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# Letter from the Editor

*Welcome to our summer edition of the medical devices newsletter.*

In this edition, we present an update in relation to our activities in 2006, which was again a busy year for the Medical Devices Department, with significant increases in both vigilance reporting and compliance activity.

We also provide an overview of the changes to the Guidelines on a Medical Device Vigilance System (MEDDEV 2.12-1 rev 5), recently published on the European Commission website. On Friday 16th November 2007, we will be holding an information day on the updated Vigilance MED.DEV and the revisions to the Medical Devices Directive 93/42/EEC.

We are pleased to have a very interesting article kindly provided to us by Dr. David Barton of the National Centre for Medical Genetics. This article details an overview of medical genetic testing in Ireland, along with the Irish involvement in the European quality initiatives in this area.

As always readers are encouraged to provide feedback particularly in relation to articles that may be of interest by contacting us at medicaldevices@imb.ie.

CONTENTS

# Activities in the Medical Devices Department 2006

*The year 2006 was a busy and productive year for the Medical Devices Department.*

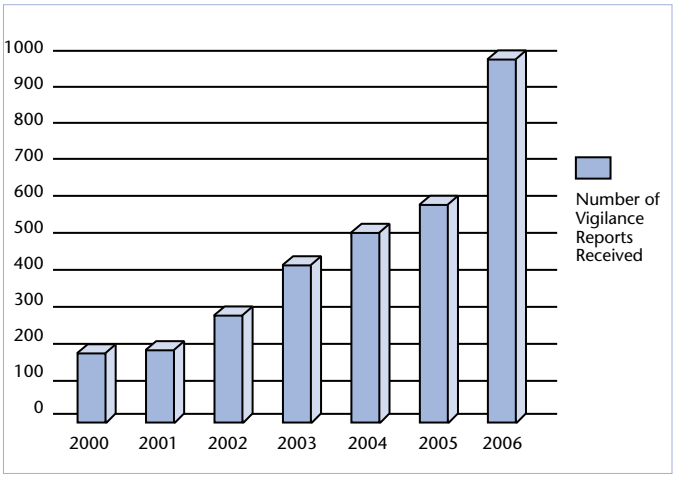
*Monitoring of safety issues on the market place continued to be a key activity.*

Trends indicate a significant increase in activity particularly in relation to the areas of vigilance and compliance.

## VIGILANCE

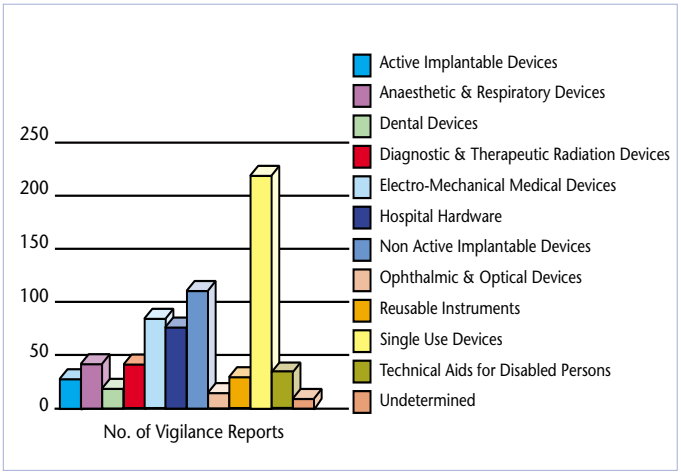
The number of vigilance reports received for medical devices continues to increase with an overall increase of 67% seen in 2006 as highlighted on figure 1.

Figure 1:
*Number of Vigilance Reports Received during 2000 to 2006*



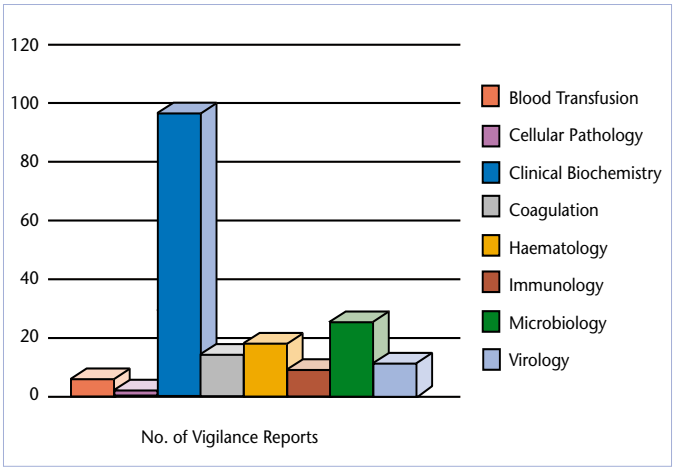

This increase was noted across all medical devices with an increase of 69% for general medical devices (GMDs), 100% for active implantable medical devices (AIMDs) and 42% for *in-vitro* diagnostic medical devices (IVDs).

