MINISTRY OF HEALTH
SINGAPORE

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All Licensees of Healthcare Establishments
All Registered Medical Practitioners

UPDATES TO CODE OF PRACTICE ON THE STANDARDS FOR THE PROVISION OF CLINICAL GENETIC/GENOMIC TESTING SERVICES AND CLINICAL LABORATORY GENETIC/GENOMIC TESTING SERVICES

The 'Standards for the Provision of Clinical Genetic/Genomic Testing (CGT) Services and Clinical Laboratory Genetic/Genomic Testing (LGT) Services' ('Standards') were issued as a Code of Practice (COP) to Private Hospitals and Medical Clinics Act (PHMCA) licensees and registered medical practitioners on 1 July 2018. The COP sets out minimum standards for the provision of CGT and LGT services and specific requirements on healthcare institutions and personnel providing these services.

2 The COP will be translated into the Clinical Genetics and Genomics Services (CGGS) Regulations under the new Healthcare Services Act (HCSA) for implementation. Further details on the implementation of these Regulations will be shared at a later date.

Key Updates to the COP

3 Since its issuance, MOH has received queries and feedback on the COP from licensees and registered medical practitioners providing CGT and LGT services. MOH also surveyed selected PHMCA licensees on the COP from December 2019 to January 2020 to gauge the operational readiness of stakeholders, and identify and review areas which may require further clarification. In consultation with the Genetic Testing Advisory Committee (GTAC), MOH has assessed the feedback and updated the COP accordingly.

4 Whilst the primary intent of each clinical genetic test remains the basis for their tiering in the COP, the tiering of level 2 and level 3 genetic tests has been further nuanced to take into account the following considerations:

(a) Likelihood of the variants/changes investigated being germline in nature or having a risk of identifying a hereditary cancer syndrome (i.e. a single gene disorder predisposing to cancer); and

(b) Whether further tests are needed for the diagnosis and/or confirmation of

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a germline variant/change/condition.

5 Other key updates to the COP are summarised in Table 1:

Table 1: Summary of Key Updates to the COP

S/N	Issue	Key Update
a	Definition of 'genetic testing'	The definition of 'genetic testing' is revised to include tests 'with the purpose of detecting a germline or somatic variant(s), genotype(s), phenotype(s) or karyotype(s)' as the policy intent is for any clinical genetic test with a genetic basis or driven by genetics to be within the scope of the COP.
b	Definition of 'biochemical genetic tests'	A definition of 'biochemical genetic tests' is included in the revised COP to provide clarity. Additional examples of such tests have also been included in Annex A.
c	Definitions of 'incidental findings' and 'secondary findings'	The definitions of 'incidental findings' and 'secondary findings' are included in the COP to provide clarity.
d	Genetic testing on minors	While the terms 'Adult' and 'Minor' continue to be used in the COP, they are no longer defined explicitly and applied specifically in the context of genetic testing. In assessing whether an individual is more appropriately considered an adult or a minor, licensees and medical practitioners should refer to prevailing standards, regulations and/or guidelines for guidance, no different from other areas of clinical practice.
e	Genetic testing on samples of deceased individuals	Specific requirements on genetic testing on samples of deceased individuals are no longer prescribed in the COP. Licensees and registered medical practitioners should refer to prevailing standards, regulations and/or guidelines for guidance, as per other areas of clinical practice.
f	Replaced the term 'required' with 'mandatory' for all consent, counselling and genetic counselling requirements	For greater consistency in our use of the term, 'required' has been replaced with 'mandatory' in the consent, counselling and genetic counselling requirements in the COP for the provision of level 1 and 2 genetic tests, and level 3 genetic tests respectively.

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g	Pre-test genetic counselling for level 2 genetic tests that may reveal a germline variant/change	For level 2 genetic tests with a reasonable chance of revealing a germline variant/change that have wider implications than drug dosing/selection (e.g. the risk of having a hereditary cancer syndrome), the requirement to *offer* pre-test **genetic** counselling to the patient is included in the revised COP to further safeguard the patient's safety and welfare.
h	Additional component for post-test genetic counselling	Consideration for testing of family members' carrier status and/or variant status to confirm the patient's condition is included as an additional component for post-test **genetic** counselling in the revised COP.
i	Competencies of clinical laboratory director	To ensure sufficient clinical laboratory personnel for the provision of LGT services, the qualification requirements for a clinical laboratory director have been expanded to include a person with a 'Master's degree in molecular genetics, biochemical genetics or cytogenetics, and has at least **10 years** of relevant working experience in molecular genetics, biochemical genetics or cytogenetics in a clinical laboratory'.
j	Clinical recommendations for genetic tests listed in Annex B and for all pharmacogenetic test reports	The requirement for clinical recommendations with regard to drug interactions and toxicity to be provided in the reports for genetic tests listed in Annex B and for all pharmacogenetic test reports, is included to allow for more tailored recommendation for the patient.
k	Annex A	A new comparative table outlining the consent and counselling requirements for the three levels of genetic tests is included in the revised COP. Examples of genetic tests across the various levels of genetic tests are updated in Annex A.
l	Annex B	The list of genetic tests approved for classification as level 1 genetic tests is updated in the revised COP.
m	Annex C	The decision matrix to guide the tiering of genetic tests is updated to reflect the more nuanced tiering of level 2 and 3 genetic tests (as described in para 4 above).
n	Annex E	The Clinical Pathology Accreditation (UK) is removed from the list of agencies that endorse and/or provide external quality assessment schemes (EQAS).

