

Audit of low volume endocrine testing in Scotland (2017)

This Scotland-wide audit is intended to evaluate reporting procedures for esoteric endocrine tests, for which standardisation may be poor. Where there is variation in the units and reference ranges employed for the same analyte there is potential risk to patient care, and is an impediment to the harmonisation of patient care pathways. This audit will identify tests where efforts could be made to harmonise reporting. The audit also affords an opportunity to provide a baseline of what testing is currently provided and to make recommendations that seek to improve services.

Representatives from Health Boards received a questionnaire asking about analytical platform/method, reported units and reference ranges, 2016-2017 workload, or if analysis is not performed locally, for details of the reference laboratory, for the following tests:

[Androstenedione](#)

[Dehydroepiandrosterone sulphate \(DHEAS\)](#)

[17-hydroxyprogesterone \(OHP\)](#)

[Dihydrotestosterone \(DHT\)](#)

[11-Deoxycortisol \(11-DOC\)](#)

[Renin](#)

[Aldosterone](#)

[Insulin](#)

[C-peptide](#)

[Anti-Müllerian Hormone \(AMH\)](#)

[Adrenocorticotrophic Hormone \(ACTH\)](#)

[Growth Hormone \(GH\)](#)

[Insulin-like Growth Factor \(IGF\)-1](#)

[Insulin-like Growth Factor \(IGF\)-2](#)

[Calcitonin](#)

[Thyroglobulin](#) and [Thyroglobulin Antibodies](#)

[Thyroid stimulating hormone receptor antibody \(TRAb\)](#)

[Plasma metadrenalines/catecholamines](#)

[Urinary metadrenalines/catecholamines](#)

[Urinary 5-Hydroxyindoleacetic acid \(HIAA\)](#)

[Urinary Cortisol](#)

[Prednisolone](#)

[Chromogranin A](#)

Responses were received from the following Health Boards: Ayrshire and Arran, Dumfries and Galloway, Fife, Forth Valley, Greater Glasgow and Clyde, Grampian, Highlands, Lanarkshire, Lothian and Tayside representing approximately 96% of Scotland's population.

Click on the hyperlinks to navigate to the full details of the responses in Appendix B.

Main findings

Where an assay is available in Scotland the majority of testing is performed by a Scottish laboratory, with the exception of the rarely requested 11-DOC test. The audit has provided a baseline for which centres are currently offering analysis and typical annual workloads for these tests within Scotland. Discrepancies between reported units and reference ranges in use have been highlighted and recommendations made towards harmonising these. Further recommendations have been made towards best practice and standardisation.

Summary of recommendations:

ANALYTE	RECOMMENDATION
Dehydroepiandrosterone-Sulphate (DHEAS)	Where the same method is in use, reference ranges should be harmonised.
11-Deoxycortisol (11-DOC)	Requests for 11-deoxycortisol should be sent to Glasgow Royal Infirmary for analysis.
Dihydrotestosterone (5-DHT)	Numbers are too low to recommend developing an assay in Scotland. 5-DHT analysis should be by tandem mass spectrometry.
Chromogranin A	Where possible, analysis of Chromogranin A should utilise Glasgow Royal Infirmary's service. Results are not comparable between methods and with a method change, patients being monitored with Chromogranin A require a new baseline to be established through parallel measurements.
C-peptide	C-peptide should be reported in pmol/L. It is not appropriate to report a reference range derived from a healthy population for C-peptide.
Insulin	Insulin should be reported in pmol/L. It is not appropriate to report a reference range derived from a healthy population for Insulin.
ACTH	ACTH should be reported in ng/L. It is not appropriate to report a reference range derived from a healthy population for ACTH.
IGF-1	Laboratories should confirm that their assay is calibrated to the WHO 02/254 International Standard. IGF-1 should be reported in nmol/L.
Growth Hormone (GH)	Laboratories should confirm that their assay is calibrated to the WHO International Standard (98/574). Dynamic stimulatory or inhibitory tests are used for the diagnosis of GH deficiency or excess. Random measurements of GH are difficult to interpret and are not recommended.
Urinary 5-HIAA	Quantitative rather than qualitative tests should be used for 5-HIAA analysis.

	5-HIAA should only be tested in patients with known or suspected carcinoid syndrome.
Metadrenalines/catecholamines	The principal recommended tests for known or suspected pheochromocytoma/paraganglioma are either plasma free metanephrines, OR 24hr urinary fractionated metanephrines. Analysis of plasma/urine 3-methoxytyramine is also recommended.
Thyroglobulin and Thyroglobulin Antibody	<p>There should be a robust and consistent approach to detection of Thyroglobulin Antibody interference employed across Scotland.</p> <p>It is not appropriate to report a reference range derived from a healthy population for Thyroglobulin or Thyroglobulin Antibody.</p> <p>Measurement of Thyroglobulin Antibody should be quantitative and cut-off levels of Thyroglobulin Antibody indicating interference should be robustly established for the local method.</p> <p>High sensitivity Thyroglobulin assays are preferred and should be available when TSH-stimulation testing is not performed.</p>
TRAbs	Where the same method is in use, reference ranges/cut-offs should be harmonised.

It is further recommended that laboratories performing low numbers of analyses (<10 per week) consider the practicalities and cost implications of analysing locally against sending samples to an external laboratory for analysis.

Click on the hyperlinks to navigate to further information on the recommendations in Appendix A.

Appendix A.

Dehydroepiandrosterone-Sulphate (DHEAS)

Findings: Three sites in Scotland offer DHEAS analysis, using two different methods. The same units are used by all sites. Lothian and GGC have the same method but report different reference ranges.

	METHOD	UNITS	REPORTED REFERENCE RANGE	WORKLOAD																														
GGC	Abbott Architect	µmol/L	Prepubertal: <2.5 µmol/L* Adult male: 2.5-16 µmol/L Adult female: 2.0-12.5 µmol/L	1617 (04/16-03/17)																														
Grampian	Siemens Immulite	µmol/L	Males: 2.0-15.2 µmol/L Females: 1.0-11.7 µmol/L	428																														
Lothian	Abbott Architect	µmol/L	<table border="1"> <thead> <tr> <th></th> <th>Female</th> <th>Male</th> </tr> </thead> <tbody> <tr> <td>≤01Y</td> <td>none</td> <td>none</td> </tr> <tr> <td>1-6Y</td> <td>0 - 2.5</td> <td>0 - 2.5</td> </tr> <tr> <td>6-15Y</td> <td>0 - 10.3</td> <td>0 - 10.3</td> </tr> <tr> <td>15-20Y</td> <td>1.3 - 12.5</td> <td>2.4 - 17.2</td> </tr> <tr> <td>20-25Y</td> <td>3.6 - 11.1</td> <td>6.5 - 14.6</td> </tr> <tr> <td>25-35Y</td> <td>2.0 - 13.9</td> <td>4.6 - 16.1</td> </tr> <tr> <td>35-45Y</td> <td>2.0 - 11.1</td> <td>3.8 - 13.1</td> </tr> <tr> <td>45-55Y</td> <td>1.5 - 7.7</td> <td>3.7 - 12.1</td> </tr> <tr> <td>55-120Y</td> <td>0.8 - 4.9</td> <td>1.3 - 9.8</td> </tr> </tbody> </table>		Female	Male	≤01Y	none	none	1-6Y	0 - 2.5	0 - 2.5	6-15Y	0 - 10.3	0 - 10.3	15-20Y	1.3 - 12.5	2.4 - 17.2	20-25Y	3.6 - 11.1	6.5 - 14.6	25-35Y	2.0 - 13.9	4.6 - 16.1	35-45Y	2.0 - 11.1	3.8 - 13.1	45-55Y	1.5 - 7.7	3.7 - 12.1	55-120Y	0.8 - 4.9	1.3 - 9.8	442 (04/16-06/17)
	Female	Male																																
≤01Y	none	none																																
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*A prepubertal reference range is not reported. A comment is appended if >2.5 µmol/L.

Recommendation: Recommend Lothian and GGC to report DHEAS using a harmonised reference range.

[Return to recommendations](#)

11-Deoxycortisol (11-DOC)

Findings: 11-DOC is rarely specifically requested with several sites not indicating a referral laboratory. 11-DOC is analysed by Glasgow Royal Infirmary as part of the androgen profile. Results are not reported unless specifically requested.