Figure 2:
*Family Groups of Devices Implicated in Vigilance Reports in 2006 – General Medical Devices and Active Implantable Medical Devices*




General category IVDs represent the majority of vigilance reports received for IVDs with a large proportion relating to clinical chemistry as highlighted in figure 3. In 2006, there was a 14% increase in the number of user reports received by the IMB.

Figure 3:
*Family Groups of Devices Implicated in Vigilance Reports in 2006 – In-vitro Diagnostic Medical Devices*




The principal issues encountered during 2006 included reports relating to single use devices, implantable devices, blood glucose meters and various devices used in cardiovascular interventions.

Quality issues and software problems were found to be the root cause of many of the vigilance issues relating to electro-mechanical medical devices and IVDs. Device maintenance and management problems have been identified as the root cause of a number of vigilance cases.

During 2006, there were a number of major recalls of medical devices. These included a recall of a contact lens solution which was thought to be associated with an increased incidence of a serious eye infection and the recall of three automatic external defibrillators due to component problems. In all instances, the IMB had considerable involvement in overseeing the manufacturer recall. A large replacement programme of various manufacturers' blood glucose meters was undertaken in Ireland during 2006 following incidents associated with the unit of measurement inadvertently changing from mmol/l to mg/dl.

## COMPLIANCE

Following-on from 2005, another significant increase in the number of compliance cases handled was noted in 2006. The number of cases increased from 70 to 172, which represents an increase of 246% between 2005 and 2006. This increase

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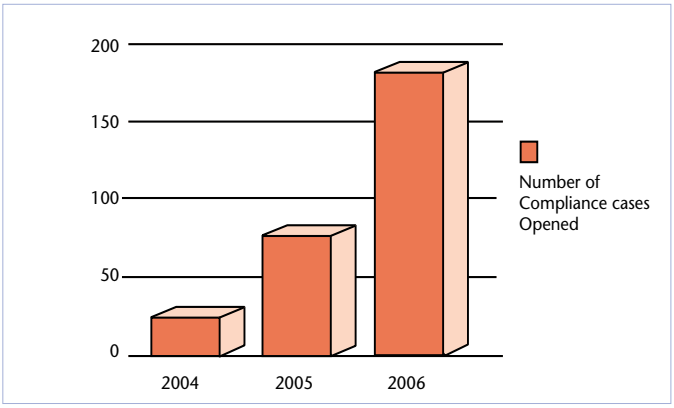
was due to more focused compliance activities carried out by the Medical Devices Department as well as increased awareness in the market-place. The majority of cases were in relation to reactive issues




A number of proactive compliance activities were undertaken in 2006, including projects relating to systems and procedure packs and continuous positive airway pressure machines. These proactive projects identified issues in relation to a lack of understanding and knowledge of the requirements of the legislation. As a consequence of these activities a considerable number of manufacturers became compliant in 2006. A total of 46 compliance visits, both proactive and reactive, were conducted in 2006.

The area of splinting was also looked at with regards to classification as custom-made or class I medical devices and a position paper was published early this year. This document is now available on the IMB medical devices website www.medicaldevices.ie.

### POST MARKET SURVEILLANCE AUDITS

In 2006, seven post market surveillance audits were carried out. Four manufacturers were audited following issues arising from field safety corrective actions. One of these manufacturers required a follow up audit due to inadequate product design. Two audits were conducted with the compliance section of the Medical Devices Department relating to flammability concerns. The program of custom-made device audits continued this year and a total of twenty three audits took place.

# *Revision of the Guidelines on a Medical Device Vigilance System*

## *(MEDDEV 2.12-1 rev 5)*

Ireland has played an active role in the revision of the Guidelines on a Medical Device Vigilance System (MEDDEV 2.12-1 rev 5) at a European level. After much debate and discussion we are pleased to announce that the document has now been finalised and is available on the European Commission's medical device website. To assist manufacturers to determine what impact the new guidelines will have on their handling of vigilance issues we have summarised eleven key changes below.

