



External Quality Assessment
Enzyme Analysis for Lysosomal Storage Diseases



Pilots “large scale”

2006 (36)

2007 (46)

2008 (55)

2009 (59), DBS (27)



2010 (58)EBV

2011 (61)EBV

2012 (24)DBS Pilot



ENZYMES 2012 PROFICIENCY TESTING DRIED BLOOD SPOTS

Hurler/Scheie (MPS I) α -L-iduronidase **D5**

Krabbe Galactocerebrosidase **D5B**

Niemann Pick A/B Sphingomyelinase

Fabry α -galactosidase **D3**

Gaucher β -Glucosidase **D4**

Hunter iduronate sulphatase **D7**

MPS VI, Arylsulphatase B **D2**

GM₁ (Morquio B) β -Galactosidase

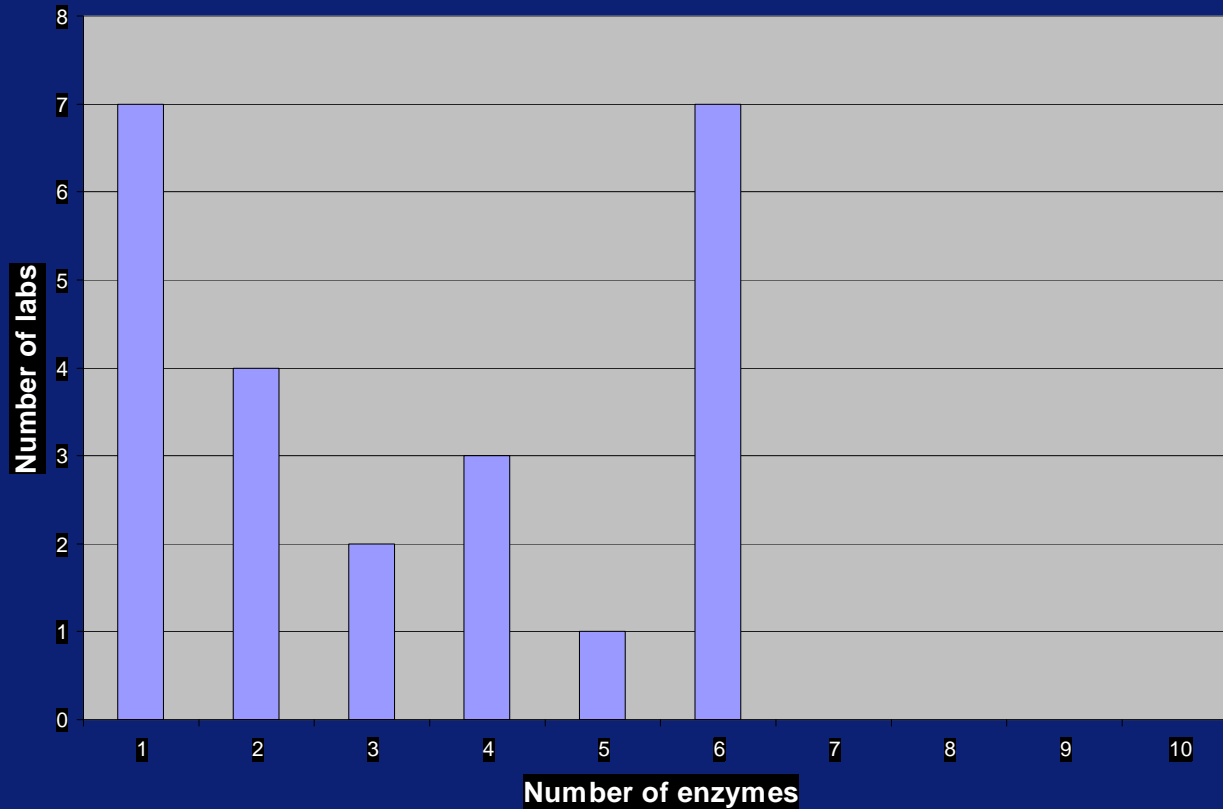
GM₂ β -Hexosaminidase A+B

Pompe α -Glucosidase **D7B**

D 1 + 6 control DBS used for determination CV

RESULTS 2012

NUMBER OF ENZYMES MEASURED



Reproducibility of Arylsulfatase B 2012 duplicate samples DBS

2	65
7	131
9	7
11	52;D+
13	32
21	126;d-d+
22	3;d-

D- enzyme activity
patient sample >
30% control DBS

D+ enzyme activity
other samples < 20
% control DBS

D0 patient sample
not measured

N=7	2012
D correct	57%
CV<25	29%
CV>25	71%

Mean CV 59 ± 52 %

D incorrect 43%

Reproducibility of β -Galactosidase 2012 duplicate samples DBS

1	
1b	
5	6
7	36
9	8
10	36
11	42
13	35
14	4
15	29
19	52
21	123
22	38
23	
24	12

Mean CV 37 ± 33 %
D incorrect 0%

N=15	2012
No data	25%
CV<25	25%
CV>25	50%

D- enzyme activity
patient sample > 30%
control DBS

D+ enzyme activity
other EBV < 20 %
control DBS

D0 patient sample not
measured

Reproducibility of β -Glucosidase 2012 duplicate samples DBS

2	23:D+
4	60
5	57
7	200;D-D+
7b	63;d0
7c	
8	171;D-
9	17
11	60
13	71;D-
15	13;D-
19	17
20	60
21	123
22	138
23	

Mean CV 63 ± 60 %
D incorrect 31 %

N=16	2012
D correct	50%
No data	13%
CV<25	38%
CV>25	50%

D- enzyme activity
patient sample > 30%
control DBS

D+ enzyme activity
other samples < 20 %
control DBS
D0 patient sample not
measured

Reproducibility of α -Galactosidase 2012 duplicate samples DBS

1	
2	69
3	189;d+
4	6
5	43
6	199
7	29
8	148;D+
9	25
10	17
11	24
12	-
13	25
14	7
15	19
16	7
17	9;d0
18	37
19	17
20	38
21	156
22	8
23	D0
24	

