



European
Diagnostic
Manufacturers
Association

Genetic Testing

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Definitions

Genetic testing is the analysis *in vitro* of structural properties of DNA (sequence and/or chemical modifications of nucleotides), or of those properties of RNA, proteins, or metabolites that are the direct and sole consequences of their DNA template structure, to provide information about inherited or acquired traits that are transmitted during cell division and that affect all subsequent generations of cells (somatic) or offspring (germinal).

Medical genetic testing is application of *Genetic Testing* to derive information relevant to health-care, as it relates to disease risk prediction, disease diagnosis, disease treatment, and reproductive health.

Non-medical genetic testing comprises the application of *Genetic Testing* for purposes of DNA identification, (e.g. paternity and forensic testing), or presence of animal and plant materials in foods.

Whereas *Genetic Testing* of micro organisms is conventionally not included under the definition of *Medical Genetic Testing*, both are commonly included under the term *Molecular Diagnostics*.

Background

The use of medical tests to obtain information about the genetic constitution of individuals for clinical purposes (medical genetic testing) is not new. For example, the value of detection of sickle cell anaemia (a disease with high prevalence in families of African and Southern European descent) by examining blood cells is well established and allows the saving of many lives.

DNA-based technology available today has greatly expanded the amount and precision of genetic data that can be generated. While this is viewed by many as welcome progress,

there exists also public concern about use of genetic data that may violate individual privacy and result in disadvantages.

It is widely recognized that in health and disease both external (environment and life-style) and intrinsic (inherited, i.e. genetic) influences are co-operative.

Medical Genetic Testing: Impact

Scientifically, all genetic data are part of the overall spectrum of medical data and cannot be classified as a separate category. Genetic data cover a broad range of information content, ranging from extremely high (for genetic data related to rare inherited diseases) to modest or low (for the vast majority of all genetic data).

Pragmatically, two major disease categories may thus be distinguished, based on the relative importance of inherited factors on the one side and environmental and life-style factors on the other.

- Rare, single-gene, "classic heritable" diseases represent the extreme end of the spectrum where the impact of the genetic mutation is causative and outweighs all other influences. In these diseases, the notion that "genetics" play a "deterministic" role is a reasonable approximation of clinical reality (e.g. Huntington's disease, cystic fibrosis, hemophilia). However, even in single-gene disorders, environmental factors may be quite important as a trigger of clinical events; and substantial variation exists regarding disease manifestations (e.g. severity, age of onset, etc) that are attributable to environmental and life-style factors, including treatments, as well as to the effect of variation in other genes ("genetic background").
- Common complex diseases (e.g. heart disease, diabetes, arthritis, etc.) represent the great majority of all disorders and consequently impact the health care

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burdens of different societies. In these diseases the relative contributions of external and genetic factors are more balanced, the latter representing the combined effects of several gene variants, and the knowledge about genetic factors only aids in achieving somewhat more accurate diagnoses or predictions, very similar to the impact of other currently obtained medical information (such as plasma cholesterol or smoking status). Information on genetic variants in common complex disease is therefore “probabilistic” (i.e. raising or lowering likelihood of a correct diagnosis or an accurate prediction), and must always be seen in the context of environmental or lifestyle factors with which they interact.

The salient difference between these two contrasting categories is the magnitude of the information content of the genetic test with regard to the disease (i.e. its positive and negative predictive value, or its sensitivity and specificity, respectively). The higher this content, the more powerful and “deterministic” (for future risk-assessment) will a particular piece of information be.

It is logical that high information content raises the sensitiveness of data, and thus the potential for use to the disadvantage of the individual. This is true for all medical, including genetic, data. Thus, not the nature of the data (genetic or not), but the magnitude of information content is the relevant characteristic. The information content of any medical data, however, is highly contextual, i.e. dependent on the particular circumstances and the question to which it is applied. Thus, a series of Single Nucleotide Polymorphisms (SNPs) may hold no information content at all with regard to health-related issues, when at the same time its information content with regard to forensic or paternity studies may be extremely high.

Therefore, since the information content of any medical data may change substantially depending on circumstances, it should be self-evident that all medical information must comply with the same rigorous standards of data quality and must be afforded the same high degree of confidentiality. Special considerations, if appropriate based on information content, should always apply to

the bearer of the information, not the information per se.

