King's College Hospital
NHS Foundation Trust

Please note: This is for clinical guidelines only and **not** for Patient Information Leaflets (PIL). Also, if the content of this document must be followed at all times and describes departmental process then consider registering as a Trust Policy on Kingsdocs rather than a clinical guideline on KCGS. Advice can be sought from the Patient Outcomes Team.

Full Guideline Name (Do not use abbreviations)			
Version Number	1.0	**Please complete all fields**	
Is this a new guideline?		Yes	
If no, please state the title of superseded guideline			
Guidance type Clinical Guideline, Protocol, Care Pathway, Patient Information Leaflet or other**.**		Clinical Guideline	
Summary A couple of sentences to help people assess whether the document is the guidance they need. Text is viewable on search.		WGS testing in children	
Review date All local guidelines need to have a full review at least every 3 years.		1/7/28	
Any drugs-related information included? Guidelines that include any kind of medication need to be reviewed and approved by a Specialty Lead Pharmacist. Specialty Lead Pharmacists may judge that the guideline needs to be approved at Drugs & Therapeutics Committee.		No	**Name of Specialty Lead Pharmacist consulted** (blank)
Lead Specialty responsible for reviewing and ratifying the document		Paediatric Neurology	
Principal author responsible for the document's authorship, update and governance. Please state full Name and Job Title.		Jon Gadian, Paediatric Neurology	
Secondary Author(s) please state full Name and Job Title.			
Specialties/staff groups affected for the latest version only. All staff affected by this document need to be consulted. Please include full Name and Job Title		Clinical Genetics, General Paediatrics	
ED / acute medical pathway included? If the document includes a pathway that starts from ED, please liaise with the relevant ED liaison clinician.		No	**Name of ED Liaison clinician consulted** (blank)
Approved for use at which sites Please state which site(s) this guideline applies to making sure all relevant groups have ratified this document before uploading on to KCGS (King's Clinical Guidelines System) or contacting the Patient Outcomes Team.		NB: Guidelines need to be written for use across all KCH sites unless there is a specific reason not to. Please ensure the guideline has been approved by the appropriate Committee for all relevant sites. Trust-wide / Denmark Hill only / PRUH only	
Approval Committee(s) name For the latest version only. E.g. Drugs & Therapeutics Committee, Care Group Risk & Governance Committee, Infection Prevention & Control Committee.		**Please list ALL Committees that have ratified this document.**	**Approval date**
		(blank)	(blank)
How will the document be disseminated? E.g. department/ward based education, training, email, team briefings.		Department education	
How will the document be monitored? E.g. clinical audit, risk/incident monitoring, benchmarking.		Clinical audit	
Key words these help intranet users to find the guideline they need.		Genetics, paediatric, children, WGS, whole genome sequencing	
Guidance conflict guidelines authors and approvers must be assured that the guideline does not conflict with NICE, Royal Marsden Guidance, Trust policies or other local guidelines.		n/a	

Drug Safety information, alerts and updates Guidelines authors and approvers must be assured all relevant advice issued from national bodies e.g. The MHRA, NPSA, NHS England and NHS Improvement has been considered and incorporated.	n/a
References Not required when references included in document annex.	Based on guidance by SE Genomics. With thanks to Dr Tom Rossor.

WGS Testing in Children

Table of Contents

Introduction

Whole genome sequencing gives clinicians outside of clinical genetics access to detailed genetic testing. Being able to request this test is a required competency for CCT in general paediatrics. However, for non-geneticists, the process is not always intuitive.

