Response To:


By

The Royal College of Pathologists

The Royal College of Pathologists (RCPPath) is a professional membership organisation with charitable status, concerned with all matters relating to the science and practice of pathology. The total membership is almost 8600, of which over 6600 are based in the United Kingdom. Fellowship (denoted by the letters FRCPPath) is obtained either by examination, by submission of published research work or by invitation of Council. College Fellows work mostly in hospitals, universities and industry. Our Fellowship includes several Nobel Laureates.

The main specialties of pathology that the College represents are Clinical Biochemistry, Cytopathology, Dermatopathology, Clinical Embryology, Forensic Pathology, Genetics (both Molecular and Cytogenetics), Haematology, Histocompatibility and Immunogenetics, Histopathology, Immunology, Medical Microbiology, Metabolic Medicine, Neuropathology, Oral Pathology, Paediatric Pathology, Toxicology, Transfusion Medicine, Veterinary Pathology and Virology.

The aims of the College relevant to this response are to:

• advance the science and practice of pathology, and
• promote research in pathology and disseminate the results.

The ways in which the College does this include:

• setting standards for and overseeing the education and training in pathology
• setting standards of practice and organising workplace-based assessments and examinations
• monitoring workforce statistics and the appointment of pathology consultants
• updating our members via scientific meetings and symposia
• ensuring and monitoring a programme of continuing professional development for members and non-members
• developing and publishing guidelines on aspects of best practice
• maintaining standards of practice by promoting audit and quality assurance in pathology disciplines, and supporting accreditation for all pathology laboratories
• funding research, in association with industry and other partners in science
• advising Government departments, national organisations, medical and academic bodies on all matters relating to pathology
The constitution of the College includes a Specialty Advisory Committee (SAC) for each discipline, as well as a number of Joint Committees, where, for example, direct clinical care include both clinical and laboratory components, e.g. genetics, immunology and haematology. Many of these committees will be making their own responses to this consultation.

The terms “in house” and “home brew” have been applied to tests developed by individual laboratories, as opposed to those tests developed by industry. In this submission, the College prefers the term “Laboratory Developed Tests” (LDT), as used in the United States.[ref: Association for Molecular Pathology’s Comments at the FDA/CDRH Public Meeting: Oversight of Laboratory Developed Tests July, 2010]

The College considers that quality (which includes safety) in all aspects of pathology is essential, and quality is best maintained by a variety of measures, only one of which is the quality control of reagents, kits, equipment and softwares produced by industrial manufacturers. As well as training, examination, qualifications and personal professional registration of individuals, the College considers the accreditation of laboratory services to defined, objective and measurable standards to be one of the most important. In this respect would be meant accreditation to EN ISO 15189:2007 “Medical laboratories — Particular requirements for quality and competence”.

The College has been a component part of the structure of Clinical Pathology Accreditation UK Ltd (CPA) since its inception in 1993. CPA adheres to EN ISO 15189:2007, and in 2009 was absorbed into the UK Accreditation Service (UKAS).

Accreditation by CPA to EN ISO 15189:2007 necessarily means that all tests provided by such a medical laboratory are based on scientific evidence, have been validated as to their performance and are performed in the setting of a Quality Management System (including both internal Quality Control (QC) and External Quality Assurance (EQA)). This would also include a necessity to maintain constant vigilance as to test performance, scientific advances, and audit. In the UK, external Quality Assurance schemes are themselves provided by accredited services (the various National External Quality Assessment Schemes (NEQAS)).

In addition, CPA accreditation also necessitates adherence to professional guidelines, such as those produced by the RCPPath, as well as various other professional bodies. This also helps to ensure the availability of safe, effective, appropriate, and patient-oriented tests.

Thus, whether such accredited laboratories choose to provide services based on tests developed by manufacturers, or their own LDT, patients and their clinicians can be assured that the result is clinically valid, safe, reliable and reproducible.

If a manufacturer should wish to offer tests based on its own reagents or kits, for example, then so long as it should do this through an appropriately accredited laboratory (which may be its own), i.e. in the UK accreditation by CPA to EN ISO 15189:2007, then the RCPPath would consider that this satisfies the requirements of upholding safety and quality standards.

The College also believes that any regulatory systems should not interfere negatively with the practice of medicine, but should enhance it. Any requirement that requires more time and expense, without significantly improving quality, is thus a disbenefit. This is especially the case within the confines of relatively fixed resources.

The College welcomes all measures to improve regulation, so long as these measures improve the outcome of medical practice. If there are aspects of laboratory accreditation which may be improved then these should be introduced, but increasing such requirements over existing measures must be carefully considered in terms of cost and benefit.

LDT are an essential and central component of medical practice. Laboratory professionals who perform such tests have a critical role in working with other clinicians to provide services to patients. LDT are frequently the way by which laboratory medicine advances the overall practice
of medicine, hence any barriers or impedance to test development would seriously negatively impact on medicine. Without LDT, major advancements in the diagnosis and management of inherited diseases, as well as a wide range of cancers, would not have been possible. Also, genetic LDT account for the vast majority of genetic tests which are available, for both diagnosis and prediction of risk in those liable to inherited diseases. They are also used to monitor the clinical course of leukaemia – indeed, bespoke LDT applicable only to specific individuals are absolutely essential in managing many cases of this disease. These are but a few examples of the hundreds of types of LDT available. Without such tests, the practice of medicine would be severely reduced in scope, to the detriment of patients.

The Royal College of Pathologist’s responses are thus based on these principles.

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QUESTIONNAIRE

1. Classification

Question 1:

- Would you consider the adoption of a **risk-based classification** for *in vitro* diagnostic medical devices as an improvement of the current European regulatory framework?

The RCPath supports the adoption of a risk-based classification *in principle*, for example, as the UK Human Genetics Commission has argued in *Genes Direct/More Genes Direct* and their *Principles for Direct-to-consumer genetic testing services*. It is important, however, that for laboratory developed tests (LDT), using non-CE-marked reagents, developed by and used in laboratories accredited to EN ISO 15189 (such as conferred by CPA(UK) Ltd), there is not an unnecessary requirement for CE marking. In effect, accreditation of a laboratory means that any tests it performs are carried out to defined and high standards, equivalent to (and arguably better than) CE marking.

- Are you aware of any **consequences** for the protection of **public health**?