IVD manufactures will note that the specific requirements for *in-vitro* diagnostic (IVD) medical devices are better addressed and more integrated into the new document.

### 1. THE STRUCTURE

The structure of the document has been changed, where specific chapters identify the key roles that stakeholders are involved in the vigilance system, and their roles in the process are detailed.

- Introduction
- Definitions
- Manufacturers Role
- Responsibilities of the Competent Authority
- Role of the Notified Body
- Role of the Commission
- Role of the Users

### 2. THE REMOVAL OF THE TERM 'NEAR INCIDENT'

The term near incident has been removed from the document because it was felt that the definition of an incident already included the concept of near incident. There is still a requirement for incidents that might lead to or might have led to the death of a patient, or USER or of other persons or to a serious deterioration in their state of health to be reported.

"Any malfunction or deterioration in the characteristics and / or performance of a device, as well as any inadequacy in the labelling or the instructions for use which, directly or indirectly, ***might lead to or might have led to the death of a patient***, or USER or of other persons or to a serious deterioration in their state of health."

### 3. FIELD SAFETY CORRECTIVE

A new definition of a 'Field Safety Corrective Action' (FSCA) has replaced the no longer existing European recall definition.

A 'field safety corrective action' taken by a manufacturer to prevent or reduce the risk of death or serious deterioration in the state of health associated with the use of a medical device.

These may include:

- the return of a medical device to the supplier
- device modification
- device exchange
- device destruction
- retrofit by purchaser of manufacturer's modification or design change
- advice given by manufacturer regarding the use of the device (e.g. where the device is no longer on the market or has been withdrawn but could still possibly be in use, e.g. implants)

### 4. REPORTING CRITERIA

Any event which meets **all** three basic reporting criteria **A – C** listed below is considered as an INCIDENT and must be reported to the relevant national Competent Authority. The criteria are that:

*a) An event has occurred*

Typical events include, but are not limited to:

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(i) A malfunction or deterioration in the characteristics or performance. A malfunction or deterioration should be understood as a failure of a device to perform in accordance with its INTENDED PURPOSE when used in accordance with the MANUFACTURER's instructions.
(ii) False positive or false negative test result falling outside the declared performance of the test.
(iii) Unanticipated adverse reaction or unanticipated side effect
(iv) Interactions with other substances or products
(v) Degradation / destruction of the device (e.g. fire)
(vi) Inappropriate therapy
(vii) An inaccuracy in the labelling, instructions for use and/or promotional materials.

*b) The MANUFACTURER's device is suspected to be a contributory cause of the INCIDENT*

*c) The event led, or might have led, to one of the following outcomes:*

- death of a patient, USER or other person
- serious deterioration in state of health of a patient, USER or other person
- A serious deterioration in state of health can include:
- life-threatening illness
- permanent impairment of a body function or permanent damage to a body structure
- a condition necessitating medical or surgical intervention to prevent a) or b)

## 5. REPORTING METHODS

### *Standard Vigilance Reports*

The initial and final vigilance report forms have been replaced with a single form which can be used for either functions, this form is the 'Report Form for Manufacturer's Incident Report' (Annex 3). In addition, a new form for the reporting of Field Safety Corrective Actions has been introduced (Annex 4).

### *Reporting Methods*

Two new additional reporting mechanisms are now available to manufacturers for reporting incidents.

*a) Summary Report*

PERIODIC SUMMARY REPORTING is an alternative reporting regime that is agreed between the MANUFACTURER and the national Competent Authority for reporting similar INCIDENTs with the same device or device type in a consolidated way where the root cause is known or an FSCA has been implemented

*b) Trend Report*

A reporting type used by the MANUFACTURER when a significant increase in events not normally considered to be INCIDENTS according to section 5.1.3. occurred and for which predefined trigger levels are used to determine the threshold for reporting. Examples of these include

- already reportable INCIDENTs
- INCIDENTs that are usually exempt from reporting
- events that are usually not reportable

The IMB would emphasis that the manufacturer and the Competent Authority must work closely together to agree such reporting mechanisms

## 6. USE ERROR

USE ERROR and abnormal use are now reportable by the MANUFACTURER to the national Competent Authority when a MANUFACTURER:

– notes a significant change in trend (usually an increase in frequency), or a significant change in pattern (see annex 7 GHTF SG2 N36) of an issue that can potentially lead to death or serious deterioration in state of health or public health threat)

– initiates corrective action to prevent death or serious deterioration in state of health or SERIOUS PUBLIC HEALTH THREAT

## 7. REPORTING TIMELINES

The timelines for reporting have been further clarified. The most significant change being the introduction of a two day timeline for the reporting of a serious public health issue as outlined below.

