A GUIDE TO THE PROVISION OF NON-CLINICAL GENETIC TESTING

MINISTRY OF HEALTH

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Contents

1 Objective

1.1 This guide acknowledges the rapid advancements in the field of genetics and genomics and was developed with the intention of providing information to providers of non-clinical genetic testing who are operating or wish to operate in Singapore to ensure the safety, welfare and privacy of the consumers. While this guide is not primarily designed for consumers, it may also help to inform and guide the expectations of potential consumers of non-clinical genetic testing.

2 Background and Definition of Direct-To-Consumer Genetic Testing

2.1 Direct-to-consumer (DTC) genetic testing[1] is a method of providing genetic tests directly to consumers without the involvement of a healthcare provider (i.e. where such tests are NOT 'ordered' by a medical practitioner). Upon purchase of such products, the consumer would typically need to collect a DNA sample, commonly by performing a cheek swab or saliva spit, and mail the sample back to the company located in Singapore or overseas. The company would send the test report directly to the consumer. Notably, this deviates from the traditional process where a medical practitioner orders the appropriate test from a laboratory, collects and sends the sample, interprets the test result and manages the follow-up of the individual.

2.2 DTC genetic tests have been gaining prominence and new companies have sprung up rapidly over the years. With the expanding landscape, it is imperative for companies who intend to manufacture, distribute, market and sell such products in Singapore to understand the existing regulatory controls.

3 Scope of 'Clinical Genetic Testing'

3.1 Broadly, genetic testing can be categorised into clinical and non-clinical genetic testing. Two factors can be used to distinguish between clinical and non-clinical genetic testing: (a) purpose of the genetic test and (b) conditions and terms reported in the test report. A genetic test would be considered as a clinical genetic test –

(a) if it is used for any one of the following purposes[2]:
    (i) to confirm or exclude the presence of a genetic disease in a symptomatic person (diagnostic genetic testing)
    (ii) to predict the risk of having affected children (carrier testing)

[1] Genetic testing means the analysis of an individual's human chromosomes, DNA, RNA, gene and/or gene products to detect genetic variants.

[2] Refer to Paragraph 2 - Interpretation of the Code of Practice on the Standards for the provision of clinical genetic/genomic testing services and clinical laboratory genetic/genomic testing services ('Standards')

(iii) to predict a genetic condition in an asymptomatic person for a disease that will occur later in life (predictive screening/testing)
(iv) to predict a person's drug response (pharmacogenetic testing)
(v) to predict a person's risk of developing a disease or condition (whether inherited or not inherited)
(vi) any purposes that purport to assess, diagnose, prevent, alleviate or treat a medical condition or disorder

or

(b) if the test reports conditions and terms which connote meanings similar to medical conditions or induce consumers to seek further medical solutions.

3.2 In order to determine if a genetic test is a clinical genetic test, it is also important to consider (a) the context of the gene(s)/ variant(s) selected in the test panel, and (b) whether and/or how the genetic test reports on the association of a medical condition. A test that:

(i) has the potential to detect variants in genes that cause single gene disorder or medical condition; or
(ii) may inform the susceptibility of an individual to a clinically significant medical condition,

would also be considered a clinical genetic test.

Some examples are as follows:

Gene	**Medical Condition**
BRCA 1 & 2	Hereditary Breast and Ovarian Cancer
LDLR, APOB, PCSK9	Familial Hypercholesterolemia
HBA1, HBA2, HBB	Thalassemia
SMN1	Spinal Muscular Atrophy
COL4A3	Alport Syndrome
PAX1	Otofaciocervical Syndrome
TWIST1	Craniosynostosis
GFAP	Alexander Disease
MSH2	Lynch Syndrome
RB1	Retinoblastoma
APC	Familial Adenomatous Polyposis
RET	Familial Medullary Thyroid Cancer
VHL	Von Hippel-Lindau syndrome
RYR2	Catecholaminergic Polymorphic Ventricular Tachycardia
NF2	Neurofibromatosis Type 2

3.3 On the other hand, <u>non-clinical genetic testing</u> refers to genetic testing for non-clinical purposes such as general wellness and recreational purposes, which are **<u>not</u>** used to assess, diagnose, prevent, alleviate or treat a medical condition or disorder. Genetic tests for general wellness have intended uses that relate to the maintenance or promotion of a general state of health or a healthy activity.

