Sgrinio Smotyn Gwaed Newydd-anedig Cymru

Newborn Bloodspot Screening Wales

Congenital Hypothyroidism Referral and clinical management Guidelines for Newborn Bloodspot Screening Wales

September 2019 Version 2

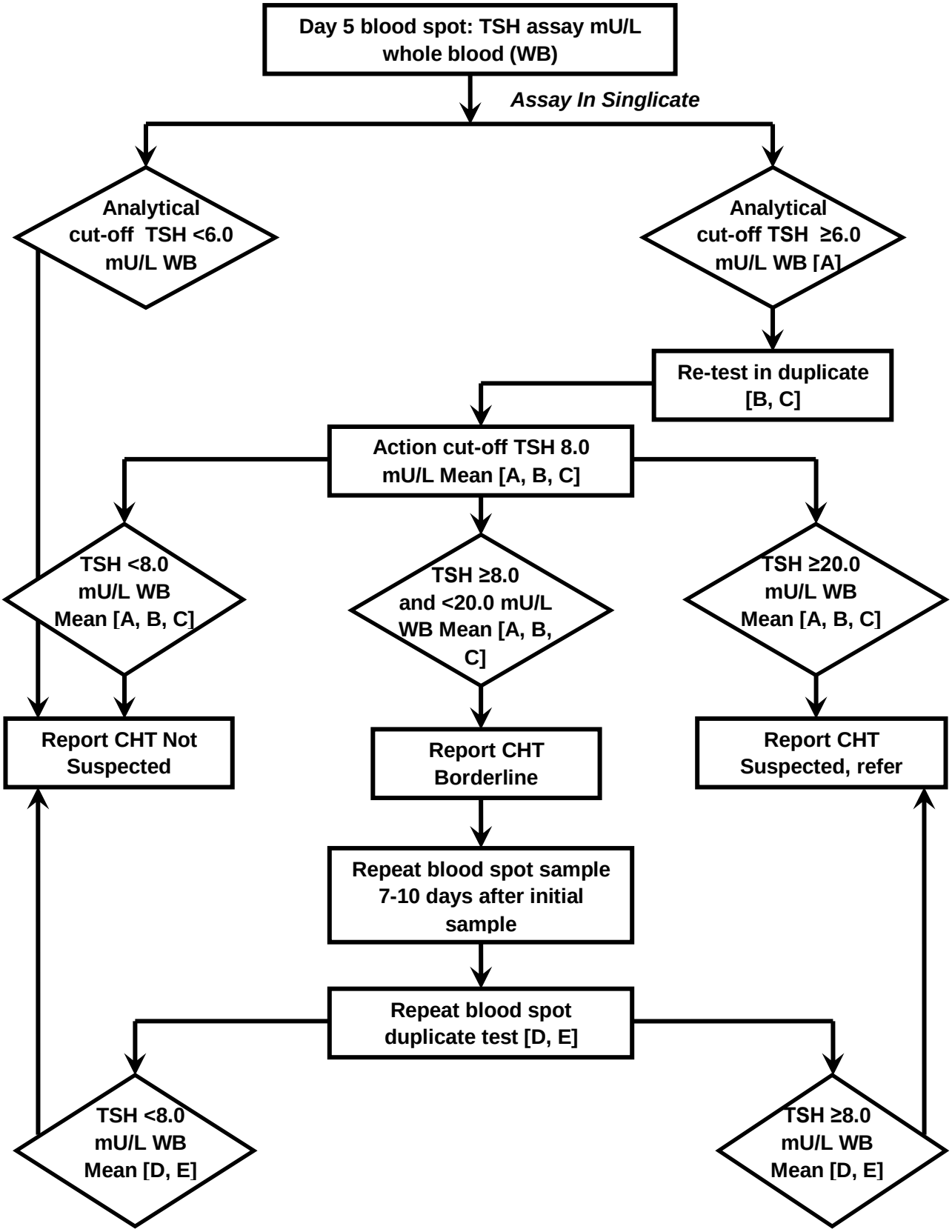
Based on the CHT initial Clinical Referral Standards and Guidelines in the UK

https://www.gov.uk/government/publications/congenital-hypothyroidism-screening-laboratory-handbook/addendum-to-cht-screening-laboratory-handbook#contents

https://www.gov.uk/government/publications/congenital-hypothyroidism-screening-laboratory-handbook Jacob H & Peters C. Screening, diagnosis and management of congenital hypothyroidism: European Society for Paeditric Endcrinology Consensus Guideline. Atch Dis Child Educ Pract Ed 2015:100:260-263.