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Extension of 'sunrise period'

6 The current 'sunrise period' for PHMCA licensees to comply with the COP was scheduled to end on 31 December 2020. In view of the COVID-19 situation, MOH will be **extending the 'sunrise period' until the new CGGS Regulations is implemented under HCSA, which will be announced at a later date**. In the interim, licensees and registered medical practitioners are strongly encouraged to comply with the revised COP (2021) and use this further extension of the 'sunrise period' to review and make the necessary changes to their current processes.

7 The revised COP (2021) and FAQ are attached below. Should you require further clarification or feedback to the COP, please send us your queries via email at eLIS@moh.gov.sg.

Thank you.

Best regards

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MINISTRY OF HEALTH

SINGAPORE

REVISED CODE OF PRACTICE (2021)

STANDARDS FOR THE PROVISION OF CLINICAL GENETIC/GENOMIC TESTING SERVICES

STANDARDS FOR THE PROVISION OF CLINICAL LABORATORY GENETIC/GENOMIC TESTING SERVICES

Contents

PART A: APPLICATION AND INTERPRETATION

1. Application

1.1 This Code of Practice (also known as "Standards") sets out the minimum standards required for the provision of clinical genetic/genomic testing ("CGT") services, and clinical laboratory genetic/genomic testing ("LGT") services. The Code of Practice places specific requirements on healthcare institutions, licensees and personnel (including doctors) providing CGT and LGT services.

1.2 In this Code of Practice, genetic tests, as defined in paragraph 2.11, are categorised into 3 levels, each with its respective ordering restrictions and associated requirements (details of the categorisation are set out at paragraphs 4, 9 and 14 below, and examples of genetic tests in **Annex A**). For the purpose of this document, the terms "genetic test(s)" and "genetic testing" include genetic and genomic test(s), and genetic and genomic testing, respectively. The 3 levels of genetic tests have been tiered according to the:

- Impact of the tests to the patient and his/her family, including the follow-up management required;
- Risk of inappropriate ordering of genetic tests; and
- Predisposition to wrong interpretation of test results.

1.3 The Code of Practice does **not** apply to the provision of CGT and LGT services in the following areas:-

a. genetic testing solely for research, education or any other non-clinical purposes;

b. genetic testing on samples of deceased individuals;

c. genetic analysis of non-human DNA, RNA, chromosomes;

d. preimplantation genetic diagnosis (PGD);

e. forensic testing;

f. identity/relationship testing (e.g. paternity or kinship testing); or

g. tests that are used primarily for the diagnosis of non-genetic diseases but may contribute to the diagnosis of genetic diseases or disorders (e.g. blood smears and certain serum chemistries such as lipid profile).

1.4 In addition to this Code of Practice, any licensee and/or personnel (including doctors) providing CGT and LGT services shall refer to and ensure compliance with all other applicable laws and regulations. These include the Private Hospitals and Medical Clinics (PHMC) Act, the Personal Data Protection Act, the Health Products Act, the Mental Capacity Act, the Human Biomedical Research Act, Intestate Succession Act and Application of Muslim Law Act, the Regulations made thereunder, and all other licensing terms and conditions, directives or guidelines (e.g. Singapore Medical Council Ethical Code and Ethical Guidelines) which may be issued by the Ministry of Health (MOH), or other relevant agencies/bodies from time to time.

2. Interpretation

In this Code of Practice, unless the context otherwise requires –

2.1 **"Actionable"** means having the ability to modify a patient's medical management, a patient's own health-related actions, and/or a patient's life-plan (e.g. relating to reproduction or marriage decisions).

2.2 **"Analytical validity**" means the ability of a test to accurately measure the presence or absence of the analyte it tests e.g. the chromosomes, DNA, RNA, genes and/or gene product such as proteins or metabolites.

2.3 **"Biochemical genetic tests"** means tests that evaluate the quantity, structure and/or activity level of a protein/metabolite for the diagnosis of inborn errors of metabolism. These tests enable the evaluation, diagnosis, treatment and monitoring, and carrier testing of inborn errors of metabolism with an underlying genetic basis.

2.4 **"Clinical validity"** means the accuracy with which a test identifies a patient's clinical status.