A risk-based classification would allow for graded application of regulations, but a requirement for CE-marking of all LDT would seriously negatively impact in many areas, including, for example, tests needing to be developed quickly in response to clinical threats, such as new infectious conditions, or urgent situations where individuals might require bespoke analyses that can only be provided by LDT.

- Can you provide **economic data** linked to a change-over to this GHTF classification system?

The RCPath does not envisage any negative economic impact, so long as hospital-based testing is not compromised by a necessity for using CE-marked reagents in LDT. If, however a necessity for CE-marking should be brought in, it would put at risk a considerable proportion of the approximately 28,000 staff employed in UK clinical laboratories.

In monetary terms, newborn screening laboratories provide one specific example. Here, a necessity to use CE-marked reagents would increase costs in a typical NHS region (~3M population) by >£250k (~£6.2m pa for all UK) with no foreseeable public health benefit, indeed the extra costs within a fixed budget would amount to a disbenefit. Across the UK the increased costs for newborn screening for phenylketonuria (PKU) and medium-chain acyl-CoA dehydrogenase deficiency (MCAD) would alone amount to £2.5m pa.

2. Conformity assessment procedure

Question 2:
In the context of a possible adoption of a **risk-based classification** according to the **GHTF model** (see above 1.) do you see a need for amending the current conformity assessment procedures for *in vitro* diagnostic medical devices?

No. Given that laboratory accreditation ensures quality and safety, in part through the combination of within-laboratory validation of LDT as part of their overall Quality Management System (including internal Quality Control (QC) and External Quality Assurance (EQA)). It is mandatory that CPA (UK) Ltd., responsible for external laboratory accreditation in the UK, are notified when new tests are introduced and that evidence of validation is provided. Hence, if risk-based classification is adopted such validation by accredited laboratories would ensure conformity. Laboratories offering LDT would, of course, require to be accredited (to EN ISO 15189).

**Question 3:**

If yes, in your view which are the **conformity assessment procedures** that should be **deleted or amended** and **why**?

**Question 4:**

Would you consider [it] appropriate to **require for all IVDs**, except for those in class A of the GHTF classification, at least the **pre-market control** of the manufacturer's **quality management system** by a third party as laid down in GHTF/SG1/N046:2008?

If all clinical genetic testing is performed by laboratories accredited to EN ISO 15189, effective checking and quality control will be carried out by them anyway, so this extra checking would be superfluous.

**Question 5:**

In the context of the "**batch release verification**", do you consider that a **control of each batch** of manufactured **high-risk IVDs** should be required prior to their placing on the market?

Yes. Changes or differences in reagents can lead to critical changes in test performance characteristics, e.g. specificity and sensitivity. All accredited laboratories test all batches of reagents (CE-marked or not) and monitor their performance as part of their internal Quality Management, to ensure the highest standards are maintained.

If yes, what would be the **purpose of batch release verification** and which IVDs should be subject to such a control?

Batch by batch variation in reagents may cause critical, clinically significant, differences in test performance. This is well described in all laboratory disciplines, but, for example, it is recognised in immunology with tests supporting diagnosis of autoimmune or allergic disease, and in haematology with tests for coagulation, which impacts on Warfarin dosing for patients. Any IVD involved in clinical care should be subject such controls. As stated above, in effect, reagents used in LDT by accredited laboratories are subject to batch by batch quality control.
UK RCPath IVD Response

If yes, **how** (testing, verification of the results of the tests) and **by whom** (manufacturer under the control of notified bodies, notified bodies, independent laboratories) these controls should be performed?

Any reagents or tests kits produced by manufacturers should be subject to the same quality standards that accredited laboratories demand of themselves. The principles of EN ISO 15189 should apply.

**3. Scope**

**Question 7:**
Would it be necessary **to maintain** the exemption provided for by article 1(5) of Directive 98/79/EC and why?

Yes. It is essential to maintain the exemption provided for by article 1(5) of Directive 98/79/EC for the following reasons:

1. **Clinical Risk**

If it should not be possible to use non-CE marked reagents in LDT, then the diagnosis of many conditions would not then be possible, which would bring with it increased clinical risk. In haematology, for example, this would have a major impact on the diagnosis of leukaemias and lymphomas. Similarly, in histopathology there are some 200 different immunohistochemical tests for specific markers, most of which are used in the diagnosis and monitoring of cancers, both rare and common. In such cases, without these tests the risk is that an incorrect diagnosis would be made and as a consequence the incorrect or inappropriate treatment would be given.

2. **Rare Disease testing**

Tests for rare diseases (conditions affecting not more than 5 in 10,000 persons in the EU) are inherently carried out less often than tests for common conditions. Although a few conditions in this category are common enough that commercial production of IVDs for them is viable (e.g. cystic fibrosis), the vast majority of rare disease tests will only ever be available from specialist centres. CE marking of every test offered in such centres is scientifically and financially impractical. It is certainly in the interest of patients to ensure that all such testing is carried out within an appropriate quality framework, but a requirement for CE marking would result in the loss of most rare disease testing.

It also needs to be borne in mind, that while, for example, genetic diseases may be individually rare, overall they account for a significant burden of disease, of the order of 5% of all medical conditions, and more so amongst patients receiving secondary care. In one study of paediatric care, 71% of admissions had a significant genetic component. McCandless SE, Brunger JW, Cassidy SB. The burden of genetic disease on inpatient care in a children's hospital. *Am J Hum Genet.* 2004 Jan;74(1):121-7.

In the UK in 2008-09 postnatal genetic testing was provided for over 400 disorders. Over 300 of these (74%) had a test volume of fewer than 100. Only 16 (4%) had a test volume of greater than 1000. The likelihood of any commercial provider supplying CE marked kits for such low volumes is small. There is therefore little evidence in the UK to support the claim of unfair competition between CE marked devices and LDT.

3. **Customised tests**
In some leukaemias, for example, there is a need to provide LDT based on the specific mutations which have been acquired by that patient. It is unfeasible to expect this to be provided by industrial manufacturers.

Many inherited disorders are quite common (for example, inherited forms of breast cancer may account for ~5% of all cases), but the underlying mutations are individually rare, and indeed are often unique and so confined to a single patient or family. In such circumstances, each mutation may require a specially-designed genetic test (and one that may need to be developed urgently, e.g. in a prenatal situation). It is entirely impractical to CE-mark a test that is used for a single family or a very small group of patients. To do so would arguably amount to discrimination against those at risk of rare inherited disorders and would also be at odds with the Commission’s own rare disease initiative.