Adapted for Wales in consultation with Prof John Gregory, Professor in Paediatric Endocrinology, Dr Justin Warner, Consultant in Paediatric Endocrinology and Diabetes, Dr Carol Evans, Consultant Clincial Biochemist, Medical Biochemistry & Immunology, University Hospital of Wales, Cardiff and Prof Stuart Moat, Consultant Clincial Biochemist & Director of Wales Newborn Screening Laboratory.

Figure 1 Congenital Hypothyroidism Screening Pathway in Wales



Stage of Process	No.	Standards
Newborn Bloodspot Screening Protocol for CHT in Wales	**1**	The screening strategy for CHT in the UK is based on the analysis of thyroid stimulating hormone (TSH) in bloodspots by immunoassay using the Perkin Elmer TSH AutoDelfia System. TSH analysis is performed on a single spot from the initial (day 5) dried blood spot sample. Samples with TSH ≥ a preliminary threshold (analytical cut off*) of 6.0 mU/L whole blood (WB) are re-tested in duplicate from the same card but on a different spot(s). Action is taken on the triplicate mean result. Second sample (for borderline CHT) – TSH is analysed in duplicate and action taken on the duplicate result. See Figure 1 screening pathway on page 2. Timeliness of analysis – analysis is timed to permit referral of screen positive results within 2-4 working days of sample receipt. *The analytical cut off is set below the screen action cut off of mU/L WB to allow for the natural variation in the TSH assay and to minimise the effect of volumetric variability that occurs in dried blood spots. Re-testing also acts as confirmation of correct sample identification.
Categorisation of initial screening result	**2** **3** **4**	Babies in whom the TSH concentration is <8.0 mU/L WB on the initial screening sample should be considered to have a negative screening result for congenital hypothyroidism (CHT). • Report CHT not suspected. Babies in whom the TSH concentration is ≥20.0 mU/L WB on the initial screening sample should be considered to have a positive screening result for CHT. • Report and refer as CHT suspected. Babies in whom the TSH concentration is ≥8.0 and <20.0 mU/L WB on the initial screening sample should be considered to have a borderline result for CHT.
Borderline screening	**5**	On detecting a borderline result, a second sample is to be taken 7-10 days after the initial sample. If the TSH concentration is <8.0 mU/L WB on this

	6	second screening sample, the baby should be considered to have a negative screening result for CHT. • Report CHT not suspected.
	7	If the TSH concentration is ≥8.0 mU/L WB in this second screening sample: • Report and refer as CHT suspected.
Referral of babies with positive screening results	**8**	The laboratory shall refer babies with positive screening results for CHT the same or next working day. Referral is to a paediatric endocrine team (regional specialist team) or to a clearly identified lead paediatrician with a special interest in CHT or experience of managing these patients. If the lead paediatrician is on leave then referral should be to the duty on call paediatric consultant. Appropriate local failsafe mechanisms must be in place to ensure CHT suspected babies have entered into the diagnostic pathway. Clinicians should work to a common protocol and have access to the full range of diagnostic investigations recommended. Where referral is outside a regional endocrine centre, the regional specialist team should be available to provide support and to facilitate access to diagnostic investigations where required.
	9	The first clinical appointment with the paediatrician **must** take place on the same day or the next day after parents are informed of their baby's positive screening result.
Communication flows	**10**	The Laboratory shall notify a positive screening test verbally and in writing by email (See letter in Appendix 1), to the lead paediatrician or deputy. This notification should include a link to the standardised diagnostic and initial treatment protocol. This initiates the clinical referral of screen positive cases.
	11	The result should be communicated to the parents by the clinical team and should provide the following information to the family: a) The NHS Newborn Blood Spot Screening parent