	EXTERNAL LAB	WORKLOAD
Ayrshire and Arran	None given	Not given
Dumfries and Galloway	St Thomas Hospital, London	0 (04/16-03/17)
Fife	None given	Not given
Forth Valley	St Thomas Hospital, London	2 (2016)
GGC	In house LC/MS/MS as part of steroid profile	7547 (04/16-03/17)*
Grampian	None given	Not given
Highlands	None given	Not given
Lanarkshire	Glasgow Royal Infirmary	Not given
Lothian	Glasgow Royal Infirmary	Not given
Tayside	Glasgow Royal Infirmary	0 (04/16-03/17)

* analysed as part of androgen profile and not routinely reported. 3 specific requests for 11-DOC.

Recommendation: Recommend that specific requests for 11-Deoxycortisol should be sent to Glasgow Royal Infirmary for analysis.

[Return to recommendations](#)

Dihydrotestosterone (5-DHT)

Findings: Dihydrotestosterone is requested infrequently and several sites did not specify a referral laboratory.

	EXTERNAL LAB	WORKLOAD
Ayrshire and Arran	None given	-
Dumfries and Galloway	Barts and London NHS Trust	1 (04/16-03/17)
Fife	None given	-
Forth Valley	None given	-
GGC	Barts and London NHS Trust	11 (04/16-03/17)
Grampian	Barts and London NHS Trust	-
Highlands	SAS Steroid Centre Leeds and Bradford NHS Trust	-
Lanarkshire	Barts and London NHS Trust	-
Lothian	SAS Steroid Centre Leeds and Bradford NHS Trust	10 (04/16-03/17)
Tayside	Epsom Hospital, clinical pathology	16 (04/16-03/17)

Relevant information: Epsom Hospital is withdrawing 5-DHT from their repertoire. Charing Cross (North West London Pathology) is withdrawing the current in house RIA method and plan to introduce a TMS method in 2019. Barts and London method is LC-MS/MS, £32.60, 3 week turnaround. St Thomas' (Viapath) method is LC-MS/MS, £43.25, 2 week turnaround. Leeds and Bradford is withdrawing the current in house RIA method and plan to introduce a TMS method in 2019, current cost £55 (TMS method projected to be cheaper). All details obtained direct from individual laboratories October 2018.

Recommendations: Numbers are too low to recommend developing an assay in Scotland. Recommend using a tandem mass spectrometry method for 5-DHT analysis.

[Return to recommendations](#)

Chromogranin A

Findings: The majority of Chromogranin A requests are sent to Charing Cross Hospital in London for the full gut hormone profile or Chromogranin A+B. A minority are analysed in Sheffield for only Chromogranin A.

	EXTERNAL LAB	WORKLOAD
Ayrshire and Arran	Sheffield PRU	1 (04/16-04/17)
Dumfries and Galloway	Charing Cross, London	43 (04/16-03/17)
Fife	Charing Cross, London	24 (04/16-03/17)
Forth Valley	Sheffield PRU (Chromogranin A only) Charing Cross, London (Part of gut hormone screen)	8 (2016) 29 (2016)
GGC	Charing Cross, London	105*(04/16-03/17)
Grampian	Charing Cross, London	79
Highlands	Charing Cross, London	64** (01/16-12/16)
Lanarkshire	Charing Cross, London (part of gut hormone profile)	57
Lothian	Charing Cross, London (Singly and as part of profile)	211 (04/16-03/17)
Tayside	Sheffield PRU (Chromogranin A only) Charing Cross, London Part of gut hormone screen)	187 (04/16-03/17) 55 (04/16-03/17)

*Individual CgA requests only: Full gut hormone requests not included so this is an underestimate.

**1 CgA only, 38 for CgA and B, 25 CgA+B and gut hormones

Relevant information: The Scottish Neuroendocrine Tumour Group (SCONET) guidelines (2015)¹ state that all patients with a confirmed gastroenteropancreatic neuroendocrine tumour (GEP NET) should have baseline Chromogranin A & Chromogranin B. A full gut hormone screen should be performed in all pancreatic NETs and consideration given to more detailed endocrine investigation if there are symptoms suggestive of a functioning tumour. The UK and Ireland Neuroendocrine Society Guidelines (2012)² state that in new GEP NET diagnoses, baseline tests should include plasma Chromogranin A and specific biochemical tests should be requested depending on which syndrome is suspected.

Glasgow Royal Infirmary has introduced a Chromogranin A assay (CisBio), sample type: serum; 4 week turnaround; minimum volume: 300µL; transport by first class post.

Recommendations: Requesting the full gut hormone profile for the investigation of known or suspected neuroendocrine tumour is not always necessary or appropriate. Where appropriate, Chromogranin A alone should be requested, with Glasgow Royal Infirmary being the preferred provider. Results are not comparable between methods and with a method change, patients being monitored with Chromogranin A require a new baseline to be established through parallel measurements.

[Return to recommendations](#)

C-peptide

Findings: Two sites in Scotland provide C-peptide analysis, using different methods, units and reporting ranges.

	METHOD	UNITS	REFERENCE RANGE	ANNUAL WORKLOAD
GGC	Siemens Immulite 2000	nmol/L	0.36-1.12nmol/L	1275 (04/16-03/17)
Lothian	Abbott Architect	pmol/L	400-800pmol/L	489 (04/16-03/17)

Relevant Information: There is increasing interest in the use of C-peptide as an indicator of pancreatic insulin output in diabetic populations³. The Scottish Diabetes Group have recommended that C-peptide testing in Type 1 diabetic patients should be offered across Scotland and efforts towards establishing this as a national screening project are ongoing. The UKNEQAS scheme units are pmol/L⁴.

A group representing the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), Bureau International des Poids et Mesures (BIPM), National Metrology Institute of Japan (NMIJ), National Institute of Metrology China (NIM China), and National Institute for Biological Standards and Control (NIBSC) have recommended a traceability scheme and manufacturers will soon begin to recalibrate their methods⁵. The current practice of directly calibrating with the WHO IRR (84/510 or 13/136) materials should end. The new traceability chain uses commutable matrix-based reference materials (patient serum with values assigned by a reference method).

¹ Consensus guidelines for the Management of Patients with Neuroendocrine Tumours. February 2015. Scottish Neuroendocrine Tumour Group (SCONET).

² Ramage et al., Guidelines for the management of gastroenteropancreatic neuroendocrine (including carcinoid) tumours (NETs). 2012. Gut. 61:6-32.

³ Jones, A.G., Hattersley, A.T. The clinical utility of C-peptide measurement in the care of patients with diabetes. 2013. Diabetic Medicine. 30, 803-817

⁴ Personal communication with G. Wark (UKNEQAS) 17/10/2018

⁵ Little et al., Implementing a Reference Measurement System for C-peptide: Successes and Lessons Learned. 2017. Clinical Chemistry 63:9

Recommendations: C-peptide results should be reported in pmol/L. It is not appropriate to report a reference range derived from a healthy population to aid the interpretation of C-peptide results. The group would welcome proscriptive guidance on appropriate C-peptide testing from the Diabetic Lead for Scotland. Laboratories should be aware that future recalibration efforts may affect their reported results.

[Return to recommendations](#)

Insulin

Findings: Three sites in Scotland offer analysis of insulin, using two different methods. GGC and Lothian report different units and different reference ranges, despite using the same method.

	METHOD	UNITS	REPORTED REFERENCE RANGE	ANNUAL WORKLOAD
GGC	Abbott Architect	mIU/L	<13 mIU/L (fasting)	1174 (04/16-03/17)
Lothian	Abbott Architect	pmol/L	none given	447 (04/16-03/17)
Tayside	Siemens Immulite	mIU/L	3-17 mIU/L	279 (04/16-03/17)

Relevant Information: There is an IFCC Working Group for Standardization of Insulin Assays (SWG-IA) in collaboration with American Diabetes Association (ADA), European Association for the Study of Diabetes (EASD), the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), and the International Diabetes Federation (IDF). They advocate reporting in SI units (pmol/L)^{6,7,8}. At present calibration is to mIU/L and a conversion factor is required to report in pmol/L. The conversion factor derived for the First International Standard for human insulin (83/500) is mIU/L x 6 = pmol/L however most methods are calibrated to IRP 66/304 for which there is no single recommended conversion factor. NHS Lothian (Abbott Architect) currently apply 7.175, as recommended by the manufacturer. The UKNEQAS scheme units are pmol/L, and when required UKNEQAS applies a conversion factor of 6, but scheme participants can apply any factor that they wish to⁹.