2.5 **"Clinical utility"** means the usefulness of a test used in clinical practice, and takes into account the benefits and risks of the test. Potential benefits include making a diagnosis, guiding treatment and patient-management, deriving implications relating to the patient's reproduction or marriage, more accurate risk of recurrence counselling, and prevention of a disease in the patient or his/her relative. Potential risks include financial cost, psychological stress, and effect on insurance premiums/claims.

2.6 **"Clinical Genetic ("CG") service"** means a medical practice that provides diagnostic, management, risk assessment, education and/or counselling services to an individual and/or his/her family member(s) with, or who is/are at risk of conditions that have a genetic basis. Examples of services that a CG service would provide include:-

a. evaluating an individual, making a diagnosis, ordering appropriate tests, interpreting test results, counselling and/or managing the individual and his/her family member(s);

b. evaluating an asymptomatic individual for carrier status, ordering appropriate tests, interpreting test results, counselling and/or managing the individual and his/her family member(s);

c. evaluating an asymptomatic individual for presymptomatic/susceptibility risk assessment, ordering appropriate tests, interpreting test results, carrying out treatments and/or taking other appropriate follow-up actions;

d. evaluating an individual for reproductive risk of a genetic condition(s), ordering appropriate tests, interpreting test results, discussing options for managing reproductive risk, and/or counselling regarding therapeutic interventions;

e. evaluating an implanted embryo/foetus for risk of a genetic condition(s), ordering appropriate tests, interpreting test results, discussing options for managing reproductive risk, and/or counselling regarding embryonic/foetal therapeutic interventions;

f. newborn screening for a genetic condition(s) using level 3 genetic tests; and

g. genetic screening of an individual, subpopulation or the whole population using level 3 genetic tests.

For the avoidance of doubt, "CGT services" are a subset of "CG services", as the latter encompasses more than CGT services.

2.7 "**CGT services**" means the offering and/or ordering of genetic tests, and the provision of counselling (amongst other requirements) in accordance with this Code of Practice.

2.8 A **"carrier"** is an individual who does not display any symptoms of a genetic disease/condition but who has a pathogenic genetic variant(s)/change(s) that can be transmitted to the next generation. An individual may be identified as a carrier through various "**carrier testing"** or screening methods.

2.9 **"Diagnostic genetic testing"** means genetic testing done on a symptomatic individual with the purpose of confirming or excluding a genetic condition(s). The testing may involve looking for a germline or a somatic genetic variant/change.

2.10 **"Genetic counselling"** is the process of helping a patient to understand and/or adapt to the medical, psychological and genetic contributions of a disease or condition. It includes the interpretation of family and medical histories, assessment of the likelihood of disease occurrence or recurrence, and education about the inheritance, testing, management and prevention of the disease/condition, and the relevant support resources and research available so as to allow for informed decisions to be made with regard to the disease/condition or the risk of having a disease/condition.

[*Explanatory note: The difference between counselling and genetic counselling is explained in **Annex A**.*]

2.11 **"Genetic testing"** means the analysis of an individual's human chromosomes, DNA, RNA, genes and/or gene product such as proteins and/or metabolites with the purpose of detecting a germline or somatic variant(s), genotype(s), phenotype(s) or karyotype(s). The genetic variant(s) detected can be indicative of a heritable or non-heritable change(s)/condition(s). A **"genetic test"** is the procedure used when carrying out genetic testing.

2.12 **"Germline genetic testing" is also known as "genetic testing for a heritable variant".** It is genetic testing for the primary purpose of detecting a germline variant(s)/change(s) that is present in most/all cells. Examples of such tests include:

a. carrier testing for a germline genetic condition(s) (refer to 2.8);

b. diagnostic genetic testing for a germline genetic condition(s) (refer to 2.9);

c. newborn screening for a germline genetic condition(s) (refer to 2.19);

d. predictive testing or presymptomatic testing for a germline genetic condition(s) (refer to 2.20);

e. prenatal genetic testing for a germline genetic condition(s) (refer to 2.21);

f. susceptibility testing for germline genetic condition(s) (refer to 2.28); and

g. pharmacogenetic testing for the detection of a germline variant(s)/change(s) for the purpose of informing drug selection or dosing (refer to 2.23).

2.13 **"Genetic screening for germline genetic condition(s)"** is genetic testing for the primary purpose of detecting a genetic variant(s)/change(s) that is present in most/all cells. This individual is being screened because of the population's risk structure for germline conditions e.g. age group, ethnic group. Examples of such tests include:

a. carrier screening for a germline genetic condition(s) based on ethnic group; and

b. prenatal genetic screening for an embryonic/foetal germline genetic condition(s) based on maternal age.

2.14 **"Germline variant"** means an alteration in DNA that is present within the germ cells (sperm or egg). Such a variant/change is usually also found in all other cells. Hence, a germline variant(s)/change(s) can be passed on to the next generation (i.e. heritable).