4. Cytogenetics and other whole-genome tests

Conventional karyotyping involves the culture of cells from the test subject and the examination of chromosomes using a microscope. It is one of the main genetic tests (approx. 150,000 tests per annum in the UK). As the appearance of the chromosomes is exquisitely sensitive to the stage of cell division reached at the time the cell culture is stopped, the test and its interpretation is unique for each patient and even for each cell observed. There is no prospect of such a test meeting the requirements for CE-marking (although specialist reagents employed may themselves be considered IVDs).

Modern technologies for whole-genome analysis (e.g. microarray-based comparative genomic hybridisation) are replacing karyotyping. Such testing is changing rapidly, and is not amenable to CE-marking. Hence, it is most appropriately carried out in specialist laboratories accredited to perform and interpret the results of such testing. Indeed the very development of this important new aspect of laboratory genetics necessitates laboratories having the freedom to develop LDT.

5. Seldom-used tests for common analytes

While CE-marked assays may be available for commoner diagnostic tests (although they are frequently more expensive than equivalent LDT), particular circumstances, including unexpected results from CE-marked tests, will require the application of less frequently-used tests to confirm or supplement the primary test. Although applied to commoner conditions, such tests may not be applied with sufficient frequency to create a viable market for a commercial assay. The exemption for in-house tests ensures their availability.

6. Rapid response to changes in test requirements

In recent years we have seen the rapid emergence of global health threats from infectious agents such as SARS, Influenza H5N1, H1N1 etc. Such outbreaks require the rapid development and deployment of new assays for detection, monitoring and vaccine development. It would not be possible to implement such testing in the time-scale required if each new assay had to go through the CE marking process.

7. Population-specific tests and test panels

The frequencies of mutations which cause inherited disorders vary dramatically between populations within the EU and even within individual countries in the EU. A CE-marked assay may be appropriate to one population, but entirely unsuited to another population or sub-population. Industry will develop test panels suited to the most frequently-tested populations (in the case of Cystic Fibrosis this usually means the United States), leaving other populations disadvantaged, unless local specialist laboratories are able to develop appropriate LDT suited to the population being served.
8. The safety provided through the process of external accreditation and alternatives in test methodology

When a single CE-marked assay (sometimes protected by patent) dominates the market for testing for a particular target or analyte, any systematic deficiency or weakness of that assay may go undiscovered, as alternative methods are not available to confirm the results of the dominant assay. Examples of this have been seen in the external quality assessment schemes run by the European Molecular Genetics Quality Network.

While harmonisation of test standards and comparability of results are very desirable, the RCPPath considers it more important that overall laboratory quality is maintained by accreditation. Expert professionals should be able to develop LDT, within the quality management systems already in place in accredited laboratories. There is considerable value, indeed safety, in having a variety of different LDT available for the same condition: test results using one assay can be cross checked by another, not liable to the same biases and interferences. Hence, it is essential that a variety of methods are available and in regular use for each assay or test. Specialist reference laboratories, applying their validated in-house developed tests, play an important role in this regard.

9. Economic risks

If, especially specialist, testing within the EU should be restricted because of a requirement for CE marking of all reagents, softwares and equipment used in LDT, then patients and their clinicians would be obliged to obtain such tests from laboratories outside of the EU.

This poses several additional risks:

a. tests obtained from outside the EU may well be operating in less rigorous quality and accreditation environments;

b. patients and healthcare systems would be liable to higher costs for tests, because of reduced competition and availability – a "sellers market";

c. the loss of highly skilled technical, scientific and medical jobs within the UK (and EU) associated with specialist laboratories, which would also impact on research in academia (including that students from outside the EU would no longer seek education within the EU);

d. the loss of considerable income to the UK (and EU), because of the loss to the worldwide community of tests currently only available in the UK (and EU);

e. the loss of scientific prestige, influence and resources from the UK (and EU).

The RCPPath considers that the perceived risks posed by 'non CE marked' LDT are theoretical, and are better addressed by implementation of appropriate quality assurance systems which include assay validation and laboratory accreditation based on EN ISO 15189:2007. Abolition of the exemption, resulting in the non-availability of specialist testing, would certainly be harmful to patients; it is also arguably discriminatory against those individuals who warrant having such testing.

Question 8:
If the exemption provided for by article 1(5) of Directive 98/79/EC should be clarified or limited, which of the following items you would consider as appropriate in order to clarify the scope of this exemption and ensure a high level of safety:

Item 1:
Better **define the concepts** of "in-house test", "health institution", “premises of a manufacture or premises in the immediate vicinity”. Could you suggest an appropriate definition for these terms?

**“In-house test”**

As discussed, the term “Laboratory Developed Test” (LDT) is preferred to “In-house test”. By LDT is meant those tests developed and validated within the quality management system of an accredited laboratory, where all reagents are inherently subjected to internal quality control (QC), and the tests themselves are assessed where possible by external quality assessment (EQA) (to have EQA schemes for all genes/mutations would be unfeasible).

**“Health Institution”** should mean any organisation whose primary purpose is healthcare, rather than a commercial for profit company providing a service to a healthcare setting.

As, in the RCPath’s view, the exemption should continue to apply only to health institution laboratories, and such laboratories come under the regulatory supervision of the national authority, which is a Member State competence, then quality and safety are assured. Thus, the RCPath suggests this definition: “A Health Institution is a body whose primary purpose is the care and/or promotion of public health. Such a body may comprise a single institution at one location or a network of institutions with a shared governance structure.”

The definition of “Premises of a manufacture or premises in the immediate vicinity” should recognise that what is important for the maintenance of patient safety and quality is to have in place adequate systems of clinical governance. This is assured by accreditation of laboratories. Where laboratories are organised in networks, and accredited as networks (which in itself improves standardisation), it does not matter that individual facilities may not be physically close. Because the laboratories are accredited as a network, with a common governance structure (itself a condition of accreditation to EN ISO 15189) then safety and quality are assured.

**Item 2:**

Require that all "in-house tests" fulfill the **essential requirements** of the Directive 98/79/EC, **without being subject to a CE marking**?

No. Requiring LDT to fulfil the essential criteria even without formal CE marking would still place an unacceptable burden on laboratories, as in effect these would amount to duplication of the requirements of EN ISO 15189.

**Item 3:**

Require that all **high risk** "in-house tests" are **excluded from the exemption** provided for by article 1(5) of Directive 98/79/EC and then have to fulfil the essential requirements of the Directive 98/79/EC including the involvement of a notified body?

