Proposed Units of Activity/Currency Measurement for Cytogenetic Samples in NHS Diagnostic Cytogenetics Laboratories.

A Report to the Joint Medical Genetics Committee

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Proposal

NHS Cytogenetics Laboratories should adopt a common system of 13 core currencies with relative values as listed in Table 1, to be used for future Contracting processes. These have been designed to take into account current working practice, ease of collecting data within laboratories and the need to incorporate likely new tests; they should be applicable to > 97% of diagnostic samples. It is appreciated, however, that due to variations in specimen mix and local priorities these relative weightings cannot reflect all current circumstances in all laboratories. Likewise, some will alter with time due to changing technology. Attention is drawn to areas which may be particularly sensitive to such effects in the text. It is suggested that a suitable review process is put into place to monitor the effectiveness of these currencies and their relative values and to modify them where necessary.

N.B. FISH analyses have been divided into three main categories in the first instance, plus a specific currency for AneuVision screening and similar techniques. This approach was chosen to allow for future developments to be incorporated into the proposed system.

Sources of Information.

The timescale for this exercise precluded the collection of data specific to this report. Data has been drawn from a variety of existing sources including:

- unit costs for different sample types currently used by 24 NHS laboratories for contracting purposes and/or charging for private samples - this data was summarised in 'Laboratory Services for Genetics, August 2000: Report of an expert working group to the NHS Executive and the Human Genetics Commission' - data has been re-analysed to excluded 2 laboratories which do not have a differential rate for different specimen types/tests
- consensus relative workload units produced following London Regional Heads of Laboratories Meetings, December 2000
- the prices charged for comparable diagnostic analyses in private cytogenetic laboratories in the UK, Europe and the USA
- consensus data from Trent Laboratories for 1998
- personal experience from the Newcastle, Kennedy-Galton, Nottingham and other Laboratories

A summary of most of these data is included in Table 2. It should be made clear that it has not been possible to establish the absolute comparability of data derived from all of these sources. In particular, private laboratories will operate under different financial pressures and the figures available will not take into account factors such as offsetting costs between sample categories for commercial reasons.

General Principles

1. The currencies and their relative values have been designed for use in regional or large sub-regional laboratories with a broad case mix in line with current national patterns. For smaller and specialist centres (mainly Haematology/Malignancy Laboratories), some currencies will not apply

and some adjustment of the relative values of the remainder may be necessary if the case mix within any currency is atypical.

2. It is assumed that the laboratory is CPA Accredited, or at a standard equivalent to this status, operates within the Professional Standards guidelines as designated by the Association of Clinical Cytogeneticists and complies with current performance guidelines of UK NEQAS in Clinical Cytogenetics.

3. Each currency will contain a mixed caseload of referrals which will require different cell analysis patterns, with the need for additional conventional staining techniques or other handling steps (e.g. cell storage or onward transport to other centres for DNA analysis) in an appropriate number of cases. These effects have been taken into account in setting relative values of currencies.

4. Each currency is designed to be applied to the total number of specimens received. Within certain currencies there may be a small number of samples which are not processed e.g. because an earlier sample has been received and reported (voids), or are rejected because of inadequate specimen quality, or fail to produce a complete analysis. The latter consideration applies particularly to analysis of pregnancy losses and to a lesser extent malignancy samples. An allowance has been made for the reduced work involved with these samples in the proposed relative values of currencies. It has assumed that laboratories will strive to minimise void samples and that overall culture/analysis failure rates fall within the normal range reported through NEQAS.

5. FISH analyses will include those which are specifically requested by clinicians, those initiated by the laboratory based on current 'good practice' for certain referral categories, plus those necessary to follow-up abnormal findings on conventional staining. It is considered essential that laboratories are in a position to initiate appropriate FISH analysis in the latter two circumstances without having to re-contact the referring clinician, but it is also essential that laboratories are applying 'good practice' at all times and are not creating unnecessary work.

6. Currencies for FISH and chromosome breakage syndromes are additional to those given for the specimen type. (see Currencies 8 and 13 for examples of this)

7. An allowance for associated molecular tests, such as UPD and methylamine studies, has not been included in the proposed currencies.

Proposed Currencies

1) Blood samples, value 1.0 unit

This group covers all urgent and non-urgent postnatal and all prenatal referrals. An allowance has been made for the variation in numbers of standard cultures which need to be set up for different

referrals (particularly neonatal and prenatal samples) and for the additional staining techniques (excluding FISH) which will be required for some cases.

Comment - Within this group, neonatal and prenatal referrals have a higher inherent workload content and it may be appropriate to separate this group at some time in future.

