



**SCOTTISH NEWBORN SCREENING LABORATORY**

**INSTITUTE OF MEDICAL GENETICS  
YORKHILL HOSPITAL  
GLASGOW**

**ANNUAL REPORT**

**APRIL 2009-MARCH 2010**

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## 1. INTRODUCTION

The Scottish Newborn Screening Laboratory (SNSL) is housed in the Biochemical Genetics Department in the Institute of Medical Genetics at Yorkhill, Glasgow. It is the sole newborn screening laboratory in Scotland and one of the largest in the UK. The Consultant Clinical Scientist in charge of Biochemical Genetics is the designated director of the Newborn laboratory screening service. The current staff complement in the SNSL consists of a Laboratory Newborn Screening Coordinator managing the laboratory, one Clinical Scientist (0.6 wte), three Health Care Scientists (2.5 wte) and four Administration and Clerical staff (3.0 wte).

The remit of the laboratory is:-

- To screen all babies born in Scotland (currently around 60,000 per annum) for phenylketonuria (PKU), congenital hypothyroidism (CHT) and cystic fibrosis (CF);
- To ensure the reporting of all negative results to the proper authorities and the prompt referral of all positive cases for treatment;
- To provide data on the incidence of these conditions to the Scottish Office as required;
- To review new technology with a view to the incorporation of new tests/methods into the screening programme;
- To undertake pilot studies and participate in research programmes related to newborn screening.

The laboratory testing is highly automated with immunoassay analysers, two bloodspot punching machines and two tandem mass spectrometers all interfaced to a state of the art Laboratory Information Management System.

## 2. ACTIVITY

Specimens in the form of dried bloodspots taken around 5 days of age are received from infants in all Health Boards in Scotland. A system of parental signed consent for testing is in operation and parents may decline some or all of the tests offered. Coverage in 2009 is estimated at 99.96%. From 1st April 2009 - 31st March 2010, actual vs. planned activity was:

<u>Actual Activity</u>	<u>Contracted Activity</u>
<b>61,557</b>	58,000

*Table 1: Number of specimens received and tests carried out.*

a) Specimens	
Babies Screened	59,493
b) Repeat Specimens	2,064
<b>Total Specimens received</b>	<b>61,557</b>
c) Tests	
Total tests - phenylalanine	61,529
Total tests - TSH	61,529
Total tests – IRT for Cystic Fibrosis (1 test declined by parents)	61,526
<b>Total Number of Tests Carried Out</b>	<b>184,584</b>

Screening for all three conditions was declined for 23 infants (not included in the number of test/activity in table 1). In addition, screening for Cystic Fibrosis in was declined for 3 infants.

### 3. WORKLOAD, DEMAND AND REFERRAL PATTERNS

*Table 2: Number of Scottish births and babies tested 1990-2007*

<b>YEAR</b>	<b>BIRTHS</b>	<b>BABIES TESTED</b>
1990	65,973	66,765
1991	67,024	67,374
1992	65,789	66,225
1993	63,337	63,799
1994	61,656	62,070
1995	60,051	60,344
1996	59,308	59,671
1997	59,440	60,329
1998	57,319	58,340
1999	55,147	55,561
2000	53,076	53,551
2001	52,527	52,007
2002	51,270	51,450
2003	52,432	52,655
2004	53,954	54,612
2005	54,386	54,643
2006	55,690	56,356
2007	57,781	58,196
2008	60,041	60,504
2009		59,371

Each year, a proportion of specimens are received with insufficient blood to carry out the routine tests, requiring repeat specimens to be taken. The trend over the last 18 years is presented in table 3:

*Table 3: Insufficient samples*

<b>Year</b>	<b>%</b>
1992	0.58
1993	0.56
1994	0.44
1995	0.45
1996	0.46
1997	0.47
1998	0.34
1999	0.41
2000	0.42
2001	0.82
2002	1.14
2003	1.39
2004	0.93
2005	0.98
2006	0.55
2007	0.59
2008	0.55
2009	1.23

Table 4: Source of newborn blood spot cards by Health Board, April - March, 2002-2010.

	01/02	02/03	03/04	04/05	05/06	06/07	07/08	08/09	09/10
GRAMPIAN	5,188	5,503	5,326	5,705	5,618	5,973	6,315	6,539	6,585
TAYSIDE	3,819	3,803	4,062	3,977	4,020	4,210	4,630	4,631	4,723
ARGYLL & CLYDE *	4,210	4,174	4,421	4,631	4,447	4,394	4,508	4,557	4,464
DUMFRIES & GALLOWAY	1,235	1,390	1,436	1,508	1,472	1,537	1,547	1,495	1,586
FIFE	3,709	3,673	3,728	3,848	3,962	4,062	4,293	4,442	4,298
HIGHLAND*	2,061	2,031	2,121	2,264	2,260	2,229	2,400	2,559	2,420
WESTERN ISLES	226	252	252	239	226	284	260	252	229
ORKNEY	118	169	177	191	190	216	218	211	200
AYRSHIRE	3,802	3,671	3,822	3,871	3,807	4,008	4,151	4,074	3,998
LANARKSHIRE	6,162	6,347	6,417	6,537	6,603	6,787	6,705	6,883	6,829
GLASGOW*	9,665	9,669	9,954	10,120	10,007	10,155	10,863	10,968	11,012
LOTHIAN	8,483	8,346	8,812	8,652	9,268	9,309	9,997	10,252	10,238
BORDERS	1,079	1,052	1,052	1,074	1,050	1,113	1,149	1,160	1,090
FORTH VALLEY	2,887	2,932	3,241	3,261	3,283	3,448	3,522	3,506	3,549
SHETLAND	170	217	257	242	256	296	239	282	302
MISCELLANEOUS	85	35	7	11	23	31	52	39	34
<b>TOTAL SPECIMENS (inc refusals)</b>	<b>52,970</b>	<b>53,265</b>	<b>55,085</b>	<b>56,131</b>	<b>56,492</b>	<b>58,052</b>	<b>60,849</b>	<b>61,868</b>	<b>61,557</b>