No. Many of the most important tests for patients with rare diseases, such as newly emerged infectious agents and pre-symptomatic genetic testing, might be classified as high risk. Likewise, newly emerging infectious agents may pose a significant risk to the population. It is of utmost importance that specific tests are developed in a timely manner in order to monitor and control spreading of new infectious agents. Any delay in the development of LDT for these by competent specialist laboratories would, therefore, bear a higher risk than a non-CE-marked test. If they were thus to be excluded from the exemption they would cease to be provided, which would have adverse effects on individuals, families and populations with or at risk of these conditions.

Exclusion of high risk LDT from the exemption would result in them becoming unavailable and thus would pose a substantial risk to families with rare or new diseases. “Protecting” patients by
excluding some tests from the exemption may therefore have the opposite effect to that desired, placing those patients at increased risk because no test is available.

**Item 4:**
Submit the health institutions and premises referred to in Article 1(5) of Directive 98/79/EC that manufacture "in house tests" to **accreditation**, based on ISO 15189, or **equivalent regulation** at national level?

Yes. The restriction of the ‘in-house’ exemption to laboratories which are accredited to ISO 15189 or equivalent would provide appropriate quality and safety for patients who rely on these tests. Given that in general these are rare disorders, this proposal provides a proportionate response which balances the risks and benefits.

*It should be noted that the ISO definition of accreditation should be used and should not be confused with certification or licensing, neither of which provide the same assurance of quality and competence.*

Please indicate one or more items that you would consider as appropriate while explaining why you consider these items as appropriate and providing data where possible. In case you consider none of these items as appropriate or if there are, in your opinion, other options that are appropriate please indicate them.

**Question 9:**

If the exemption provided for by article 1(5) of Directive 98/79/EC **should not be maintained**, would you consider it necessary to **exempt in vitro diagnostic medical devices** intended for **diagnosis and monitoring of diseases or conditions affecting not more than 5 in 10,000 persons in the European Union** from the scope of the IVD Directive and, if yes, why?

No. Patients with rare diseases deserve the same quality of diagnostic testing as those with more common conditions. To remove the LDT exemption except for rare diseases would discriminate against those suffering from those conditions. This is in direct contradiction of the EC initiative on improved services for rare diseases.

In addition, such an exemption would allow the marketing of test kits for rare diseases with no regulatory oversight to ensure their quality, suitability or effectiveness. These kits could thus be used in laboratories not expert in their use or interpretation of the results putting families with rare diseases at risk. Accreditation would be a much better way of ensuring quality and patient safety.

Retention of the LDT exemption with the safeguard of its use only in accredited laboratories provides security, assurance of a high quality test and equity of access for those with rare disorders. In addition, the rarity of a disorder depends to some extent on the population and a rare disease in one country may be relatively common in another.

Removal of the LDT exemption would not just affect the availability of rare disease tests but also other types of specialized test where no CE marked test is available and this would do nothing to preserve those tests for patients.

If, as in the RCPPath’s opinion, the exemption for in-house tests is retained, but restricted to laboratories accredited to EN ISO 15189 (see answer to Question 8 and Item 4 above), then this provides for the availability of testing for rare diseases through **Centres of Expertise** as envisaged in the **Council of The European Union Recommendation** on action in the field of rare
3.2 Genetic tests

The interpretation of the scope of Directive 98/79/EC is that only genetic tests that have a medical purpose are covered by this Directive, e.g. prenatal diagnostic tests, diagnostic tests of diseases, tests intended to assess the answer to a medical treatment, tests used in conjunction with the use of a specific medicinal product, pharmacogenomic tests etc. However, beside these tests for which a direct medical purpose can be established, the medical purpose might be not so clear for some predictive tests, lifestyle tests, nutrigenetic tests, etc. This might lead to different interpretation on the qualification of these products within the European Union.

In addition to the above there are increasing concerns regarding genetic tests (e.g. direct to consumer genetic tests, predictive tests), including genetic tests without a clear medical purpose. These concerns are related among others to the lack of quality, lack of scientific evidence and lack of clinical validity or clinical utility of these tests.

Question 10:
Do you see a need for a clarification of the scope of Directive 98/79/EC to make clear that it covers all genetic tests that have a direct or indirect medical purpose while clarifying that tests without any direct or indirect medical purpose remain outside the scope of the Directive 98/79/EC.

If you consider that there is a need to clarify the scope of Directive 98/79/EC as regards genetic tests, which of the following items would you consider as appropriate:

Item 1:
Extend the scope to all genetic tests by adding a specific indent in the definition of in vitro diagnostic medical devices regarding devices which pursue the purpose of providing information concerning “results obtained by analysis of the genome”. Should, in this case, an exclusion be introduced in the Directive 98/79/EC as regards some categories of tests (negative list) e.g. paternity, DNA comparison?

Exclusion of some tests is problematic. Trying to define results obtained by analysis of the genome is difficult and probably not helpful, rather any definition should be based on the consequences of a test, not necessarily the means by which it was carried out, or its scientific basis.

Tests of identity can have devastating consequences for individuals and families, e.g. revealing twins as identical, when they thought they were not, or revealing them to be non-identical, when they thought they were identical. Identity tests may also reveal non-paternity/maternity, or even incest. Even seemingly innocent tests of minor non-medical characteristics may reveal identity, and so these tests should be considered to be of medical consequence. However, some tests such as those which report distant and ancient ancestry are probably low risk, although the consequences can be profound for those who thought e.g. that their origins were restricted to one ethnic background to find out that their ancestry is not as they thought.

The key to safety and quality, is for all appropriate pre-test information (counseling) to be provided, as well as for the test to be carried out to appropriate standards within the laboratory. If individuals have taken a choice as to whether to have a test, based on the possible
consequences of that test, and have thus given informed consent, then the risks of otherwise unforeseen results may be minimised.

**Item 2:**

Clarify that tests, including genetic tests, with a **direct or indirect medical purpose** are included within the scope of Directive 98/79/EC.

Indirect medical purpose covers a wide variety of possible scenarios which are undefined and further clarification would be helpful.

However, tests that may currently appear to have no medical purpose, might in the future turn out to have significant clinical consequences. A genetic test for a marker of some minor “non-medical” characteristic, might be found in the future to predict incurable disease, such as dementia. Thus, to ensure public safety all genetic tests should be kept under regular review as to whether they have a medical purpose or consequence, when previously they were thought not to have an effect. Manufacturers of tests should regularly review this. Accredited laboratories will, in any event, inherently do this as they are under an onus to justify the scientific validity and utility of any tests which they perform.