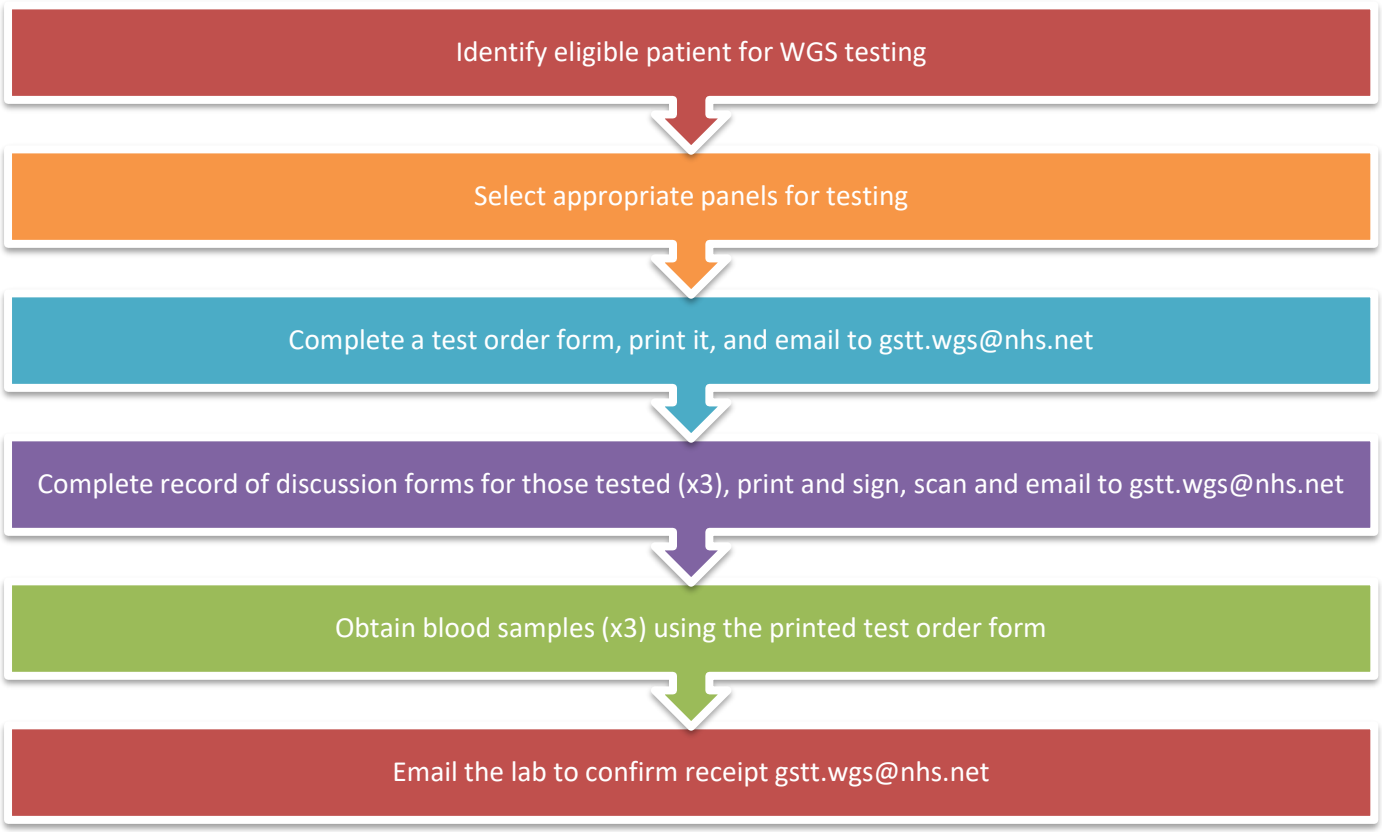
Extensive information is available through the South East Genomics, national genomics, and GSTT. This guideline attempts to collate some of this information for paediatricians in King's.

This document provides a guide on the procedural aspects of requesting whole genome sequencing testing in eligible patients with rare disease. It is not intended to address suitability for WGS testing, R14 testing (rapid testing for children in PICU/NICU), or WGS testing in cancer.

Target Audience

Paediatricians, King's College Hospital.

