

Notification of Changes to Service Provision

Immunoassay

Clinical Biochemistry

York Teaching Hospital NHS Foundation Trust

**Introduction**

York Teaching Hospital NHS Foundation Trust encompasses York Teaching Hospital and Scarborough General Hospital as well as several smaller hospitals throughout the region. Laboratory Medicine operates across the York and Scarborough sites and provides services to primary and secondary care across North Yorkshire, North East Yorkshire and Ryedale.

Within Laboratory Medicine, the contract for our current service provider for Clinical Biochemistry is close to expiration. We have recently completed a tender process for the provision of our core chemistry and immunoassay services. The tender process was undertaken with the assistance of the NHS North of England Commercial Procurement Collaborative. All of the companies who submitted bids for the tender were subject to rigorous marking criteria based on service provision and quality. We are pleased to announce that we have awarded the tender to Roche Diagnostics and feel that this will enable us to deliver the best possible service to you and, more importantly, to your patients.

The installation of the new analysers will occur in two phases. Phase one will involve the implementation of the new immunoassay analysers on the York and Scarborough sites. The expected ‘go-live’ date for the new immunoassay service is 01/08/17. This will be followed by the implementation of the core chemistry analysers early next year.

This leaflet will focus solely on those changes to our immunoassay service. Any changes to the core chemistry services will be communicated at a later date. Within immunoassay, we expect there to be minor changes to most assays, however we do not expect these changes to be clinically significant. Only information regarding expected significant changes that may impact on patient management has been included in this notification. Where changes have occurred we will alert you to these using automated comments that will appear on reports.

If you have any queries regarding the content of this notification then please do not hesitate to contact the laboratory using the contact details provided below.

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**Cardiac Markers**

***Troponin***

The troponin assay will change from a contemporary Troponin I assay (TnI) to a high sensitivity Troponin T assay (hsTnT).  **Results will be completely different to the current results and will not be comparable.** The new assay has been approved by NICE (DG15 – Myocardial infarction (acute): Early rule-out using high-sensitivity troponin tests. 2014).

The new hsTnT assay will allow some decisions to be made about patients presenting with chest pain much faster. Together with clinical assessment and ECG, hsTnT measurements taken at presentation and 1 hour later can rule out acute myocardial infarction (AMI) in approximately 75% of cases.

A new Chest Pain Pathway for suspected ACS for patients presenting with acute chest pain in secondary care will be available on the Trust Intranet.

The use of troponin to assess chest pain in primary care is not recommended.

***NT-pro-BNP***

The sample type for NT-pro-BNP will change from lithium heparin (orange top) to serum (brown top). This will mean that NT-pro-BNP can be tested on routine Biochemistry samples and a separate sample will no longer be required.

Lithium heparin samples will still be accepted.

**Tumour Markers**

The change in service provider may be associated with a change in tumour marker results for some patients. The tumour markers affected are CA12-5, CA15-3, CA19-9, CEA, AFP and hCG. Patients being serially monitored using these tumour markers for a pre-existing cancer diagnosis must have their levels re-baselined to allow for continued monitoring in the future. Re-baselining will involve measuring tumour markers levels using both the current assay (Siemens) and the new assay (Roche). A letter was sent out in June to Consultant Oncologists, Surgeons and Chemotherapy Nurses within the Trust notifying them of the expected change and the need for re-baselining. This letter can be viewed on the Trust website (<https://tinyurl.com/LabMedNews>).

***PSA***

At present we quote the referral thresholds recommended by the NHS Prostate Cancer Risk Management Programme and NICE as reference limits. These are summarised in the table below. We will continue to quote these reference limits when we move to the new assay. In addition we will also quote a reference limit for 40 – 49 year olds of <2.0 ng/mL in accordance with NICE guidance. Due to the new assay having a slight positive bias when compared with our current assay, results may be slightly higher than those reported at present. This may result in a slight increase in patients having PSA levels above the reference limits. For guidance on management of patients with elevated PSA levels please refer to NICE Guidance (<https://cks.nice.org.uk/prostate-cancer>) or to the information provided by your CCG.