Recommendations: Insulin results should be reported in pmol/L, using the manufacturer's recommended conversion factor. It is not appropriate to report a reference range derived from a healthy population to aid in the interpretation of insulin results.

[Return to recommendations](#)

⁶ Staten et al Insulin Assay Standardization: Leading to measures of insulin sensitivity and secretion for practical clinical care. 2010. Diabetes Care. 33:1; 205-206.

⁷ Manley et al Comparison of 11 Human Insulin Assays: Implications for Clinical Investigation and Research. 2007. Clinical Chemistry. 53:5; 922-932

⁸ Miller et al., Toward Standardization of Insulin Immunoassays. 2009. Clinical Chemistry. 55:5, 1011-1018.

⁹ Personal communication G.Wark (June 2010 & October 2018).

ACTH

Findings: Four sites provide ACTH analysis, using two different methods. Two different reporting units are in use, and there exist differences in the approach to reporting the reference range.

	METHOD	UNITS	REPORTED REFERENCE RANGE	ANNUAL WORKLOAD
Grampian	Siemens Immulite 2000	ng/L	0-46 ng/L	147
GGC	Siemens Immulite 2000	mU/L	No ref range provided	1743 (04/16-03/17)
Lothian	Roche Elecsys E411	ng/L	7.2-63.3 ng/L	427 (04/16-03/17)
Tayside	Siemens Immulite 2000	ng/L	9-52 ng/L	172 (04/16-03/17)

Relevant information: The UKNEQAS scheme units are ng/L¹⁰.

Recommendations: ACTH results should be reported in ng/L. It is not appropriate to report a reference range derived from a healthy population to aid in the interpretation of ACTH results.

[Return to recommendations](#)

Growth Hormone (GH)

Findings: Four sites provide GH analysis, with two different methods. All are reporting in µg/L and none report a reference range.

	METHOD	UNITS	REPORTED REFERENCE RANGE	ANNUAL WORKLOAD
GGC	Siemens Immulite 2000	µg/L	No reference range reported	2233 (04/16-03/17)
Grampian	Siemens Immulite	µg/L	No reference range reported	464
Lothian	Roche Elecsys E411	µg/L	No reference range reported	760 (04/16-03/17)
Tayside	Siemens Immulite 2000	µg/L	No reference range reported	316 (04/16-03/17)

Relevant information: The IFCC Working Group on Standardization of Growth Hormone (WG-GH) recommends reporting in µg/L and calibration with WHO International Standard 98/574. The Endocrine Society Clinical Practice Guideline on Acromegaly advises against the use of random GH levels to diagnose acromegaly¹¹. The Endocrine Society Clinical Practice Guideline on Evaluation and Treatment of Adult Growth Hormone Deficiency specifies stimulation testing to make a diagnosis of growth hormone deficiency and omits mention of random measurements¹².

Recommendations: Laboratories should confirm that their assay is calibrated to the WHO International Standard (98/574). Dynamic stimulatory or inhibitory tests are used for the diagnosis of GH deficiency or excess. Random measurements of GH are difficult to interpret and are not recommended.

[Return to recommendations](#)

¹⁰ Personal communication C Sturgeon (October 2018)

¹¹ Katznelson et al Acromegaly: An Endocrine Society Clinical Practice Guideline. JCEM. 2014. 99(22):3933-3951.

¹² Molitch et al Evaluation and Treatment of Adult Growth Hormone Deficiency: An Endocrine Society Clinical Practice Guideline. JCEM.2011; 96(6);1587-1609.

IGF-1

Findings: Two sites in Scotland offer IGF-1 analysis applying different methods and reporting units.

	METHOD	UNITS	REPORTED REFERENCE RANGE			ANNUAL WORKLOAD				
			Age	Male	Female					
GGC	IDS iSys	µg/L	<2	15-157	17-151	5579 (04/16-03/17)				
			2-4	28-247	25-198					
			5-7	46-349	39-272					
			8-10	67-442	59-371					
			11-13	89-503	82-465					
			14-16	104-510	97-502					
			17-25	105-410	96-417					
			26-39	81-249	72-259					
			40-54	63-201	57-197					
			55-65	49-191	43-170					
			65+	39-186	35-168					
			Grampian	Siemens Immulite	nmol/L		<3	1-17	2-22	894
							4-6	3-27	5-30	
7-9	5-33	7-36								
10-11	9-41	15-59								
12-13	19-66	22-69								
14-15	23-66	25-65								
16-18	23-54	25-56								
19-21	15-42	15-42								
22-24	13-38	13-38								
25-29	11-34	11-34								
30-34	9-31	9-31								
35-39	8-29	8-29								
40-44	8-29	8-29								
45-49	7-28	7-28								
50-54	6-27	6-27								
55-59	6-28	6-28								
60-64	6-29	6-29								
65-69	5-30	5-30								
70-79	5-28	5-28								
80-90	4-27	4-27								

Relevant information: A consensus statement on IGF-1 standardisation from the Growth Hormone Research Society, the IGF Society and the IFCC recommends calibration with the WHO International Standard (02/254). It does not stipulate reporting units but emphasises the importance of harmonisation and comparability of results¹³. The UKNEQAS scheme units are nmol/L.

Recommendations: Laboratories should confirm that they are calibrating against the WHO International Standard (02/254). Results should be reported in nmol/L.

[Return to recommendations](#)

¹³ Clemmons, D. Consensus Statement on the Standardization and Evaluation of Growth Hormone and Insulin –like Growth Factor Assays. 2011. Clinical Chemistry. 57:4.

5-HIAA (urinary)

Findings: Six centres provide 5-HIAA analysis using HPLC methods (in house or Chromsystems) and one qualitative screening test.

	METHOD	REPORTED UNITS	REPORTED REFERENCE RANGE	WORKLOAD
A&A	HPLC	µmol/24hr	<50 µmol/24hr	2008 (04/16-04/17)
GGC	In-house HPLC	µmol/24hr	5-42 µmol/24hr	198* (04/16-03/17)
Grampian	5-hydroxyindoles react with 1-nitroso-2-naphthol in the presence of nitrous acid to produce a purple colour **	Qualitative method POS/NEG.		171
Lanarkshire	HPLC	µmol/24hr	5-HIAA: ≤50 µmol/24h	516
Lothian	Chromsystems HPLC-ECD	µmol/24hr	10-42µmol/24hr	402 (04/2016-03/2017)
Tayside	HPLC with electrochemical detection	µmol/day	0 – 50 µmol/day	216 (04/2016-03/2017)

* GGC requests except GRI go to University Hospital Crosshouse for Urine mets and 5HIAA – 1175 (04/16-03/17)

**Screen performed in-house, quantitative analysis obtained from University Hospital Crosshouse.

Relevant information: The Scottish Neuroendocrine Tumour Group (SCONET) guidelines (2015) state that all patients with a confirmed GEP NET should have baseline 24 hour urine collection for 5-HIAA¹⁴. The UK and Ireland Neuroendocrine Society Guidelines (2012) state that for new GEP NET diagnoses, baseline tests should include urinary 5-HIAA¹⁵.

Recommendations: Quantitative rather than qualitative tests should be used for 5-HIAA analysis. 5-HIAA should only be tested in patients with known or suspected carcinoid syndrome.

[Return to recommendations](#)

¹⁴ Consensus guidelines for the Management of Patients with Neuroendocrine Tumours. February 2015. Scottish Neuroendocrine Tumour Group (SCONET).

¹⁵ Ramage et al., Guidelines for the management of gastroenteropancreatic neuroendocrine (including carcinoid) tumours (NETs). 2012. Gut. 61:6-32.

Metadrenalines/catecholamines

Findings: All Scottish laboratories send plasma metadrenaline requests to the Freeman in Newcastle (400+ a year). Six centres offer urinary metadrenalines/catecholamine testing (Five in-house or Chromsystems HPLCs and one LC-MS/MS method).