2.15 **"High-throughput sequencing"** describes a method that allows for faster sequencing of DNA and/or RNA than Sanger sequencing. Sequencing is the process of determining the precise order of nucleotides within a DNA or RNA molecule. The term "**next-generation sequencing (NGS)**" is often used to describe high-throughput sequencing. In this Code of Practice, "**NGS"** includes all forms of high-throughput sequencing.

2.16 **"Incidental findings"** means non-intended findings that arise and are outside the original purpose for which the test or procedure was conducted. This is distinct from "secondary findings", which are not the primary target/goal but nonetheless intended to be sought.

2.17 **"LGT services"** means the provision of clinical laboratory genetic tests by a clinical laboratory with the purpose of detecting a germline or somatic variant(s), genotype(s), phenotype(s) or karyotype(s). It may include the provision of biochemical genetic tests, cytogenetic tests and/or molecular genetic tests.

2.18 **"Laboratory-developed test"** (LDT) means an *in vitro* diagnostic test that is developed, validated and/or used only for that particular clinical laboratory's in-house pathology purposes. As such, an LDT is not intended for use in or sale to other laboratories. If an LDT is made available for use in or sale to other laboratories, it would no longer be exempted from pre-market registration and prior approval will be required from the Health Sciences Authority.

2.19 **"Newborn screening for a genetic condition(s)"** means genetic testing done on babies soon after birth with the purpose of identifying babies who have a genetic condition(s) and who may benefit from early diagnosis and/or early treatment.

2.20 **"Predictive screening/testing" for germline genetic condition(s) or "presymptomatic screening/testing" for germline genetic condition(s)** means genetic testing done on an individual who displays no symptoms of any genetic condition(s) but has a significant risk of developing a single gene disorder at a later stage in life.

2.21 **"Prenatal genetic screening/testing for a germline genetic condition(s)"** means genetic testing done on an implanted embryo or foetus for the purpose of screening or diagnosing a genetic condition. Examples include prenatal karyotyping and non-invasive prenatal testing.

2.22 **"Predictive value"** means the ability of a test to accurately diagnose a disease. A positive predictive value (PPV) represents the proportion of positive test results that are truly positive. A negative predictive value (NPV) represents the proportion of negative test results that are truly negative.

2.23 "**Pharmacogenetic testing**" means genetic testing for the purpose of detecting genetic variant(s)/change(s) that can help predict an individual's response to a given drug e.g. the individual's likelihood to experience an adverse event, response to a given drug dosage, etc.

2.24 **"Registered medical practitioner"** means a person who is registered, or deemed to be registered, as a medical practitioner under the Medical Registration Act (Cap. 174).

2.25 **"Secondary findings"** means additional findings which are intended to be sought but not the primary target/goal, as determined by the practitioner. This is distinct from "incidental findings", which are not intended.

2.26 **"Somatic genetic testing"** means genetic testing done on cancer, tissue or bodily fluid for the primary purpose of detecting a non-heritable variant/change in an individual's human chromosomes, DNA, RNA, genes and/or gene product.

2.27 **"Somatic variant"** means an alteration in DNA that had occurred after conception and is not present within the germ cells (sperm or egg). Hence, somatic variant(s)/change(s) cannot be passed on to the next generation (i.e. non-heritable).

2.28 **"Susceptibility screening/testing" for germline genetic condition(s)**, sometimes also known as **predisposition screening/testing,** means genetic testing done on an individual who displays no symptoms of any genetic condition(s) but is at risk of developing a complex genetic disorder later on in life. These types of tests generally look for genetic risk factors of developing a particular complex disorder(s).

PART B: PROVISION OF GENETIC TESTS

3. General principles of provision of genetic tests

3.1 The ethical principles of beneficence, non-maleficence and respect for autonomy apply to the provision of genetic tests. In particular, there must be:

a. proper regard for the safety and welfare of individuals;

b. respect for vulnerable individuals;

c. consent properly obtained for all genetic tests; and

d. appropriate protection of the privacy and confidentiality of personal data.

PART C: PROVISION OF LEVEL 1 GENETIC TESTS

4. Level 1 genetic tests

4.1 Level 1 genetic tests are:

a. tests that are likely to be appropriately ordered and correctly interpreted by most registered medical practitioners;

b. tests where most registered medical practitioners are likely to be able to appropriately explain the test results to the patient; and

c. tests where most registered medical practitioners are likely to be able to implement the appropriate referrals, investigations and/or follow-up plans based on the test results.

4.2 Level 1 genetic tests consist of:-

a. biochemical genetic tests (e.g. enzyme activity, metabolite analysis);

b. haemoglobin electrophoresis for detecting haemoglobinopathies;

c. genetic tests of variants/changes important in tissue typing for transplant;

d. genetic tests of variants/changes important in blood typing and blood product transfusion (including platelet transfusion and work-up for transfusion reactions); and

e. any other tests approved for classification as level 1 genetic tests by the Director of Medical Services ("DMS") in **Annex B**.

4.3 Level 1 genetic tests may only be provided by a registered medical practitioner. No other person may provide level 1 genetic tests.