		information leaflet 'Congenital hypothyroidism is suspected' (via hard copy or web link). Details of which are provided on the referral letter from laboratory. b) Details of the time and date of the appointment with the paediatrician and appropriate contact telephone numbers.
	12	The outcome of the first appointment should be reported to the newborn screening laboratory via email: new.screening.cav@wales.nhs.uk The Wales Newborn Screening Laboratory should also be informed about diagnostic outcome to facilitate national audit using the form sent with the intial referral letter from the laboratory (see form in Appendix 2).
Clinical evaluation and confirmatory diagnostic tests	**13**	The clinician responsible for assessing the baby with a positive screening result shall take a clinical history and perform a clinical exam. Note 1: Babies with CHT are more likely to have associated anomalies, particularly congenital heart defects and hearing loss and require careful neonatal examination and follow up. A complete history, including maternal thyroid status (previous history of thyroid dysfunction, maternal anti-thyroid medications), maternal diet (e.g. vegan or other low iodine diet) and family history should be obtained.
	14	Diagnostic tests considered essential in the baby are: a) Free T4 (plasma or serum) b) TSH (plasma or serum) Note 2: Diagnosis using free T4 and TSH should be performed on a plasma or serum sample using the appropriate age-related reference ranges as defined by the local clinical laboratory in relation to the equipment used. These diagnostic tests require a rapid turn around time (within 2 hours in a working day) and this can be achieved if there is close working between the clinician and the local laboratory.
Desirable additional diagnostic tests	**15**	Appropriate imaging techniques (radioisotope and/or ultrasound scans) may help to establish whether the thyroid gland is: a) Normally situated and normal in size and shape