	METHOD	UNITS	REPORTED REFERENCE RANGE	ANNUAL WORKLOAD																
Ayrshire and Arran	HPLC	µmol/24hr or nmol/24hr	VMA * µmol/24hr 5HIAA ≤50 µmol/24hr HVA ≤40 µmol/24hr Noradrenaline ≤900 nmol/24hr Adrenaline ≤230 nmol/24hr Dopamine ≤3300 nmol/24hr fNMA ≤65 nmol/24hr fMA ≤350 nmol/24hr	2008 [§]																
GGC	In-house HPLC	nmol/24hrs	Adrenaline <230 Noradrenaline <900 Dopamine <3300	567 ^{&} (04/16-03/17)																
Grampian	Chromsystems [£]	µmol/24h	Normetadrenaline <3.0 µmol/24h Metadrenaline <1.4 µmol/24h 3-Methoxytyramine <2.5 µmol/24h	692																
Lanarkshire	HPLC	µmol/24h	Noradrenaline: up to 900 µmol/24 Adrenaline: ≤ 230 µmol/24h	577																
Lothian	HPLC-ECD Chromsystems	µmol/24hr	Normetadrenaline 0.4-3.4µmol/24hr Metadrenaline 0.3-1.7µmol/24hr	863 [^] (04/16-03/17)																
Tayside	LCMS	nmol/day	<table border="1"> <thead> <tr> <th>Analyte</th> <th>Unlikely</th> <th>Possible</th> <th>Likely</th> </tr> </thead> <tbody> <tr> <td>Normetadrenaline (nmol/24 h)</td> <td><3000</td> <td>3000-6550</td> <td>>6550</td> </tr> <tr> <td>Metadrenaline (nmol/24 h)</td> <td><1000</td> <td>1000-2880</td> <td>>2880</td> </tr> <tr> <td>3-methoxytyramine (nmol/24 h)</td> <td><2300</td> <td>2300-5000</td> <td>>5000</td> </tr> </tbody> </table>	Analyte	Unlikely	Possible	Likely	Normetadrenaline (nmol/24 h)	<3000	3000-6550	>6550	Metadrenaline (nmol/24 h)	<1000	1000-2880	>2880	3-methoxytyramine (nmol/24 h)	<2300	2300-5000	>5000	New (previous annual workload for NA, A&D was 835)
Analyte	Unlikely	Possible	Likely																	
Normetadrenaline (nmol/24 h)	<3000	3000-6550	>6550																	
Metadrenaline (nmol/24 h)	<1000	1000-2880	>2880																	
3-methoxytyramine (nmol/24 h)	<2300	2300-5000	>5000																	

[&]GGC requests except GRI go to University Hospital Crosshouse for Urine mets and 5HIAA – 1175 (04/16-03/17)

* reference range not stated.

[§]includes 350 paediatric samples: 3MT analysed on all samples but only routinely reported on paediatric samples

[£]Positive results are sent to University Hospital Crosshouse for confirmation.

[^]53 paediatric samples – sent to University Hospital Crosshouse

Relevant information: There is compelling evidence that measurements of plasma free or 24 hour urinary fractionated metanephrines are superior to other tests of catecholamine excess for diagnosis of pheochromocytoma and paraganglioma¹⁶. Endocrine Society Clinical Practice guidelines on pheochromocytomas and paragangliomas recommend that initial biochemical testing should include HPLC or tandem mass spectrometry measurements of plasma free metanephrines or 24 hour urinary fractionated metanephrines¹⁷. Scottish Neuroendocrine Tumour Group (SCONET) guidelines (2015) state that pheochromocytoma and paraganglioma should be investigated using plasma or urine metanephrines¹⁸. The measurement of 3-methoxytyramine in urine or plasma is not discussed in guidelines, but may slightly improve diagnostic sensitivity and identify rare dopamine-

¹⁶ Lenders, J. Et al. Pheochromocytoma. Lancet. 2005: 366;665-675.

¹⁷ Lenders, J. Pheochromocytoma and Paraganglioma: An Endocrine Society Clinical Practice Guideline. 2014. JCEM. 99(6):1915-1942.

¹⁸ Consensus guidelines for the Management of Patients with Neuroendocrine Tumours. February 2015. Scottish Neuroendocrine Tumour Group (SCONET).

secreting tumours^{19,20,21,22}. To provide equity across Scotland, measurement of 3-methoxytyramine in plasma or urine is recommended.

Recommendations: For the investigation of suspected pheochromocytoma and paraganglioma plasma free metanephrines or 24 hour urinary fractionated metanephrines should be available. 3-methoxytyramine is useful in the investigation of rare dopamine-secreting tumours and should be available.

[Return to recommendations](#)

Thyroglobulin (Tg) and Thyroglobulin Antibody (TgAb)

Findings: Four sites provide Tg testing, using two different methods. Two strategies to identify potential interference are employed: measurement of TgAb (Siemens Immulite used in all cases) or Tg confirmation by radioimmunoassay (Birmingham)²³. The latter approach is employed by Lothian.

THYROGLOBULIN	METHOD	UNITS	REPORTED REFERENCE RANGE	ANNUAL WORKLOAD
GGC	Siemens Immulite 2000	µg/L	<55 µg/L	2150 (04/16-03/17)
Grampian	Siemens Immulite	µg/L	<60µg/L	375
Lothian	Beckman Access	µg/L	None provided	1081 (04/16-03/17)
Tayside	Siemens Immulite 2000	µg/L	None provided	410 (04/16-03/17)
THYROGLOBULIN ANTIBODY	METHOD	UNITS	REPORTED REFERENCE RANGE	ANNUAL WORKLOAD
GGC	Siemens Immulite 2000	IU/mL	<40 IU/mL	2161 (04/16-03/17)
Grampian	Siemens Immulite	IU/mL	<40 IU/mL	375
Lothian	N/A	N/A	N/A	N/A
Tayside	Siemens Immulite 2000	N/A	Reported as positive or negative	410 (04/16-03/17)

Relevant information: GGC is currently evaluating the Beckman Access for analysis of Tg and Lothian is evaluating the Roche ElecSys method for both Tg and TgAb. For reasons of cost and resilience, Lothian plan to adopt measurement of Tg and TgAb to detect interference, therefore all laboratories in Scotland will be measuring TgAb alongside Tg measurement.

Guidelines state that TgAb should be measured by a quantitative method^{24,25,26}. Despite standardisation by calibration against international standards (BCR 457: Tg; IRP 65/93: TgAb), large variability exists for both Tg and TgAb assays. For both Tg and TgAb, guidelines recommend consistent use of the same assay and same laboratory over the course of follow-up. If methods

¹⁹ Eisenhofer, G. Et al. Biochemical diagnosis of chromaffin cell tumours in patients at high and low risk of disease: plasma versus urinary free or deconjugated O-Methylated catecholamine metabolites Clin Chem 2018; 64:11

²⁰ Rao, D. Et al. Plasma methoxytyramine:clinical utility with metanephrines for diagnosis of pheochromocytoma and paraganglioma. 2017. Eur J Endo. 177:103-13.

²¹ van Duinen, N. Et al. Increased urinary excretion of 3-methoxytyramine in patients with head and neck paragangliomas. JCEM. 2010;95(1);209-214.

²² Davison, A. Clinical evaluation and treatment of pheochromocytoma. 2017. ACB;55(1); 34-48.

²³ Crane, M. et al. Discordance in thyroglobulin measurements by radioimmunoassay and immunometric assay: a useful means of identifying thyroglobulin assay interference. 2013. AC: 50(5);421-432.

²⁴ Perros et al., British Thyroid Association Guidelines for the Management of Thyroid Cancer Third Edition. Clinical Endocrinology. Vol 81, Supp 1, 2014.

²⁵ Pacini et al European consensus for the management of patients with differentiated thyroid carcinoma or the follicular epithelium. Eur J Endo 20016: 154, 787-803.

²⁶ Giovanella et al Thyroglobulin measurement using highly sensitive assays in patients with differentiated thyroid cancer: a clinical position paper. Eur J Endo. 2014. 171:2 R33-R46.

change a new baseline should be established through parallel measurements^{27,28}. Manufacturer established cut-offs for TgAb assays may identify autoimmunity rather than interference in Tg assays, therefore cut-offs for predicting interference should be validated by laboratories^{29,30,31}. Guidelines do not currently recommend use of high sensitivity Thyroglobulin assay (functional sensitivity $\leq 0.1\mu\text{g/L}$) however there is a growing body of evidence for the usefulness of these assay and they are the only acceptable alternative when TSH-stimulation testing is not performed^{32,30}.

Recommendations: There should be a robust and consistent approach to detection of interference employed across Scotland. Measurement of thyroglobulin antibody should be quantitative and cut-off levels of Thyroglobulin Antibody indicating interference should be robustly established for the local method. It is not appropriate to report a reference range derived against a healthy population for Thyroglobulin or Thyroglobulin Antibody. High sensitivity thyroglobulin assays are preferred and should be available when TSH-stimulation testing is not performed.