\*Figures have been compiled for the original Argyll and Clyde, Highland and Greater Glasgow Health Board areas to allow comparison with previous years

### Presumptive positive cases detected

A total of 80 infants with a presumptive positive diagnosis of PKU, CHT or CF following the newborn bloodspot screening tests were referred for further investigation to the appropriate paediatrician.

Table 5 summarises the referrals over the last 8 years. Note CF screening commenced in February 2003 and the 5 cases identified in 2002/03 represent only two months screening.

Table 5: Referrals of presumptive positive cases, 2003-2008

Year	02/03	03/04	04/05	05/06	06/07	07/08	08/09	09/10
PKU	6	8	9	10	12	15	9	12
CHT	35	31	31	25	38	29	31	31
CF	(From 01.02.03) 5	26	30	29	34	30	34	37
Total	46	65	70	64	84	74	74	80

## Referral Pattern of presumptive positive cases 2009-2010

### Phenylketonuria

Table 6: Twelve cases with high or persistently raised levels of phenylalanine were referred to paediatricians in 6 Health Board areas:

Number of cases	Area/Health Board
2	Argyll & Clyde
1	Fife
3	Glasgow
2	Grampian
3	Lanarkshire
1	Lothian

Table 7: Outcome of cases with high or persistently raised levels of phenylalanine

4	PKU
3	Hyperphenylalaninaemia
2	Transient
3	No information yet

### Congenital Hypothyroidism

Table 8: Thirty one cases with high or persistently raised levels of TSH were referred to paediatricians in 11 Health Board areas to be investigated for congenital hypothyroidism

Number of Cases	Area/Health Board
2	Argyll & Clyde
4	Ayrshire & Arran
1	Fife
1	Forth Valley
6	Glasgow
5	Highland
4	Lanarkshire
5	Lothian
1	Orkney
1	Shetland
1	Tayside

Table 9: Outcome of cases with high or persistently raised levels of TSH

11	Confirmed Congenital Hypothyroidism - on treatment.
1	Confirmed Congenital Hypothyroidism, no further information
3	? Transient, on treatment
16	No Information

## **Cystic Fibrosis**

443 cases (0.72%) with an initial raised level of IRT were sent for mutation analysis.

*Table 10: Thirty seven cases with suspected CF or possible CF were referred to paediatricians in 11 Health Board areas:*

<b>Number of cases</b>	<b>Area/Health Board</b>
1+2*	Argyll & Clyde
1*+2 sweat test neg	Ayrshire & Arran
1	Borders
2+1 sweat test neg	Forth Valley
8+1*+1 sweat test neg	Glasgow
1+1*	Grampian
1+1 sweat test neg	Highland
3+2*	Lanarkshire
3+2*	Lothian
2	Tayside
1	Western Isles

\*cases awaiting outcome of sweat test (n=9).

*Table 11: Outcome of cases with high or persistently raised levels of IRT*

20	Two CF mutations (one detected Manchester-cousin of known case)
6*	One mutation + two raised IRT – No further information
3	One mutation + two raised IRT – positive sweat test
1	One mutation + two raised IRT – negative sweat test
	One mutation + second specimen taken too late to perform reliable IRT testing – No further information
3	No Mutations + two raised IRT – No further information
4**	No Mutations + two raised IRT – negative sweat test

\*One Lanarkshire baby had one mutation but no second specimen, counted with sweat tests awaited.

\*\*One Ayrshire baby where first specimen was taken too late for IRT testing, no mutations, no second specimen, ancestry group C.

In addition, 39 cases with 1 mutation (probable CF carriers) were reported to General Practitioners in Health Boards across Scotland.

#### 4. RESPONSE TIMES

All cases (100%) with high or persistently raised levels of PHE, TSH or IRT were telephoned on the day of confirmation within the laboratory, to the appropriate authority. Results were confirmed in writing to the appropriate Consultant Paediatrician within 2 working days of the initial report.

Reports were issued within 2 working days of receipt on **99.03%** of all specimens. Target - 95% of results issued within 2 working days of receipt of specimen.

*Table 12: Sample turn-around times April 09 - March 10*

<b>Time period</b>	<b>Reports within 2 working days (%)</b>	<b>Average reporting time in days</b>
Apr-09 – March 10	99.03	1.10

#### 5. QUALITY AND ACCREDITATION

##### Quality Assurance

The laboratory continues to participate in the following External Quality Assurance schemes:

- The UK National External Quality Control Scheme (UK NEQAS) for TSH and PHE. (See appendix 1, pages 11-14).
- The Centre for Disease Control in Atlanta for IRT and PHE. (See appendix 1, page 15).
- The German Quality Control Scheme for TSH (See appendix 1, page 16)

Overall performance in all schemes is satisfactory.