5. Provision of predictive/presymptomatic testing and susceptibility testing using level 1 genetic tests

5.1 Predictive/presymptomatic and susceptibility testing using level 1 genetic tests shall only be offered:

a. if there is evidence of clinical validity and clinical utility; and

b. where medically indicated.

6. Genetic testing on adults (with vs without mental capacity) or minors using level 1 genetic tests

Genetic Testing on a symptomatic adult (with vs without mental capacity) or minor

6.1 If an adult (with vs without mental capacity) or minor has symptoms suggestive of a genetic condition, diagnostic genetic testing using level 1 genetic tests may be carried out on him/her, subject to paragraphs 7 and 8.

Genetic testing on an asymptomatic adult (with vs without mental capacity) or minor (e.g. carrier/ presymptomatic/predictive/susceptibility testing and/or screening)

6.2 Carrier/presymptomatic/predictive/susceptibility testing and/or screening using level 1 genetic tests may be offered and carried out on an asymptomatic adult (with vs without mental capacity) or minor, subject to paragraphs 5.1, 7 and 8.

7. References to "the patient" in paragraph 8

7.1 All references to "the patient" in paragraph 8 shall refer to:

a. the patient if he/she is an adult with mental capacity;

b. in the case of a patient who is a minor, the appropriate person(s) with the authority to make decisions for the said minor; or

c. in the case of a patient who is an adult who lacks mental capacity, the appropriate person(s) with the authority to make decisions on behalf of the adult who lacks mental capacity under the Mental Capacity Act (Cap. 177A).

8. Counselling, consent, and disclosure of level 1 genetic test results

8.1 Pre-test counselling is **mandatory** and shall be provided to the patient by the registered medical practitioner who ordered the genetic test(s) *(ordering doctor)*, before the conduct of the level 1 genetic test(s). The counselling shall be conducted in accordance with the clinical practice standards applicable to any other diagnostic procedure.

8.2 Consent for all level 1 genetic tests is **mandatory** and shall be obtained from the patient in accordance with the clinical practice standards applicable to any other diagnostic procedure.

8.3 Level 1 genetic test results shall be disclosed to the patient by the ordering doctor or by a team member who is supervised by the ordering doctor, and shall follow the clinical practice standards applicable to any other diagnostic procedure.

8.4 It is mandatory to offer post-test counselling to the patient after the results of the level 1 genetic test(s) are known. The post-test counselling (*where provided*) shall be conducted by the ordering doctor in accordance with the clinical practice standards applicable to any other diagnostic procedure.

8.5 Counselling for level 1 genetic tests may be outsourced to suitably qualified healthcare professionals, but the licensee and the ordering doctor shall still remain responsible for the safety and welfare of the patient and the quality of the counselling.

PART D: PROVISION OF LEVEL 2 GENETIC TESTS

9. Level 2 genetic tests

9.1 Level 2 genetic tests are:

a. tests that would require the skills of appropriately trained registered medical practitioners to be correctly ordered;

b. tests that would require the skills of appropriately trained registered medical practitioners to correctly interpret the test results;

c. tests that would require the skills of appropriately trained registered medical practitioners to correctly explain the test results to the patient; and

d. tests that would require the skills of appropriately trained registered medical practitioners to implement the appropriate referrals, investigations or follow-up plans based on the test results.

9.2 Level 2 genetic tests consist of:-

a. genetic tests carried out on tumour(s), cancer, and/or cancer associated tissues or bodily fluids that predominantly investigate somatic variants/changes but may potentially reveal the presence of germline variants/changes, and where further tests[1] would be needed for the diagnosis and/or confirmation of the germline variant/change/condition;

b. genetic tests carried out on tumour(s), cancer, and/or cancer associated tissues or bodily fluids that predominantly investigate variants/changes that are invariably/almost certainly germline, and where these variants/changes have no risk of identifying a hereditary cancer syndrome (i.e. a single gene disorder predisposing to cancer);

c. pharmacogenetic tests that involve testing for a germline genetic variant(s)/change(s) with the primary purpose of informing drug selection or dosing (unless that specific gene/variant is listed as a level 1 genetic test in **Annex B**); and

d. any other test approved for classification as a level 2 genetic test by DMS.

9.3 Level 2 genetic tests may only be provided by a registered medical practitioner who meets **any of the following requirements:**

a. has:-

(i) relevant qualifications or training in clinical genetics;

(ii) at least 2 years of relevant working experience in clinical genetics; **and**

(iii) is able to choose the appropriate level 2 genetic test(s) to recommend to the patient

b. has:-

(i) relevant qualifications or training in managing a disease or condition;

(ii) at least 2 years of relevant experience in working with the genetics of that particular disease or condition; **and**

(iii) is able to choose the appropriate level 2 genetic test(s) to recommend to the patient

c. is under the direct supervision of a registered medical practitioner who meets criteria (a) or (b);

or

d. has otherwise obtained DMS' specific approval to order a particular level 2 genetic test.