Upon becoming aware that an event has occurred and that one of its devices may have caused or contributed to that event, the medical device manufacturer must determine whether it is an incident.

The following time lines apply in a case of:

- Serious public health threat: IMMEDIATELY (without any delay that could not be justified) but not later than **2 calendar days** after awareness by the MANUFACTURER of this threat.
- Death or UNANTICIPATED serious deterioration in state of health: IMMEDIATELY (without any delay that could not be justified) after the MANUFACTURER established a link between the device and the event but **not later than 10 elapsed calendar days** following the date of awareness of the event.
- Others: IMMEDIATELY (without any delay that could not be justified) after the MANUFACTURER established a link between the device and the event but **not later than 30 elapsed calendar days** following the date of awareness of the event.

## 8. THE ROLE OF THE NATIONAL COMPETENT AUTHORITY

The document further clarifies the role of the national Competent Authority. This is detailed in chapter 6. The concept of a lead / coordinating Competent Authority is outlined. The circumstances when such a coordinating Competent Authority may be required are clearly outlined. The role of the coordinating Competent Authority and the area relating to the dissemination of information are also detailed.

## 9. THE NOTIFIED BODY ROLE IN THE VIGILANCE SYSTEM

The document for the first time considers the role of the Notified Bodies. This is outlined in chapter 7. It highlights that although Notified bodies do not play a key operational role in the medical device vigilance system, the overall performance of the medical device vigilance system is supported by the Notified Body activity in the following areas:

- Assessment of vigilance procedures
- Audit of the implementation of the vigilance procedures, and link with other systems e.g. Corrective and Preventive Action (CAPA) , FSCA
- Assessment of the impact of vigilance issues on the certification granted

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- Liaison with the national Competent Authority if required, e.g. specific investigations / audits based on a request of the national Competent Authority

### 10. THE ROLE OF THE COMMISSION

The key roles of the Commission are outlined in chapter 8. These include:

- The Commission shall ensure that appropriate coordination and cooperation is put into place between the Competent Authorities of all Member States to allow the medical device vigilance system to deliver the high level of protection for the health and safety of patients and USERS.
- In order to reinforce a common understanding and a common approach towards the identification and resolution of vigilance cases, the Commission shall:
- facilitate the exchange of experience and best practices between the national Competent Authorities of the Member States,
- facilitate the transmission of relevant data through the appropriate data exchange system,
- when appropriate, in cooperation with national Competent Authorities, develop and organise training programs.

### 11. THE USERS ROLE IN THE VIGILANCE SYSTEM

Chapter 9 highlights the importance of the Users role in the vigilance system. It acknowledges that there is no legal requirement within the Directives obliging USERS to have an active role in the vigilance system. Yet for the successful operation of the vigilance system their involvement is vital.

## Regulatory Update

A Medical Devices Expert Group (MDEG) meeting took place in May 2007. It consisted of a closed session for Competent Authorities and an open session for all stakeholders. It was clarified that the timeline for adoption of the revisions to the Medical Devices Directive 93/42/EEC will be autumn 2007, with 15 months for transposition of the agreed amendments into national law and a further 15 months for implementation. The European Commission also outlined the reasons for the questionnaire on reprocessing of medical devices which has been issued to Member States for completion.

MDEG discussed the revision of the common technical specification for *in-vitro* diagnostic (IVD) medical devices and the extension of the scope of the Active Implantable Medical Devices Directive 90/385/EC to include TSE requirements. Concern was also raised with regard to the overlap of the Machinery Directive 2006/42/EC and the Medical Devices Directive 93/42/EEC. The Machinery Directive has recently been reviewed, and the text regarding the exclusion of medical devices from its scope has been removed and consequently manufacturers of medical devices may now have to comply with the essential requirements of the Machinery Directive. The European Commission proposes to review this position from a legal perspective.