##### Clinical Pathology Accreditation (CPA, UK) Status

The Biochemical Genetics Laboratories were inspected on 3<sup>rd</sup> and 4<sup>th</sup> September 2008. One observation and 26 non conformances (all minor) were identified. All have been rectified and the Laboratories have full Accreditation Status.

## 6. AUDIT

### Completeness of Screening

Completeness of screening was checked against a cohort of 5916 names and addresses issued from the Registrar's Office for 4<sup>th</sup> quarter of 2008 and first 3 quarters of 2009, 19 babies did not have newborn screening results in the reporting system under the information given. Of these, 11 babies had died, 7 are English, and 1 was a parental refusal.

Breakdown of figures per quarter are:

4<sup>th</sup> Qtr 2008 = 1454. There were no results in 6 (2 died, 4 are English babies)

1<sup>st</sup>Qtr 2009 = 1450 babies. There were no results in 5 (4 died, 1 English)

2<sup>nd</sup> Qtr 2009 = 1486 babies. There were no results in 3 (3 died)

3<sup>rd</sup> Qtr 2009 = 1526 babies. There were no results in 5 (2 died, 2 English and 1 Parental Refusal)

### Clinical follow-up and audit

Work is currently ongoing on the backlog of all referred cases in order to complete clinical outcomes.

### Tests declined

An audit of the number of parents declining some or all of the screening tests offered has been carried out since 2003 when the system of signed consent was introduced.

*Table 13: Number and type of tests declined by parents 2003-2009.*

Year	Declined: All tests	Declined: CF only	Declined: CHT only	Declined: PKU only	Declined: CF+CHT	Declined: CF+PKU	Declined: CHT+PKU
2003	40	15	0	0	1	0	0
2004	35	7	0	0	0	0	0
2005	37	6	1	0	0	0	0
2006	22	0	0	0	0	0	0
2007	16	4	0	0	0	0	0
2008	20	0	0	0	0	0	0
2009	25	4	0	0	0	0	0

In 2009 the vast majority of parents accepted newborn blood spot testing with less than 0.05% of parents declining some or all tests.

## 7. TEACHING AND RESEARCH ACTIVITIES.

### Teaching

Formal lectures on newborn screening are provided for students enrolled in the 1 year taught course in Medical Genetics (Med Sci) at the University of Glasgow.

Specialist Registrars from Clinical Genetics and Biochemistry have visited the department as part of their overall training programme. This involves them spending a few hours in the laboratory where they are introduced to the rationale behind newborn screening and the practical aspects of assay preparation and the interpretation of results. The laboratory also continues to receive Medical Students undergoing a Special Study Module in Community Medicine and Clinical Scientists in training as part of their study module on Metabolic Biochemistry.

### Research/Development Activities

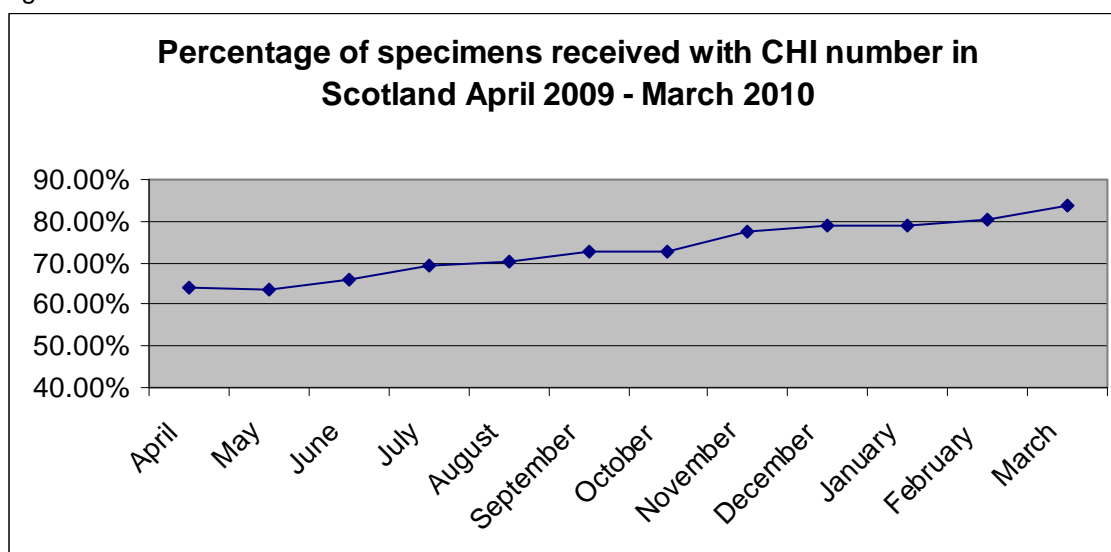
#### Screening developments

Equipment and resources to support the planned expansion of the newborn screening programme to include Medium Chain Acyl CoA Dehydrogenase Deficiency (MCADD) and Sickle Cell Disorder (SCD) from 1<sup>st</sup> October 2010 have been procured. The equipment includes a second Tandem Mass Spectrometer, HPLC system, Isoelectric Focusing system and a second Multipuncher. Assay development and instrument validation testing has been completed. Upgrades to the Laboratory Information Management System have also been carried out in preparation for the expanded test repertoire.