[Return to recommendations](#)

TRAbs

Findings: Three biochemistry laboratories provide analysis of TRAbs, using two different methods. Tayside and GGC use the same method but employ different approaches to reporting of results.

	METHOD	UNITS	REPORTED REFERENCE RANGE	ANNUAL WORKLOAD
GGC	RSR Elisa	U/L	<1 negative 1-2 equivocal >2 positive	2995 (04/16-03/17)
Lothian	Roche Elecsys E411	U/L	<1.6 IU/L	2312 (04/16-03/17)
Tayside	RSR Elisa	U/L	0 – 0.4 U/L	528 (04/16-03/17)

NB Highlands and Grampian TRAbs are handled by microbiology and immunology, respectively so no data were provided.

Recommendations: Where the same method is in use, reference ranges/cut-offs should be harmonised.

[Return to recommendations](#)

²⁷ Perros et al., British Thyroid Association Guidelines for the Management of Thyroid Cancer Third Edition. Clinical Endocrinology. Vol 81, Supp 1, 2014.

²⁸ Pacini et al European consensus for the management of patients with differentiated thyroid carcinoma or the follicular epithelium. Eur J Endo 20016: 154, 787-803.

²⁹ Katrani et al Analytical and clinical performance of thyroglobulin autoantibody assays in thyroid cancer follow-up. Clin Chem Lab Med. 2017: 55(12):1987-1994.

³⁰ Evans, C et al. Thyroglobulin in differentiated thyroid cancer. Clin Chim Acta. 2015. 444:310-317

³¹ Spencer et al Current Thyroglobulin Autoantibody (Tab) Assays Often Fail to Detect Interfering TgAb that can result in the reporting of falsely low/undetectable serum Tg IMA values for patients with differentiated thyroid cancer. JCEM 2011; 96(5):1283-1291

³² Giovanella et al Thyroglobulin measurement using highly sensitive assays in patients with differentiated thyroid cancer: a clinical position paper. Eur J Endo. 2014. 171:2 R33-R46.

Appendix B: Full list of tests and responses

<u>Androstenedione</u>					
REGION	METHOD	UNITS	RRs	ANN WORK	EXTERNAL?
Ayrshire and Arran				1 (04/16-04/17)	GRI
Dumfries and Galloway				129 (04/16-03/17)	GRI
Fife				104 (04/16-03/17)	GRI
Forth Valley				285 (2016)	GRI
Grampian	Siemens Immulite	nmol/L	Males: 2.1-10.8 Females: 1.0-11.5	440	
Greater Glasgow and Clyde	Extraction – LC/MS/MS	nmol/L	<18 year old: no range Females age 18-40: <5.5 Females age >40: <3.0 Males >18: <5.5	7547* (04/16-13/17)	
Highlands				93 (06/16-05/17)	GRI
Lanarkshire				211	GRI
Lothian				400 (04/16-03/17)	GRI
Tayside				117 (04/16-03/17)	GRI

*Analysed as part of the androgen profile

Forth Valley provided 10 years of workload data showing a considerable jump in androstenedione requesting since 2015 (doubled). 2017 data so far already reached 312.

UKNEQAS scheme units are nmol/L³³

[Return to recommendations.](#)

³³ Taken from uknegas.org.uk/programmes/result/?programme=steroid-hormones Accessed 17/10/2018

DHEAS							
REGION	METHOD	UNITS	RRs			ANN WORK	EXTERNAL?
Ayrshire and Arran						0 (04/16-04/17)	GRI
Dumfries and Galloway						58 (04/16-03/17)	GRI
Fife						123 (04/16-03/17)	Lothian
Forth Valley						104 (2016)	GRI
Grampian	Siemens Immulite	µmol/L	Males: 2.0-15.2 Females: 1.0-11.7			428	
Greater Glasgow and Clyde	Abbott Architect	µmol/L	Prepubertal: <2.5 µmol/L Adult male: 2.5-16 µmol/L Adult female: 2.0-12.5 µmol/L			1617 (04/16-03/17)	
Highlands						74 (06/16-05/17)	GRI
Lanarkshire						184	GRI
Lothian	Abbott Architect i2000	µmol/L		Female	Male	442 (04/16-03/17)	
			≤01Y	none	none		
			1-6Y	0 - 2.5	0 - 2.5		
			6-15Y	0 - 10.3	0 - 10.3		
			15-20Y	1.3 - 12.5	2.4 - 17.2		
			20-25Y	3.6 - 11.1	6.5 - 14.6		
			25-35Y	2.0 - 13.9	4.6 - 16.1		
			35-45Y	2.0 - 11.1	3.8 - 13.1		
			45-55Y	1.5 - 7.7	3.7 - 12.1		
			55-120Y	0.8 - 4.9	1.3 - 9.8		
Tayside						81 (04/16-03/17)	GRI

Forth Valley included 10 years of workload data. DHEAS had increased steadily from 26 in 2007 to 104 in 2016.

UKNEQAS scheme units are µmol/L³⁴

[Return to recommendations](#)

³⁴ Taken from uknegas.org.uk/programmes/result/?programme=steroid-hormones Accessed 17/10/2018.

17-OHP					
REGION	METHOD	UNITS	RRs	ANN WORK	EXTERNAL?
Ayrshire and Arran				1 (04/16-04/17)	GRI
Dumfries and Galloway				135 (04/16-03/17)	GRI
Fife				85 (04/16-03/17)	GRI
Forth Valley				264 (2016)	GRI
Grampian				303	GRI
Greater Glasgow and Clyde	Extraction followed by LC/MS/MS	nmol/L	Adults (>18): <6 nmol/L no paediatric ranges	7547 Part of androgen profile Also performed on blood spots (data not included) (04/16-03/17)	
Highlands				95 (06/16-05/17)	GRI
Lanarkshire				158	GRI
Lothian				401 (04/16-03/17)	GRI
Tayside				131 (04/16-03/17)	GRI

Forth Valley provided 10 years of workload data. A steady rise in requesting is seen from 14 in 2007 to 301 already in 2017 (already more than the whole of 2016).

UKNEQAS scheme units are nmol/L³⁵

[Return to recommendations](#)

³⁵ Taken from ukneqas.org.uk/programmes/result/?programme=steroid-hormones 17/10/2018

<u>Dihydrotestosterone</u>					
REGION	METHOD	UNITS	RRs	ANN WORK	EXTERNAL?
Ayrshire and Arran					rarely done
Dumfries and Galloway				1 (04/16-03/17)	Barts and London NHS Trust
Fife				-	
Forth Valley				-	
Grampian					Barts and London NHS Trust
Greater Glasgow and Clyde				11 (04/16-03/17)	Barts and London NHS Trust
Highlands				0 (06/16-05/17)	SAS Steroid Centre Leeds and Bradford NHS Trust
Lanarkshire					Barts and London NHS Trust
Lothian				10 (04/16-03/17)	SAS Steroid Centre Leeds and Bradford NHS Trust
Tayside				16 (04/16-03/17)	Epsom Hospital, clinical pathology

<u>11-Deoxycortisol (11-DOC)</u>					
REGION	METHOD	UNITS	RRs	ANN WORK	EXTERNAL?
Ayrshire and Arran					rarely done
Dumfries and Galloway				0 (04/16-03/17)	St Thomas Hospital, London
Fife				-	
Forth Valley				2014 – 1 2015 – 2 2016 – 2 2017 – 0 to date	St Thomas Hospital, London
Grampian					no response
Greater Glasgow and Clyde	LC-MS/MS	nmol/L		7547*	
Highlands				-	
Lanarkshire				Not known	GRI
Lothian				unknown	GRI – done as part of steroid profile
Tayside				0 (04/16-03/17)	GRI

*Analysed as part of the androgen profile and not routinely reported. 3 specific 11-DOC requests received

[Return to recommendations](#)

Renin					
REGION	METHOD	UNITS	RRs	ANN WORK	EXTERNAL
Ayrshire and Arran				6 (04/16-04/17)	GRI
Dumfries and Galloway				73 (04/16-03/17)	GRI
Fife				76 (04/16-03/17)	Lothian
Forth Valley				109 (2016)	GRI
Grampian				153	GRI
Greater Glasgow and Clyde	Diasorin Liaison	mIU/L	Adult Supine: <40 mIU/L Adult Upright: <52 mIU/L Infants <1year: <450mIU/L 1-5yrs: <380 mIU/L 6-15 yrs: <125 mIU/L	1766 (04/16-03/17)	
Highlands				109 (06/16-05/17)	GRI
Lanarkshire				186	GRI
Lothian	DiaSorin Liaison PRC	mU/L	Adult ranges Supine (>30mins): 5-40 mU/L Sitting (>15mins): 5-45mU/L Erect (>1hour): 16-63mU/L Paediatric supine reference ranges: <1 week: no range 1 week – 1 month: 10 – 450 mIU/L 1 month – 10 years: 8 – 200 mIU/L 10 years – 16 years: 8 – 70 mIU/L	819 (04/16-03/17)	
Tayside				229 (04/16-03/17)	GRI

Neither GGC or Lothian routinely report a value for aldosterone:renin ratio but may comment on it, if appropriate.