Discussion also took place in relation to the impact of the proposed changes to the New Approach legislation, particularly with regard to the use of accreditation for Notified Bodies. All stakeholders voiced their concerns over using this approach for medical devices, as it is felt that the use of the Designating Authorities handbook and the activities of the Notified Body Operations Group (NBOG) have strengthened the control over medical device Notified Bodies. A questionnaire has been issued to Member States to gather information on how Notified Bodies in the medical devices area are designated and monitored

The revised guidance MEDDEV 2.12-1 rev 5 on the medical device vigilance system was adopted by the MDEG and recently published on the European Commission website. This document may be downloaded from the medical devices section of the European Commission website at http://ec.europa.eu/enterprise/medical_devices/index_en.htm

At the recent meeting of the IVD Technical group, the revisions to the common technical specifications for Annex II list A IVDs was discussed and finalised. The document will be sent by the European Commission to the Article 7 Regulatory Committee in the autumn for endorsement.

TThe European Commission outlined its plan for 2007 and stated that the following subjects are included:finalisation of the amendment to the Medical Devices Directive 93/42/EEC, the finalisation of the Decision on EUDAMED and the repeal of legislation on Electromechanical Equipment for Veterinary Use. Also being considered is the need to create a working group to develop guidance on e-labelling for medical devices as the legal basis is included in the revised text of 93/42/EEC.

A Competent Authority meeting took place under the Portuguese presidency of the EU. Market surveillance issues were discussed and a new terms of reference and work programme for the Market Surveillance Operations Group (MSOG) was agreed. It was also agreed to change the name of the group to the Medical Devices Compliance and Enforcement Group. The area of genetic testing and the IVD Directive was considered. A workshop titled 'Future 2014' took place and considered what challenges may lie ahead regarding the regulation of medical devices.

## Upcoming Events

The IMB Medical Device Department will be holding an information day on the 'Revisions to the Medical Devices Directive 93/42/EEC and the Vigilance MED.DEV' on Friday 16th November 2007. This event will take place in the Crowne Plaza Hotel, Dublin Airport.

The day will be split into 3 sessions:

***Session 1*** – general information on the Medical Devices Department of the Irish Medicines Board and an overview of the changes to the medical device legislation.

***Session 2*** – key changes to the Medical Devices Directive 93/42/EEC

***Session 3*** – key changes to Vigilance MED.DEV

The agenda and registration forms will be available on the IMB medical devices website www.medicaldevices.ie from mid August 2007. A booking fee is being charged for this conference. Refreshments, lunch and conference documentation are included in this fee.

# Overview of Genetic Testing in Ireland

*Heralded as the 'new face of medicine', lambasted as 'scientists playing God', genetic testing has rarely been out of the news over the past twenty years.*

It is rolled up into debates over stem cell research, human cloning, *in-vitro* fertilisation and genetically-modified organisms. In reality, medical genetic testing has little to do with any of these subjects, confining itself (for the moment, at least) to identifying mutations in genes for inherited disorders. This short article seeks to describe the current status of medical genetic testing in Ireland, and to set it into the international context.

## DEFINITION OF GENETIC TESTING

There are many different definitions of genetic testing, which can be taken to mean all testing involving analysis of nucleic acids, but for the purposes of this article I shall take the definition from the Disability Act 2005 (more of which below):

*"Genetic Testing" means:*
*the examination of samples taken from a living person for the purpose of analysing the person's deoxyribonucleic or ribonucleic acid by means of chromosomal analysis or by any other means for the purpose of –*

*a)* confirming the identity or nature of an existing symptomatic disease,
*b)* ascertaining whether the person has a genetic predisposition or susceptibility to a disease, or
*c)* identifying the carrier of a disease.

This definition neatly introduces the three main types of genetic testing: diagnostic testing, presymptomatic (or predictive) testing and carrier testing. Genetic testing can provide information about the future health of an individual or their children, because (in general) we have the same DNA in every cell of our bodies from the moment we are conceived. We pass half of this DNA information on to our children, with the other half being contributed by the other parent.

## MEDICAL GENETICS

Medical Genetics is the branch of medicine concerned with disorders which are inherited or due to changes in the genetic material (DNA or chromosomes), such as cystic fibrosis or haemochromatosis. Within the specialty, Clinical Genetics is where the patients are seen and clinical diagnoses made, Cytogenetics involves the analysis of chromosomes by microscopy and Molecular Genetics involves the study of DNA. Unlike other medical specialties, Medical Genetics considers not just the patient presenting in the clinic but the whole family. Clinical Genetics consultants are supported in their work by specialist Genetic Counsellors.

