Genetic Units (GenUs) 2016 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.

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 laboratories may use numbers internally but they can be misinterpreted and could lead to inequities.
4. **Investigations into unclassified variants** should not receive additional weightings.
5. **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.
6. **Tests on duplicate samples should NOT be scored twice**. If internal policies require a laboratory to test duplicate samples (eg. for HD predictives), these should not be given double the GenUs.

7. **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.

8. **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.

    All samples received and booked into the LIMS will receive a band A and will include processing through DNA extraction or cell culture. Therefore the number of band A will equal the number of samples received. The actual testing for the sample will then fall into ONE band only.

    An additional band A will be counted for long term cell storage in liquid nitrogen or cell culture for export to another laboratory only where this is the only work being carried out on the sample.

Specific points: Cytogenetics

A band A is applied to every sample that is booked into the LIMS to cover extraction or cell culture to the point that material, either DNA or cell suspension, is stored or available for analysis. Each sample that is analysed will then have ONE band only applied to it in addition to the band A for booking in. Any additional testing required to provide a clinical report is now included within the band for that test. E.g. any follow up FISH required to confirm an abnormality found by karyotype or array is included in the band and not added to the total score.

The activity associated with FISH testing has been correlated with the number of hybridisations completed in line with the number of amplicons tested. This recognises the fact that the number of FISH tests being undertaken on a sample will vary, often in line with local requirements, particularly for haematology samples. A single hybridisation may include two informative probes e.g. the ATM/TP53 combination probe would count as a single hybridisation band B.

Both postnatal and prenatal whole genome analysis can be by either karyotype or microarray. Where a rapid aneuploidy test is carried out prior to the array or karyotype this is included in the band and is not additional.

Rapid aneuploidy only testing for prenatal samples is counted as band C if it is normal. If this test is found to be abnormal and a karyotype/array is undertaken on the prenatal sample it is then counted as band E activity not band C.

Haematology/solid tumour testing has been split depending on the reason for referral this is to reflect where a full analysis is required in the case of diagnostic, relapsed or transformed samples compared to those analysed for monitoring purposes which are counted as follow up samples.

PGD embryo preparation should be counted in the band for the type of testing undertaken. Where a laboratory only prepares the embryos for testing this should be counted as band B.

Specific points: molecular

Haemato/oncology tests with more than a single amplicon should be scored according to the number of amplicons.

Triplet repeats should be scored as follows:

- HD, SCAs, Frax PCR, SBMA – Band B
- DM and FA – Band C to allow for TP PCR being routine practice for most labs.

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

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:

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

NGS. Multi-gene analysis using NGS has been allocated to Band G and H of the GenU system. However, where NGS is used as a replacement technology to sequence less than the equivalent of 50 amplicons the band assigned should be the same as the Sanger sequencing band.

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 B includes a single FISH hybridisation

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; this can be by QF-PCR or FISH

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

Laboratory Genetic Units (GenUs): 2016 Version

Note internal transport of DNA/cell culture samples between co-located laboratories should not be counted as exports

Shared activity within co-located laboratories only attracts the GenU (single band) for the shared activity

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 all sample types. 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, DNA extraction	▪ 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). ▪ Proband samples processed as a positive control for other family members
A	**1**	▪ DNA/cell culture sample export	▪ An additional A is counted for any exports only of DNA or cell cultures
		▪ Cell freezing/storage – long term liquid nitrogen storage	▪ Freezing/storage – this is a one-off charge for potentially 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
		▪ Embryo preparation of PGD analysis ▪ FISH only testing for constitutional or acquired samples with a single FISH hybridisation as the only test ▪ Follow up FISH testing for all sample types with a single FISH hybridisation as the only test	▪ Only includes preparation for testing. ▪ A single hybridisation can include two informative probes e.g. ATM/TP53 combination probe ▪ Follow up of microarray findings using a single FISH probe