#### Community Health Index (CHI)

The laboratory information management system (LIMS) continues to be used to provide information on the use of the CHI number on the blood spot cards (Figure 1). The figures are distributed to the CHI Programme Manager at SGHD and Health Board Coordinators throughout Scotland. The information is also sent to Nursing, Medical and Administration staff within a number of Health Boards.

Figure 1



## **8. FINANCIAL PROFILE**

See Appendix 2.

## **9. SUMMARY AND CONCLUSIONS**

The workload of the screening laboratory in 2009 shows little change from the previous year with around 61,500 specimens received which exceeds the contracted activity of 58,000. The increased activity will be reflected in new SLA from April 2010 onwards where the figure of 62,000 births will be used and reviewed annually.

There has been an unexplained rise in the number of insufficient samples received in 2009 (1.23% vs. 0.55% in 2008) necessitating repeat requests.

The number of parents declining some or all testing for their baby in 2009 was 29 (<0.05%) compared to 20 in 2008). This refusal rate is comparable to the levels which existed before signed consent was introduced.

A total of 80 infants with a presumptive positive diagnosis of PKU, CHT or CF were identified following the newborn bloodspot screening tests and were referred for further investigation to the appropriate paediatricians.

The laboratory continues to comfortably exceed the standards for reporting and sample turn-around times.

Although the use of CHI numbers on bloodspot cards has shown a steady rise in 2009 to almost 90%, there is some variation between Health Boards.

Prior to the implementation of screening for Medium Chain Acyl CoA Dehydrogenase Deficiency (MCADD) and Sickle Cell Disorder (SCD) on 1<sup>st</sup> October 2010, increased staffing (1.0 wte Band 8a Healthcare Scientist) will be recruited to service the increased workload.



**UKNEQAS** for Neonatal Screening

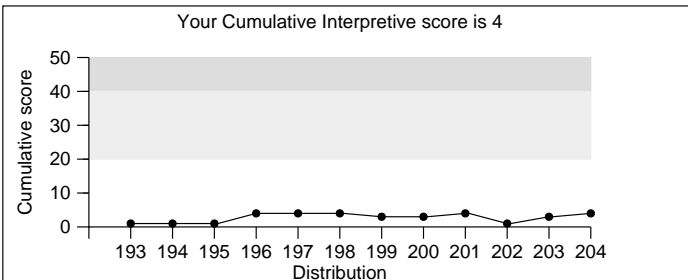
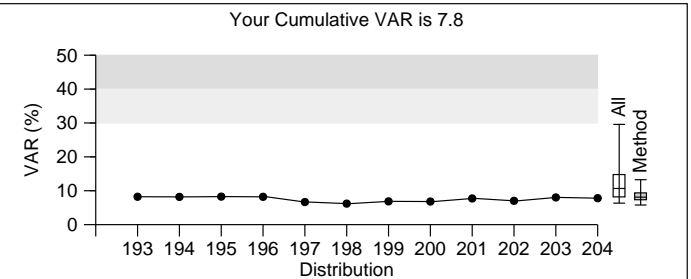
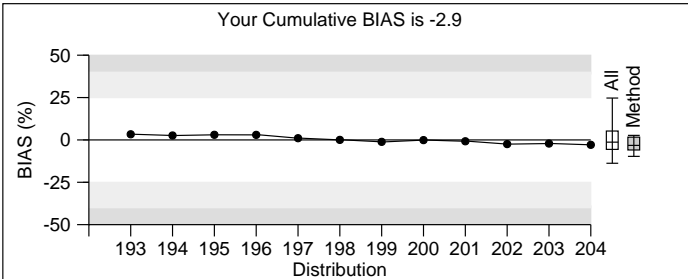
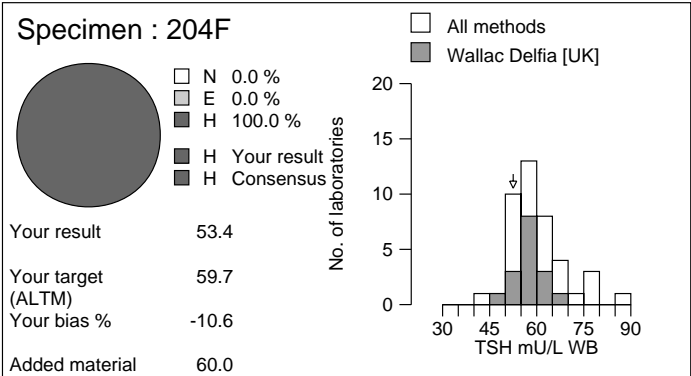
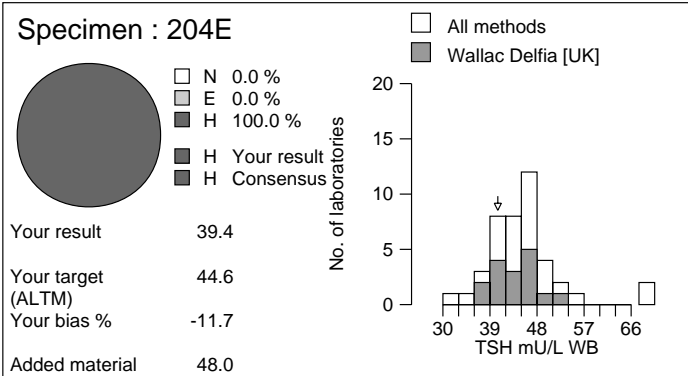
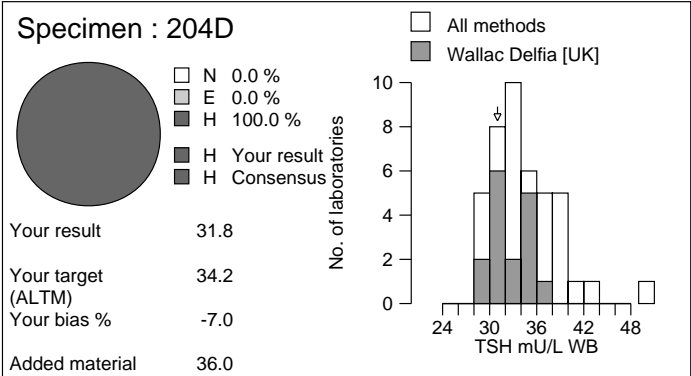
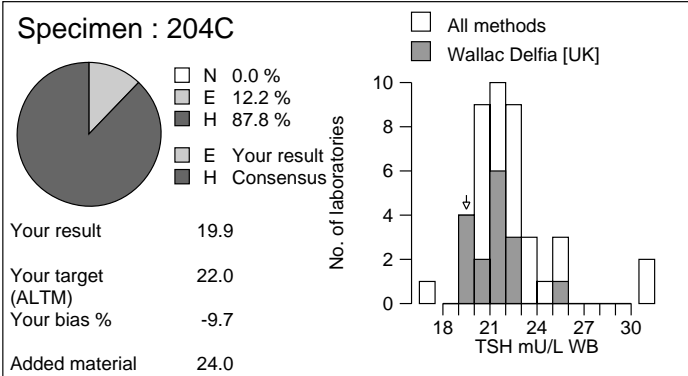
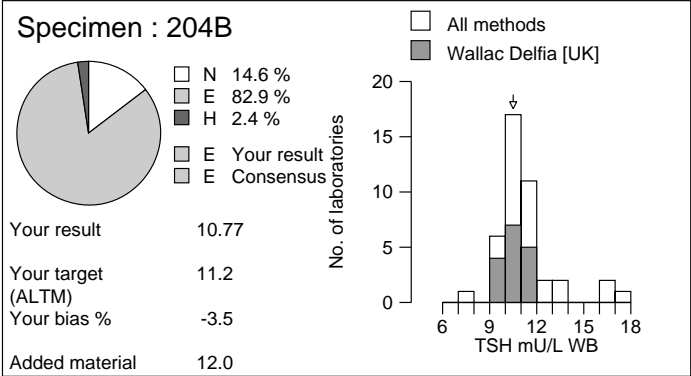
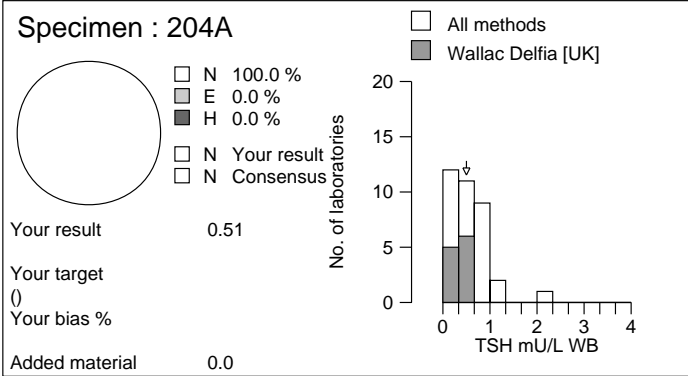
Laboratory : **10934**