## MEDICAL GENETIC TESTING IN IRELAND

Although some genetic testing services were offered in the past by university-based laboratories, Medical Genetics really only appeared in the Irish health service with the establishment of the National Centre for Medical Genetics (NCMG) in 1994. The centre originally comprised a small team with one consultant and a few laboratory scientists, but now employs over seventy-five people and is still expanding. The centre also houses the UCD Department of Medical Genetics; the Director of the Centre, Dr Andrew Green, is UCD Professor of Medical Genetics. Demand for testing continues to grow year by year (see Figure 1), with signs that the trend, linear for many years, is accelerating in 2007.

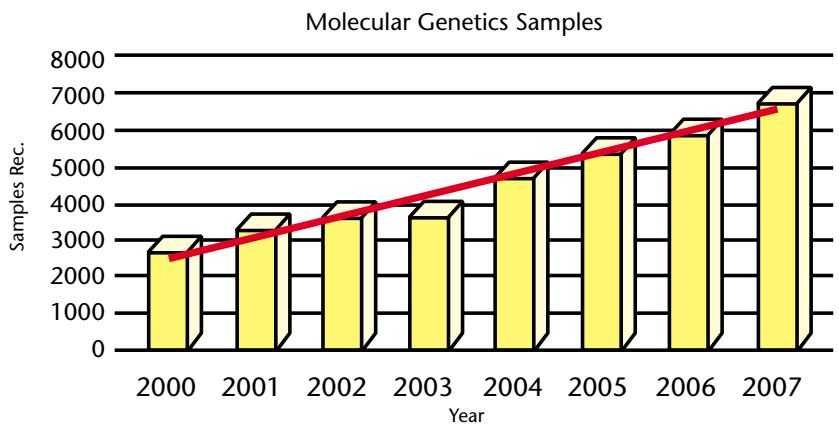
The Cytogenetics and Molecular Genetics laboratories at NCMG offer a wide range of genetic tests, although the diverse nature of the requests received means that much testing is still sent to expert laboratories abroad. The centre's website at www.genetics.ie has lots of additional information and useful links.

## REGULATORY SITUATION FOR GENETIC TESTING

### *The Disability Act, 2005*

Because genetic test results can have such life-changing implications for tested individuals and their families, and because most tests will only be carried out once in the individual's lifetime, special attention to quality is essential in genetic testing. The implications of genetic test results for an individual's future health status, and the potential for discrimination that arises from this, have led to the introduction of laws and regulations at various levels to protect those undergoing genetic testing. In Ireland, the Disability Act of 2005 (reference 1) has a special section on genetic testing. This section is designed to provide limitations on the use of information obtained from genetic testing, to

Figure 1:
*Samples received for molecular genetic testing each year since 2000. The figure for 2007 is extrapolated from numbers received to July. The red line indicates the linear trend.*



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ensure that people who may be affected by genetic disorders will not be subject to unreasonable requirements from an employer or an insurance or mortgage provider (reference 2). Specifically, the Act makes it an offence to carry out genetic testing on a person unless their consent has been obtained in accordance with the Data Protection Acts. Once testing has been carried out, it is an offence to process the resulting 'genetic data' for the purposes of insurance, employment, a pension or a mortgage application. Before genetic data are processed, the subject of the data (i.e. the individual tested) must be supplied with "all appropriate information concerning the purpose and possible outcomes of the proposed processing, and any potential implications for the health of the subject which may become known as a result of the processing". This latter provision makes some form of genetic counselling mandatory, but strangely only comes in after the test has been carried out; it is commonly-accepted practice in Medical Genetics world-wide to counsel the individual about the possible outcomes of the test and their implications before testing was carried out. Unless this happens, the consent to testing which is made mandatory by the Act cannot be said to be a truly informed consent.