Flowchart



Algorithm

This algorithm is based on the South East Genomics crib sheet available at - WGS-RD-Crib-Sheet-V4.pdf

1) **Identify the genetic panels to be tested** (R number) using one of the following methods:
   - If you know which genetic panels you wish to test, include these in the order form using the appropriate R number, or if not search for it using either
     NHS England | Public Genetic Test Directory
     NHS England » National genomic test directory

   - If unsure of which genetic test should be performed, or if requesting R14 for an acutely unwell child, then please discuss with the clinical genetics team before sending samples. NB – R14 is sent using a different pathway – do not use the forms in this document, but instead refer to the separate KCH R14 pathway - https://www.exeterlaboratory.com/genetics/genome-sequencing

   - If required, discussion with clinical genetics can be done in the weekly MDT as follows:
     - On EPIC - request MDT discussion for patient (type MDT950 into orders or search for Genetics – NICU Genetics Cross-Site MDT (GSTT-KCH)) or, contact the Clinical Genetics registrar email at gstt.geneticsregistrar@nhs.net
     - Join the Monday 4pm MS Teams clinical genetics meeting:

Subject: KCH Genetics Ward Round
When: Occurs every Monday effective 04/01/2021 from 16:00 to 17:00 (UTC+00:00) Dublin, Edinburgh, Lisbon, London.
Where: Microsoft Teams Meeting

Microsoft Teams meeting

Join on your computer or mobile app
Click here to join the meeting
Join with a video conferencing device
109325872@teams.bjn.vc
Video Conference ID: 126 062 025 7
Alternate VTC dialing instructions
Learn More | Meeting options

---

2) **Complete a request form (test order form)**
   - Whole genome sequencing is likely to identify a lot of variants. It is therefore generally preferable to test parents at the time of testing the affected child (trio), as this can reduce the number of false positives, improve speed and accuracy of diagnosis. Therefore the request form needs to include parent details.
   - If parental samples cannot be provided, it may be possible to test as a duo or singleton. Explain this when emailing the genetics team (gstt.wgs@nhs.net).
   - Complete the test order form. NB – this is not available on EPIC. All forms need to be completed electronically. The test order form is available from one of the following (double clicking on the PDF also links the consent forms):

Adobe Acrobat Document

If not available, then please use one of the following links:
https://southeastgenomics.nhs.uk/wp-content/uploads/2024/08/WGS-Rare-Disease-Order-Form.pdf
Test order forms - South East Genomics : South East Genomics
NHS England » NHS Genomic Medicine Service test order forms

- On page 2, include the clinical features present in the patient, and whether or not they are present in the parents. This needs to be listed in HPO terms (and not taken from the list at the bottom of the page). If the terms are not in an HPO format the form will be returned to you. To identify the HPO term search for it using the link provided (Human Phenotype Ontology) and click on the Term tab to find the Term Identifier (should start HP:0….)
- Save the completed test order form and email it to gstt.wgs@nhs.net together with the completed record of discussion forms (see 3).
- Print the form if you wish to use it as the order form for blood tests (see 4).
- A sample annotated form is included in the appendix, created by SE genomics.

3) Obtain consent (Record of discussion)

- If trio testing is performed, then you will need to complete 3 record of discussion forms – one signed by a parent/guardian on behalf of the child, and one for each parent tested.
- Patient information is available at the following

Adobe Acrobat Document

Patients and public - South East Genomics : South East Genomics (website)
genome-sequencing-rare-disease-patient-information.pdf (printable form)
genome-sequencing-rare-disease-patient-information-easy-read.pdf (easy read)
NHS England » Whole genome sequencing patient information leaflets (scroll down past the cancer forms)

- Complete the consent forms either via the linked PDF above (see 2 – complete a request form), or 3x individual ROD forms available at one of the following:

Adobe Acrobat Document

nhs-genomic-medicine-service-record-of-discussion-form.pdf
NHS England » NHS Genomic Medicine Service record of discussion form

- The forms (x3) will need to be printed off, signed by the family and clinician, scanned in and emailed to gstt.wgs@nhs.net
- A sample annotated form is included in the appendix, courtesy of the SE genomics.