[Return to recommendations](#)

Aldosterone					
REGION	METHOD	UNITS	RRs	ANN WORK	EXTERNAL?
Ayrshire and Arran				6 (04/16-04/17)	GRI
Dumfries and Galloway				68 (04/16-03/17)	GRI
Fife				62 (04/16-03/17)	Lothian
Forth Valley				103 (2016)	GRI
Grampian				126	GRI
Greater Glasgow and Clyde	Diasorin Liaison	pmol/L	Adults Supine 100-400 Adults Upright 100-800 <1month: 1000-5500 1-6months:500-4500 6-12 months: 160-3000 2-4yrs: 70-1000 5-15yrs: 70-600	1942 (04/16-03/17)	
Highlands				112 (06/16-05/17)	GRI
Lanarkshire				162	GRI
Lothian	DiaSorin Liaison	pmol/L	Adult ranges Supine: 30 – 440 pmol/L Sitting (>15 minutes): 70 – 570 pmol/L Erect: 110 – 860 pmol/L Paediatric ranges (supine): <1 month: 1000 – 5000 pmol/L 1 month – 1 year: 100 – 4500 pmol/L 1 – 10 years: 100 – 1000 pmol/L 10 – 16 years: 50 – 700 pmol/L	496 (04/16-03/17)	
Tayside				208 (04/16-03/17)	GRI

Neither GGC or Lothian routinely report a value for aldosterone:renin ratio but may comment on it, if appropriate.

UKNEQAS scheme units are pmol/L³⁶

[Return to recommendations](#)

³⁶ Taken from uknegas.org.uk/programmes/result/?programme=steroid-hormones 17/10/2018

<u>Insulin</u>					
REGION	METHOD	UNITS	RRs	ANN WORK	EXTERNAL?
Ayrshire and Arran				7 (04/16-04/17)	GRI
Dumfries and Galloway				180* (04/16-03/17)	GRI
Fife				53 (04/16-03/17)	Lothian
Forth Valley				122 (2016)	GRI
Grampian				75	GRI
Greater Glasgow and Clyde	Abbott Architect	mU/L	Fasting <13	1174 (04/16-03/17)	
Highlands				27 (06/16-05/17)	GRI
Lanarkshire				328	GRI
Lothian	Abbott Architect	pmol/L	None given	447 (04/16-03/17)	
Tayside	Siemens Immulite 2000	mU/L	3-17 mU/L	279 (04/16-03/17)	

*these are the number of requests. These requests are vetted therefore actual numbers sent to Glasgow will be lower.

Forth Valley provided 10 years of workload data showing fairly stable levels of requesting since 2009.

Glasgow don't routinely report an insulin:glucose ratio but may comment on it, depending on circumstances.

UKNEQAS scheme units are pmol/L³⁷

[Return to recommendations](#)

³⁷ Personal communication with G.Wark 17/10/2018

<u>C-peptide</u>					
REGION	METHOD	UNITS	RRs	ANN WORK	EXTERNAL?
Ayrshire and Arran				8 (04/16-04/17)	GRI
Dumfries and Galloway				179* (04/16-03/17)	GRI
Fife				26 (04/16-03/17)	Lothian
Forth Valley				35 (2016)	GRI
Grampian				44	GRI
Greater Glasgow and Clyde	Siemens Immulite 2000	nmol/L	Fasting 0.36-1.12 nmol/L	1275 (04/16-03/17)	
Highlands				22 (06/16-05/17)	GRI
Lanarkshire				270	GRI
Lothian	Abbott Architect	pmol/L	400-800pmol/L (young, healthy, fasted population)	489 (04/16-03/17)	
Tayside				164 (04/16-03/17)	GRI

*these are the number of requests. These requests are vetted therefore actual numbers sent to Glasgow will be lower.

C-peptide: Glasgow and Edinburgh, using different methods. Different reporting units. Discussion to be had over the appropriate uses of C-peptide and what values to use for these purposes.

Forth Valley provided 10 years of workload data showing an increase between 2007 (20) to 2011 (172) then a reduction since then with a drop in 2016 to 35 from 122 in 2015.

UKNEQAS scheme units are pmol/L³⁸

[Return to recommendations](#)

³⁸ Personal communication with G.Wark 17/10/2018

<u>AMH</u>					
REGION	METHOD	UNITS	RRs	ANN WORK	EXTERNAL?
Ayrshire and Arran				17 (04/16-04/17)	GRI
Dumfries and Galloway				15 (04/16-03/17)	GRI
Fife				1 (04/16-03/17)	GRI
Forth Valley				9 (2016)	GRI
Grampian				80	GRI
Greater Glasgow and Clyde	Beckman Access	pmol/L	No female range Age specific male ranges up to 51 weeks 390 -1300 1-4 years 300 - 1700 5-8 years 260 - 1200 9-12 years 100 - 1000 13-16 years 40 - 560 17 - 20 years < 520 over 20 years < 100	4635 (04/16-03/17)	
Highlands				12 (06/16-05/17)	GRI
Lanarkshire			Individual interpretation	Not known	GRI
Lothian				480 (04/16-03/17)	GRI
Tayside				1 (04/16-03/17)	GRI

Lothian have recently introduced local AMH testing on the Roche E411. Units are pmol/L. References ranges are not routinely reported but interpretative comments are reported for Edinburgh Fertility and Reproductive Endocrine Centre:

- <1.5 Risk of negligible response to gonadotrophin treatment
- 1.5-7.5 Risk of reduced response to gonadotrophin treatment
- 7.5-22.4 Probable normal response to gonadotrophin treatment
- 22.4-37.5 Risk of high response to gonadotrophin treatment. Increased risk of OHSS
- >37.5 High risk of high response to gonadotrophin treatment. High risk of OHSS

GRI's locally established male ranges and data from a 2016 clinical biochemistry paper may be used as a guide but these are not routinely reported.

[Return to recommendations](#)

ACTH					
REGION	METHOD	UNITS	RRs	ANN WORK	EXTERNAL?
Ayrshire and Arran				17 (04/16-04/17)	GRI
Dumfries and Galloway				193* (04/16-03/17)	GRI
Fife				54 (4/16-03/17)	GRI
Forth Valley				63 (2016)	GRI
Grampian	Siemens Immulite	ng/L	0-46 ng/L	147	
Greater Glasgow and Clyde	Siemens Immulite 2000	mU/L	No ref range (interpretation given in relation to clinical details and paired cortisol if available)	1743 (04/16-03/17)	
Highlands				62 (06/16-05/17)	GRI
Lanarkshire				199	GRI
Lothian	Roche Elecsys E411	ng/L	7.2-63.3 ng/L	427 (04/16-03/17)	
Tayside	Siemens Immulite 2000	ng/L	9-52 ng/L	172 (04/16-03/17)	

*these are the number of requests. These requests are vetted therefore actual numbers sent to Glasgow will be lower.

Forth Valley have provided 10 years of workload data, showing fairly stable ACTH requesting.

UKNEQAS scheme units are ng/L³⁹

[Return to recommendations](#)

³⁹ Personal communication with C.Sturgeon 17/10/2018

Growth Hormone (GH)					
REGION	METHOD	UNITS	RRs	ANN WORK	EXTERNAL?
Ayrshire and Arran				24 (04/16-04/17)	GRI
Dumfries and Galloway				73 (04/16-03/17)	GRI
Fife				104 (04/16-03/17)	Lothian
Forth Valley				118 (2016)	GRI
Grampian	Siemens Immulite	µg/L	No reference range provided	464	
Greater Glasgow and Clyde	Siemens Immulite 2000	µg/L	No reference range provided	2233 (04/16-03/17)	
Highlands				92 (06/16-05/17)	GRI
Lanarkshire				215	GRI
Lothian	Roche Elecsys E411	µg/L	No reference range provided	760 (04/16-03/17)	
Tayside	Siemens Immulite 2000	µg/L	No reference range provided	316 (04/16-03/17)	

Forth Valley have provided 10 years of workload data showing stable GH requesting.