Distribution : **204**

Date : 21-Mar-2010

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Analyte : TSH mU/L WB



For TSH there are 3 possible responses

Screen negative, which I will call N, and which is defined as less than 10 mU/L WB  
Borderline, which I will call E, and which is defined as lying between 10 and 20 mU/L WB inclusive  
Screen positive, which I will call H, and which is defined as greater than 20 mU/L WB.

Birmingham Quality is part of the University Hospitals Birmingham NHS Foundation Trust and provides this UK NEQAS service from PO Box 3909, Birmingham B15 2UE, UK. To contact us, email ClinChem@ukneqas.org.uk or phone us on 0121 414 7300. The simplest way for you to return your results is via the Online Results and Reports Service. FAXing completed Results documents to 0121 414 1179 is still currently permissible.

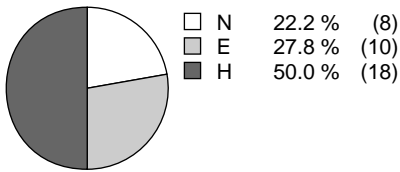
© The data in this CPA(EQA) Accredited UK NEQAS report is confidential.  
For this Scheme, the Organiser is Finlay MacKenzie.  
www.birminghamquality.org.uk  
Published at 14:10:11 on Wednesday 24 March 2010



		204A		204B		204C		204D		204E		204F	
	n	Mean	GCV	Mean	GCV	Mean	GCV	Mean	GCV	Mean	GCV	Mean	GCV
All methods	42			11.2	12.3	22.0	9.1	34.2	11.9	44.6	12.3	59.7	14.7
Wallac Delfia [non-UK]	17			10.9	10.2	22.3	8.6	34.5	13.2	45.0	12.2	59.3	11.6
Wallac Delfia [UK]	16			10.8	8.5	21.3	6.8	32.9	8.2	43.5	10.6	57.7	8.7