It may involve claims about sustaining or offering general improvement to functions associated with a general state of health that do not make any reference to diseases or medical conditions. Any genetic testing that perform the same function as clinical genetic testing would be considered clinical, **regardless of any disclaimers used**. Some examples of non-clinical genetic testing are as follows:

Types of non-clinical genetic testing	Purpose	Example
Ancestry testing	Test intended to provide information about an individual's relatedness to a certain ancestor or ancestral group and/or how much of an individual's genome is likely to have been inherited from ancestors from particular geographical areas or ethnic groups.	Test that presents algorithmic-based ethnicity or genetic heritage in a pie chart.
Innate behavioural/ lifestyle testing	Test intended to provide information about an individual's: • Behavioural propensities or talents • Performance capacity (physical or cognitive) • Response to certain environmental conditions (e.g. stress) and that are designed to assist the individual to manage his/her lifestyle patterns and behaviour (e.g. through customised fitness programmes) but does not include treatment advice or recommendations.	Test that claims to predict artistic, musical ability, emotional intelligence, or propensity to travel based on genetic information.
Nutrigenomics testing	Test intended to provide information about an individual's response to certain diets.	Test that claims to predict whether an individual would require more nutrients (e.g. genetic markers that influence a person's nutrition and fitness)

4 Regulatory Approach for Clinical and Non-Clinical Genetic Testing

4.1 The regulation of healthcare services in Singapore falls under the purview of the Private Hospitals and Medical Clinics Act (PHMCA). On 1 July 2018, MOH promulgated the Code of Practice on the Standards for the provision of clinical genetic/genomic testing services and clinical laboratory genetic/genomic testing services ('Standards'), which is meant as a 'guidance document' to all licensees regulated under the PHMCA. In particular, the Standards stipulate that clinical genetic testing services can only be provided to consumers by healthcare institutions licensed under the PHMCA. Clinical genetic testing services cannot be offered or provided by manufacturers or suppliers directly to consumers, whether for a fee or other reward. This means that clinical genetic tests **cannot be offered as DTC tests** in Singapore.

4.2 The genetic tests for non-clinical purposes such as general wellness (e.g. testing for innate behaviour or talents, fitness and nutrigenomics) are considered as 'low risk' to consumers and may be offered directly to consumers. These tests should be marketed as 'recreational or for non-clinical' purposes (e.g. to encourage individuals to maintain or adopt a particular lifestyle).

5 Good Practices for the Providers of Non-Clinical Genetic Testing to Safeguard Consumers' Safety, Welfare and Privacy

5.1 Consumers' Safety

(a) Concerns regarding the misinterpretation of health-related predictions in the test report – While some genetic tests are marketed as 'recreational or for non-clinical' purposes, the test report may contain genetic risks of certain medical conditions such that the consumer may misinterpret the results as susceptibility or diagnostic genetic testing (which would be considered as clinical genetic testing and not allowed to be offered as DTC tests). In addition, certain advice or recommendations in the report may be reported in an ambiguous manner such that they do not provide any meaningful information to consumer. This may needlessly alarm the consumers.

Good practices for non-clinical genetic testing providers:

(i) When advertising non-clinical genetic tests, the providers should be mindful of the controls set out in Sections 3 and 4 of the Medicines (Advertisement and Sale) Act relating to certain diseases, medical skills and services.

(ii) The advertisement, marketing material, test report containing results, as well as subsequent follow-up services (e.g. real-time enquiry platform and e-consultation with relevant experts such as dieticians) **must not carry any medical information and/or**

advice to assess, predict, diagnose, treat, prevent or alleviate an ailment, a condition, disability, disease or disorder, implied or otherwise, affecting any part of the human body or mind. A list of examples of prohibited diseases, conditions and disorders is provided in *Annex A*.

Below are some examples of statements which are considered medical information and/or advice and should be avoided. These include the use of layman's terms to connote meanings similar to medical conditions or to induce consumers to seek further medical solutions.

Statements that are considered as medical information and/or advice
You are more likely to have inflammation which could lead to arthritis.
Your results show that you need a higher intake of antioxidants. A low intake of antioxidants puts you at higher risk of cancer, Parkinson's disease, auto-immune diseases and more.
This genetic test report will help you to prevent diseases such as type 2 diabetes, cardiovascular disease, cancer and more.
Understanding the factors that contribute to the inflammatory process will help you prevent cancer.

(iii) Providers should **include disclaimers** in the pre-purchase page/form, marketing materials, consent form and test report to inform the consumer that *'the test cannot be used to assess the risk of disease or conditions, detect, diagnose, manage or treat any health or medical disease/conditions. Any results from the test should not be regarded as medical information and/or advice.'*

The inclusion of disclaimers recommended here is to serve as a good practice in the context of the provision of non-clinical genetic testing. As mentioned in paragraph 3.3, any genetic testing that performs the same function as clinical genetic testing would still be considered clinical, regardless of any disclaimers used.