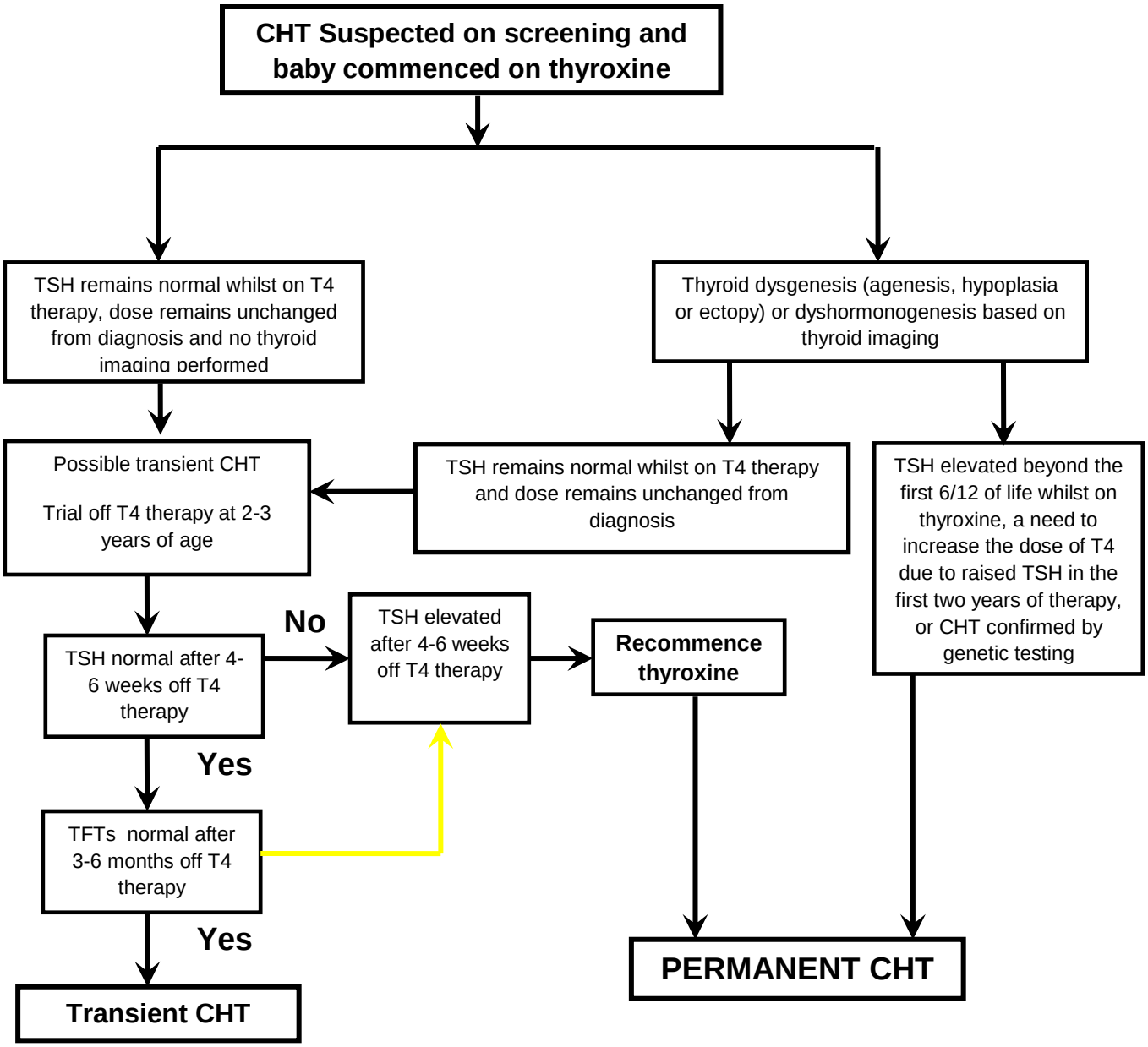
		b) Normally situated but abnormal in size and shape c) Ectopic d) Absent Note 3: Access to expert radiological advice is advocated as both isotope scanning and thyroid ultrasound in neonates require specialist skills and can potentially generate misleading results. A radioisotope scan and an ultrasound examination may establish the cause of the child's CHT and indicate whether the condition is likely to be permanent. Initiation of treatment should not be delayed whilst waiting for an isotope scan. However, ideally it should be performed within 5 days after starting therapy. An ultrasound scan can be performed at any stage and investigation need not be confined to the neonatal period. These investigations may increase awareness of potentially related problems such as deafness and can provide information about recurrence risk. Recurrence is unusual in the case of thyroid dysgenesis but there is likely to be autosomal recessive inheritance with a 1:4 recurrence risk for families of babies with thyroid dyshormonogenesis.
	16	In addition, the following test may be helpful: a) Thyroglobulin Note 4: Plasma thyroglobulin needs to be measured on a sample taken prior to the start of treatment; this must not delay initiation of treatment. If plasma thyroglobulin is detectable then there must be some thyroid tissue present. Concentrations will be low/undetectable in thyroid agenesis.
Advisable tests in the mother	**17**	Diagnostic tests considered advisable in the mother to exclude interference in the infant's TSH measurement and to exclude thyroid dysfunction in the mother include: a) Free T4 (plasma or serum) b) TSH (plasma or serum) Maternal history should be written on the request form These investigations should be extended to include an assessment of TSH receptor blocking antibody status (TRAB) in mothers with a current or previous history of autoimmune thyroid disease. NB – TSH-R stimulating assays (TSI) are not suitable for the follow-up of babies with possible CHT.
Timely receipt into clinical care & Treatment	**18**	A baby in whom a diagnosis of CHT has been made should commence treatment with oral levothyroxine by: a) CHT suspected on initial (day 5) screening sample 14 days of age (100% of infants)

		b) CHT suspected on a repeat blood spot sample that follows a borderline TSH 21 days of age (100% of infants)
	19	Treatment thresholds for CHT and recommended action: Serum TSH concentrations (mU/L) **<6 – Normal**, no need to repeat. **6-20 – Investigate.** If free T4 within neonatal range, consider withholding treatment for 2 weeks then retest.***** **>20 – Commence treatment.** ***** Treatment decision should be made in discussion with parents. It may appropriate to remain off treatment with repeat testing if the free T4 remains within the reference range and the TSH is improving. The starting dose of oral levothyroxine should be 10-15 mcg/kg/day, with a maximum dose of 50 mcg/day. The objective of treatment is to normalise TSH within the first month. The dose of levothyroxine may need to be reduced if TSH is suppressed or if the baby is showing signs of overtreatment. Babies with significant endogenous thyroid hormone production may need smaller initial doses. Note 5: Treatment with levothyroxine should lead to normalisation of free T4 and a 50% reduction in TSH within days. However, TSH normalisation can take weeks and timing does not correlate well with the administered levothyroxine dosage or the severity of the underlying diagnosis. The aim of treatment is therefore to increase free T4 close to the upper reference range within the first 2 weeks of treatment and to normalise the TSH within the first month. Free T4 concentrations may exceed the normal reference range at the time of TSH normalisation but significant elevation should be avoided. Regular dose adjustments may be required.
	20	Only licensed solutions and tablets of levothyroxine should be used. Suspensions may be unreliable. Parents should be shown how to administer preparations and accompanying written information should be provided.
	21	Once levothyroxine treatment has been started, TSH

