# Establishment of a unit to measure test activity to serve as a common currency in a genetics laboratory network

Running Title**:** **Common activity currency for genetic tests**

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**Abstract**

Laboratory activity is measured for many reasons. These include trend analysis, comparing activity between providers, commissioning and performance management. Challenges in this area include determining suitable units of measurement, establishing equivalence between similar tests, data collection, changing technology and relating activity to cost. Methods used to measure activity in genetics have previously been based on simplistic counting of samples, reports, requests and staff time. Here, a simple system was devised based on weighted bands for molecular genetic laboratory activities. Over the past six years this has been used by laboratories within the UK Genetic Testing Network, extended to cytogenetic test activities and monitored through a number of national audits and quality assessment schemes. The band units (GenU) also have potential for use in costing and have been used by some participants for contractual arrangements. The measure of activity remains consistent but the price per unit may be differentially calculated for different sections of work and updated in line with changing costs. It has proved to be a relatively robust, practical, and effective means of monitoring workload that also serves as a common currency for use in a genetic testing network.

**Introduction**

Genetic testing services for inherited disorders in the United Kingdom are generally organised on a regional or national basis that reflects the relatively rare and specialist nature of the investigations. These services operate as part of an informal national NHS network.

A measure of laboratory work is needed to act as an accepted standard for measuring activity, allow comparison of the same activity and of equivalent inter- and intra-laboratory activities and be suitable for use in contracting purposes. This in turn facilitates resource management,

benchmarking of service provision, performance management and equity of access to network services. The system should promote efficiency, be robust and future proof, easy to implement and monitor, transparent, link to best clinical practice and relate to funding mechanisms. Measures historically used include simple counts of sample, reports, test or request numbers and the Welcan labour units.

The specific challenges associated with genetic tests and associated pre- and post-analytical activities are that they vary considerably in complexity and in the volume of individual activities. Significant numbers of samples (10%) may be for storage only; others may undergo multiple tests over several years, and some activities may require multiple sample types or family members. For this reason a simple count of sample number is a poor indicator of laboratory activity. Likewise, reports may vary from the result on a single PCR fragment size through to sequence analysis of 500 genes. Counting tests requires a definition of the components that fall within the activity. Similarly, counting requests can be problematic when reflex testing, which may result in different levels of investigation, is involved. In 1986 a system for weighting clinical laboratory procedures was devised, based on the relative staff input time[1]: one Welcan unit was equal to one minute of technical, clerical or aide time. An average cost could then be applied based on average staff costs and batch size. The strengths and weaknesses of this approach for Clinical Biochemistry have been well reviewed[2]. Key issues concern the identification and recovery of all costs, both direct and indirect, distinction between manual and more automated versions of analyses and the relatively poor correlation with a full costing system. Over the past 20 years a number of different methods for measuring molecular genetic test activity have been used. A workload system was introduced in 2004 based on the principles of the Welcan system. This was not applied consistently and in 2007 the UKGTN initiated a working group to develop a new measure of genetic testing activity in order to compare work load across the Network laboratories. This was required

urgently for molecular genetics because of the expansion in the volume and repertoire of tests and rationality for these to be offered on a Network basis. It was proposed that the new measure should also take into account the relative complexity of a test in addition to the time taken and be adaptable for introduction of new technologies.

**Material and Methods**

A working group including key molecular genetic laboratory and commissioning stakeholders was convened in 2007 to devise a new system based around the patient report as a transparent measure of activity, with each report assigned to one of a number of weighted bands according to its complexity. Initial work was undertaken to determine the number of bands needed.

For the first main study six bands (A-F) were used that were evaluated against five different models of numerical weighting. The weighting was based on the number of amplicons analysed, consumable costs and the complexity of the analysis. For example band A, with a unit weight of one, covered DNA extraction and storage. Band B with a unit weight of two covered a single amplicon. Where a test could be undertaken by equivalent methods that fell in different bands, it was allocated to the lowest to promote efficiency. Most investigations could be easily classified and consensus was sought where necessary.

By multiplying the number of reports in each band by the weight of that band and summing the results, a value (initially termed Molecular Units – MolUs) was obtained representing total reportable laboratory activity. To assess the impact on costs, the total laboratory expenditure (staff costs, consumables, maintenance, capital charges, quality assurance,

institutional overheads etc.) was divided by the total number of MolUs to derive a notional 'cost per MolU'. From this the price of any particular test could be calculated by multiplying the price per MolU by the band weight of that test.

Following acceptance of the scheme for molecular activity it was expanded to include cytogenetics. Units were assigned to activities by a combined approach of aligning common activities such as aneuploidy screening, conversion of existing measures and consideration of relative complexity.

**Results**

The results of 12 months' data from six representative molecular genetic laboratories under the five different weighting models were presented at a national meeting. See summary in table one below. This showed that models 3 and 4 produced test prices that provided the greatest consistency between the different providers.