(iv) Providers should provide information to aid consumers in understanding how to interpret the test results.

(v) Providers should inform the consumers of all risks associated with testing, including psychological risks and risk to family members.

(b) Concern about the return of raw genetic information to consumers – Other than returning the report of the genetic test results, some providers may provide the option of returning raw genetic information to the consumer. Providers need to be cognisant of the potential risks involved for the consumers where they may subsequently engage online 'third-party

interpretation' services to analyse and interpret the raw genetic information. These 'third-party interpretation' services could potentially provide the consumers with more information about their disease risk and traits without the medical guidance which is required in making important medical decisions, such as providing the necessary follow up, counselling and support to the individual.

Good practice for non-clinical genetic testing providers:

Providers should educate consumers on how the raw genetic information should or should not be used, and include suitable disclaimers that the provision of the raw genetic information is only for information and is not suitable for clinical use such as the stopping or starting of treatment therapies. Providers should also include an advisory note to direct consumers to seek an appropriate medical professional on the interpretation of raw genetic information.

5.2 Consumers' Welfare

(a) Concern regarding misleading statements made by providers - In some cases, statements made regarding non-clinical genetic testing may be exaggerated or unsupported by scientific evidence. Moreover, it has also been observed overseas that some companies have claimed that the specific advice or recommendation provided was based on the consumer's genetic information. However, most of these recommendations were found to be medically unproven or simply computed based on background information submitted by the consumer upon purchase of the test (rather than based on the genetic information of the consumer). Such misleading or unproven claims may result in consumers purchasing the product with false expectations of the benefits of such testing.

Good practices for non-clinical genetic testing providers:

(i) Providers should inform consumers of the strength of scientific evidence of the tests and any claims of benefits of the outcomes of such tests, as well as any scientific limitations of the tests and technology used.

(ii) Providers should avoid misleading statements and scientifically and/or clinically unsupported recommendations. Below are some examples of statements that should be avoided.

Examples of misleading statements	MOH's position
Our lab's genomic sequencing is 99.5% accurate.	This statement could potentially be misleading to the consumer, who may interpret that the outcomes stated in the report are 99.5% accurate in

		correlating to the particular gene or its variant they have, when this is not the case. This statement here only refers to the accuracy of the test in detecting the presence of a particular genetic variant.
	Your genetic sequence will inform you of your wellness traits.	This statement is misleading as there are many other factors such as lifestyle behaviour and diet that could contribute to the specific wellness trait.
	You may refer to the recommendation in this report to reverse the effect of your genes.	This statement may connote that (a) one's genetic make-up is the main causal factor to the onset of a condition and (b) adopting the recommendation will affect the expression of genes, which is scientifically unproven.
	An individual gene is responsible for a particular behavioural trait.	Specific human behaviours are the result of the interaction among multiple genes and numerous environmental factors.
	Your genetic makeup contains this variant of *CYP24a2* gene which predisposes you to Vitamin D deficiency.	This statement may give the impression that one's genetic make-up is the main causal factor for the vitamin deficiency. However, the lack of adequate intake of Vitamin D and lack of appropriate exposure to sunlight also contribute to Vitamin D deficiency.

(iii) Providers should **disclose the sensitivity, specificity, and predictive value of the genetic test**, and the populations for which this information is known, in an understandable and readily accessible manner. For example, if the variants included in the test are most common in people of certain descent/populations and do not represent the majority of gene variants in the general population, it should be disclosed to the consumers.

(b) Concerns about consumers being misled into buying 'personalised' fitness programmes and supplements based on genetic information – Currently, there is a lack of valid scientific evidence to prove that genetic information

can be used as the main factor to effectively recommend nutritional choices or to customise or personalise dietary supplements or cosmetics. In some cases overseas, reports have shown that these 'customised' supplements were merely a base formula of ingredients that were beneficial to the general population with additional nutrients supplemented based on the 'deficiencies' identified by the genetic test.

Good practice for non-clinical genetic testing providers: Providers should provide a cautionary note to inform the consumers of the limitations (e.g. lack of valid scientific evidence) when offering such 'customised' products.