The discussion should therefore be restated into a debate about the appropriate use of any medical data independent of its information content, rather than about the appropriate level of confidentiality of genetic vs. other medical data. Special considerations should be afforded to individuals who carry medical information with very high information content (which would include a positive HIV-test prior to becoming overtly sick) as compared to other medical data with lower, less predictive information content (such as cholesterol level, blood pressure, as well as the great majority of all DNA-derived data that do not pertain to genetic diseases), but not to the information per se and its nature (genetic or not). High information content, regardless of the nature of the test, may warrant protective measures for patients who are at risk for discrimination, such as have been afforded HIV-positive patients, in the interest of social justice and protection of the individual.

Public Perception

The current discussion about genetic information is, to a large extent, influenced by the misperception that all genetic data convey exceptionally high information content. This perception is related to the equally erroneous view that all our physical and psychological characteristics are simply a consequence of inherited properties (Genetic Determinism).

This public perception that genetic data represent a category of its own, and are more sensitive and require different standards of confidentiality and data protection than other medical data is understandable because (i) the vast majority of currently available genetic tests pertain to either to rare genetic diseases or to paternity and forensic testing, i.e. they have very high information content, and (ii) among all medical tests that have exceptionally high information content, the vast majority are tests predictive of rare genetic diseases. Therefore, current experience with genetic data and testing is largely restricted to examples where these tests indeed have

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very high information content. So far, the public has had very little exposure to or experience with other (DNA-derived) genetic tests, the vast majority of which carry low information content and where consequently no special considerations would apply.

It should be noted that as long as the public is not reassured that genetic information, like all other information, will be used based on its information content, and as long as such use is tolerated, all genetic information, regardless of its information content, will continue to be perceived as different and potentially discriminatory, reinforcing the sentiment of genetic exceptionalism. Only a rational public policy governing the use of all medical, including genetic data to protect the individual from abuse will stop this self-perpetuating dynamic.

Information and Education

The diagnostic industry, as well as the pharmaceutical industry, recognizes the importance of education and information if society is to benefit from current progress in biology and genetics. So, it is eager to participate in efforts to improve public knowledge and understanding of genetics, in general, and of genetic testing in particular. As one (obvious) aspect of this, it is recognized that manufacturers should therefore provide relevant information about their test products to the users of these tests and to the general public.

The in vitro diagnostics industry would like to see the new molecular diagnostic technology used and accepted positively as part of the established process to gain information, to treat and cure diseases and to improve the quality of life, while respecting the right of the person concerned to strict confidentiality.

The Individual and Genetic Testing

Individual genetic information is personal and private. It must be left to the individual to decide whether or not personal genetic information should be determined by genetic testing and what this information may be used for. Neither employers nor insurance companies, nor indeed governments or

medical professionals should decide about this.

Confidentiality of Medical Data

All personal medical information, including that from genetic testing, should be confidential. Legislation (such as the European Directive 95/46/EC on Personal Data Protection) is being introduced to protect the confidentiality of medical and personal information.

Medical information (including genetic information) should not be disclosed without the informed consent of the person concerned.

Informed Consent for Medical Tests

Similar to any tests, genetic tests should only be carried out after informed consent has been obtained. Informed consent includes full disclosure of the benefits, risks and limitations of the test, including alternatives to the tests, therapeutic and preventive options after testing. Some medical tests (especially genetic tests) provide information that can be determinant for the future life of the individual concerned and his or her family. In such cases, testing should only be performed after counselling and with informed consent of the individual concerned.

Genetic Testing and Benefits

Genetic testing can only be recommended if there is a benefit to the individual (or family) concerned. In addition to any benefit from the impact of genetic testing on further preventive or therapeutic measures for the person(s) concerned, this also includes psychological benefits for the individual tested (e.g. decreased anxiety) and information that the individual considers important for planning his or her life in future.

Genetic Testing and Professional Guidance

The way genes affect individual people is biologically complex and difficult to understand. In certain rare disorders (monogenic diseases) nucleic acid based

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testing provides (almost) categorical information about disease risk. In such cases, the need for specialised explanation and psychological assistance (“genetic counselling”) is generally acknowledged.

On the other hand, the incremental contribution towards overall disease risk in common complex diseases conveyed by inherited factors is likely to be quite comparable to that represented by external and life-style factors. Thus, if and when this is understood, the dialogue between patients and health professionals about such risk factors will not require expertise and procedures different from those currently employed in physicians’ offices with regard to life-style risk factors or to diseases like cancer.

Therefore, authorities should avoid restrictive legislation in this area. It is important that informed and concerned individuals should have access to genetic tests and to their own genetic information if they so decide.