		and thyroid hormone concentration should be checked at an appointment with a paediatrician at approx-imately 2 weeks, 4 weeks, 8 weeks, 3 months, 6 months, 9 months and 12 months after treatment is started, and thereafter as indicated. More intensive biochemical monitoring may be required. (See note 5)
	22	Assessment of permanence of hypothyroidism. In cases where the cause or persistence/permanence of hypothyroidism has not been confirmed (see Figure 2 Diagnostic Protocol Flow Diagram, p9), confirmatory testing should be undertaken by stopping thyroxine at 2-3 years of age with thyroid function tests checked 4-6 weeks later. It may be appropriate for a specialist referral for those who are borderline and remain on a small dose of levothyroxine. The outcome should be fed back to the regional endocrine centre to facilitate regional and national audit.

Figure 2 Congenital Hypothyroidism Diagnostic Protocol

(Guideline for re-investigation)



Appendix 1

Newborn Bloodspot Screening Wales
Sgrinio Smotyn Gwaed Newydd-anedig Cymru

Wales Newborn Screening Laboratory
Department of Medical Biochemistry & Immunology
tel 029 20 744 032, fax 029 20 744 065

Private and Confidential

01 September 2018

Dr XXXX
Consultant Paediatrician
Hospital
Town/City
Post code

Dear Dr XXXX

Name, DOB, NHS No:
Address (inc post code), Family GP - Dr XXXX, address & Tel:XXXX

Positive Congenital Hypothyroid Screening Test Result for Follow-up

This infant's newborn blood spot sample collected XX/09/18 (received into the laboratory XX/09/18) was found to have a positive screening test result for Congenital Hypothyroidism. The blood spot TSH was XX mU/L (mean of triplicate results).

Please arrange to see both the infant and the mother for further investigation of thyroid function urgently (within 48 hours of this notification). The results should be communicated by a member of the clinical team and should provide the CHT is suspected leaflet; Information on newborn screening for CHT can be found on GOV.UK, including the 'CHT is suspected' leaflet. Simply go to www.gov.uk and search for 'CHT suspected'.

Recommended diagnostic investigations to be undertaken in the baby:

- First review appointment to take place either today or tomorrow
- Urgent thyroid function test (FreeT4 and TSH).
- Measurement of thyroglobulin.
- Appropriate imaging to investigate whether the thyroid gland is either present, situated normally, of normal size and shape and demonstrates normal isotope uptake.

The following tests in the mother should also be undertaken to aid diagnosis:

- Thyroid function test (FreeT4 and TSH)
- TSH receptor blocking antibodies (TRAb) if there is a current or previous history of autoimmune thyroid disease.

All samples should be sent to your local laboratory. Please inform me of the results from the above investigations (using the CHT follow-up form attached) as these data are required for auditing the Congenital Hypothyroid Newborn Screening Programme in Wales.