## THE IVD DIRECTIVE

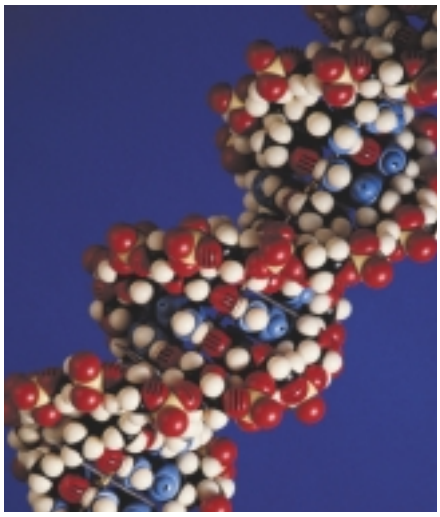
On the broader front, genetic testing is regulated (like all other clinical testing) under the provisions of Directive 98/79/EC of the European Parliament and of the Council of 27 October 1998 on *in-vitro* diagnostic medical devices – the IVD Directive. There is only one special mention for genetic testing in the Directive, in recital 30:

*"Whereas it is essential that manufacturers notify the Competent Authorities of the placing on the market of 'new products` with regard both to the technology used and the substances to be analysed or other parameters; whereas this is true in particular of high-density DNA probe devices (known as micro-chips) used in genetic screening"*.

It is surprising that 'micro-chips' are specifically mentioned, as multiplex testing technologies which are not based on chips can perform exactly the same genetic tests as chip-based devices. While there are no issues around the IVDD which are absolutely unique to genetic testing, genetic testing does bring to light issues which affect specialist testing in general, and the special focus on all matters involving genetic testing serves as a useful channel for discussion of such issues. One such issue is the exemption from regulation under the IVDD of tests manufactured and used in the same health intuition, often referred to as "the in-house exemption". The exemption is significant in genetics because genetic testing is heavily reliant on laboratory-developed tests which are delivered within 'health institutions'.

Some confusion has arisen because the term health institution is not defined in the Directive. There has been much debate about the scope of this exemption, and some Member States hold the view that the exemption does not apply if specimens from outside the health institution are tested with the device. However, DG Enterprise has issued an opinion (reference 3) indicating that the origin of specimens tested is not relevant to the exemption. There has also been discussion about whether commercial pathology laboratories could fall under the exemption. The European Commission has said that commercial service providers were not covered by the exemption. This is particularly important given that some new genomic tests are being delivered as in-house tests provided by a single reference laboratory.

There is also concern that the exemption may allow unregulated tests to be put into service, in countries where Member States have not enacted alternative regulatory mechanisms. However, there is a counter-balancing concern that specialist laboratories which (at least in some countries) are already subject to accreditation requirements might become subject to two overlapping regulatory domains, having to fulfil the same requirements twice but in different ways, thus increasing the regulatory burden without necessarily improving patient safety. It has been suggested that compliance with an appropriate laboratory accreditation standard such as ISO 15189 would ensure that in-house assays were properly validated, and could act as an alternative form of regulation where the exemption applies. Ireland has no provision for the mandatory accreditation of clinical laboratories, although many Irish labs have achieved accreditation independently. Interestingly, the new OECD guidelines for quality assurance in genetic testing mandate that all laboratories issuing genetic test results should be accredited for this activity. As an OECD member, Ireland is covered by these guidelines.



There is general acceptance that the in-house exemption performs an important role in allowing the availability of highly-specialised and 'orphan' assays for which a commercial market may never exist. This 'orphan' classification depends on test complexity and volume of requests. A related category of tests which may be more significant in other areas (e.g. infectious disease) are new targets (e.g. SARS) for which assays must be developed at short notice.

At the NCMG, most tests in use are developed and validated in-house rather than being CE-marked IVDs. This is because no CE-marked IVDs exist for most genetic tests. In cases where CE-marked IVDs do exist, they are often not well tailored to the requirements of the Irish population. So we are buying in reagents, developing our own assays (or adapting research-use assays) and validating them according to guidelines issued by international bodies. This approach allows us to offer the most appropriate tests for the population we serve. It also allows us to adapt to changing scientific information, which is difficult for CE-marked devices. A case in point would be adapting assays to deal with new information on DNA variations which might interfere with an existing assay. All molecular genetic tests involve the hybridisation of short DNA sequence (probe and/or primer) to their matching sequence in the patient's DNA. Such hybridisation is disrupted by mismatches between the primer/probe and the patient's DNA sequence. Indeed, this is the basis of discriminating the normal DNA sequence from the disease-causing mutation. However, normal variation in nearby DNA sequences not associated with disease can also interfere with the hybridisation, and give false-negative or false-positive results. Molecular genetics labs (and some IVD manufacturers) regu-

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larly check the ever-expanding databases of DNA variants to see if new variants which might interfere with their assay have been reported. If such an interfering variant is identified, the genetic testing lab can easily adapt its in-house assay and perform a limited re-validation proportionate to the significance of the change made, whereas the task of re-certifying a commercial IVD is much more onerous, and manufacturers tend simply to list the new variant as a possibly interfering variant on their website and package insert.