9.4 No other person may provide level 2 genetic tests.

[1] It is not mandatory to perform diagnostic and/or further confirmatory testing to differentiate between somatic and germline origin. However, where relevant, such diagnostic and/or further confirmatory testing should be offered to the patient. As such testing is voluntary, the patient's consent is required before proceeding.

9.5 Any private hospital or medical clinic seeking to provide level 2 genetic tests shall **notify** MOH of such level 2 genetic tests it intends to provide, and furnish MOH with any other information related to the genetic tests, in accordance with MOH's requirements and any other conditions that may be prescribed by MOH.

10. Provision of predictive/presymptomatic testing and susceptibility testing using level 2 genetic tests

10.1 Predictive/presymptomatic and susceptibility testing using level 2 genetic test shall only be offered:

a. if there is evidence of clinical validity and clinical utility; and

b. where medically indicated.

11. Genetic testing on adults (with vs without mental capacity) or minors using level 2 genetic tests

Genetic testing on a symptomatic adult (with vs without mental capacity) or minor

11.1 If an adult (with vs without mental capacity) or minor has symptoms suggestive of a genetic condition, diagnostic genetic testing using level 2 genetic tests may be carried out on him/her, subject to paragraphs 12 and 13.

Genetic testing on an asymptomatic adult (with vs without mental capacity) or minor (e.g. carrier/ presymptomatic/predictive/susceptibility testing and/or screening)

11.2 Carrier/presymptomatic/predictive/susceptibility testing and/or screening using level 2 genetic tests may be offered and carried out on an asymptomatic adult (with vs without mental capacity) or minor, subject to paragraphs 10.1, 12 and 13.

12. References to "the patient" in paragraph 13

12.1 All references to "the patient" in paragraph 13 shall refer to:

a. the patient if he/she is an adult with mental capacity;

b. in the case of a patient who is a minor, the appropriate person(s) with the authority to make decisions for the said minor; or

c. in the case of a patient who is an adult who lacks mental capacity, the appropriate person(s) with the authority to make decisions on behalf of the adult who lacks mental capacity under the Mental Capacity Act (Cap. 177A).

13. Counselling, consent, and disclosure of level 2 genetic test results

13.1 Pre-test counselling is **mandatory** and shall be provided to the patient by the ordering doctor, before the conduct of the level 2 genetic test(s). The counselling shall be conducted in accordance with the clinical practice standards applicable to any other diagnostic procedure.

13.2 Pre-test genetic counselling is not mandatory but can be offered to the patient if there is a reasonable chance of a level 2 genetic test revealing a germline variant/change that has wider implications than drug dosing/selection (e.g. the risk of having a hereditary cancer syndrome); and if provided, shall be conducted and documented by appropriately trained personnel (per paragraph 19.1) and shall follow the requirements set out in paragraph 20.

13.3 Consent for all level 2 genetic tests is **mandatory** and shall be obtained from the patient in accordance with the clinical practice standards applicable to any other diagnostic procedure.

13.4 Level 2 genetic test results shall be disclosed to the patient by the ordering doctor or by a team member who is supervised by the ordering doctor, and shall follow the clinical practice standards applicable to any other diagnostic procedure.

13.5 It is mandatory to offer post-test counselling to the patient after the results of the level 2 genetic test(s) are known. The post-test counselling (*where provided)* shall be conducted by the ordering doctor in accordance with the usual clinical practice standards applicable to any other diagnostic procedure.

13.6 Post-test genetic counselling is highly recommended for any abnormal level 2 genetic test that has implications other than drug dosing and/or if the individual is found to be at risk of having a germline genetic variant/change/condition; and if provided, shall be conducted and documented by appropriately trained personnel (per paragraph 19.1) and shall follow the requirements set out in paragraph 23.

13.7 Counselling for level 2 genetic tests (with the exception of the pre-test and post-test genetic counselling referred to in paragraphs 13.2 and 13.6) may be outsourced to suitably qualified healthcare professionals but the licensee and the ordering doctor shall still remain responsible for the safety and welfare of the patient and the quality of the counselling.

13.8 The pre-test and post-test genetic counselling referred to in paragraphs 13.2 and 13.6 may be outsourced according to paragraph 19.2.

PART E: PROVISION OF LEVEL 3 GENETIC TESTS

14. Level 3 genetic tests

14.1 Level 3 genetic tests are:

a. tests that would require the skills of appropriately trained registered medical practitioners to be correctly ordered;

b. tests that would require the skills of appropriately trained registered medical practitioners to correctly interpret the test results;

c. tests that would require the skills of appropriately trained registered medical practitioners to correctly explain the test results to patients;

d. tests that would require the skills of appropriately trained registered medical practitioners to implement the appropriate referrals, investigation or follow-up plans based on the test results; and

e. tests that would require the skills of appropriately trained personnel to correctly provide appropriate genetic counselling.