It must also be borne in mind that by no means all genetic tests involve tests of DNA, RNA or even protein. A physical examination by a doctor, an ECG, neurophysiological, ultrasound or X-ray examination can all amount to genetic tests.

The RCPath considers it important to concentrate on the impact of tests, and the uncertainty in this area seems to be centred around tests with a (claimed) predictive value. This could be addressed, therefore, by simply adding “prediction” to the definition of a medical device in Article 1(2)(a) viz:

(a) 'medical device’ means any instrument, apparatus, appliance, material or other article, whether used alone or in combination, including the software necessary for its proper application, intended by the manufacturer to be used for human beings for the purpose of:

- diagnosis, prevention, monitoring, treatment, prediction or alleviation of disease.

**Question 11:**

Do you see a need to create **additional requirements or restrictions for direct-to-consumer genetic tests** in order to ensure a better level of health protection? If yes, on which aspects?

Yes. The RCPath agrees that direct-to-consumer tests should be subject to a degree of control, as per the UK Human Genetics Commission’s recent report *A Common Framework of Principles for direct-to-consumer genetic testing services* (available at http://www.hgc.gov.uk/).

These *Principles* determine the standards in the UK that test providers should work within when providing genetic testing services directly to the public. They apply to all situations where it is possible for a consumer to purchase a test without prescription from a qualified medical professional, including tests that are ordered directly by a consumer or a non-medical intermediary acting on the consumer’s behalf. They cover all aspects of direct-to-consumer genetic testing services including:

- the marketing of tests
- information for consumers
- counselling and support
- consent and data protection
- the laboratory analysis of biological samples and
- the levels of support that should accompany the genetic test results

The Principles are given in the Appendix.

The RCPath is disappointed that as yet there is no mechanism by which these recommended codes of practice can be enforced or at least recognized as being adhered to by providers outside the EU, for example: EU recognition for laboratories either meeting EN ISO 15189 or utilizing CE-marked reagents and meeting the best practice guidelines outlined by the Human Genetics Commission’s report would be very beneficial. We feel further consideration of this could usefully be given to this area.

3.3 Diagnostic services

There are an increasing number of tests which are performed within an economic operator's facility (within the EU or outside) without placing the in vitro diagnostic medical devices on the market. The economic operator receives the body specimen and provides the result either directly to the patient or to a physician. Sometimes, different operators act at different steps in order to obtain the results of the test: specimen reception, specimen tests, statistical analysis, results. Despite Recital 11 and Article 9(13) of Directive 98/79/EC it may not always be clear that IVD’s used in such a situation are subject to Directive 98/79/EC. There are increasing concerns regarding the validity and the reliability of the results of such tests and the understanding of the result by lay users. In principle, these tests performed by the manufacturer should be subject to the same requirements than in vitro diagnostic medical devices that are placed on the market.

**Question 12:**
Do you see a need to amend the definition of "putting into service" to make it clear that it covers also the in vitro diagnostic medical devices that are not placed on the market but used for the delivery of results within the Community?

The RCPath takes the view that providing any tests for medical reasons amounts to providing a service. Thus, the moment that a laboratory offers to carry out such tests amounts to providing a service, whether it issues any reports or not. If any such service was required to be provided by a laboratory accredited to EN ISO 15189, then quality and patient safety would be ensured. Thus, a manufacturer wishing to offer a service would be subject to the same requirements as a clinical laboratory in a health institution.

**Question 13:**
Do you see a need to introduce other specific requirements for tests used for diagnostic services, especially when the results of the tests are provided directly to consumers, such as minimum requirements for advertising?

Yes. As in our answer to question 11, the RCPath would refer to the Human Genetics Commission’s recent report A Common Framework of Principles for direct-to-consumer genetic testing services (available at [http://www.hgc.gov.uk/](http://www.hgc.gov.uk/)).

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3 Article 9(13) Directive 98/79/EC states: "The provisions of this Article shall apply accordingly to any natural or legal person who manufacturers devices covered by this Directive and, without placing them on the market, puts them into service and uses them in the context of his professional activity."
### 3.4 Point-of-care / near-patient in vitro diagnostic medical devices

There is a growing number of tests which are performed outside a laboratory environment but near to a patient by a healthcare professional, who is not necessarily a laboratory professional, in order to make a diagnosis and to determine the appropriate treatment. These tests are often referred to as "point-of-care" or "near-patient" tests.

**Question 14:**
Do you see a need to add specific requirements for "point of care" or "near-patient" in vitro diagnostic medical devices? If yes, regarding which aspects (e.g. information supplied by the manufacturer)?

The RCPath considers that the use and provision of point of care and near patient tests should be subject to the same degree of oversight and clinical governance as required by accredited laboratories. Such testing should ideally be carried out under the auspices of an accredited laboratory service, and hence subject to the same internal quality control, and where applicable, external quality assurance, as a test carried out within laboratory premises. As per our answer to question 8, item 1, we would take the view that if such testing is carried out under the clinical governance framework of an accredited laboratory, patient safety is assured.

### 4. Clinical evidence

**Question 15:**
Do you see a need to further clarify the requirements regarding clinical evidence for in vitro diagnostic medical devices?

#### 4.1 Clinical validity

The clinical validity is the demonstration of the performance characteristics supporting the intended use of the in vitro diagnostic medical devices and includes diagnostic sensitivity, diagnostic specificity based on the true disease status of the patient and negative and positive predictive values based on the prevalence of the disease. These two last elements (negative and positive predictive values based on the prevalence of the disease) are currently not clearly mentioned in the Directive 98/79/EC.

**Question 16:**
On the basis of the above, do you see a need to extend the requirements regarding the demonstration of the clinical validity in Directive 98/79/EC?

Yes. It is most important that the clinical validity of any test should be demonstrated. However, with tests for rare conditions it may not be possible to gather a large body of data together, sufficient for a manufacturer to justify production of a kit or reagents. For this reason, amongst others, such tests may only be practical and feasible as a LDT, and hence, why LDT should continue to be exempt as provided for by article 1(5) of Directive 98/79/EC. After introducing

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4. GHTF/SG1/N045:2008 regarding Principles of In Vitro Diagnostic (IVD) Medical Devices Classification (see above footnote 6) defines "near-patient testing" as "testing performed outside a laboratory environment by a healthcare professional not necessarily a laboratory professional, generally near to, or at the side of, the patient".