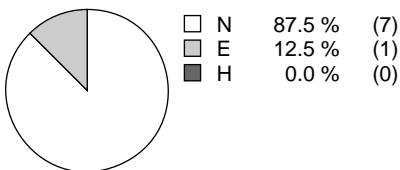
%Recovery Added Material		204A	204B	204C	204D	204E	204F
	n						
All methods	42	0.0	12.0	24.0	36.0	48.0	60.0
Wallac Delfia [non-UK]	17		93.0	91.8	95.0	93.0	99.5
Wallac Delfia [UK]	16		90.8	92.8	95.8	93.7	98.8
			89.8	88.8	91.4	90.6	96.2

Specimens distributed in each category

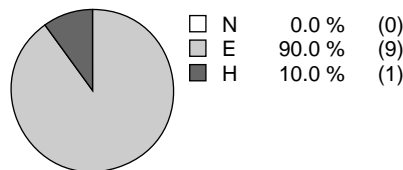


Your interpretation for each category

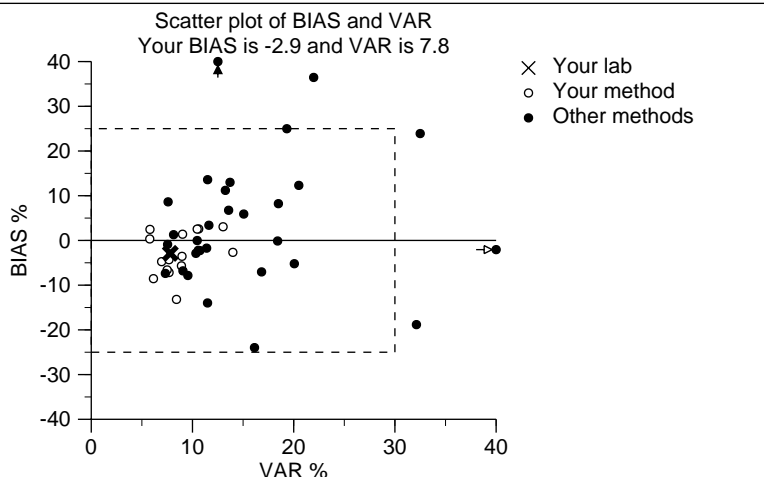
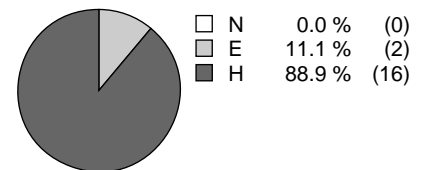
Normal



Equivocal

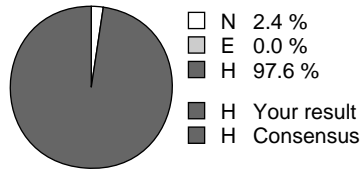


High

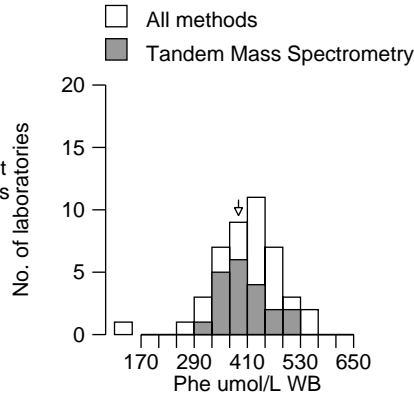




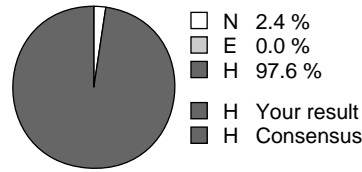
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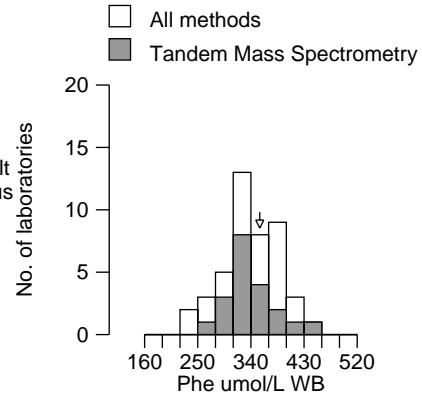
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 Your target (ALTM): 410  
 Your bias %: -1.1  
 Added material: 400.0



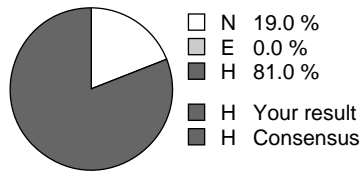
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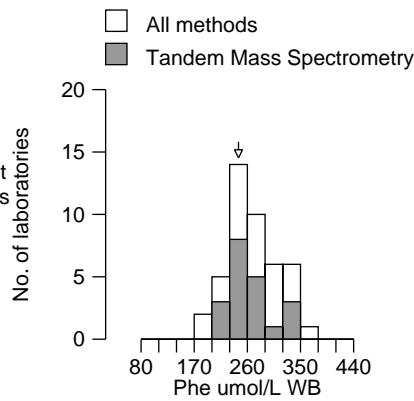
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 Your target (ALTM): 340  
 Your bias %: +2.0  
 Added material: 320.0



