

## CMGS Workload Units Scheme 2004-05 (v1.1)

PROCEDURE PREPARATION	TOTAL WLUS
<b>Specimen handling</b>	
Inappropriate referral	20
Sample reception and booking-in	10
Exporting sample	20
<b>DNA Extraction</b>	
ProteinaseK / phenol-chloroform	32
Salting-out	16
Automated / "Kit" / Direct (e.g. "boiled")	8
Fixed tissue extraction	45
RNA extraction – kit	30
RNA extraction – manual	45
Pulsed-field block preparation	45
Storage of tumour samples	30
OD quantitation	6
<b>ANALYSIS</b>	
1. Real-time PCR (No gel)	25
2. Simple PCR 1	35
PCR (single or multiplex) → Direct analysis (agarose) → UV-visualisation → Analysis (e.g. ARMs analysis, IVS8 polyT, multiplex analysis NOT including Elucigene CF29 kit)	
3. Simple PCR 2 (e.g. STRs, SSCP, Heteroduplex, WAVE, single RED)	45
PCR (single or multiplex) → Direct analysis (PAGE) → EtBr staining → UV-visualisation → Analysis	
Silver-staining → Analysis	
Autoradiography → Analysis	
Direct analysis on Genescanner → Analysis	
Direct analysis on DHPLC → Analysis	
PCR (single or multiplex) → RE digestion → Electrophoresis (agarose) → UV-visualisation → Analysis	
4. Complex PCR 1 (INCLUDING all 4 tubes for Elucigene CF29 kit)	65
(1) → PCR (single or multi) → (2) → Electrophoresis (PAGE, agarose or Genescanner) → (3) → Analysis	
Where additional steps a, b or c include:	
(a) = Pre-PCR treatment e.g. Bisulphite PCR, RT-PCR	
(b) = Post-PCR treatment e.g. PTT analysis, OLA, multiple REDs	
(c) = Post-electrophoresis blotting / hybridisation	
5. Complex PCR 2 (Dosage by QF-PCR, MAPH or MLPA)	120
Multiplex PCR → post-PCR purification → Electrophoresis (Genescanner) → Matrix analysis	
6. Sequence analysis (per sequence primer for all platforms)	
PCR → Check gel → Purify → Sequence reaction(s) → (Purify) → Electrophoresis → Detection → Analysis	
Known sequence change	110
Unknown sequence change (apply to both directions if bidirectional)	160
7. Southern analysis	110
RE digest → Electrophoresis (agarose) → Blot → Probe-labelling / Hybridisation → Autoradiography → Analysis	
<b>REPORTING</b>	
1. DNA Banking	10
2. Simple report (Using report template)	15
3. Complex (Requiring additional analysis/interpretation post-data checking)	60
Urgent prenatal analysis	Add 50% to total reception/extraction, analysis and reporting WLUs
Urgent mutation analysis during pregnancy for potential PND	ditto
Urgent predictive analysis	*Add 50% to total reception/extraction, analysis and reporting WLUs
Urgent mutation analysis for gene therapy	Add 50% to total reception/extraction, analysis and reporting WLUs
* applied per report not per replicate samples on the same report	

**Other urgent categories only as approved by Steering group (contact via NorbuG@gosh.nhs.uk)**

## CMGS Workload Units : Guidelines

A workload unit (WLU) represents the laboratory and administrative operations completed in a minute. WLU breakdowns are available for all individual operations and have been used to calculate banded WLU scores for routine molecular genetic procedures. The WLU "Toolkit" can be applied to any new procedures or to modifications of existing procedures. Details of any procedures not included or urgency factors should be submitted to the Audit sub-committee for WLU assignment.

Medium through-put (plate format, multi-channel pipettes) apply  $\frac{1}{4}$  factor to appropriate analytical WLUs  
High through-put (plate format, robotic liquid handling) apply  $\frac{1}{10}$  factor to appropriate analytical WLUs

**The total WLUs for an analysis report is calculated by the addition of the WLUs of the all procedures executed (sample reception , DNA extraction, analysis and report.) If more than one analysis is performed the analysis score is multiplied appropriately:**

Eg. DHPLC analysis of 20 fragments with subsequent sequence analysis for one fragment would accumulate a total analysis score of  $(20 \times 45 \text{ DHPLC analysis}) + (2 \times 160 \text{ unknown sequence change}) = 1220 \text{ WLU}$

The total score for a blood sample received for this analysis resulting in a complex report would be:  $(10 + 32 \text{ sample reception /DNA extraction}) + (1220 \text{ analysis}) + (60 \text{ report}) = 1322$

**The total WLU may usefully be recorded on the patient's report for subsequent auditing purposes. WLUs will be audited by disorder (for CMGS annual audit), by Health authority or PCT (for local activity) and by NEQAP**

*The total WLUs per staff WTE (regardless of grade) for a year is 82,500. This represents approximately 50% total working time, accounting for time spent on non-WLU-generating activities such as development, training, audit, administration, seminars...etc.*

### Specimen Handling / DNA Extraction

- A sample will acquire a sample reception / booking-in score regardless of the sample type (blood, DNA or other.)
- Inappropriate referrals should include samples requiring phone calls to establish referral reason, referring consultant, mislabelled tubes, inadequate or eligible request information. It also includes the re-issue of mislaid reports.
- Samples for referral to another laboratory acquire WLU scores for sample reception + sample referral + banking report (if it is local practice to issue a report at this stage.)