Following acceptance of the methodology, all UKGTN member laboratories agreed to participate in a larger study using the most recent data. Cytogenetic tests were also included and the units renamed as Genetic Units (GenUs). The results of this data collection led to some further refinement and recognition of the need to review the scheme on an annual basis. These are incorporated into the published schemes[3,4] the latest of which is presented below. Recent revisions have largely related to accommodating parallel screening of much larger gene panels and further refinement of certain cytogenetic tests reflecting the relative immaturity of the scheme for this subspecialty

To assess consistency in scoring reports, laboratories submit the unit-level data for scrutiny as part of the annual ACGS activity audit, which collects test-level data by reports and units and to the UKGTN audit that collects number of reports by weighted band. The results of these data collection exercises show that laboratories have generally correctly allocated the number of units in accordance with the published scheme for their test repertoire and volume.

Annual UK external quality assessment schemes for Genetics Laboratories analyse a collection of three clinical cases for each disease or clinical scenario for which a service is provided, affording an ideal opportunity to quality-check the use of workload units at individual report level. Results have been reviewed for both molecular genetics and cytogenetic schemes. In the few instances where discrepancies arose the reasons were explored with the individual laboratories and additional clarification was provided. For example, for postnatal constitutional microarray, only one of 19 participants scored differently to the published band D because of undertaking an additional test.

**Discussion**

The use of a weighted banding system for measuring genetic test activity has been found to be a relatively simple and adaptable means to standardize data collection and allow comparison of laboratory activities. Assuming the test weight is set correctly, the process also drives efficiency since laboratories delivering most units from the lowest cost base will have a lower cost per unit (GenU). The correct use of units can be monitored through audits and external quality assurance. Joint management by key stakeholders, UK Genetic Testing Network and Association for Clinical Genetic Science, ensures it remains fit for purpose. Laboratories are required to seek a band allocation for any new test activity and reference this on their application for UKGTN approval as an NHS commissioned service.

The units can be converted to a cost per unit either on a total or sub-laboratory level. Despite concerns in the initial costing exercise about variation in what operational costs different laboratories included, the overall laboratory cost per unit across each of the UK Molecular Genetics Laboratories was similar (table 1). However it should be noted that these may not reflect external market prices because costs are generally spread across a mixed work load, and volumes of individual tests are generally similar between providers. Under a different, more consolidated service model this arrangement may change but it should be possible to apply internal adjustments for example by calculating different unit costs per test area.

No conflict of interest

**References**


1. National Hospital Productivity Improvement Program. Canadian workload measurement system laboratory. A Schedule of unit values for clinical laboratory procedures. 1986-87 Edition, Toronto, Ontario. Laboratory Workload Measurement Secretariat
2. Tarbti IF. J Clin Pathol 1990:43:92-97. Laboratory costing system based on number and type of test; its association with the Welcan workload measurement system.
3. ACGS Activity and Genetic Unit Data. http://www.acgs.uk.com/committees/quality-committee/acgs-activity-datagenus/
4. UKGTN Reports on GenUs http://ukgtn.nhs.uk/our-work/ukgtn-reportsguidelines/genetic-units-genus/

**Figure Legends**

Table 1 Modelling (2008)

Table 2. Laboratory Genetic Units (GenUs): 2016

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

| Model | Band | Weight | min £ | max £ | Average £ | SD |
|---|---|---|---|---|---|---|
| 1 | A | 1 | 23 | 62 | 39 | 4 |
| | B | 2.5 | 58 | 155 | 97 | 33 |
| | C | 3.5 | 79 | 186 | 125 | 36 |
| | D | 12 | 278 | 743 | 451 | 166 |
| | E | 36 | 835 | 2230 | 1392 | 479 |
| | F | 75 | 1739 | 4646 | 2900 | 999 |
| 2 | A | 1 | 23 | 53 | 36 | 10 |
| | B | 2.5 | 56 | 133 | 89 | 26 |
| | C | 4 | 186 | 214 | 190 | 16 |
| | D | 12 | 271 | 637 | 427 | 123 |
| | E | 36 | 813 | 1910 | 1282 | 370 |
| | F | 40 | 1694 | 3978 | 2671 | 771 |
| 3 | A | 1 | 41 | 53 | 47 | 4 |
| | B | 3 | 124 | 160 | 142 | 12 |
| | C | 4 | 166 | 214 | 190 | 16 |
| | D | 10 | 415 | 534 | 474 | 39 |
| | E | 15 | 622 | 801 | 711 | 59 |
| | F | 20 | 829 | 1068 | 948 | 78 |
| 4 | A | 1 | 34 | 49 | 41 | 5 |
| | B | 3 | 103 | 145 | 122 | 15 |
| | C | 4 | 137 | 194 | 162 | 21 |
| | D | 12 | 412 | 583 | 487 | 62 |
| | E | 20 | 687 | 971 | 812 | 103 |
| | F | 40 | 1374 | 1942 | 1623 | 206 |
| 5 | A | 1 | 30 | 48 | 38 | 6 |
| | B | 3 | 89 | 144 | 114 | 19 |
| | C | 4 | 118 | 192 | 152 | 25 |
| | D | 12 | 355 | 577 | 455 | 75 |
| | E | 25 | 739 | 1202 | 949 | 156 |
| | F | 50 | 1478 | 2424 | 1898 | 313 |