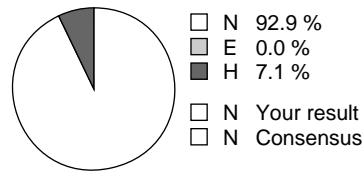
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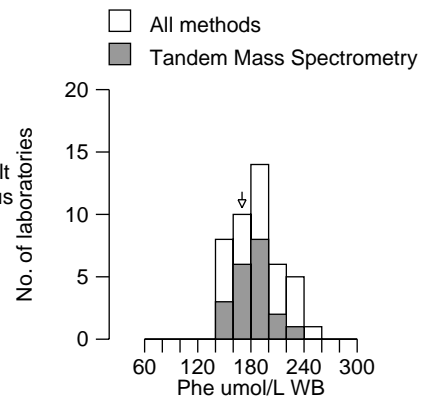
Your result: 259  
 Your target (ALTM): 267  
 Your bias %: -2.9  
 Added material: 240.0



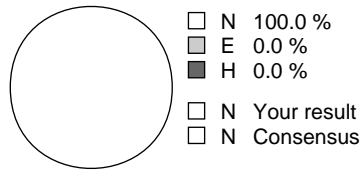
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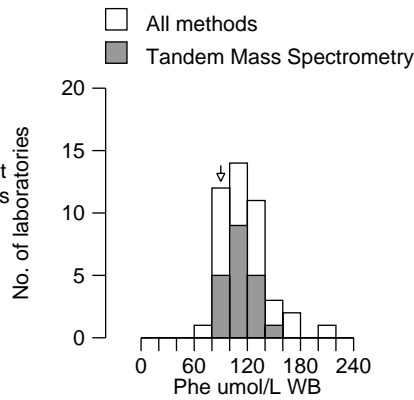
Your result: 175  
 Your target (ALTM): 185  
 Your bias %: -5.6  
 Added material: 160.0



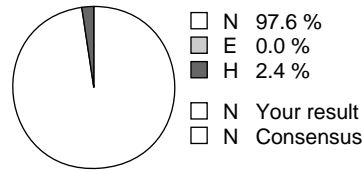
**Specimen : 204E**



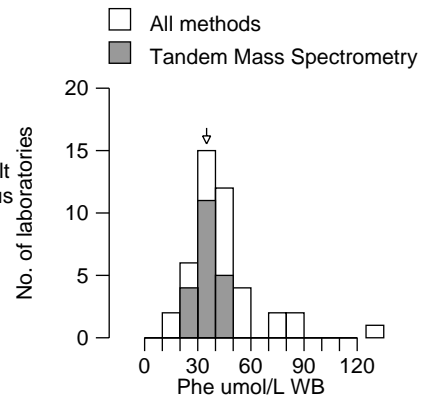
Your result: 99  
 Your target (ALTM): 112  
 Your bias %: -11.6  
 Added material: 80.0



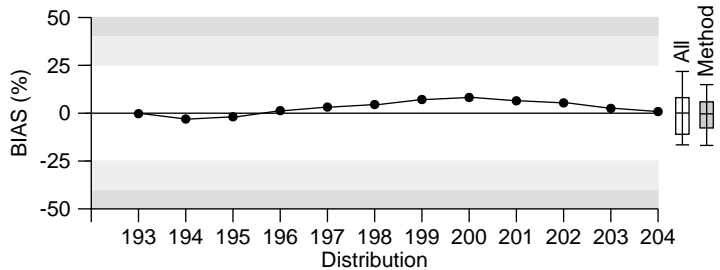
**Specimen : 204F**



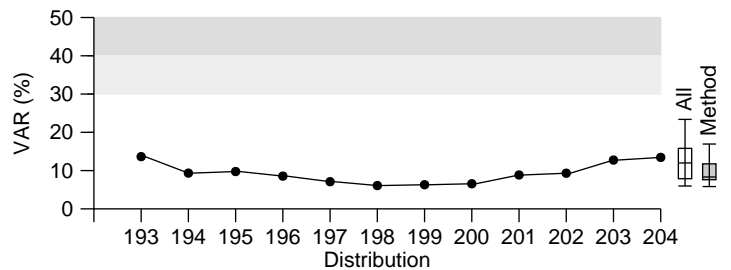
Your result: 36  
 Your target (ALTM): 41  
 Your bias %: -11.6  
 Added material: 0.0



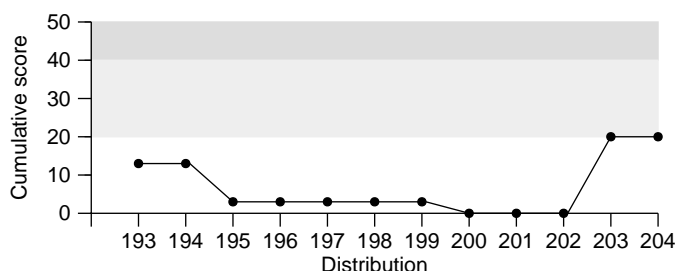
Your Cumulative BIAS is +0.8



Your Cumulative VAR is 13.4



Your Cumulative Interpretive score is 20



For Phenylalanine there are only 2 possible responses

Screen negative, which I will call N, and which is defined as less than or equal to 240 umol/L  
 Screen positive, which I will call H, and which is defined as greater than 240 umol/L

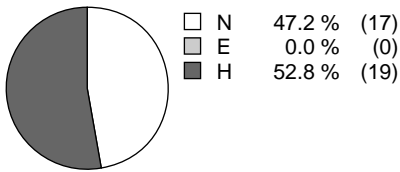
Any laboratory reporting E, or Intermediate or N/H etc for Phenylalanine, will be classified as not being Screen negative, so will be entered as H in my system.