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| **Reference Limits for PSA** | |
| Age Group | Reference Limit |
| 50 – 59 years | < 3.0 ng/mL |
| 60 – 69 years | < 4.0 ng/mL |
| >70 years | < 5.0 ng/mL |

**Thyroid Function Tests**

There will be changes in reference ranges for TSH, FT4 and FT3. The changes are summarised in the table below. Specific pregnancy and paediatric related reference ranges will be applied to reports where appropriate. These new reference ranges originate from an extensive study performed by Roche diagnostics.

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| **Changes in Reference Ranges (Adults)** | | |
| Assay | Current Reference Range | New Reference Range |
| TSH | 0.55 – 4.8 mU/L | 0.27 – 4.2 mU/L |
| FT4 | 9 – 23 pmol/L | 12 – 22 pmol/L |
| FT3 | 3.5 – 6.5 pmol/L | 3.1 – 6.8 pmol/L |

The change in TSH reference range will mean you may see more patients with slightly elevated TSH results. National guidance1 recommends that patients with borderline-raised TSH results should be repeated after an appropriate time interval; we will continue to recommend repeat testing in 4 – 6 weeks. The laboratory will add on TPO antibodies to persistently elevated TSH results and comment appropriately to help guide patient management.

The change in TSH reference range will mean you may see fewer patients with slightly low TSH results. A clinical audit performed within the laboratory revealed that only a very small percentage of patients (0.9%) with TSH results between 0.1 and 0.55mU/L (the lower limit of our current reference range) had abnormal FT4 levels indicative of overt thyroid disease. Common causes of low TSH levels include non-thyroidal illness and medication e.g. glucocorticoids and dopamine. These causes should be excluded first before subclinical thyroid disease is considered. It is also important to note that low TSH levels are a common finding in the elderly without the presence of identifiable thyroid disease. We will continue to add on FT3 levels and comment where appropriate. For further guidance on the interpretation of thyroid function tests please refer to <http://www.british-thyroid-association.org/>.

Please help us to help you by telling us on the request form if your patient is taking thyroxine or other thyroid-modifying drugs.

[1] UK Guidelines for the Use of Thyroid Function Tests (<http://www.acb.org.uk/docs/default-source/guidelines/TFTguidelinefinal.pdf> Accessed 19/07/2017)

***TPO Antibodies***

Numerical values for TPO antibodies between the old and new methods will not be comparable. However, results should be interpreted as positive or negative based on the new cut-off provided on reports. Repeat measurement of positive TPO antibodies is not informative. Negative antibodies should not be repeated within 12 months.

**Ferritin**

The reference ranges for ferritin will change. These changes are summarised in the table below.

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| **Changes in Reference Ranges for Ferritin** | |
| Current Reference Ranges | New Reference Ranges |
| Male: 22 – 322 µg/L  Female: 20 – 291 µg/L | Male: 30 – 400 µg/L  Female: 13 – 150 µg/L |

We expect all ferritin results to be approximately 15% higher when using the new assay. Please be mindful of this when using ferritin levels to guide patient management. The new reference range for males will be higher to compensate for this. Conversely, the new reference range in females is significantly lower. The new reference ranges are those quoted by the assay manufacturer. We have undertaken further verification work in our laboratory which confirms that these reference ranges are appropriate for our patient population. Please note that the female reference range was derived from a population of mostly pre-menopausal women. Further work will be carried out at a later date to define reference ranges in children and post-menopausal women. When interpreting ferritin levels in post-menopausal females please be aware that levels may be higher in this patient population.

Due to the decrease in reference range for females you may see an increase in the number of elevated ferritin levels in women. We will continue to add iron levels to first time elevated ferritin results to identify genuine cases of iron overload. Interpretive comments will be added where appropriate.