2) Amniotic Fluid samples - full cytogenetic analysis, value 1.3 units

Includes an allowance for additional work-up of mosaic cases.

3) Chorionic Villus samples - analysis of cultured cells only, value 1.4 units

Includes an allowance for work-up of mosaic cases; UPD testing has not been included.

Comment - It was considered that CVS involved slightly more work than an amniotic fluid due to the importance of cleaning up the initial specimen and the higher percentage of cases where mosaicism will need to be investigated.

4) Chorionic Villus samples - analysis of both direct preparations and cultured cells, value 2.1 units.

Includes an allowance for work-up of mosaic cases; UPD testing has not been included. An allowance has been made in the relative value given for the small number of cases (<10%) which will not produce a result from direct preparations. Where it is laboratory policy to apply both direct and culture techniques to all samples, these latter cases should not be reassigned to currency category 3.

Comment - There is some considerable variation in how much analysis of direct preparations is being undertaken in different laboratories and how this is being reported. A typical figure of adding about 50% to costs has been used.

N.B. No figure has been given for Chorionic villus samples analysed by direct preparations only, as this does not fall within Professional Guidelines.

5) Solid tissues, value 1.4 units

This group will include a significant number of cases where no result is obtainable but which still incur considerable workload and expenditure on consumables. An allowance has been made for limited local cell banking of selected chromosomally abnormal cases and others; an estimate for the current levels of expense related to documentation of foetal samples and safe onward transport to Pathology Departments or return to Hospitals of origin has also been included. Any future changes in legislation in this latter area will affect the proposed relative value. Additional work such as routine cell banking of larger categories of referrals, photography of foetuses etc., has not been included.

Comment - It was considered that as solid tissues involve cleaning up of the initial specimen that the currency would be equivalent to that of CVS cultured cells only. It is appreciated that there is considerable variation in local policy for processing foetal samples which may affect the applicability of the proposed relative value in individual laboratories.

6) Haematology samples, value 2.5 units
(includes investigations of lymph nodes and infiltration of bone marrow in other malignant conditions)

There will be considerable variation in the workload and costings for different referral groups within this currency, some samples requiring detailed analysis of 20 or more cells, whereas others (such as for transplantation follow-up) are often essentially screens for sex chromosomes only. A typical referral pattern from both children and adults has been assumed. An allowance has been made for the levels of interpretation which is required for a high percentage of haematological cases, which will be reflected in the skill mix of staff undertaking this work. It may be desirable to subdivide this currency in the future, particularly to provide a more sensitive costing mechanism for smaller units concentrating on Malignancy cytogenetics.

Comment - In general, the work was considered to be a bit more complex than a full CVS analysis, particularly because of the extra interpretation required in many cases.

7) Tumour tissue, value 3.0 units

The proposed relative value for this currency is for the typical pattern of referral to laboratories, i.e. primarily childhood solid tumours such as neuroblastoma, Ewing's, rhabdomyosarcoma; it is unlikely to be appropriate for laboratories where the case mix is atypical. It should be treated as a guideline only, as local practices vary considerably. Currently, these specimens do not fall within NEQAS. Some cases will involve a considerable amount of work and expense without producing a useful result.

8) Simple FISH analysis, value +0.7 units per test.
This includes 0.2 units related to the capital costs of large items of dedicated equipment.

This currency includes analysis based on commercially available probes for single microdeletions, two colour sexing, fusion probes and similar for malignancies, single chromosome paints, single centromeric probes and subtelomeric probes for single chromosomes. It also includes prenatal aneuploidy screening for single chromosomes only. An allowance has been made for the high cost of capital equipment related to FISH analysis (also applies to all other FISH currencies).

N.B. The relative value assumes that full cytogenetic analysis has already been or will be performed on the same sample and that suitable fixed cells are available for FISH analysis. For example, full chromosome analysis of a blood sample (1.0 unit) plus one simple FISH test (0.7 units) equals 1.7 units, full chromosome analysis of a bone marrow sample (2.5 units) plus two simple FISH tests

(2x0.7 units) equals 3.9 units. This same method of calculation applies to all simple, intermediate and complex FISH analyses in any combination.

9) Intermediate FISH analysis, value +3.0 units per test.
This includes 0.3 units related to the capital costs of large items of dedicated equipment.

Includes Octochrome type test and others falling between the extremes more fully defined in the Simple and Complex categories.

10) Complex FISH analysis, value +5 units per test.
This includes 0.5 units related to the capital costs of large items of dedicated equipment.

