
60	14;d-
61	86
62	32
63	12
64	4;d0

N=55	2012
No data	18%
CV<25	76%
CV>25	11%

**D-** enzyme activity  
patient sample > 30%  
control Fibroblast

**D+** enzyme activity  
other Fibroblast < 20  
% control Fibroblast

**D0** patient sample not  
measured

Mean CV  $12 \pm 16$  %  
D incorrect 16 %

# Reproducibility of $\beta$ -Galactosidase 2012 duplicate samples Fibroblasts

1	33
2	8
3	21
4	5
5	7
6	40
7	0
8	2
9	d+
10	34
11	3
12	5
13	2
14	17
15	2
16	18
17	8
18	2
19	7
20	4

Mean CV  $10 \pm 13\%$   
D incorrect 3%

21	1
22	2
23	72;D+
24	10
25	1
43	14
26	8
27	17
28	22
29	4
30	-
31	0
32	16
33	12
34	2
35	0
36	0
37	10
38	12
39	9
40	2

41	
42	6
44	5
45	-
46	3
47	15
48	0
49	33
50	6
51	1
52	3
53	17
54	-
55	0
56	13
57	4
58	-
59	-
60	9
61	1
62	20
63	11
64	16

N=64	2011	2012
No data	20%	19%
CV<25	43%	83%
CV>25	37%	8%

**D-** enzyme activity  
patient sample > 30%  
control Fibroblast

**D+** enzyme activity  
other Fibroblast < 20 %  
control Fibroblast

**D0** patient sample not  
measured

# Reproducibility of $\alpha$ -Glucosidase 2012 duplicate samples Fibroblasts

2	4
4	6
5	11
6	8
7	9
8	8
9	70
10	7
11	5
14	13
15	0
16	17
17	3
18	1
19	6

20	7
21	4
25	3
43	11
26	3
27	10
29	5
32	10
33	15
34	6
35	9
37	
44	6

45	1
46	9
48	200;d+
49	31
52	3
53	8
54	-
56	7
57	49
58	
59	
60	10
61	0
62	23
64	

N=42	2012
No data	24%
CV<25	81%
CV>25	10%

**D-** enzyme activity  
patient sample > 30%  
control Fibroblast

**D+** enzyme activity  
other Fibroblast < 20 %  
control Fibroblast

**D0** patient sample not  
measured

Mean CV  $16 \pm 33$  %  
D incorrect 2 %



# Reproducibility of $\beta$ -Glucosidase 2012 duplicate samples Fibroblasts

1	24
2	
3	0
4	5
5	4
6	0;d-
7	0
8	7
9	30
10	20
11	2
12	69
14	13
15	0
16	9
17	0
18	4
19	7
20	7
21	5

22	-
23	4;2d+
25	2
43	16
26	4
27	7
28	1
29	2
30	
31	3
32	4
33	4
34	
35	10
36	1;d0
37	3
38	7
39	1
41	d0

44	3
45	1
46	23
47	2
48	7;d-
49	24
51	5
52	7
53	17
54	-
56	72;d0
57	7
58	
59	35;d-
60	14
61	14;d-d+
62	15
63	2
64	7

N=58	2012
No data	21%
CV<25	81%
CV>25	7%

**D-** enzyme activity  
patient sample > 30%  
control fibroblasts

**D+** enzyme activity  
other samples < 20 %  
control fibroblasts

**D0** patient sample not  
measured

Mean CV  $10 \pm 15$  %  
D incorrect 9%

# Reproducibility of $\beta$ -Hexosaminidase A+B 2012 duplicate samples Fibroblasts

2	14
4	9
5	13
6	9
7	4
8	10
9	105
10	3
11	30
12	2
13	1
14	21
15	4
16	11
17	8
18	1
19	8
20	11
21	1
22	10
24	4

25	1
43	5
26	11;d+
27	2
28	2
30	
31	15
32	8
33	11
34	4
35	4
36	7
37	3
38	6
39	6
40	4
41	
42	3

