Genetic Units (GenUs) 2012 version: Instructions for use and table of GenU bands

The following notes are designed to ensure laboratories collect and report workload data consistently for UKGTN annual returns and NHS commissioners. Laboratories may use the GenUs system differently for internal laboratory purposes but submissions of data to UKGTN and to NHS commissioners need to adhere to the following instructions.

Next generation Sequencing (NGS). The GenUs system is not yet fully workable for measuring NGS workload. Laboratories are requested to record workload on reports that have been issued, where the assay used NGS, as a separate table and to explain the rationale for the measure they have used. This will be reviewed by the UKGTN Laboratory Membership & Audit working group and the Association for Clinical Genetic Science to develop a fair and workable measure to inform the next stage of this work. For example does the number of base pairs analysed, perhaps split into blocks such as 500bp or 1kb work? Can the preparation time be taken into consideration?

General instructions

1. **Please report only the workload directly attached to a report.**
2. Note internal transport of DNA/cell culture samples between co-located laboratories should not be counted as exports.
3. **Please use the letter which applies to the band** (A to H for molecular and A to E for cytogenetics) NOT the weight or A =1, B= 2, C = 3 etc. We understand that for convenience labs may use numbers internally but they can be misinterpreted and could lead to inequities.
4. **Haemato/oncology tests with more than a single amplicon** should be scored according to the number of amplicons.
5. **Investigations into unclassified variants** should not receive additional weightings.
6. **Failures:**
    a. A failure as a consequence of a failed laboratory process/procedure should not be counted. In these situations it is recognised that this will require some tests to be repeated in order to achieve a result. This has been factored into the unit score for each test, and this category of failed analysis does not attract any **additional** unit score for the failed element. If the failed sample has been booked in **and** processed (DNA extracted or cultures set up) then a single band A should be scored.
    b. Failures due to the inherent nature of the sample (notably marrows and tumours) should attract the same unit score as successful analyses as it is recognised that this category of failed analyses often involves considerable amounts of work.
7. **Tests on duplicate samples should NOT be scored twice**. If internal policies require a lab to test duplicate samples (eg. for HD predictives), these should not be given double the GenUs.
8. **Triplet repeats should be scored as follows**:
    a. HD, SCAs, Frax PCR, SBMA – Band B
    b. DM and FA – Band C to allow for TP PCR being routine practice for most labs.
9. **Multi-gene sequencing**. This is very difficult to score correctly and fairly. One of the underlying principles of the new scheme is that a ‘disease/service’ should, wherever possible, be in a single band. Another is that inefficiencies should not be rewarded with additional GenUs. At the present time, because of local practices, neither of these are 100% possible for diseases with multiple candidate genes. The following scoring systems are recommended with the expectation that a greater number of labs will adopt parallel sequencing in the future.
    a. Sequencing of two or more genes in parallel that are reported on a single report should be scored according to the total number of amplicons tested.

b. Sequencing of two or more genes in series should be given the additive score of the two appropriate bands.

10. **Multi-level testing**. Where possible, a disorder/service should be assigned to a single band even when multilevel testing is the routine practice, eg FH.

    In cases where there is a discrete test for a common mutation that is carried out as a pre-screen, then two bands should be assigned – one for the pre-screen and one for the full screen.

11. **MLPA as part of a gene sequencing mutation search should be regarded as two additional amplicons and the test scored accordingly.**

Clarification of specific points raised by member labs

Band A

ALL DNA extractions (inc from FFPE samples) should be scored in band A with a GenU score of 1. This score should be applied to samples that are extracted and tested locally, extraction followed by DNA banking and extraction followed by sample export. The last category, samples exported after extraction are then given another Band A for the work involved in the export. Any extractions carried out in molecular labs for cytogenetics should be counted, but should not be scored in both systems

Band B

Band B is to include single amplicon molecular diagnostic tests (including testing for somatic mutations).that have not traditionally been part of genetics, when these are performed in a molecular genetics laboratory eg.JAK2 (V617F), BRAF V600E/K, factor V, prothrombin.

Haemochromatosis, C282Y and H63D. EACH amplicon should be counted as band B.

Band C

Maternal cell contamination checks should be regarded as an *integral* part of a PND. Together these should be scored in band C.

Rapid aneuploidy testing should be scored in band C. This should allow for the urgency of the test results.

CF couple reports should be scored as 2 x band C. There is very little economy of scale when testing a couple versus two individuals.

Predictive, carrier and mutation confirmation tests that are carried out by SEQUENCING should be scored in band C. This extra weighting has been given to allow for the number of control samples that are required for such tests.

Micro Satellite Instability is in Band C

MYH – common mutations is in Band C but **full sequencing** should be recorded in the appropriate band **according to the number of amplicons**.

Connexin 26 / 30 should be in Band C

Band H

An additional band (band H with 40 GenUs has been added. This is to allow for very large numbers of amplicons in multi-gene tests.