4) Obtain blood samples

- If the child has had genetic testing in the past, check if there is saved DNA suitable for WGS testing by emailing gstt.viapathgeneticsadmin@nhs.net
- If in outpatients and there is no saved DNA, the paediatric phlebotomists will often be happy to take bloods from parents and the child at the same time, so that all three samples go together using the test order form. If inpatient, consider requesting the ward team to take all 3 samples at the same time so they can be easily linked.
- If the child has saved DNA and parent testing required, then please ask parents to either obtain a sample from their GP (EDTA 4ml), or book an appointment in adult phlebotomy:

Online Appointment Healthcare Platform | Swiftqueue (Denmark Hill)
Online Appointment Healthcare Platform | Swiftqueue
Phlebotomy - Kingsweb

- The genetic teams are happy to accept the child's test order form with parental hand-labelled blood samples providing the section "**Samples** *being sent to GLH DNA extraction lab (only required if also using this form for sample collection)"* (see appendix) has been completed.
- However, if parents attend adult phlebotomy or have bloods tested in the community, a form in each parents' name is required to get the correct blood bottle to the correct place. This needs to include the details of the parent and the child (child's NHS number, and WGS reference number if obtained), trio bloods, sample type (EDTA), and volume required (4ml). These forms are included in the PDF in step 2 if required, or at

Adobe Acrobat Document

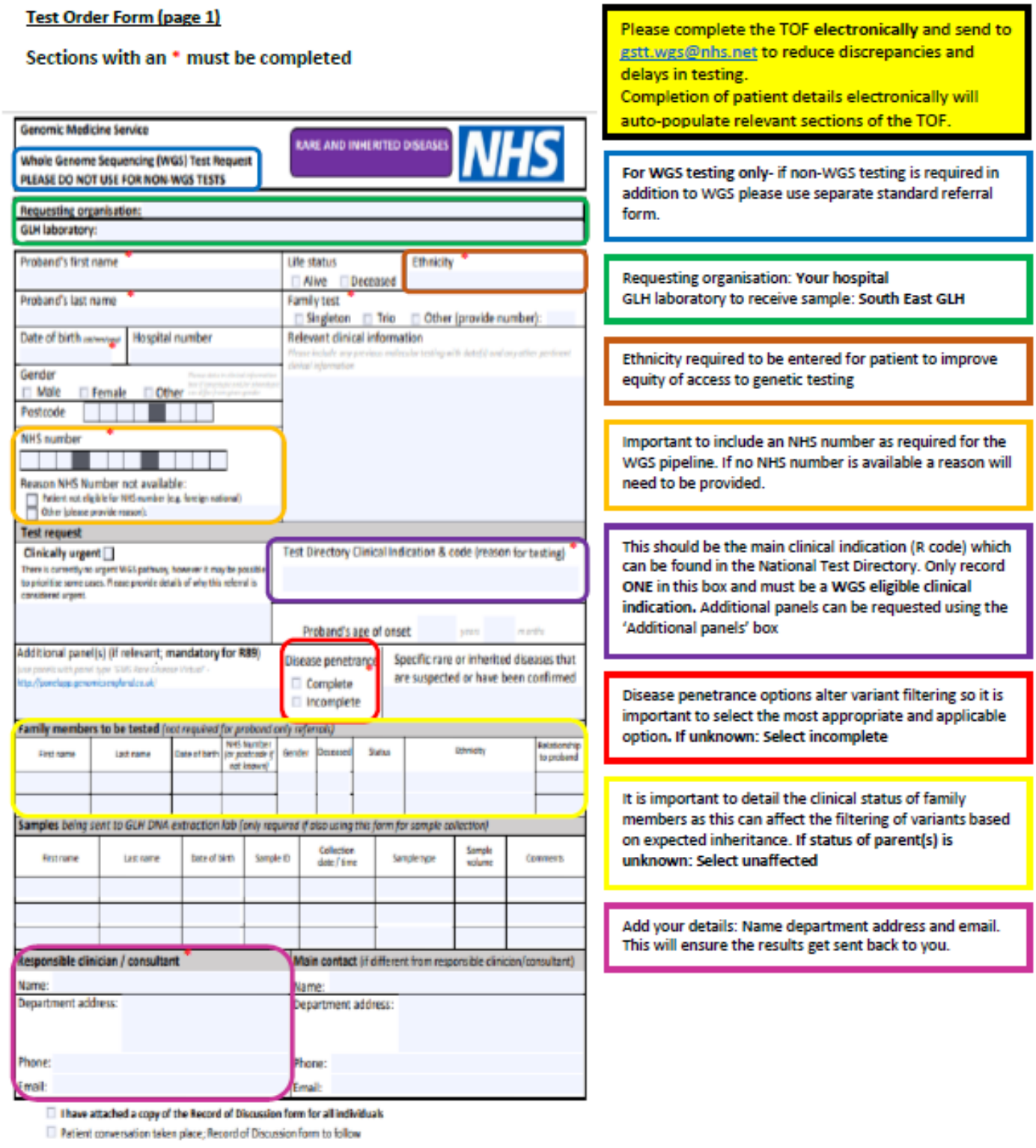
2.Rare-Disease-Test-Request-Form-editable.pdf
Test order forms - South East Genomics : South East Genomics (Test order form for Rare Diseases)
The samples need to be sent to South East GLH, Genetics Specimen Reception
5th floor Tower Wing, Guy's Hospital, London, SE1 9RT