For further information on the investigation of hyperferritinaemia please refer to the Trust website (<https://tinyurl.com/PrimaryCareInfo>).

**Cortisol**

There will be changes in the reference range for cortisol. The changes are summarised in the table below. Results will be lower when measured using the new assay, but the reference range will also be lower to compensate for this. The new assay is standardised against an international reference material and compares better with the reference method.

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| **Changes in Reference Ranges for Cortisol** | |
| Current Reference Range | New Reference Range |
| 9am: 150 – 650 nmol/L | 6 – 10am: 133 – 537 nmol/L |

**Prolactin**

There will be changes in reference ranges for prolactin. The changes are summarised in the table below. The new reference ranges were derived during a study performed by Roche Diagnostics and were verified by an independent study published in Clinical Chemistry2.

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| **Changes in Reference Ranges for Prolactin** | |
| Current Reference Ranges | New Reference Ranges |
| Male: 45 – 375 mU/L  Female: 59 – 620 mU/L | Male: 86 – 324 mU/L  Female: 102 – 496 mU/L |

The upper limits of the reference range for both males and females will decrease following the introduction of the new assay. This may result in an increase in elevated prolactin results. We will continue to add further tests and interpretive comments where appropriate. Physiological and pharmacological causes of hyperprolactinaemia should be excluded first before pathological causes are considered. Please refer to <https://tinyurl.com/PrimaryCareInfo> for further information on the causes of hyperprolactinaemia.

[2] Beltran L, Fahie-Wilson MN, McKenna J *et al*. Serum Total Prolactin and Monomeric Prolactin Reference Intervals Determined by Precipitation with Polyethylene Glycol: Evaluation and Validation on Common Immunoassay Platforms. *Clin Chem* 2008; 54 (10): 1673 - 1681

**Testosterone**

There will be changes in the reference ranges for testosterone and sex hormone binding globulin (SHBG). The changes are summarised in the table below. In both cases, reference ranges are age- and sex-related. The implementation of these reference ranges will allow for more appropriate interpretation of testosterone levels in the context of the patient’s age. The new lower limit of the reference range in men greater than 50 years of age will reduce the number of patients inappropriately identified as having hypogonadism. We will continue to add further investigations and interpretive comments where appropriate.

There will be a decrease in the upper reference limit for female testosterone. We expect female testosterone results to be lower on the new assay, which is less prone to interference from other steroid hormones. We will continue to send samples with an elevated female testosterone result to a referral laboratory for confirmation by a more specific method.

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| **Changes in Reference Ranges for Testosterone** | | |
| Sex | Current Reference Range | New Reference Range |
| Male | 8.1 – 29 nmol/L | **20 – 49 years**: 8.64 – 29.0 nmol/L  **≥ 50 years**: 6.68 – 25.7 nmol/L |
| Female | 0.5 – 2.6 nmol/L | **20 – 49** **years**: ≤1.67 nmol/L  **≥ 50 years**: ≤1.42 nmol/L |

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| **Changes in Reference Ranges for SHBG** | | |
| Sex | Current Reference Range | New Reference Range |
| Male | 10 – 57 nmol/L | **20 – 49 years**: 18.3 – 54.1 nmol/L  **≥ 50 years**: 20.6 – 76.7 nmol/L |
| Female | 18 – 144 nmol/L | **20 – 49 years**: 32.4 – 128 nmol/L  **≥ 50 years**: 27.1 - 128 nmol/L |

In view of the changes in testosterone and SHBG reference ranges in females there will be an associated change in the free androgen index reference range. The changes are summarised in the table below.

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| **Changes in Reference Ranges for Free Androgen Index** | | |
| Sex | Current Reference Range | New Reference Range |
| Female | 2 – 10 % | **20 – 49 years**: 0.3 – 5.6 %  **≥ 50 years**: 0.2 – 3.6 % |