[Return to recommendations](#)

IGF-1							
REGION	METHOD	UNITS	RRs			ANN WORK	EXTERNAL?
Ayrshire and Arran						30 (04/16-04/17)	GRI
Dumfries and Galloway						225 (04/16-03/17)	GRI
Fife						202 (04/16-03/17)	GRI
Forth Valley						278 (2016)	GRI
Grampian	Siemens Immulite	nmol/L	<3 4-6 7-9 10-11 12-13 14-15 16-18 19-21 22-24 25-29 30-34 35-39 40-44 45-49 50-54 55-59 60-64 65-69 70-79 80-90	1-17 3-27 5-33 9-41 19-66 23-66 23-54 15-42 13-38 11-34 9-31 8-29 8-29 7-28 6-27 6-28 6-29 5-30 5-28 4-27	2-22 5-30 7-36 15-59 22-69 25-65 25-56 15-42 13-38 11-34 9-31 8-29 8-29 7-28 6-27 6-28 6-29 5-30 5-28 4-27	894	
Greater Glasgow and Clyde	IDS iSYS	µg/L	Age <2 2-4 5-7 8-10 11-13 14-16 17-25 26-39 40-54 55-65 65+	Male 15-157 28-247 46-349 67-442 89-503 104-510 105-410 81-249 63-201 49-191 39-186	Female 17-151 25-198 39-272 59-371 82-465 97-502 96-417 72-259 57-197 43-170 35-168	5579 (04/16-03/17)	
Highlands						253 (06/16-05/17)	GRI
Lanarkshire						355	GRI
Lothian						760 (04/16-03/17)	GRI

Tayside				1404 (04/16-03/17)	GRI
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IGF-1: All going to Glasgow except Grampian, who are doing their own. Different methods and units in use. Grampian ranges don't reflect any gender differences in adults.

Forth Valley provided 10 years of workload data showing steady small year on year increases.

UKNEQAS scheme units are nmol/L⁴⁰

[Return to recommendations](#)

⁴⁰ Personal communication with G. Wark 17/10/2018.

IGF-2					
REGION	METHOD	UNITS	RRs	ANN WORK	EXTERNAL?
Ayrshire and Arran					rarely done
Dumfries and Galloway				2 (04/16-03/17)	SAS Peptide Section, Royal Surrey County Hospital
Fife				-	
Forth Valley				2011-3 2012-3 2015-3 2016-14 2017-2	SAS Peptide Section, Royal Surrey County Hospital
Grampian					N/A
Greater Glasgow and Clyde				5 (04/16-03/17)	SAS Peptide Section, Royal Surrey County Hospital
Highlands				1	SAS Peptide Section, Royal Surrey County Hospital
Lanarkshire				Not known	SAS Peptide Section, Royal Surrey County Hospital
Lothian				data not available	SAS Peptide Section, Royal Surrey County Hospital
Tayside				7 (04/16-03/17)	SAS Peptide Section, Royal Surrey County Hospital

Calcitonin					
REGION	METHOD	UNITS	RRs	ANN WORK	EXTERNAL?
Ayrshire and Arran				0 (04/16-04/17)	GRI
Dumfries and Galloway				9 (04/16-03/17)	GRI
Fife				4 (04/16-03/17)	GRI
Forth Valley				6 (2016)	GRI
Grampian				8	GRI
Greater Glasgow and Clyde	Diasource IRMA	ng/L	<15ng/L	354 (04/16-03/17)	
Highlands				31 (06/16-05/17)	GRI
Lanarkshire				21	GRI
Lothian				94 (04/16-03/17)	GRI
Tayside				29 (04/16-03/17)	GRI

[Return to recommendations](#)

<u>Thyroglobulin</u>					
REGION	METHOD	UNITS	RRs	ANN WORK	EXTERNAL? + strategy for interference
Ayrshire and Arran				9 (04/16-04/17)	GRI - no strategy stated
Dumfries and Galloway				41 (04/16-03/17)	Lothian
Fife				140 (04/16-03/17)	Lothian
Forth Valley				39 (2016)	GRI
Grampian	Siemens Immulite		<60µg/L	375	
Greater Glasgow and Clyde	Siemens Immulite 2000	µg/L	<55 - Try only to measure post radical thyroidectomy – no ref range should apply	2150 (04/16-03/17)	
Highlands				136 (06/16-05/17)	GRI
Lanarkshire				119	GRI
Lothian	Access	µg/L	none given	1081 (04/16-03/17)	*
Tayside	Siemens Immulite 2000	µg/L	No reference range reported	410 (04/16-03/17)	

* sample also sent to Birmingham for Thyroglobulin RIA result.

Forth Valley provided 10 years of workload data showing steady requesting of Thyroglobulin.

<u>Thyroglobulin Antibodies</u>					
REGION	METHOD	UNITS	RRs	ANN WORK	EXTERNAL?
Ayrshire and Arran					rarely done
Dumfries and Galloway				As per Lothian	
Fife				As per Lothian	
Forth Valley				43 (2016)	GRI
Grampian	Siemens Immulite		<40 IU/mL	375	
Greater Glasgow and Clyde	Siemens Immulite 2000	IU/mL	<40 IU/mL	2161 (04/16-03/17)	
Highlands				136 (06/16-05/17)	GRI
Lanarkshire				119	GRI
Lothian				not done	
Tayside	Siemens Immulite 2000		Positive or Negative	410 (04/16-03/17)	

Forth Valley provided 10 years of workload data –fluctuating workload, doesn't reflect thyroglobulin requesting, usually more are requested: likely inappropriate requesting. [Return to recommendations](#)

<u>TRABs</u>					
REGION	METHOD	UNITS	RRs	ANN WORK	EXTERNAL?
Ayrshire and Arran				16 (04/16-04/17)	GRI
Dumfries and Galloway				118 (04/16-03/17)	GRI
Fife				371 (04/16-03/17)	Lothian
Forth Valley				194 (2016)	GRI
Grampian				Immunology	
Greater Glasgow and Clyde	RSR Elisa	U/L	<1 negative 1-2 equivocal >2 positive	2995 (04/16-03/17)	
Highlands				microbiology	
Lanarkshire				Not known	GRI
Lothian	Roche Elecsys E411	IU/L	<1.6 IU/L	2312 (04/16-03/17)	
Tayside	ELISA – RSR Ltd	U/L	0 – 0.4 U/L	528 (04/16-03/17)	

Forth Valley provided 9 years of workload data showing fairly steady increasing levels of TRAB requesting, though possibly levels out 2015-2016.

[Return to recommendations](#)

Plasma metadrenalines/catecholamines					
REGION	METHOD	UNITS	RRs	ANN WORK	EXTERNAL?
Ayrshire and Arran				0 (04/16-04/17)	Freeman Hospital, Newcastle
Dumfries and Galloway				62 (04/16-03/17)	Freeman Hospital, Newcastle
Fife				1 (04/16-03/17)	Freeman Hospital, Newcastle
Forth Valley				No data available, very small numbers received.	Freeman Hospital, Newcastle
Grampian				<10	Freeman Hospital Newcastle
Greater Glasgow and Clyde				238 (04/16-03/17)	Freeman Hospital, Newcastle
Highlands				3 (06/16-05/17)	Freeman Hospital, Newcastle
Lanarkshire				43	Freeman Hospital, Newcastle
Lothian				data not available	Freeman Hospital, Newcastle
Tayside				46 (04/16-03/17)	Freeman Hospital, Newcastle

Urine metadrenalines/catecholamines					
REGION	METHOD	UNITS	RRs	ANN WORK	EXTERNAL?
Ayrshire and Arran	HPLC: NORA, A, DOP, fNMA, fMA, 3MT	nmol/24hr - then gives units for VMA/5HIAA and HVA as umol/24hr! confusing	VMA * $\mu\text{mol}/24\text{hr}$ 5HIAA $\leq 50 \mu\text{mol}/24\text{hr}$ HVA $\leq 40 \mu\text{mol}/24\text{hr}$ Noradrenaline $\leq 900 \text{ nmol}/24\text{hr}$ Adrenaline $\leq 230 \text{ nmol}/24\text{hr}$ Dopamine $\leq 3300 \text{ nmol}/24\text{hr}$ fNMA $\leq 65 \text{ nmol}/24\text{hr}$ fMA $\leq 350 \text{ nmol}/24\text{hr}$ 3MT analysed but reported only on paediatric	2008 ^s (04/16-04/17)	3MT reported only on children but analysed on all samples (all samples age specific reference range).
Dumfries and Galloway				138 (04/16-03/17)	Monklands Hospital, Airdrie
Fife				205 (04/16-03/17)	Lothian
Forth Valley				284 (2016)	GRI
Grampian	Chromsystems ^f	$\mu\text{mol}/24\text{h}$	Normetadrenaline $< 3.0 \mu\text{mol}/24\text{h}$ Metadrenaline $< 1.4 \mu\text{mol}/24\text{h}$ 3-Methoxytyramine $< 2.5 \mu\text{mol}/24\text{h}$	692	