5) **Email the WGS team**
   - Email gstt.wgs@nhs.net to provide them copies with the completed forms. Testing will not occur until all forms are received and complete. If you have completed the process correctly you should have the following:
     - 1x WGS test order form (electronically completed and emailed)
     - 3x record of discussion (printed, signed, scanned in, and emailed)
     - 3x blood samples sent to the lab (with 1x WGS test order form +/- 2x rare disease test request forms if parents samples taken separately).

6) **Results**
   - For queries, email gstt.wgs@nhs.net
   - Current turn around times are listed at https://southeastgenomics.nhs.uk/professionals/service-turn-around-times/ (see Rare Disease, Whole Genome Sequencing)

Additional Information

Professionals FAQ - Professionals FAQ - South East Genomics : South East Genomics
Information on turn-around-times can be found at - Service Turnaround Times - South East Genomics : South East Genomics
Extract from South East Genomics crib sheet below: WGS-RD-Crib-Sheet-V4.pdf



Test Order Form (page 2)

Sections with an * must be completed

Proband first name	Proband last name	Date of birth (dd/mm/yyyy)	NHS number

HPO terms are important for the analysis and interpretation of WGS data.
Please enter valid HPO terms present in the proband/family members being tested
HPO terms can be copied from the lists below

HPO Terms - Please ensure those given match those available at (https://hpo.jax.org/app/) *						
	Present	Absent	Present	Absent	Present	Absent

Intellectual disability, developmental and metabolic
Intellectual disability - mild
Intellectual disability - moderate
Intellectual disability - profound
Intellectual disability - severe
Autistic behaviour
Global developmental delay
Delayed fine motor development
Delayed gross motor development
Delayed speech and language development
Generalized hypotonia
Feeding difficulties
Failure to thrive
Abnormal facial shape
Abnormality of metabolism/homeostasis
Microcephaly
Macrocephaly
Tall stature

Craniosynostosis
Bicoronal synostosis
Unicoronal synostosis
Metopic synostosis
Sagittal craniosynostosis
Lambdoidal craniosynostosis
Multiple suture craniosynostosis

Skeletal dysplasia
Disproportionate short stature
Proportionate short stature
Short stature
Skeletal dysplasia

Diabetes
Neonatal insulin-dependent diabetes mellitus
Transient neonatal diabetes mellitus

Renal
Multiple renal cysts
Nephronophthisis
Hepatic cysts
Enlarged kidney
Renal insufficiency

Neurology
Muscular dystrophy
Myopathy
Myotonia
Fatigable weakness
Peripheral neuropathy
Distal arthrogryposis
Arthrogryposis multiplex congenita
Cognitive impairment
Parkinsonism
Spasticity
Chorea
Dystonia
Ataxia
Cerebellar atrophy
Cerebellar hypoplasia
Dandy-Walker malformation
Olivopontocerebellar hypoplasia
Diffuse white matter abnormalities
Focal White matter lesions
Leukoencephalopathy
Cortical dysplasia
Heterotopia
Lissencephaly
Pachygyria
Polymicrogyria
Schizencephaly
Holoprosencephaly
Hydrocephalus
Neurodegeneration
Dementia

Epilepsy
Seizures
Generalized seizures
Focal seizures
Epileptic spasms
Infantile encephalopathy
Atonic seizures
Generalized myoclonic seizures
Generalized tonic seizures
Generalized tonic-clonic seizures
EEG with focal epileptiform discharges
EEG with generalized epileptiform discharges
Multifocal epileptiform discharges