5. The GHTF is currently working on a guidance document on clinical evidence for IVDs.

such tests, accredited specialist laboratories will inherently audit test performance, ensuring quality and patient safety.

4.2 Clinical utility
Beside the notion of clinical validity, the notion of clinical utility is the demonstration of the potential usefulness and added value to patient management decision-making. The notion of clinical utility for the purpose of this document does not include cost/benefit assessment, reimbursement issues and/or health economics issues. If a test has a utility, it means that the results provide valuable information for the purpose of making decisions about effective treatment or preventive strategies.

Question 17:
In the context of the above, do you see a need to require the demonstration of the clinical utility of the parameter in Directive 98/79/EC? If yes, how should the clinical utility be demonstrated?

Yes. It should be the norm that the clinical utility, as well as scientific validity, of a test is demonstrated prior to its application and that this should be transparent, i.e. open to inspection by any individual.

5. Others

5.1 “Conditional CE marking”

Question 18
Would you consider the possibility of a conditional CE marking in certain situations useful? Which situations would you think of and which conditions, including procedural requirements, would you consider necessary?

No. It would amount to the same degree of extra work and time as required by CE marking, and if all tests should be provided by laboratories accredited to EN ISO 15189, then any LDT would, as stated, be provided to assured quality and safety standards. In effect, an accredited laboratory is “CE marked”, and hence any of its products or services are likewise equivalently “CE marked”.

5.2. Companion in vitro diagnostic medical devices (e.g. pharmacogenomic assays, biomarker assays)

There are a growing number of tests which are developed and/or used in direct combination with specific medicinal products or which are co-developed with new medicinal products. These tests may be used for the selection of patients suitable for the respective medication, for optimal and individualized dosing of medicinal products, for the exclusion of populations expected to suffer from severe adverse side effects and/or other medicinal products-related indications. Currently, most companion diagnostics are self-certified by the IVD manufacturer.

Question 19:
Which options do you see to guarantee a high quality of IVD medical devices used as companion diagnostics?

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7 The Additional Protocol mentioned in the previous footnote also introduces the notion of clinical utility.
For such tests to be offered only by laboratories accredited to EN ISO 15189, for all the reasons stated above. This would include that they be subject to the risk-based classification in question 1.

Appendix

The UK Human Genetics Commission’s:

Principles for the provision of genetic testing services directly to the consumer

(available at http://www.hgc.gov.uk/)

1. Purpose and scope
1.1 These Principles are intended to ensure good practice in the provision of genetic testing services directly to the consumer. The test provider should strive to provide a high-quality service that meets the expectations of the consumer whilst safeguarding their interests.
1.2 The Principles apply to tests marketed to or ordered directly by a consumer or by a non-medical intermediary acting on the consumer’s behalf; they are not intended to apply to tests ordered by a medical professional on biological material taken from an individual as part of a professional investigative or diagnostic procedure in respect of that individual by that professional.

2. Marketing and advertising
2.1 Where relevant, the test provider should comply with any legislation or voluntary codes for advertising of medical tests, including genetic tests or other clinical services and they should also comply with more general guidance (including legal guidance) covering consumer advertising.
2.2 Promotional and technical claims for genetic tests should accurately describe both the characteristics and the limitations of the tests offered, and the test provider should not overstate the utility of a genetic test.
2.3 Where a claim is made about the clinical validity of a genetic test, the claim should be supported by relevant evidence published in peer reviewed scientific literature and the test provider should give standard references to this literature.
2.4 The test provider should be aware of the risk of bias when quoting evidence and ensure that evidence is presented transparently with reference to the criteria used to include and/or exclude published literature when this is cited as evidence of the applicability or effectiveness of the test.
2.5 Information about tests which are available only in the context of a consultation with a health professional or are only provided to consumers with both individualised pre- and post-test counselling should make it clear that tests are available only in that context.

3. Regulatory Information
3.1 The test provider should make available the evidence of the association between a genetic marker and a disease, condition or trait for the genetic tests that they supply. Ideally, the associations should be validated at genome wide significance level in more than one large case control study and in a cohort of the ethnic/geographic background relevant to the client. The associations should be published in peer-reviewed scientific journals, they should be undertaken in line with the recommendations made in the STREGA statement*, and the provider should supply standard references for these publications.

3.2 Standard statistical methodologies accepted by the scientific community should be used to calculate the risk of the disease, condition or trait, and the evaluation of the algorithms used should be made available by the test provider for standard review and scrutiny.
4. Information for prospective consumers

4.1 The test provider should supply easily understood, accurate, appropriate and adequate information, which is also available in accessible formats, to consumers before obtaining consent for a genetic test. The following should be provided:

- general information about genetics to enable a consumer to understand the scientific basis of genetic testing, the role of genes in health and disease, and conditioning phenotypes, and the technologies applied to generate the knowledge
- a clear explanation of the relative roles of genetics, environmental factors, lifestyle choices and other factors in determining health, disease and phenotype
- specific information about genetic tests offered
- information about counselling offered in connection with the test including whether counselling is included in the cost of the test and for what costs the consumer will be liable if they withdraw following pre-test counselling
- information about the presentation of results in statistical form, such as relative and absolute risk assessments or likelihood of inclusion/exclusion as a genetic relative, so that an individual can understand test results that are provided
- information about measures taken by the test provider and laboratories to ensure the confidentiality of personal records and security of biological samples
- information about the maximum period of storage of the biological sample and personal records, and procedures for storage, transfer and disposal of biological samples and personal records
- information about whether biological samples may be used for any secondary purposes, such as additional research purposes, and about or whether personal genetic information may be passed on to third parties and, if so under what conditions and to whom
- information about procedures for handling and resolving consumer complaints
- information about the manner in which the test results will be provided and, if applicable to the genetic test, information about the requirement for pre- and post-test counselling
- a statement that the results of the test might be able to reveal information about genetic relationships
- a statement that the results of the genetic test might have implications when purchasing life insurance
- a statement that third parties, such as law enforcement agencies, may have access to consumers’ biological samples without their consent if laws exist that would permit this
- information about specific procedures that might need to be followed if the test is to be used for official purposes, such as certain chains of evidence that might need to be maintained in some jurisdictions, if the test is to be used in the courts of law
- a statement that taking DNA from someone else without their consent is generally ethically inappropriate and is a criminal offence in some jurisdictions
- information about what will happen to consumers’ biological samples, and personal and genetic data, if the company ceases trading

4.2 The test provider should provide information to consumers about the association between a genetic variant and a disease, condition or trait for each genetic test that they offer in a format that is easy to understand.