NHS

UK Genetic Testing Network

Laboratory Genetic Units (GenUs)
October 2012
Note internal transport of DNA/cell culture samples between co-located laboratories should not be counted as exports.
Yellow shading aligns to molecular techniques and blue shading aligns to cytogenetic techniques

Band	GenU Score	General examples	Specific examples
A	1	▪ All DNA extractions to include o extract > test locally o extract > DNA banking ▪ All RNA extraction	
		▪ Sample receipt, booking in, and processing of blood sample, haematological blood/bone marrow sample, PET samples. Covers: o Sample preparation, setting up of culture(s) and processing of sample to provide a cell suspension for cytogenetic analyses, processing of PET samples for FISH ***or*** o DNA extraction and banking for molecular studies	▪ Samples processed for both Cytogenetic and Molecular Genetic Studies are considered as separate. ▪ Interpretation/undertaking segregation of results from another laboratory. ▪ Re-issue of report for sample previously tested (repeat request for same test).
A	1	▪ DNA/cell culture sample export	
		▪ Cell freezing/storage	▪ Freezing/storage in liquid nitrogen. This is a one-off charge for long-term storage.
B	2	▪ Single amplicon (genotyping or sequencing)	▪ FraX PCR ▪ Haemochromatosis ▪ Factor V ▪ Jak2 ▪ HD (diagnostic and predictive tests) ▪ Other triplet disorders where a single PCR is required (eg SBMA) ▪ Y deletions ▪ FLT3 ▪ NPM1
		▪ Sample receipt, booking in, and processing of amniotic fluid sample, CV sample, solid tissue sample, lymph node, tumour sample. Covers: o sample preparation, setting up of culture(s) and processing of sample to provide a cell suspension for cytogenetic analyses ▪ Embryo preparation of PGD analysis	
C	4	▪ Genotyping 2-4 amplicons ▪ Sequencing: Very small gene with 2-4 exons/amplicons ▪ Sequencing: Predictive tests, confirmations and carrier tests ▪ MS-PCR	▪ CF-ARMS, CF-OLA, CF-HT ▪ AS/PWS ▪ FraX if Southern blotted ▪ DM, Friedreich's ataxia

NHS

UK Genetic Testing Network

Band	GenU Score	General examples	Specific examples
		▪ MLPA with no other test (including DMD) ▪ Prenatal tests to include the MCC ▪ 1 lane on Southern ▪ Triplet disorders that require two PCRs (allele specific and TP-PCR) ▪ Aneuploidy (to include 13, 18, 21 and X/Y) ▪ Identity/paternity tests	▪ RT PCR BCR/ABL1
		▪ Direct CVS analysis ▪ Rapid aneuploidy (to include 13, 18, 21 and X/Y (QF-PCR /FISH) ▪ Simple FISH test defined as a single interpretative event using commercial probe/kit ▪ Kit based MLPA ▪ Targeted array CGH follow up studies	▪ Includes slide making/G-banding and FISH preparation ▪ Microdeletion testing ▪ Break apart probes ▪ Fusion probes (includes BCR/ABL) ▪ Post bone marrow transplant XY donor scoring ▪ Targeted array CGH follow up can be by FISH or aCGH
D	**7**	▪ Blood, Amniotic fluid, CVS culture, or Solid Tissue G-band constitutional analysis ▪ Haematological (marrow, blood, lymph node, effusion) or tumour G-band analysis	▪ Includes slide making and G-banding ▪ G-band analysis appropriate to referral reason and if necessary other conventional staining (eg C band, NOR) to aid interpretation.
E	**10**	▪ 5-19 amplicons (MLPA to count as 2 amplicons when part of full screen) ▪ All linkage tests including UPD	▪ Sequencing MECP2 ▪ DMD linkage ▪ AS/PWS if linked markers used
		▪ Array CGH (whole genome analysis) ▪ Chromosome breakage studies, eg FA, AT ▪ Combined FISH analysis of probes that must be applied and interpreted together to provide a single diagnostic/prognostic report	▪ Includes processing steps post DNA extraction. ▪ Includes SCE preparation and analysis for FA and scanning for chromosome 7 and 14 rearrangements for AT. ▪ FISH panels typically 2-4 probes e.g CLL FISH panel; most NHL FISH panels; MLL, BCR-ABL & ETV6-RUNX1applied to presentation ALL; myeloma limited to clinically relevant abnormalities.
F	**15**	▪ 20-49 amplicons (MLPA to count as 2 amplicons when part of full screen)	▪ Sequencing factor 8
G	**25**	▪ 50-100 amplicons (MLPA to count as 2 amplicons when part of full screen)	▪ Sequencing FBN1 ▪ Sequencing BRCA1+BRCA2
H	**40**	▪ Over 100 amplicons	▪ Sequencing a group of genes in parallel that contribute to a single report