Greater Glasgow and Clyde	In-house HPLC	nmol/24hrs	Adrenaline <230 Noradrenaline <900 Dopamine <3300	567 ^{&} (GRI requests only) (04/16-03/17)	*																
Highlands				222	University Hospital Crosshouse																
Lanarkshire	HPLC	µmol/24h	Noradrenaline: up to 900 µmol/24 Adrenaline: ≤ 230 µmol/24h Dopamine: ≤3300 µmol/24h Normetadrenaline: ≤3.8 µmol/24h Metadrenaline: ≤2.2 µmol/24h	577																	
Lothian	HPLC-ECD Chromsystems	µmol/24hr	Normetadrenaline 0.4-3.4µmol/24hr Metadrenaline 0.3-1.7µmol/24hr	863 [^] (04/16-03/17)																	
Tayside	LCMS	nmol/day	<table border="1"> <thead> <tr> <th>Analyte</th> <th>Unlikely</th> <th>Possible</th> <th>Likely</th> </tr> </thead> <tbody> <tr> <td>Normetadrenaline (nmol/24 h)</td> <td><3000</td> <td>3000-6550</td> <td>>6550</td> </tr> <tr> <td>Metadrenaline (nmol/24 h)</td> <td><1000</td> <td>1000-2880</td> <td>>2880</td> </tr> <tr> <td>3-methoxytyramine (nmol/24 h)</td> <td><2300</td> <td>2300-5000</td> <td>>5000</td> </tr> </tbody> </table>	Analyte	Unlikely	Possible	Likely	Normetadrenaline (nmol/24 h)	<3000	3000-6550	>6550	Metadrenaline (nmol/24 h)	<1000	1000-2880	>2880	3-methoxytyramine (nmol/24 h)	<2300	2300-5000	>5000	Newly introduced – no figures yet. 835 for previous method (noradrenaline, adrenaline, dopamine)	
Analyte	Unlikely	Possible	Likely																		
Normetadrenaline (nmol/24 h)	<3000	3000-6550	>6550																		
Metadrenaline (nmol/24 h)	<1000	1000-2880	>2880																		
3-methoxytyramine (nmol/24 h)	<2300	2300-5000	>5000																		

*Reference range not stated.

[&]GGC requests except GRI go to University Hospital Crosshouse for Urine mets and 5HIAA – 1175 (04/16-03/17)

* reference range not stated.

[§]includes 350 paediatric samples: 3MT analysed on all samples but only routinely reported on paediatric samples

^fPositive results are sent to University Hospital Crosshouse for confirmation.

[^]53 paediatric samples – sent to University Hospital Crosshouse

[Return to recommendations](#)

Urine 5HIAA					
REGION	METHOD	UNITS	RRs	ANN WORK	EXTERNAL?
Ayrshire and Arran	HPLC	µmol/24hr	<50	2008 (04/16-04/17)	
Dumfries and Galloway				110 (04/16-03/17)	Monklands Hosp, Airdrie
Fife				88 (04/16-03/17)	Lothian
Forth Valley				115 (2016)	GRI
Grampian	5-hydroxyindoles react with 1-nitroso-2-naphthol in the presence of nitrous acid to produce a purple colour	Qualitative method POS/NEG		171	Screen performed in-house, quantitative analysis sent to University Hospital Crosshouse.
Greater Glasgow and Clyde	In-house HPLC	µmol/24hr	5-42 µmol/24hr	198 (GRI requests only) (04/16-03/17)	*
Highlands				222 (cats screen)	University Hospital Crosshouse
Lanarkshire	HPLC	µmol/24hr	5-HIAA: ≤50 umol/24h HMMA (VMA): ≤35umol/24h infants (to 1 year) up to 9 umol/mmol creatinine <i>Other analytes in the screen include:</i> HVA: ≤40 umol/24h infants (to 1 year) up to 20 umol/mmol creatinine	516	
Lothian	HPLC-ECD Chromsystems	µmol/24hr	10-42µmol/24hr	402 (04/16-03/17)	
Tayside	HPLC with electrochemical detection	µmol/day	0 – 50 µmol/day	216	

* GGC requests except GRI go to Crosshouse for Urine mets and 5HIAA – 1175 (04/16-03/17)

Forth Valley provided 10 years of workload data showing steadily increasing requesting levels, possibly levelling off in the last few years.

[Return to recommendations](#)

Urinary cortisol					
REGION	METHOD	UNITS	RRs	ANN WORK	EXTERNAL?
Ayrshire and Arran				6 (04/16-04/17)	EGR
Dumfries and Galloway				135 (04/16-03/17)	GRI
Fife				63 (04/16-03/17)	Lothian
Forth Valley				73 (2016)	GRI
Grampian	Siemens Immulite	µmol/mol creat nmol/24hr	Early morning: <25 µmol/mol creat. 55-248 nmol/24 hr	209	
Greater Glasgow and Clyde	LC/TMS	nmol/24hrs nmol/mmol creat	<165 nmol/24hrs <40 nmol/mmol creat	2374 (04/16-03/17)	
Highlands				142 (06/16-05/17)	GRI
Lanarkshire				56	GRI
Lothian	Urinary free cortisol: Abbott Architect	nmol/24hr	20-180nmol/24hr	259 (04/16-03/17)	
Tayside				121 (04/16-03/17)	GRI

Forth Valley provided 10 years of workload data, showing a steady but clear decline in requesting.

UKNEQAS scheme units for urinary free cortisol are nmol/L⁴¹

[Return to recommendations](#)

Prednisolone					
REGION	METHOD	UNITS	RRs	ANN WORK	EXTERNAL?
Ayrshire and Arran				0 (04/16-04/17)	Heart of England, Heartlands
Dumfries and Galloway					South Manchester Hospital, Wythenshawe
Fife				-	

⁴¹ Taken from ukneqas.org.uk/programmes/result/?programme=steroid-hormones 17/10/2018

Forth Valley				2010-5 2011-2 2012-4 2013-5 2014-3 2015-3 2016-7 2017-5	South Manchester Hospital, Wythenshawe
Grampian					South Manchester Hospital, Wythenshawe
Greater Glasgow and Clyde				69 (04/16-03/17)	South Manchester Hospital, Wythenshawe
Highlands				3 (06/16-05/17)	South Manchester Hospital, Wythenshawe
Lanarkshire				Not known	South Manchester Hospital, Wythenshawe
Lothian				data not available	
Tayside				not done	

[Return to recommendations](#)

Chromogranin A					
REGION	METHOD	UNITS	RRs	ANN WORK	EXTERNAL?
Ayrshire and Arran				1 (04/16-04/17)	Sheffield PRU
Dumfries and Galloway		pmol/L	0-60	43 (04/16-03/17)	Charing Cross, London
Fife				24 (04/16-03/17)	Charing Cross, London
Forth Valley		nmol/L pmol/L	0-6 0-60	8 (2016) 29 (2016)	Sheffield PRU Charing Cross, London – part of gut hormones screen
Grampian				79 (gut hormone profile)	Charing Cross, London
Greater Glasgow and Clyde				105 (04/16-03/17) These are individual Cg requests. Many additional full gut hormone profiles sent to Charing Cross.	Charing Cross, London
Highlands				64 01.01.16-31.12.16 (1 CgA only 38 for CgA and B 25 CgA+B and gut hormones)	Charing Cross, London
Lanarkshire		pmol/L	<60pmol/L	57 (part of the gut hormone profile)	Charing Cross, London
Lothian				211 (04/16-03/17)	Charing Cross, London
Tayside				187 (Cg A only) 55 (Gut hormone profile) (04/16-03/17)	Sheffield PRU Charing Cross, London

Forth Valley provided 7 years of workload data showing fairly steady levels of requesting.

[Return to recommendations](#)