Genetic Testing of Children (and others under control of a legal guardian)

The primary goal of medical genetic testing of infants, children or other persons under the control and guidance of a legal guardian should be their well being. Medical benefits to the child through early diagnosis or preventive measures and therapies may justify genetic testing and screening.

However, the number of diseases that can be successfully treated once identified is still quite limited. If no individual benefits are perceived, or, if no medical benefits of testing accrue before adulthood (which may be the case for such adult-onset disorders as Alzheimer’s disease), testing should be deferred until the child is of legal age and competent to make his or her own decision.

Pre-implantation Genetic Testing

Pre-implantation genetic testing may be offered to couples undergoing *in vitro* fertilisation to detect congenital disease in an embryo before implantation in the uterus. This testing can be of value to families wanting to know if they are at risk of

transmitting a genetic disorder to their children.

Because of divergence of religious beliefs and opinions about the ethics of pre-implantation diagnostic testing, this is the subject of important public and political debate in many countries.

Prenatal Genetic Disease Screening

A number of prenatal diagnostic tests are accepted as standard care and are routinely offered during pregnancy (e.g. maternal serum alpha-fetoprotein screening and chorionic villus sampling).

However, there is public concern and growing controversy that prenatal genetic testing might be misused for selection purposes, based on medically irrelevant or socially unacceptable criteria. This is an issue not unique to genetic testing (sex-selection based on ultrasonography data being the most common example) that may require regulatory oversight based on societal consensus. However, it should be noted that with regard to the vast majority of pregnancy terminations we defer today in most countries fully to women’s autonomous decisions, without any consideration of medical justification or lack thereof.

Ethical Issues and Medical Practice

As is evident from the foregoing, genetic testing has the potential of raising important ethical, religious and social issues with regard to when such testing should be carried out (pre-implantation, prenatal, newborn, postnatal, childhood, adolescent and adult) and to what use should be made of the results. These issues will need to be addressed responsibly by an informed dialogue among all stakeholders at national and international levels to achieve consensus and compromise that will then be reflected in appropriate guidelines, regulations, or legal frameworks. Industry will play its role in this process.

It is the diagnostic industry’s position that appropriate guidelines for or regulation of medical practice with regard to genetic testing is needed to resolve these issues.

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Quality and Safety of Genetic Tests

Medical genetic tests that are manufactured by industry must be produced in compliance with the In Vitro Diagnostic (IVD) Medical Device Directive 98/79/EC.

However, some health institution laboratories presently carrying out genetic testing do not use products manufactured in compliance with IVD Directive 98/79/EC but use tests developed in-house. This is because the Directive contains an exemption relating to test products that are made in, and used only within one and the same health institution. Thus, in such institutions, genetic tests that have been developed by the professional users themselves can be, and are, used.

Therefore, industry recommends that such in house products be regulated according to the same standards as manufactured products, and that all laboratories offering genetic testing services have relevant quality management systems and are accredited for the type of specialised testing they are performing.

The Future of Genetic Testing

Progress in human molecular genetics has broadened the opportunities for the application of genetic testing with regard to:

- development of new diagnostic tests for medical disorders;
- selection of patients more likely to respond to drug treatment (pharmacogenetics);
- more precise prediction of future disease risks.

Who Decides About Medical Genetic Testing and What it is Used for?

An active debate is currently ongoing about whether this information should be collected and how it should be used, largely as a result of today's lack of experience of the predictive power of molecular diagnostic data for common complex diseases. Given the fact that genetic testing results are not qualitatively different from any other kind of medical data, this debate should be refocused on the magnitude of information content of medical data, and on appropriate

governance of what medical information ought or ought not be used for.

The IVD industry firmly opposes any inappropriate discrimination against or unlawful differential treatment of individuals based on their present or future health status, and on medical data including genetic information. In any case, safeguards on the use of medical data should not impede the ability to carry out research necessary for innovation.

Therefore, the IVD industry strongly endorses a dialogue among all interested parties, including patient advocacy groups, health care providers (e.g. physicians, nurses, pharmacists), health authorities, ethicists, health policy makers, governments, health insurance organisations, as well as other health industries to reach consensus on how medical information should provide individual and societal benefits, and which uses of this information should not be allowed. Such a consensus would define best practice principles, ensure high ethical standards, and by actively protecting the individual patient would help reduce concerns about possible misuse of medical information. It would further serve to provide a balance between allowing important medical research to continue while simultaneously safeguarding the interests of individuals and society.

**EDMA Public Relations Committee
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