14.2 Level 3 genetic tests consist of:-

a. genetic tests carried out on tumour(s), cancer, and/or cancer associated tissues or bodily fluids that predominantly investigate variants/changes that are invariably/almost certainly germline, and where these variants/changes have risks of identifying a hereditary cancer syndrome (i.e. a single gene disorder predisposing to cancer);

b. genetic tests carried out on tumour(s), cancer, and/or cancer associated tissues or bodily fluids, whose sole purpose is to identify the presence or absence of germline variants/changes associated with a hereditary cancer syndrome (i.e. a single gene disorder predisposing to cancer);

c. genetic tests that will identify the presence (or absence) of a germline variant/change that is actionable other than informing drug selection or dosing;

d. all other genetic tests not categorised as level 1 and level 2 genetic tests; and

e. any other test approved for classification as a level 3 genetic test by DMS.

[*Explanatory note: Licensees and ordering doctors are to refer to **Annex C** for guidance in determining the classification of the genetic tests.*]

14.3 For avoidance of doubt, all genetic tests that sequence and report the whole genome [whole genome sequencing (WGS)] and/or whole exomes [whole exome sequencing (WES)] are categorised as level 3 genetic tests. Genetic tests which involve WGS and/or WES, but report only specific gene panels requested by the ordering doctor shall be categorised according to the decision matrix in **Annex C**.

[Explanatory note: A distinction is drawn between genetic tests that report the whole genome/exome sequences and genetic tests that only report specific gene panels.]

14.4 Level 3 genetic tests may only be provided by a registered medical practitioner who meets **any of the following requirements**:

a. has:-

(i) relevant qualifications or training in clinical genetics;

(ii) at least 2 years of relevant working experience in clinical genetics; **and**

(iii) is able to choose the appropriate level 3 genetic test to recommend to the patient

b. has:-

(i) relevant qualifications or training in managing a disease or condition;

(ii) at least 2 years of relevant experience in working with the genetics of that particular disease or condition; **and**

(iii) is able to choose the appropriate level 3 genetic test to recommend to the patient

c. is under the direct supervision of a registered medical practitioner who meets criteria (a) or (b);

or

d. has otherwise obtained DMS' specific approval to order a particular level 3 genetic test.

14.5 No other person may provide level 3 genetic tests.

14.6 Any private hospital or medical clinic seeking to provide level 3 genetic tests shall **notify** MOH of such level 3 genetic tests it intends to provide, and furnish MOH with any other information related to the genetic tests, in accordance with MOH's requirements and any other conditions that may be prescribed by MOH.

15. Provision of predictive/presymptomatic testing and susceptibility testing using level 3 genetic tests

15.1 Predictive/presymptomatic and susceptibility testing shall be offered only:

a. if there is evidence of clinical validity and clinical utility; and

b. where medically indicated.

16. Genetic testing on adults (with mental capacity) using level 3 genetic tests

Genetic testing on a symptomatic adult

16.1 If an adult has symptoms suggestive of a genetic condition, diagnostic genetic testing using level 3 genetic tests may be carried out on him/her, subject to paragraphs 19, 20, 21, 22 and 23.

Genetic testing on an asymptomatic adult (e.g. carrier/presymptomatic/predictive/susceptibility testing and/or screening)

16.2 Carrier/presymptomatic/predictive/susceptibility testing and/or screening using level 3 genetic tests may be offered and carried out on an asymptomatic adult, subject to paragraphs 15.1, 19, 20, 21, 22 and 23.

17. Genetic testing on minors using level 3 genetic tests

Genetic testing on a symptomatic minor

17.1 If a minor has symptoms suggestive of a genetic condition, diagnostic genetic testing using Level 3 genetic tests may be carried out on the minor, subject to the counselling and consent requirements set out in paragraphs 19, 20, 21, 22 and 23.

Genetic testing on an asymptomatic minor (e.g. carrier/presymptomatic/predictive/susceptibility testing and/or screening)

17.2 If a minor does not have symptoms suggestive of a genetic condition, testing using level 3 genetic tests should be deferred until he/she is an adult.

17.3 Notwithstanding paragraph 17.2 above, carrier/presymptomatic/predictive/susceptibility testing using level 3 genetic tests, and/or screening using level 3 genetic tests may be offered and carried out on a minor in any of the following circumstances:

a. where there is beneficial intervention, treatment or prevention available for the minor at that point in time;

b. where the minor needs to make decisions relating to reproduction or marriage and has sufficient intelligence and capacity to understand the relevant issues and risks, and gives valid consent to the level 3 genetic test(s); or

c. where otherwise approved by DMS

subject to paragraphs 19, 20, 21, 22 and 23.

18. Genetic testing on adults who lack mental capacity using level 3 genetic tests

Genetic testing on a symptomatic adult who lacks mental capacity

18.1 If an adult who lacks mental capacity has symptoms suggestive of a genetic condition, diagnostic genetic testing using level 3 genetic tests is allowed, subject to paragraphs 19, 20, 21, 22 and 23.

