

CMGS Workload Units : Proposed Scheme

<u>Procedure</u>	<u>Total WLUs</u>
Specimen handling	
Inappropriate referral	20
Sample reception and booking-in	10
Exporting sample	20
DNA Extraction	
ProteinaseK / phenol-chloroform	32
Salting-out	16
Automated / "Kit" / Direct (e.g. "boiled")	8
OD quantitation	6
Analysis	
• <u>Simple PCR 1</u>	35
PCR (single or multiplex) → Direct analysis (agarose) → UV-visualisation → Analysis (e.g. ARMs analysis, multiplex analysis)	
• <u>Simple PCR 2</u>	45
PCR (single or multiplex) → Direct analysis (polyacrylamide) → EtBr staining → UV-visualisation → Analysis → Silver-staining → Analysis → Autoradiography → Analysis → Direct analysis on Genescanner → Analysis → Direct analysis on DHPLC → Analysis (e.g. STRs, SSCP, Heteroduplex, WAVE)	
PCR (single or multiplex) → RE digestion → Electrophoresis (agarose) → UV-visualisation → Analysis	
• <u>Complex PCR 1</u>	65
(1) → PCR (single or multiplex) → (2) → Electrophoresis (PAGE, agarose or Genescanner) → Analysis Where additional steps 1 or 2 included (1) = Pre-PCR treatment e.g. Bisulphite PCR (2) = Post-PCR treatment e.g. PTT analysis, OLA	
• <u>Complex PCR 2 (Dosage)</u>	
Multiplex PCR → post-PCR purification → Electrophoresis (Genescanner) → Matrix analysis	
• <u>Sequence analysis</u> (per sequence primer for all methods of analysis)	
PCR → Check gel → Purify → Sequence reaction(s) → (Purify) → Electrophoresis → Detection → Analysis	
Known sequence change	110
Unknown sequence change	160
• <u>Southern analysis</u>	70
RE digest → Electrophoresis (agarose) → Blot → Probe-labelling / Hybridisation → Autoradiography → Analysis	
Reporting	
• Simple report (e.g. DNA bank, CF, FraX, simple linkage)	15
• Medium report (e.g. Simple risk, linkage & pedigree)	30
• Complex report (e.g. Complex risk, complex linkage, novel mutation)	60

CMGS Workload Units : Rules

A workload unit (WLU) represents the laboratory and administrative operations completed in a minute. The WLUs assigned to the procedures described have been calculated following time and motion studies by the Scottish Laboratories. The Scottish laboratories and the GOS (North Thames East) laboratory are now using these units for all procedures and therefore have validated the units assigned. WLU breakdowns are available for all individual operations and have been used to calculate banded WLU scores for routine molecular genetic procedures (as described.) The WLU “Toolkit” can be applied to any new procedures or to modifications of existing procedures (or to any we have missed out!) Details of any procedures not included should be submitted to the audit sub-committee for WLU assignment.

The total WLUs for an analysis report may be calculated by the addition of the WLUs of the procedures executed (sample reception , DNA extraction, analysis and report.) The CMGS audit committee aim to replace the Genotype with WLUs in the annual data collection process.

DNA Extraction

As duplicate samples received for predictive / pre-symptomatic analysis will be extracted separately, the WLU score should be doubled accordingly. Similarly, if a prenatal sample is extracted as two aliquots, the extraction WLU score should be double accordingly.

Analysis

- Six sets of analysis procedures have been compiled in which procedures requiring similar WLUs have been grouped (banded.) Variation within analysis groups is unavoidable by this method, but reduces the need for multiple WLU scores which are less easily audited and communicated (both locally for purchasers, and nationally.) A maximum WLU for each set of procedures is assigned for each analysis type. This is necessary to group sets of similar procedures and accommodates differences in batch size and the number of controls used.
- WLUs for the six types of analysis have been calculated for a **minimum batch size** including appropriate controls (i.e. positive, normal and water.) The analysis of samples in larger batches does not lead to sufficiently lower WLU scores to alter the WLU band assigned. (The alternative assignment of WLUs to samples per batch leads to different scores for the same analysis, which is obviously confusing for the service purchaser.)
- **Controls should not be included in the WLU score for a sample (as for genotypes.)** An analysis will have the same number of controls unrelated to the number of test samples. (As above, inclusion of a WLU score particular to the number of controls used leads to different WLU scores for the identical analysis of samples analysed in different sized batches.) The banded nature of the analysis groups should accommodate the use of a limited variation in the numbers of controls. The WLU factor for controls has been estimated specifically for each analysis group.
- **Samples requiring repeat analysis (due to failure) should only be assigned WLUs for the reported result.** The WLUs for failed analyses will continue to be audited nationally (and locally, presumably.)

- **WLUs for development work** should be collected separately and will continue to be audited annually.
- A PCR represents a single analysis tube, the products of which are analysed on a single track of a gel. Therefore, an ARMs reaction (2 tubes) will generate twice the number of WLUs.
- The WLU score for a sequencing reaction represents sequence analysis from a single primer (e.g. forward reaction only) and includes the initial amplification of the PCR product to be sequenced. The WLUs associated with the PCR component of sequence analysis have been calculated assuming that the majority of sequencing templates are sequenced in both directions.
- For those samples analysed in duplicate (e.g. pre-symptomatics / prenatals / dosage) the WLU score for all relevant procedures should be double accordingly.

Reports

Simple report: Report requiring little explanation, no risk analysis, and no literature review, usually resulting from direct mutation analysis for a known mutation.

- e.g. CF diagnostic report (positive or negative.)
 FraX diagnostic report (positive or negative.)
 HD, SCA's, FA, HCT, DM, AS, PWS, DMD/BMD deletion...
 (DNA banking report.)

Medium report: Report requiring simple explanation of risk analysis or linkage analysis, and/or pedigree drawing.

- e.g. Simple Bayes calculation for familial CF mutation.
 Simple DMD risk calculation and pedigree.
 Recurrence risks in AS/PWS.
 "Grey area" expansions for HD.
 Pre-mutations for FraX.

Complex report: Report requiring extensive risk or linkage analysis, and/or pedigree drawing. Report following identification of novel mutation (requiring literature review.)

- e.g. Extended Bayes calculation.
 Risk analysis requiring MLINK.
 Novel missense mutation.