Mean CV 52 ± 63 %
D incorrect 17%

N=24	2012
D correct	83%
No data	21%
CV<25	38%
CV>25	45%

D- enzyme activity
patient sample > 30%
control DBS

D+ enzyme activity
other DBS < 20 %
control DBS

D0 patient sample not
measured



Reproducibility of α -Iduronidase 2012 duplicate samples DBS

1b	
2	14;D-
4	169
5	4
7	8
9	50
11	6
13	96
15	13
19	-
20	39
21	128
22	46
23	
24	2

Mean CV 52 ± 56 %
D incorrect 7 %

N=15	2012
Dcorrect	73%
No data	20%
CV<25	36%
CV>25	40%

D- enzyme activity
patient sample > 30%
control DBS

D+ enzyme activity
other DBS < 20 %
control DBS

D0 patient sample not
measured

Reproducibility of Iduronidate sulphatase 2012 duplicate samples DBS

2	D0
7	7
9	1;D-
11	33
13	5
15	29
21	76
22	28

Mean CV 25 ± 26 %
D incorrect 25 %

N=8	2012
No data	13%
CV<25	38%
CV>25	50%

D- enzyme activity
patient sample > 30%
control DBS

D+ enzyme activity
other DBS < 20 %
control DBS

D0 patient sample not
measured

Reproducibility of α -Glucosidase 2012 duplicate samples DBS

24

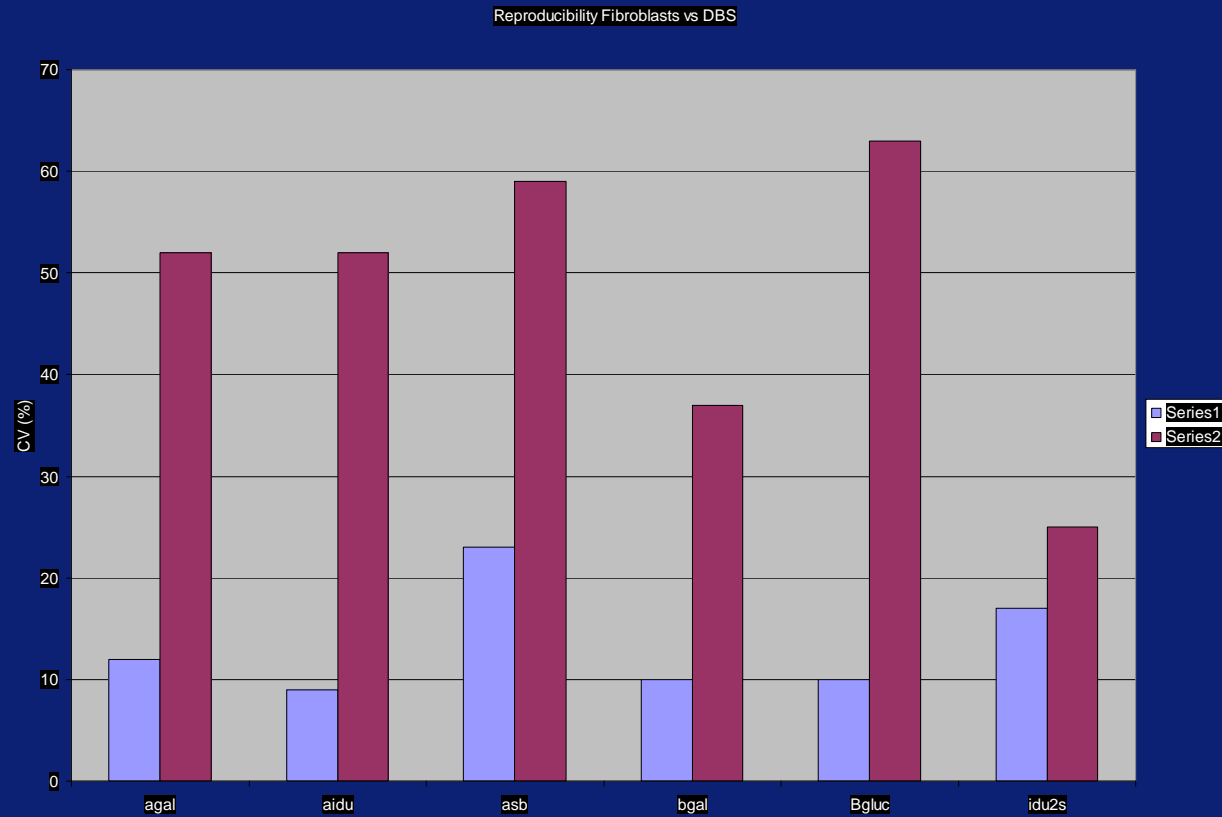
8;D-

Only one participant for α -Glucosidase

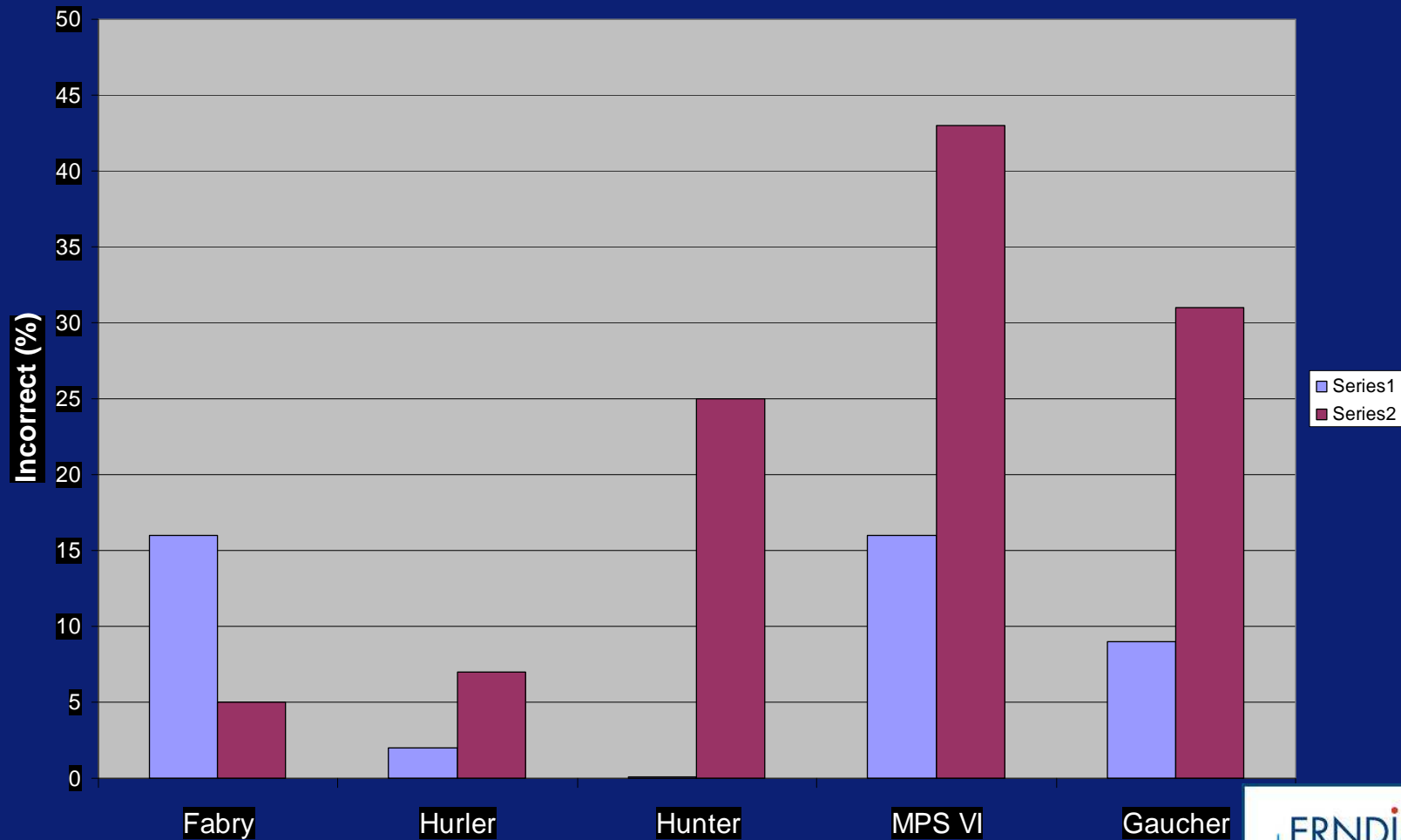
Activity in patient sample not different from activity in other DBS samples