Yours sincerely,

Prof Stuart J Moat, FRCPath
Consultant Clinical Biochemist & Director – Wales Newborn Screening Laboratory

Appendix 2

Wales Newborn Screening congenital hypothyroidism presumptive positive follow-up form

Name			
Date of birth		**NHS number**	

Date referral received	
Date of first contact with family and by whom	
Date of first assessment by Paediatrician	
Please state whether or not the initial assessment was undertaken by a Consultant	

Please indicate the infant's plasma thyroid function test results from the first clinic assessment.					
TSH (mU/L)		**fT4 (pmol/L)**		**Thyroglobulin (µg/L)**	
Date of blood test:					

Please indicate the mother's serum thyroid function test results					
TSH (mU/L)		**fT4 (pmol/L)**		**TRABS (IU/L)**	
Please provide any relevant thyroid medical, dietary (eg vegan) and family history:					

Please indicate the infant's Thyroid ultrasound results
Not performed/Normal / Absent / Ectopic / Hypoplastic / Enlarged / other (please give details)

Please indicate the infant's thyroid radio isotope uptake scan results
Not performed / Normal / Agenesis / Dysgenesis / Ectopic / Mild dysplasia / Other (please state)
Date of scan:

Was this infant commenced on thyroxine?	**Yes / No**	
If thyroxine replacement therapy was started please state:		
Start date	Preparation used	Dose/day

Form completed by			
Contact details		Date	

This information is required by the Wales Newborn Screening Programme. Data will be anonymised before being collated on a national basis.

Please return this form to The Wales Newborn Screening Laboratory by email to: stuart.moat@wales.nhs.uk

Appendix 3 Communication Guidelines: When CHT is suspected

The following guidelines have been developed by the NHS Newborn Bloodspot Screening Programme to support healthcare professionals in their communication of screening results to parents when Congenital Hypothyroidism (CHT) is suspected.

Guidelines for communicating screening results that indicate CHT is suspected	**Reasoning**
Parents should be told their baby's result as soon as possible.	If the diagnosis is confirmed, the baby should be started on daily levothyroxine treatment as soon as possible. Parental anxiety will be raised if the CHT suspected outcome result was preceded by a TSH borderline result.
The result should be communicated by a well-informed health professional and ideally face-to-face or a phone call if this is not possible. The setting must be appropriate e.g. if in person, in a quiet room; if by phone, check that the parent is free to listen. If they are alone, ask them if they would like you to contact someone to support them.	Parents prefer to be informed by someone with a good understanding of CHT and its management (ie Clinical Team). A face-to-face explanation is best as the parents can ask questions. A telephone conversation may be appropriate if a face-to-face meeting is impractical or will cause delay.
The first clinical appointment with the paediatrician must take place on the same day or the next day after parents are informed of their baby's positive screening result.	The baby must be investigated by a paediatric endocrine team (regional specialist team) or by a clearly identified lead paediatrician with a special interest in CHT or experience of managing these patients as soon as possible. Parents should not be left without a clear management plan over a weekend or bank holiday after being informed of their baby's positive screening result.
Standardised information should be provided to parents, for example: • The screening result suggests that their baby may be affected by CHT • Babies with CHT do not make enough of the hormone thyroxine, which is produced in a gland	Parents can quickly forget or misunderstand verbal information about their baby's results. Hence they should also be provided with reliable sources of information and support (as shown on the back of the 'Congenital hypothyroidism is

in the neck called the thyroid • Their baby will need further tests to confirm this result • That this treatment will improve their baby's future health and enable him or her to grow and develop normally • In most cases CHT happens by chance and the specific cause is not known. There is nothing the parents could have done to prevent it • The time and place of their appointment and the name and contact details of the member(s) of the healthcare team • That if a diagnosis of CHT is confirmed, their baby will need to be started on daily levothyroxine treatment very soon • Parents should be provided with a copy of the results leaflet 'Congenital hypothyroidism is suspected'. Information on newborn screening for CHT can be found on GOV.UK, including the 'CHT is suspected' leaflet. Simply go to www.gov.uk and search for 'CHT suspected'. • The health professional should give the family a contact number that they can call prior to their appointment with any questions or concerns	suspected' leaflet).
Parents should be informed about all newborn blood spot screening test results and all results should be recorded in the Personal Child Health Record (red book).	To ensure that the results of all five conditions for which babies are screened for, are communicated to parents. When one of the newborn screening conditions is suspected, parents do not receive a 'normal results letter' from the child health records department.
It is recommended that, where possible, health visitors are actively involved alongside specialists in the early stages of communicating results to parents, providing this does not delay communicating the result and starting treatment.	Health visitors have an on going role in supporting families.