		204A		204B		204C		204D		204E		204F	
	n	Mean	GCV	Mean	GCV	Mean	GCV	Mean	GCV	Mean	GCV	Mean	GCV
All methods	44	410	16.5	340	14.9	267	17.8	185	16.4	112	22.1	41	35.1
Fluorometric	12	421	15.2	350	14.4	274	25.0	195	20.9	113	32.7	47	123.1
HPLC	4	429		369		291		197		117		40	
Tandem Mass Spectrometry	20	403	14.4	336	11.8	260	15.1	181	12.8	109	15.2	36	19.0

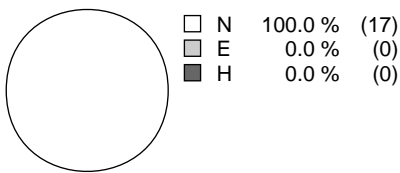
%Recovery		204A	204B	204C	204D	204E	204F
Added Material		400.0	320.0	240.0	160.0	80.0	0.0
	n						
All methods	44	92	94	94	90	89	
Fluorometric	12	94	95	95	93	83	
HPLC	4	97	103	104	98	95	
Tandem Mass Spectrometry	20	92	94	93	90	91	

Specimens distributed in each category

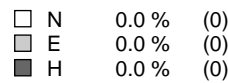


Your interpretation for each category

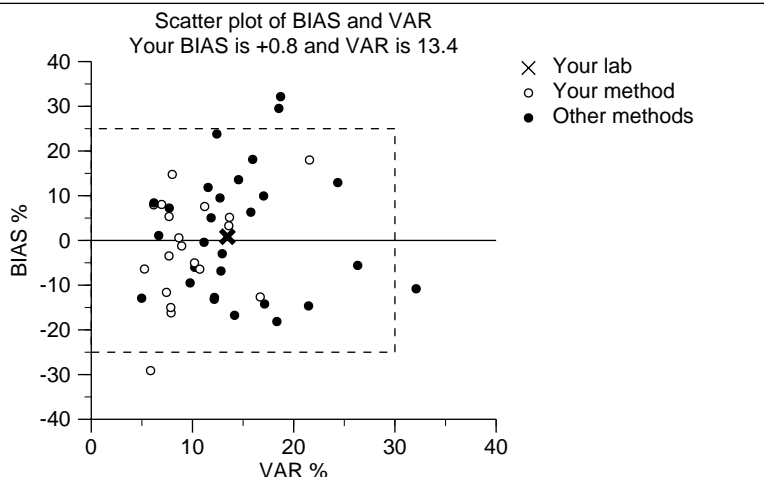
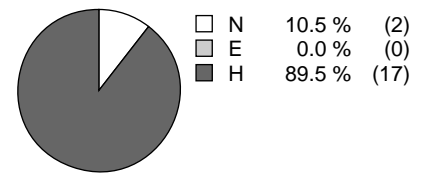
Normal



Equivocal



High



© The data in this CPA(EQA) Accredited UK NEQAS report is confidential. 14

For this Scheme, the Organiser is Finlay MacKenzie.

www.birminghamquality.org.uk

Published at 14:10:12 on Wednesday 24 March 2010

CDC Centres for Disease Control and Human Sciences

Year 2010 Quarter 1

Amino Acids

Analyte	Specimen		Specimen		Specimen		Specimen		Specimen	
Phe	1051		1052		1053		1054		1055	
	Result	Code	Result	Code	Result	Code	Result	Code	Result	Code
	66.41	1	57.87	1	68.04	1	492.96	2	62.28	1

Codes: 1= Within normal limits      2= Outside normal limits

\* = No quantitative data reported

Immunoreactive Trypsinogen

Analyte	Specimen		Specimen		Specimen		Specimen		Specimen	
IRT	1081		1082		1083		1084		1085	
	Result	Code	Result	Code	Result	Code	Result	Code	Result	Code
	5.5	1	130.1	2	29.6	1	207.9	2	6.0	1

Codes: 1= Within normal limits      2= Outside normal limits

Reviewer's comments  
 EVALUATION: No misclassifications were reported – 100% Satisfactory

## German TSH

### Latest available results – May 2009

<p>Legend: C = Certification, M = No of method, R = your result, D = difference (R-T)  Dmax = maximum allowable amount of difference in measurement  T = target value, either reference method of assigned value,  LL/UL = lower resp. upper limit</p>	<p>Certification: + = fulfilled (quotient/Dmax/<math>\leq</math> 1.0)  - = not fulfilled (quotient/Dmax/<math>&gt;</math> 1.0)  - <math>\pm</math> = certification cancelled because of technical and/or analytical reasons</p>
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	C	M	R	D/Dmax	T	LL	UL
TSH [mU/l]	+	3	A 13.0	-0.40	15.5	9.30	21.7
TSH [mU/l]	+	3	A 21.2	-0.38	25.0	15.0	35.0
TSH [mU/l]	+	3	A 5.06	-0.37	5.94	3.54	8.34
TSH [mU/l]	+	3	A 23.1	-0.28	26.0	15.6	36.4