Includes simultaneous telomere screening of all chromosomes using multi-telomeric probe devices, mFISH/SKY and CGH. These are all developing areas and the proposed relative values will be highly sensitive to individual laboratory throughput and changes in the costs of reagents and capital equipment.

11) Aneuploidy (AneuVision) screening using FISH, value 1.1 units.
This includes 0.3 units related to the capital costs of large items of dedicated equipment.

The relative value of this currency is based on AneuVision kits for chromosome 13, 18, 21, X and Y aneuploidies, but would apply to any similar combination of probes which can be analysed simultaneously. Part of the relative value reflects the price of reagent kits, which may change in future. It has been assumed that the laboratory is processing sufficient numbers of samples to achieve substantial economies of scale. See Simple FISH analysis for aneuploidy screening for single chromosomes only.

12) Aneuploidy screening using PCR, value to be developed

This recently introduced service is only available in certain centres and accurate costing is not possible at present. Currently available, *published* data suggests that if the full cost of large items of dedicated equipment is included, the cost of providing this service in individual laboratories is similar to that of FISH-based techniques (see currency 11). However, unpublished data derived from the experience in London suggests that organisation at a multi-centre level, coupled with major investment in items of high-throughput capital equipment, may provide significant long-term savings. It is proposed that the value of this currency should be developed based on the accumulating experience of the London multi-centre study, the feasibility of a multi-centre approach outside London and the value being developed for comparable techniques in Molecular Genetics.

13) Breakage syndrome analysis, value +1.5 units per test

It is assumed that the same sample will be undergoing full cytogenetic analysis. This currency is additional and will include Fanconi's anaemia, AT and Bloom syndrome. Some laboratories may be sending samples for these and rarer breakage syndromes to other centres (including non-NHS centres) for analysis. For these laboratories, it may be more appropriate for contracts to be based on the actual charges which will be incurred.

N.B. The relative value for additional breakage syndrome testing should be calculated on the same basis as for additional FISH analysis, e.g. full chromosome analysis of a blood sample (1.0 unit) plus AT testing (1.5 units) equals 2.5 units.

Table 1 - Proposed Currencies and Relative Values

	Currency	Samples/Tests covered	Value
1	Blood	All samples	1.0
2	Amniotic Fluid	All samples	1.3
3	CVS - culture only	All samples	1.4
4	CVS - culture and direct	All samples	2.1
5	Solid tissues	All samples	1.4
6	Haematology	Blood/bone marrows in leukaemias, lymph nodes, infiltration of bone marrows related to solid tumours	2.5
7	Tumour tissue	Current referral patterns	3.0
8	Simple FISH	Each additional single test procedure requiring a single interpretational step. See text for examples. Includes prenatal aneuploidy screening for a single chromosome	+0.7*
9	Intermediate FISH	See text for examples	+3.0*
10	Complex FISH	mFISH/SKY, CGH, multi-telomere probes	+5.0*
11	Prenatal aneuploidy screening by FISH	Screening for aneuploidy of several chromosomes using AneuVision kits or similar	1.1
12	Prenatal aneuploidy screening by PCR	PCR based approaches equivalent to currency 11	see text
13	Breakage Syndromes	Each additional syndrome tested	+1.5*

* Assumes that full chromosome analysis has been covered under a separate currency and that for FISH tests, fixed cells are available for analysis.

Table 2 - Summary of data used to derive relative values of currencies*

	Currency	NHS/HGC data	London consensus	Trent consensus	Private Laboratories			Proposed
					1	2	3	
1	Blood	1.0	1.0†	1.0	1.0	1.0	1.0	**1.0**
2	Amniotic Fluid	1.4	1.0†	1.5	2.0	1.3	1.0	**1.3**
3	CVS - culture only		1.2†	1.5		1.3	1.2	**1.4**
4	CVS - culture and direct	2.1	1.7†	2.5	2.0			**2.1**
5	Solid tissues	1.4	1.2†	1.0	2.0	1.3	1.2	**1.4**
6	Haematology	2.0	2.5†	3.0		2.0	1.2	**2.5**
7	Tumour tissue			3.0				**3.0**
8	Simple FISH	+1.1	+0.5†	+1.0	+1.0	+0.7		**+0.7**
9	Intermediate FISH							**+3.0**
10	Complex FISH		+3.5†					**+5.0**
11	Prenatal aneuploidy screening by FISH		0.5†					**1.1**
12	Prenatal aneuploidy screening by PCR		0.5†			1.2		**see text**
13	Breakage Syndromes		+1.5†	+1.5				**+1.5**

* See text for details.

† **Workload data only** - excludes consumable, capital and overhead costs.