Cardiology
Hypertrophic cardiomyopathy
Dilated cardiomyopathy
Cardiomyopathy

Eye Disorders
Cataract
Retinal dystrophy
Macular dystrophy
Microphthalmia
Anophthalmia
Coloboma
Developmental glaucoma
Aniridia
Abnormal anterior eye segment morphology
Nystagmus

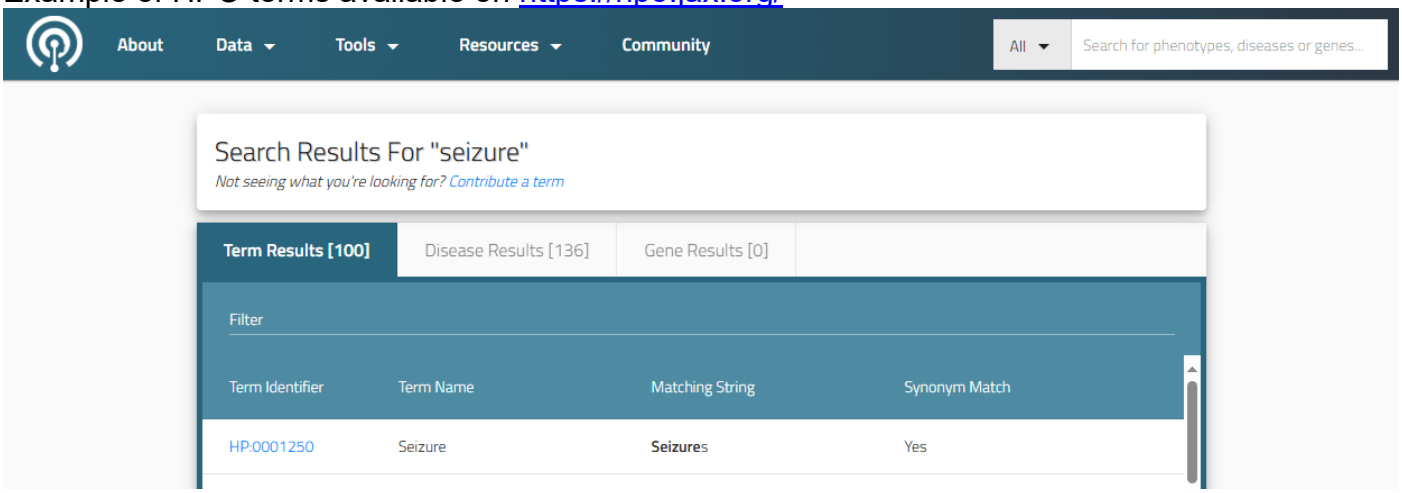
Immune Disorders
Immunodeficiency
Abnormal lymphocyte morphology
Abnormal lymphocyte physiology
Abnormal lymphocyte count
Abnormality of neutrophils
Abnormality of humoral immunity
Abnormal inflammatory response
Abnormality of complement system

Select as many specific HPO terms as possible, relevant to your patient and parents.
The more accurate the HPO terms, the more accurate the analysis and interpretation of the results.

Add HPO terms that apply to patient and tick whether these are present in proband and parents who were referred. HPO terms can be found on: Human Phenotype Ontology (jax.org)

a. We need AT LEAST ONE HPO term to be filled out – please do not leave this section blank
b. Do not abbreviate HPO terms; please write them out in full.
c. Please do not use nonstandard descriptions of HPO terms; please check on the HPO database that the HPO term you wish to record is listed.
d. There are some transcription errors of HPO terms. We should be able to pick up on most of these, but please be careful to ensure the HPO term is exactly as it appears on the database.
e. There are 10 allocated slots for HPO terms, as well as a section for additional HPO terms. Please fill in the 10 slots first before moving onto the additional section. If you need to fill in this section, please record whether the HPO term is present or absent
f. For unaffected parents, it is not necessary to record 'absent' HPO terms unless they have specifically been tested for that phenotype.

Example of HPO terms available on https://hpo.jax.org/



Monitoring & Clinical Audit

Compliance with the guideline will be monitored by clinical audit.