### Analysis

- **The analysis WLU score includes time taken in interpreting and checking of raw data.**
- Seven 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 group 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 seven 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.** An analysis batch 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.
- However, in the case of **linkage analyses**, WLUs for all samples and all markers analysed should be calculated for the reported analysis. Subsequent familial analyses should only include WLUs for individuals not previously tested and for previously identified informative markers only.

- **Samples requiring repeat analysis (due to failure) should only be assigned WLUs for the reported result.** A failure rate factor has been incorporated into each procedural band score.
- WLUs should be totalled for all negative results including mutation screening analyses (eg. WAVE analysis)
- **WLUs for development work** should be collected separately and will continue to be audited annually as part of the CMGS audit.
- 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 (2x35 = 70). **EXCEPT for Elucigene CF29 analysis where the complex PCR 1 score of 65WLU should be used as a total for all 4 tubes.**
- 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. No distinction is made between manual, ALF and ABI methods. The sequence analysis score should be selected according to whether the sample is being screened for a unknown change, requiring significant appraisal (WLU = 160) or for a known change, where the nucleotide involved is easily identified (WLU = 110).
- Urgent tests: Where two samples are received for (eg) predictive, CVS fronds, the request will be subject to a 1.5 factor with respect to urgency and each replicate prep should not be attributed additional WLUs where they are included on the same report.

### Reports

Reporting categories have been simplified from previous versions of the WLU scheme to reduce the subjectivity of application of report WLUs. **Note the "30" level was withdrawn in 2003/4**

- DNA Banking
- Simple report  
For all reports where a format is available & will include;
  - analysis for known mutations
  - situations where no mutation is detected
  - premutations for FraX
  - standard couple reports for CF
- Complex report  
Non standard reports requiring additional preparation & will include
  - additional data searches
  - evaluation of cryptic splice site
  - Novel risk calculation
  - pedigree drawing
  - evaluation of likely pathogenicity

### **Urgency**

Should only be applied to the approved situations – any other scenarios should be referred to the steering group

Mutations screen during pregnancy for possible prenatal diagnosis but **excluding CF screening because of fetal echogenic bowel**

Eg DMD mutation/linkage analysis for possible prenatal diagnosis

Mutation screen of immuno deficiency genes for possible gene therapy

**Replicate samples for predictive tests on the same report** – eg HD PST should score

[reception/extraction/OD (eg 32) + simple PCR (45) plus simple reports (15)]x1.5 for a **single sample** even if replicates are used (either true or pseudo)

Only if replicates are extracted, analysed and reported completely separately should they be scored as such.

## Appendix: WLUs for common procedures for core disorders

The WLUs assigned for the following core disorders represent values for commonly performed procedures. If they do not appear to reflect the local practice, guidance should be sought from the steering group so that the guidelines can be revised as appropriate to ensure consistency and standardisation.

### DNA Banking

Sample reception (10)+ DNA extraction + (Banking letter [10] if local practice)

### Referrals

Sample reception (10)+ DNA extraction + (Banking/Export letter [10] if local practice) + Export (20)

### AS / PWS

Southern analysis Reception / extraction + Southern analysis (110) + Simple report (15)

Bisulphite analysis Reception / extraction + Complex PCR 1 (65) + Simple report (15)

### Breast cancer

BRCA1 negative Reception / extraction + 60x[Simple PCR 2 (45)] + Simple report (15)  
(by DHPLC of 60 fragments)

BRCA1 positive Reception / extraction + 60x[Simple PCR 2 (45)] + 2x[Sequence analysis (160)] +  
(for novel missense by DHPLC of 60 fragments) Complex report (60)

### CF

- CF29 Reception / extraction + Complex PCR 1 (65) + Simple report (15)
- CF31 Reception / extraction + Complex PCR 1 (65) + Simple report (15)
- CF 29/31& polyT Reception / extraction + Complex PCR 1 (65) + Simple PCR (35) + Simple report (15)
- CF31 (PND + maternal contamination by multiplexed STRs)  
1.5x [Reception / extraction + Complex PCR 1 (65)  
+ Simple PCR 2 (35) + Simple report (15)]

### DMD / BMD

Multiplex analysis Reception / extraction + 2x Simple PCR 1 (=70) + Simple report (15)

Dosage analysis Reception / extraction + 2x Complex PCR 2 (=240) + Simple report (15)

### FraX

PCR analysis / PAGE Reception / extraction + Simple PCR 2 (45) + Simple report (15)

Southern/PCR analysis Reception / extraction + Simple PCR 2 (45) + Southern analysis (110)  
+ Simple report (15)

Southern x 2 /PCR reception / extraction = 45 + (2 x 110) + 15 = 280

### Huntington's (Diagnostic)

PCR analysis / PAGE Reception / extraction + Simple PCR 2 (45) + Simple report (15)  
(one primer set)

PCR analysis / PAGE Reception / extraction + 2x Simple PCR 2 (=90) + Simple report (15)  
(both primer sets)

### Huntington's (Presymptomatic) per report (irrespective replicate/split samples)

- 1.5 [PCR analysis / PAGE + Reception / extraction + Simple PCR 2 (45) + Simple report (15) ]

### HMSN / HNPP

• STS Dosage analysis Reception / extraction + Complex PCR 2 (120) + Simple report (15)

• STR Dosage analysis Reception / extraction + N x Simple PCR 2 (=N x 45) + Simple report (15)  
(Where N = no. of reactions)

### SCA1, 2, 3, 6 & 7

- PCR analysis / PAGE Reception / extraction + 5 x Simple PCR 2 (=225) + Simple report (15)