Band	GenU Score	General examples	Specific examples
C	4	▪ Genotyping 2-4 amplicons ▪ Sequencing: Very small gene with 2-4 exons/amplicons ▪ Sequencing: Predictive tests, confirmations and carrier tests ▪ MS-PCR ▪ 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) ▪ Identity/paternity tests	▪ CF-ARMS, CF-OLA, CF-HT ▪ AS/PWS ▪ FraX if Southern blotted ▪ DM, Friedreich's ataxia ▪ RT PCR BCR/ABL1
		▪ Direct CVS analysis ▪ Rapid aneuploidy testing for +13, +18 and +21, X/Y (QF-PCR FISH) ▪ Follow up testing all sample types by karyotype, FISH, MLPA, targeted array and FISH (if 2-4 hybridisations) ▪ Kit based MLPA ▪ FISH only testing for constitutional or acquired samples with 2-4 FISH hybridisations	▪ Includes slide making/banding and FISH preparation for all probe types ▪ Parental follow up samples: any method NB. proband sample acts as a positive control ▪ E.g. CLL FISH panel ▪ Haematology monitoring samples included as follow up
D	7	Postnatal constitutional whole genome screen by karyotyping or array analysis without a rapid aneuploidy pre-screen includes. This includes any additional conventional staining or FISH tests requested/required including confirmation of array findings, if required, for the proband	▪ Includes slide making and G-banding and processing steps post DNA extraction. ▪ Covers blood and solid tissue referrals ▪ 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 by Sanger or NGS ▪ DMD linkage ▪ AS/PWS if linked markers used
		▪ Prenatal constitutional whole genome screen by karyotyping or array analysis without a rapid aneuploidy pre-screen includes any additional conventional staining or FISH tests requested/required including array confirmation for the proband ▪ Postnatal constitutional whole genome screen by karyotyping or array analysis including a rapid aneuploidy pre-screen test. This includes any additional conventional staining or FISH tests requested/required. Includes confirmation of array findings, if required, for the proband	▪ Includes SCE prep and analysis for FA, and scanning for chromosome 7 and 14 rearrangements for AT. ▪ Transformed/relapse category includes those where a full analysis on the sample is required. ▪ Postnatal covers blood and solid tissue referrals ▪ Includes long term culture, slide making and G- banding and processing steps post DNA extraction

Band	GenU Score	General examples	Specific examples
		▪ Chromosome breakage studies, eg FA, or AT ▪ Diagnostic, transformed or relapsed Haematological (marrow, blood, lymph node, effusion) or tumour whole genome screen by karyotyping or array analysis includes any additional conventional staining or FISH tests requested/required. ▪ Haematological FISH only testing 5-19 hybridisations	▪ Rapid aneuploidy testing for +13, +18 and +21, X/Y (QF-PCR FISH)
F	**15**	▪ 20-49 amplicons (MLPA to count as 2 amplicons when part of full screen)	▪ Sequencing factor 8 by Sanger or NGS
		▪ Prenatal constitutional whole genome screen by karyotyping or array analysis including a rapid aneuploidy pre-screen test. This includes any additional conventional staining or FISH tests requested/required. Includes confirmation of array findings, if required.	▪ Includes long term culture, slide making and G- banding and processing steps post DNA extraction ▪ Rapid aneuploidy testing for +13, +18 and +21, X/Y (QF-PCR FISH)
G	**25**	▪ 50-100 amplicons (MLPA to count as 2 amplicons when part of full screen)	▪ Sequencing FBN1 ▪ Sequencing BRCA1+BRCA2
		▪ 1-50 genes analysed by NGS	▪ Sequencing 12 genes for Noonan Spectrum Disorders
H	**40**	▪ Over 100 amplicons	▪ Sequencing a group of genes in parallel that contribute to a single report
		▪ 51-500 genes analysed by NGS	▪ Sequencing 105 genes for Retinal Degeneration