## QUALITY ISSUES

A number of international projects are in place to monitor and improve the quality of genetic testing laboratories and the results they produce. Several of the initiatives have been funded by the European Commission's Framework Programmes for research and development, most prominently the European Molecular Genetics Quality Network (EMQN) and the EuroGentest Network of Excellence.

## EUROPEAN MOLECULAR GENETICS QUALITY NETWORK, EMQN

EMQN provides external quality assessment schemes for a range of genetic disorders and some technique-based schemes. EMQN also organises workshops aimed at developing consensus guidelines for best practice in molecular diagnostics. Although originally funded by the EU, EMQN is now a self-supporting not-for-profit organisation providing quality assessment to genetics laboratories world-wide. In 2006, there were 792 participations in 19 EQA schemes.

## EUROGENTEST NETWORK OF EXCELLENCE

EuroGentest has a much broader remit than EMQN, encompassing all aspects of the quality of genetic testing from test development through laboratory accreditation to information for patients and guidelines for genetic counselling. One of the network's key outputs, just launched in July, is a database of genetic testing laboratories across Europe, which includes quality indicators such as accreditation status and participation in EQA. This will help clinicians requesting genetic tests to select a laboratory with high quality standards, and will reward laboratories for the work they have put into achieving accreditation.

## OECD GUIDELINES FOR QUALITY ASSURANCE IN GENETIC TESTING

The Organisation for Economic Cooperation and Development published comprehensive guidelines for quality assurance in genetic testing in May this year. The product of several years of extensive drafting, consultation, negotiation and revision, these guidelines set standards and define best practices for genetic testing labs world-wide. The guidelines place laboratory accreditation as the central element of ensuring the quality of genetic testing, and recommend that reports on genetic tests should only be issued by laboratories demonstrated to be competent by accreditation.

This strong commitment to accreditation contrasts sharply with the situation in Ireland, where there is no regulation whatsoever of clinical laboratory testing. As Ireland is a member of the OECD, it is obliged to ensure compliance with these guidelines, and this has been brought to the attention of the HSE.

## NATIONAL CENTRE FOR MEDICAL GENETICS INVOLVEMENT IN QUALITY INITIATIVES

The NCMG is prominently involved in all of the above initiatives, represented on the management group of EMQN and providing assessors for several other EQA schemes. One NCMG scientist is always on the steering committee for the UKNEQAS for Molecular Genetics, and the Centre's Director Andrew Green is on the steering committee for Cytogenetics. David Barton, Chief Scientist in Molecular Genetics, is a partner in EuroGentest and was a member of the core drafting group for the OECD guidelines. The NCMG work in EuroGentest is focused on the development of new reference materials and on the study of the implications of the IVD Directive for genetic testing. Caitriona King and David Barton recently published best practice guidelines for molecular genetic testing of haemochromatosis, developed through a consensus process for the UK Clinical Molecular Genetics Society.

## THE FUTURE

Molecular genetic testing has evolved at a dizzying pace over the last twenty-five years, and the pace in recent years has accelerated dramatically, driven by the technical advances of the Human Genome Project and related work, and demands for ultra-high-throughput genotyping from efforts to map genes for common complex disorders such as heart disease, diabetes and hypertension. Currently, diagnostic molecular genetics uses assays focused on known mutations (e.g. in cystic fibrosis) or which scan for mutations in one or two genes (e.g. familial breast cancer), based on PCR amplification and post-PCR hybridization reactions. However, chip-based microarrays can perform millions of tests at once, and before long it will be possible to sequence a person's entire genome accurately at a reasonable cost – individual gene tests can cost several thousand euro at present, so the 'thousand dollar genome' sounds like great value! This will pose major challenges for diagnostic scientists and regulators alike, as we struggle with the information overload, the ethical issues of answering questions the patient didn't want asked and the determination of the clinical significance of the millions of DNA sequence differences between individuals.

## REFERENCES / WEB LINKS


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