Table 1

| Band | GenU Score | General examples | Specific examples |
|---|---|---|---|
| **A** | **1** | ▪ All DNA extractions to include<br>o extract > test locally<br>o extract > DNA banking<br>▪ All RNA extraction | |
| | | ▪ Sample receipt, booking in, and processing of all sample types. Covers:<br>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.<br>▪ Interpretation/undertaking segregation of results from another laboratory.<br>▪ Re-issue of report for sample previously tested (repeat request for same test).<br>▪ 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<br>▪ Haemochromatosis<br>▪ Factor V<br>▪ Jak2<br>▪ HD (diagnostic and predictive tests)<br>▪ Other triplet disorders where a single PCR is required (eg SBMA)<br>▪ Y deletions<br>▪ FLT3<br>▪ NPM1 |
| | | ▪ Embryo preparation of PGD analysis<br>▪ FISH only testing for constitutional or acquired samples with a single FISH hybridisation as the only test<br>▪ Follow up FISH testing for all sample types with a | ▪ Only includes preparation for testing.<br>▪ A single hybridisation can include two informative probes e.g. ATM/TP53 combination probe<br>▪ Follow up of microarray findings using a single FISH probe |

| Band | GenU Score | General examples | Specific examples |
|---|---|---|---|
| | | single FISH hybridisation as the only test | |
| **C** | **4** | ▪ Genotyping 2-4 amplicons<br>▪ Sequencing: Very small gene with 2-4 exons/amplicons<br>▪ Sequencing: Predictive tests, confirmations and carrier tests<br>▪ MS-PCR<br>▪ MLPA with no other test (including DMD)<br>▪ Prenatal tests to include the MCC<br>▪ 1 lane on Southern<br>▪ Triplet disorders that require two PCRs (allele specific and TP-PCR)<br>▪ Identity/paternity tests | ▪ CF-ARMS, CF-OLA, CF-HT<br>▪ AS/PWS<br>▪ FraX if Southern blotted<br>▪ DM, Friedreich's ataxia<br>▪ RT PCR BCR/ABL1 |
| | | ▪ Direct CVS analysis<br>▪ Rapid aneuploidy testing for +13, +18 and +21, X/Y (QF-PCR FISH)<br>▪ Follow up testing all sample types by karyotype, FISH, MLPA, targeted array and FISH (if 2-4 hybridisations)<br>▪ Kit based MLPA<br>▪ FISH only testing for constitutional or acquired samples with 2-4 FISH hybridisations | ▪ Includes slide making/banding and FISH preparation for all probe types<br>▪ Parental follow up samples: any method NB. proband sample acts as a positive control<br>▪ E.g. CLL FISH panel<br>▪ 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.<br>▪ Covers blood and solid tissue referrals<br>▪ G-band analysis appropriate to referral reason and if necessary other conventional staining (eg C band, NOR) to aid interpretation. |

| Band | GenU Score | General examples | Specific examples |
|---|---|---|---|
| **E** | **10** | ▪ 5-19 amplicons (MLPA to count as 2 amplicons when part of full screen)<br>▪ All linkage tests including UPD | ▪ Sequencing MECP2 by Sanger or NGS<br>▪ DMD linkage<br>▪ 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<br>▪ 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<br>▪ Chromosome breakage studies, eg FA, or AT<br>▪ 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.<br>▪ Haematological FISH only testing 5-19 hybridisations | ▪ Includes SCE prep and analysis for FA, and scanning for chromosome 7 and 14 rearrangements for AT.<br>▪ Transformed/relapse category includes those where a full analysis on the sample is required.<br>▪ Postnatal covers blood and solid tissue referrals<br>▪ Includes long term culture, slide making and G- banding and processing steps post DNA extraction<br>▪ 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 | ▪ Includes long term culture, slide making and G- banding and processing steps post DNA extraction<br>▪ Rapid aneuploidy testing for +13, +18 and +21, X/Y (QF-PCR FISH) |

| Band | GenU Score | General examples | Specific examples |
|---|---|---|---|
| | | requested/required. Includes confirmation of array findings, if required. | |
| **G** | **25** | ▪ 50-100 amplicons (MLPA to count as 2 amplicons when part of full screen) | ▪ Sequencing FBN1<br>▪ 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 |

Table 2.