Mean CV  $14 \pm 30\%$   
D incorrect 4%

44	196;d+
45	44
46	12
47	10
48	1
49	11;d+
51	10
53	17
54	-
55	2
56	24
57	1
58	
60	7
61	6
62	14
63	15
64	4

N=57	2011	2012
No data	22%	14%
CV<25	41%	86%
CV>25	27%	7%

**D-** enzyme activity  
patient sample > 30%  
control Fibroblast

**D+** enzyme activity  
other Fibroblast < 20  
% control Fibroblast

**D0** patient sample not  
measured

# Reproducibility of $\alpha$ -Iduronidase 2012 duplicate samples Fibroblasts

1	26
3	4
4	3
5	1
6	50
7	0
8	12
9	3
11	10
14	14
15	0
16	4
17	2
18	5
19	5
21	5
24	1

25	0
43	2
26	15
27	9
29	8
30	
31	6
32	12
33	2
34	11
35	4
36	42
37	3;d0
38	13;d0
39	6
44	2
45	8
46	11

47	2
48	3
49	25;d-d+
51	9
52	7
53	6;d0
54	-
55	7
56	9
57	4
58	d0
59	12
60	6
61	4
62	23;d0
64	3

N=51	2011	2012
No data	24%	18%
CV<25	31%	86%
CV>25	45%	8%

**D-** enzyme activity  
patient sample > 30%  
control Fibroblast

**D+** enzyme activity  
other Fibroblast < 20  
% control Fibroblast

**D0** patient sample not  
measured

Mean CV  $9 \pm 10$  %  
D incorrect 2 %

# Reproducibility of Iduronidate sulphatase 2012 duplicate samples Fibroblasts

2	1
3	33
4	6
5	6
7	2
8	4
9	36
11	1
14	21
15	13
17	9
18	-
19	7
20	61
21	7

25	4
26	6
27	16
29	3
30	
31	12
32	28
33	16
34	3
35	7
39	
42	2

44	0
45	75
47	9
48	7
52	3
53	24
55	51
56	11
57	0
58	
59	66
62	37
64	11

N=40	2012
No data	25%
CV<25	70%
CV>25	20%

**D-** enzyme activity  
patient sample > 30%  
control Fibroblast

**D+** enzyme activity  
other Fibroblast < 20 %  
control Fibroblast

**D0** patient sample not  
measured

Mean CV  $17 \pm 20$  %  
D incorrect 0%

# Reproducibility of Galactocerebrosidase 2012 duplicate samples Fibroblasts

5	5
6	7
7	15
8	13
9	-
10	49;d+
14	30
15	6
17	0
18	24;d+
19	8
20	20

21	3
22	31;d+
25	7
27	12
29	21
30	
33	3
34	64
36	
37	3
38	5
39	0

44	11
45	2
46	-
47	10
52	13
53	5
55	3
56	20
57	4
58	
59	55;d+
61	28
62	25
64	4

N=38	2011	2012
No data	36%	21%
CV<25	21%	71%
CV>25	43%	16%

**D-** enzyme activity  
patient sample > 30%  
control Fibroblast

**D+** enzyme activity  
other Fibroblast < 20  
% control Fibroblast

**D0** patient sample not  
measured

Mean CV  $16 \pm 16$  %  
D incorrect 11%

# Reproducibility of Sphingomyelinase 2012 duplicate samples Fibroblasts

3	13
4	3
5	6
6	8
8	3
9	-
10	28;d+
14	14
15	2
17	0
18	9
19	1
20	13

21	6
24	5
25	5
43	16
26	4
27	12
29	2
31	1
34	2
36	8
37	7
38	14;d+
39	4

44	3
46	16
47	10
50	3
52	20
53	2
55	0
56	10
57	9
58	
61	12
62	23
64	4

N=39	2011	2012
No data	28%	23%
CV<25	45%	92%
CV>25	28%	3%

**D-** enzyme activity patient sample > 30% control Fibroblast

**D+** enzyme activity other Fibroblast < 20% control Fibroblast

**D0** patient sample not measured

Mean CV  $8 \pm 7$  %  
D incorrect 5%

# OVERALL PERFORMANCE 2012

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

**33 Participants:** no false negative of positive patients