4.3 The test provider should make available to consumers, information about the scope of the test, its accuracy and limitations. Information about the analytical and clinical validity* of each of the genetic markers used in the test should be made available. Other factors, such as behaviour or environmental conditions, that will play a role in determining the development of the condition or trait under investigation should be listed.

*Clinical validity includes information about (1) the relationship between the genetic marker and the condition or trait and (2) test performance, which may include the following characteristics of the genetic marker: sensitivity, specificity, positive and negative predictive values, likelihood ratios and areas under the ROC curve.
4.4 The test provider should provide information about the likely outcomes of the genetic test and the
decisions that a consumer may face after taking the test. They should also identify prospectively any likely
further investigations that a consumer or member of their family may wish to pursue after receiving the test
results.

4.5 If a test provider intends to use a consumer’s biological samples and/or associated personal or genetic
data for research purposes, the consumer should be informed whether the research has been approved
by a research ethics committee or other competent authority, whether the biological sample and data will
be transferred to or kept in a biobank or database, and about measures to ensure the security of the
sample. The consumer should be informed of any risks or potential benefits associated with participating
in the research and whether they will receive feedback on research findings that relate to them (see
Principle 6.6).

4.6 If a test provider intends to use the results of a genetic test to make a recommendation to a consumer
to purchase a therapeutic product, such as a nutritional agent or supplement, the test provider should
make available information about the link between the genetic test result and the efficacy of the indicated
product. The test provider should also provide information about other lifestyle choices and behavioural
modifications that are known to have a preventative or therapeutic value in relation to the trait linked to the
genetic markers tested and whether the consumer can purchase the recommended therapeutic product
elsewhere.

4.7 Where the test result indicates that the consumer may benefit from an alteration in the dosage of a
medicine, or from an alternative medicine to one currently being taken, the test provider should make
available information about the link between the genetic test result and the metabolism of the indicated
medicines (see Principles 3.1 and 11.3).

4.8 The test provider should make it clear how and whether a consumer can receive updated test results
as part of the service they supply.

4.9 Where appropriate, outside the context of a consultation with a suitably qualified health professional,
the test provider should inform consumers about recommendations or known actions that may help the
consumer to take informed decisions about their health or welfare in the light of the test results, including
informed interaction with the health care system.

4.10 Where appropriate, the test provider should supply consumers with information about health
professionals who are able to offer further advice or support.

4.11 For tests in categories 1–6, an appropriately qualified professional, with recognised training and
qualifications, employed by or representing the test provider, who is regulated by an appropriate
professional body, should be responsible for ensuring that consumers are provided with all of the
information specified in this section of the Principles. This requirement should apply to tests in other
categories where similar professional structures exist.

5. Counselling and support

5.1 Where the test is a genetic test in the context of inherited or heritable disorders, that test should only
be provided to consumers who are given a suitable opportunity to receive pre- and post-test counselling.

5.2 The counsellor should have the appropriate skills and competencies and should be accountable to a
relevant professional body.

5.3 After receiving the information provided in part 4 and receiving any offer of pre-test counselling,
consumers should have the opportunity to cancel purchase of the test without incurring further costs
relating to the test.

6. Consent

6.1 In designing a direct-to-consumer genetic testing service, the test provider should give consideration,
not only to the nature of the test and the information that it generates, but also to the personal and familial
circumstances that may be relevant to consumers.

6.2 A genetic test should be carried out only after the person concerned has given free and informed
consent. Informed consent can only be provided when a consumer has received sufficient relevant
information about the genetic test to enable them to understand the risks, benefits, limitations and
implications (including the implications for purchasing insurance) of the genetic test.

6.3 The test provider should take reasonable steps to assure themselves that a biological specimen
provided for testing was obtained from the person identified as the sample provider.
6.4 The test provider should require consumers to sign a statement confirming that they give their informed consent to the specific genetic tests to be undertaken on their biological material. The document should record the sample provider’s age and that they have read and understood the information with which they have been provided. The statement should include an explanation of what will happen to the consumer’s biological samples and personal data if the controlling share of the company is taken over by a third party.

6.5 The test provider should retain documentary evidence of the provision of informed consent by the consumer for the duration of storage of the consumers’ biological samples and personal records.

6.6 Separate, specific, informed consent should be requested by the test provider if the test provider wishes to perform further tests that are not covered by the original consent or if biological samples are to be stored by the test provider after the consumer has been provided with the genetic test results. Likewise, separate informed consent should be requested by the test provider before biological samples are used for any secondary purposes, e.g. research, or before any third party is permitted access to biological samples. Consumers’ biological samples and personal genetic data should only be used for research that has been approved by a research ethics committee (REC) or other relevant competent authority.

6.7 Except in exceptional circumstances provided for by law and appropriate guidance, companies offering direct-to-consumer genetic tests should not provide tests to adults unable to provide informed consent.

6.8 Companies offering direct-to-consumer genetic tests should be aware of the laws that exist in some countries prohibiting DNA theft, which make it illegal to obtain or test DNA without the consent of the person from whom it originated. In line with these laws a test provider should make consumers aware of the law and should not perform a test if they have reason to believe that a biological sample they have been provided with for genetic testing purposes has been taken from a third party who has not given their consent for the tests to be performed. Requests to recover DNA for genetic testing purposes from secondary objects or materials, when there is reason to believe that the person from whom the DNA originates is still alive, should raise suspicion and should be declined.

6.9 The following principle applies to tests in categories 1-3, 5 and 6 (and categories 7 and 8 where these have been evaluated as ‘high impact’ – see ‘How to use the Principles’). Genetic tests in respect of children when, according to applicable law, that child does not have capacity to consent should normally be deferred until the attainment of such capacity, unless other factors indicate that testing during childhood is clinically indicated. If postponement would be detrimental to the child’s health, or the management of the child’s health may be altered significantly depending on the test result, then testing should be organised by a health professional who has responsibility for ensuring that any medical intervention or screening indicated will be arranged and proper arrangements made for any subsequent care.

7. Data protection

7.1 Genetic information is sensitive personal data and requires the highest level of security and confidentiality. Records containing personal data and genetic information that can be linked to an identifiable person should be subject to privacy protection and security in accordance with professional guidance and applicable laws on data protection and confidentiality.