5.3 Consumers' Privacy

(a) Concern about how consumer data may be used or disclosed – Personal data submitted by the consumers upon purchase of the genetic tests (e.g. name and contact details linked to genetic information) **should not be used or disclosed without obtaining consent from the consumers**. The Data Protection Provisions under the Personal Data Protection Act (PDPA) requires organisations to, among other things, notify an individual of the purposes and obtain his consent for the collection, use and disclosure of his personal data, unless any relevant exception under the Second, Third and Fourth Schedules to the PDPA applies such that personal data can be collected, used and disclosed without consent. This is to ensure that consumers are provided with sufficient information about the purposes of the genetic test and use of personal data (e.g. how their personal data and results of the test will be used, whether there could be any risks or impact to the individual etc.) so as to allow them to make an informed decision.

(b) Other than informing consumers of the providers' privacy practice, it is important for the providers to put in place **robust data security measures or arrangements to prevent unauthorised access of any databases** containing personal data by third parties as required under the PDPA.

Good practices for non-clinical genetic testing providers: (i) Providers should disclose the extent and measures to which personal data will be kept confidential and whether the personal data will be disclosed and used for other purposes. (ii) Providers must obtain consent from the individuals whose personal data they intend to disclose to others unless any of the relevant exceptions under PDPA apply. (iii) Providers should disclose whether the samples will be stored, discarded and used for secondary purposes. (iv) Providers should inform consumers on what will happen to consumers' samples and personal data if the company ceases operation.

(c) Concern about receiving marketing messages when the consumer's telephone number is in the Do Not Call (DNC) Registry – The DNC Provisions under the PDPA will apply to organisations that send specified messages to Singapore telephone numbers. A specified message may be in the form of a voice call, text message or fax message, and is defined in Section 37 of the PDPA. In most instances, a marketing message of a commercial nature would be a specified message within the meaning of the PDPA.

Good practices for non-clinical genetic testing providers:

Providers who wish to send messages that market a product or service (e.g. health supplements and non-clinical genetic tests) would have to check the DNC Registry and ensure that they do not send specified messages to numbers that are registered, unless:

(i) the individual has given clear and unambiguous consent in evidential form to receive such messages from the provider;
(ii) the provider has an ongoing relationship with the individual; or
(iii) the message is excluded from the definition of 'specified message'.

6 Other Legislation

Any provider of non-clinical genetic testing shall ensure compliance with all other relevant laws and regulations, where applicable. These include the PDPA, the Human Biomedical Research Act, the Regulations made thereunder, all other directives or guidelines which may be issued by MOH or other relevant agencies/bodies from time to time.

7 Contact Information

For genetic testing providers or potential consumers of DTC genetic testing who like to seek further clarification or information on

- the provision of genetic testing in Singapore, please contact MOH via email at: [eLIS@moh.gov.sg]
- data protection provisions or DNC provisions, please contact Personal Data Protection Commission (PDPC) via email at: [Info@pdpc.gov.sg]
- matters of transactional nature, please contact the Consumer Association of Singapore (CASE) via CASE Consumer Hotline at: 6467 9055

Annex A

Examples of Diseases/Conditions/Disorders Not Allowed for Non-Clinical Genetic Testing

Body system/Organs	Examples of related claims not allowed
Circulatory system	Hypertension, stroke, cholesterol disorders, reduces cholesterol, regulates platelet aggregation, coagulation defects, arteriosclerosis
Eye, Ear, Nose	Blindness, cataract, deafness, inflammation
Digestive system	Periodontitis, ulcers, gastritis, hepatitis, liver cirrhosis, fatty liver, diarrhoea, constipation, inflammation of the intestines/liver/pancreas
Endocrine system	Diabetes, thyroid disorders, hypothyroidism, prostate diseases, thymus disorders, hormonal regulation
Metabolic system	Obesity
Respiratory system	Asthma, tuberculosis, bronchitis, sinusitis
Skin, Hair, Nails	Fungal infection, eczema, ulcers, warts, moles, pigmentation disorders
Immune system	Leprosy, AIDS, allergies, immunisation
Muscular, connective tissues and skeletal systems	Osteoporosis, arthritis, sclerosis, autoimmune diseases, sclerosis, inflammation of joints
Nervous system	Epilepsy, fits, paralysis, Alzheimer's disease, Parkinsonism, dementia, neuropathies, drug addictions, depression, eating disorders
Renal system	Kidney stones, renal failure, nephritis, urinary tract infection, incontinence, cystitis
Reproductive system	Menstrual disorders, sexual dysfunction, infertility, frigidity, impotency, conception, pregnancy
Others	Cancers, infectious diseases

The above list is not exhaustive and may be revised from time to time.

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