Reproducibility one participant <25%

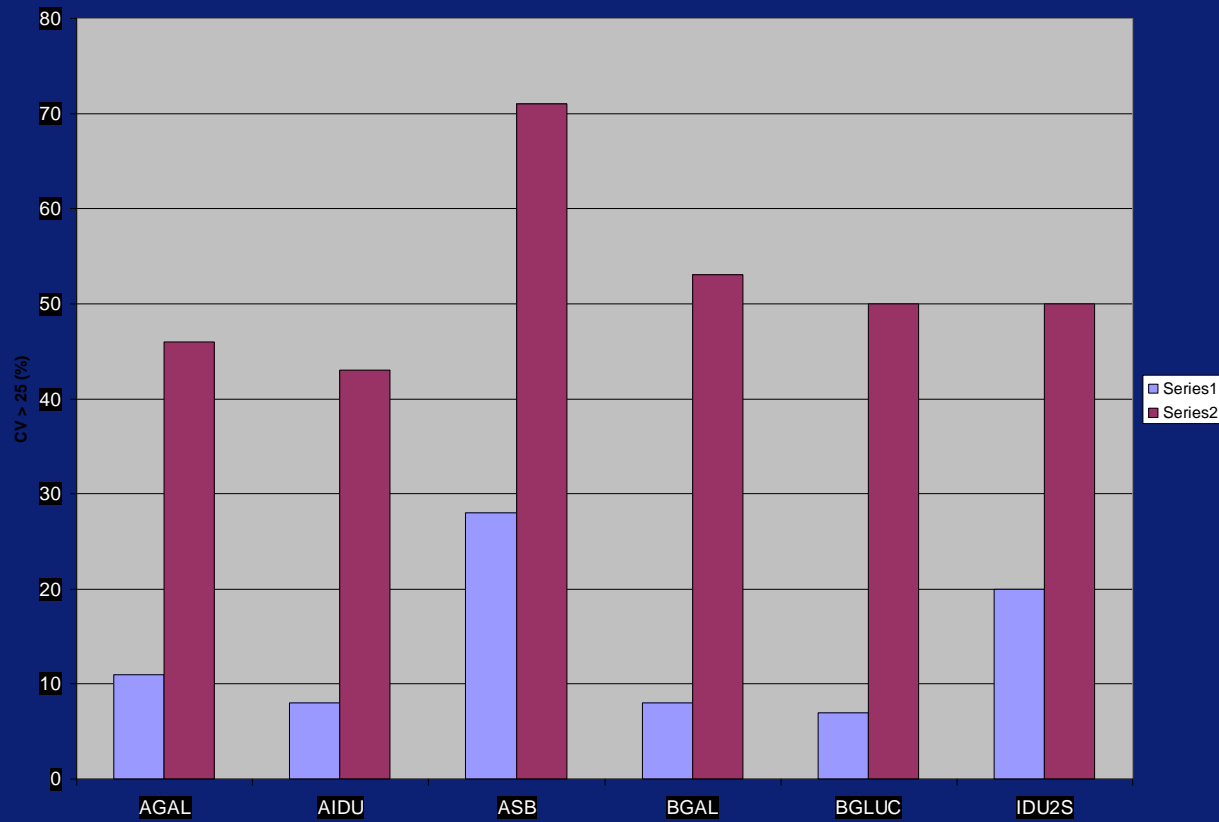
Reproducibility fibroblasts vs DBS



DIAGNOSIS FIBROBLASTS VS DBS



% Participants CV>25 Fibroblasts vs DBS



CONCLUSION COMPARISON FIBROBLASTS VS DBS

Diagnostics DBS Fabry, Hurler comparable with fibroblasts

**Diagnostics Hunter, Gaucher, MPS VI, Pompe much better in fibroblasts
and unreliable in DBS**

Reproducibility activity measurements in DBS insufficient