7.2 The test provider and laboratories should not release biological samples or records containing personal data and genetic information that can be linked to an identifiable person to any third party without the prior consent of the person to whom they relate, unless required to do so in accordance with national legislation for example, pursuant to a Court order.

7.3 Companies who wish to record consumers’ details on to a database that will be held by the test provider, a laboratory or a professional associated with the testing procedure, should obtain prior consent from the consumers. Consent should also be obtained prospectively for consumers to be contacted in the future by these organisations or individuals.

7.4 If a test provider ceases trading, they should dispose of personal and genetic data securely or provide for transfer of responsibilities in accordance with the terms of consent given by the consumer.

8. Sample handling
8.1 The use, storage, transfer and disposal of biological samples provided for genetic testing should be
carried out in accordance with applicable legal, ethical and professional standards. The nature, purpose
and maximum duration of the storage should be specified.
8.2 Biological samples should be used, stored, transferred and disposed of in conditions that ensure their
security.
8.3 If a test provider ceases trading, they should dispose of consumers’ biological samples securely or
provide for transfer of responsibilities in accordance with the terms of consent given by the consumer.

9. Laboratory processes
9.1 The analysis of biological samples for the purpose of providing genetic testing services should be
provided by competent laboratories. Competence can be established by accreditation to the International
Organisation for Standardisation (ISO) standards 15189 or 17025 or other equivalent recognition
consistent with the OECD* guidelines for quality assurance in molecular genetic testing. Achievement of
laboratory accreditation requires monitoring the quality of laboratory performance through proficiency
testing.
9.2 Genetic tests used as part of a direct-to-consumer genetic testing service should be able to identify the
genotype of interest both accurately and reliably.
9.3 Laboratories should have policies in place to apply corrective measures if their performance falls
outside of parameters determined by the laboratory’s quality assurance programme.
9.4 Laboratory personnel should have appropriate professional qualifications that meet recognised
standards, underpinned by education and training, to assure competence in laboratory procedures in the
provision of genetic tests.

Assurance in Molecular Genetic Testing’, www.oecd.org

10. Interpretation of test results
10.1 For tests in categories 1–6, interpretation of genetic test results should be carried out under the
responsibility of an appropriately qualified professional, with recognised training and qualifications,
working within the standards determined by an appropriate professional body and regulated by this
professional body, employed by or working on behalf of the test provider. Similar standards should apply
to tests in other categories where similar professional structures exist. There should be no remuneration
structure in place that would allow this individual to benefit directly from any particular interpretation of the
test results or the sale of any services or products related to those results.
10.2 The qualified professional responsible for the interpretation of genetic test results should ensure that
the interpretation of genetic test results is accurate and take steps to ensure that these results are
comprehensible to the consumer.
10.3 Where genetic test results are provided in the form of a risk assessment, the risk assessment should
be based on robustly evaluated algorithms. Standard statistical methodologies should be used to convert
risks reported in scientific literature to the risk of a disease, condition or trait for an individual compared
with the general population risk, as well as lifetime risks or lifetime incidences. Results should make clear
the distinction between relative risks and absolute risk.
10.4 Test providers should regularly review the available evidence on which their interpretation is based.

11. Provision of results
11.1 The results of genetic tests and the significance that should be attributed to a particular genetic test
result should be described to the consumer in a format that is easy to understand.
11.2 When testing for a condition or trait, where such conditions or traits are determined, at least in part,
by other, non-genetic factors in addition to genetic markers, the test provider should make consumers
aware of these other factors when providing results of genetic tests. In addition, the test provider should
supply an indication of the level of significance that an individual should attribute to the genetic test results
in comparison with the significance of these other factors, and this should be provided to the consumer in
a format that is easy to understand.
11.3 When providing consumers with the test results for tests in category 6 (pharmacogenetic tests), the
test provider should strongly recommend that the consumer does not alter the dosage of any existing
medication on the basis of the test results and to take the results of the pharmacogenetic test to a medical
practitioner for personalised interpretation of the test result. The test provider should give the consumer
appropriate information to take with them to their medical practitioner to aid the interpretation of the test results.

11.4 The test provider should take care not to overstate the value or significance of the results of the genetic test when providing the test results.

11.5 The test provider should state clearly when a genetic test result can only give an indication of relative risk in relation to the general population as opposed to an absolute risk, bearing in mind that either might only be calculable in the context of a family history analysis.

11.6 The test provider should have in place a process to evaluate how well consumers are able to understand the background information and test results they have received, and take steps to improve their information and results provision in accordance with the findings.

11.7 The test provider should ensure that the provision of genetic test results is undertaken in such a way as to retain the confidentiality of personal and genetic data. When genetic test results are provided electronically, the test provider should ensure that appropriate security measures are in place to maintain the confidentiality of data transmitted. If the option of sending test results via email is offered by the test provider, consumers should be made aware that this method is generally not secure.

11.8 The test provider should not release genetic test results to any third parties, including insurance companies, health professionals, solicitors or other medical practitioners without the specific prior consent of the sample provider.

11.9 Test providers who interpret un-interpreted data obtained from genetic tests that have been provided by a third party laboratory should comply with all the aspects of these Principles that are relevant to the services they provide. Likewise, test providers who only undertake the genetic analysis and do not interpret the test results should comply with all the aspects of these Principles that are relevant to the services they provide.

12. Continuing support

12.1 For tests in categories 1–6 (and categories 7 and 8 where these have been evaluated as ‘high impact’ – see ‘How to use the Principles’) the test provider should be able to provide consumers, at the time of testing or at any subsequent stage, with information about opportunities that are available for any further consultation with health professionals.

13. Complaints

13.1 The test provider should have written procedures in place for acknowledging and investigating complaints. Staff who manage and respond to complaints should have received appropriate training.

13.2 The test provider should nominate a member of staff to oversee the handling of complaints. This person should be responsible for the management of the investigation of the complaint and the effective operation of the complaints procedure.

13.3 The complaints procedure and the name and contact information of the person to contact regarding complaints should be easily accessible to consumers. This information should be available in formats that are accessible for people who are unable to access standard print.

13.4 The test provider should ensure that complaints are dealt with in a reasonable time-period and consumers should be informed promptly of the outcome of the complaint.

13.5 If a consumer remains dissatisfied with the investigation or outcome of their complaint, they should be made aware of what further recourse might be available to them.