Genetic testing on an asymptomatic adult who lacks mental capacity (e.g. carrier/presymptomatic/predictive/susceptibility testing and/or screening)

18.2 Carrier/presymptomatic/predictive/susceptibility testing and/or screening using **level 3 genetic tests** may only be offered and carried out on an asymptomatic adult who lacks mental capacity in the following circumstances:

a. where there is beneficial intervention, treatment or prevention available for the said adult at that point in time;

b. where (i) it is in the best interests of the said adult or (ii) there is compelling family interest, provided it does not detract from the best interests of the said adult;

c. where the test relates to decisions regarding the said adult's reproduction or marriage; or

d. where otherwise approved by DMS

subject to paragraphs 19, 20, 21, 22 and 23.

18.3 Any consent or permission obtained in relation to adults who lack mental capacity shall be in accordance with the Mental Capacity Act (Cap. 177A), and shall include the categories of the consent set out in paragraph 21.

19. Qualifications of personnel doing genetic counselling

19.1 Genetic counselling shall be provided **only by any of** the following persons:

a. a genetic counsellor who has a recognised genetic counselling degree or certification, which is supported or recognised by credible bodies such as the Accreditation Council for Genetic Counselling, Human Genetics Society of Australasia and Genetic Counsellor Registration Board, and has at least 2 years of relevant working experience in clinical genetic counselling;

b. a registered medical practitioner who has the relevant qualifications or training in genetic counselling for that particular disease or condition, and has at least 2 years of relevant working experience in clinical genetic counselling for that particular disease or condition;

c. a registered medical practitioner who has the relevant qualifications or training in clinical genetics, and at least 2 years of relevant working experience in clinical genetics;

d. a genetic counsellor, registered medical practitioner, or other suitable professional who is under the direct supervision of a person who meets criteria (a) or (b) or (c); or

e. a person specifically approved by DMS.

19.2 Pre-test and post-test genetic counselling for level 3 genetic tests may be outsourced to appropriately trained personnel (with the qualifications set out in paragraph 19.1) but the licensee and the ordering doctor shall still remain responsible for the safety and welfare of the patient and the quality and outcome of the counselling.

20. Pre-test genetic counselling

20.1 Pre-test genetic counselling **is mandatory for all level 3** genetic tests.

20.2 Pre-test genetic counselling shall only be conducted and documented by appropriately trained personnel (with the qualifications set out in paragraph 19.1).

20.3 Pre-test genetic counselling shall be provided to and conducted in a manner appropriate to the needs and comprehension of:-

a. the patient if he/she is an adult with mental capacity;

b. in the case of a patient who is a minor, the appropriate person(s) with the authority to make decisions for the said minor; or

c. in the case of a patient who is an adult who lacks mental capacity, the appropriate person(s) with the authority to make decisions on behalf of the adult who lacks mental capacity under the Mental Capacity Act (Cap. 177A).

20.4 At the minimum, the following components of pre-test genetic counselling shall be discussed and documented for each genetic test:

a. the nature of the condition or genetic variant/change abnormality to be tested, including its symptoms, natural history and inheritance pattern;

b. the condition or genetic variant/change's effect on the patient; and the risk of the patient transmitting this condition or genetic variant/change to the next generation;

c. a general description of the genetic test and the purpose of the test;

d. the genetic testing procedure, including the type of sample required, its cost, and other reasonably foreseeable risks, discomforts or inconveniences to the patient arising out of the genetic test;

e. the effectiveness and limitations of the genetic test (e.g. analytical sensitivity and specificity);

f. the foreseeable outcomes of the genetic test and their interpretations, including the discussion on the institutional and laboratory policies on the return of incidental and/or secondary findings;

g. any foreseeable consequences to the patient arising out of the genetic test, such as psychological stress, impact on insurability and employment, and implications on family members;

h. the turn-around time of the genetic test and how the results will be disclosed to the patient and/or person giving consent;

i. the option to withdraw from genetic testing before the completion of the test, or to postpone the receipt of test results;

j. where the patient is found to have a condition or genetic variant/change, the treatment and management options of the condition or genetic variant/change, and their potential outcomes. Where there are no treatment options for the patient's condition or genetic variant/change, there should be a discussion on whether there are any alternative procedures or treatments available, and the potential benefits, risks and limitations of such alternatives;

k. the option of not being tested and its potential benefits and limitations;

l. the alternatives to genetic testing and the benefits and limitations of these alternatives;

m. the person or categories of persons or organisations to whom the test results may be disclosed (e.g. those involved in the care of the patient);

n. the extent to which information and records identifying the patient will be kept confidential (refer to paragraphs 22 and 37);

o. any further use and management of the patient's genetic information (*including the use and management of the genetic information after death, where possible);* and

p. any further use, management and disposal of the patient's samples (*including the use, management and disposal of the samples after death, where possible).*

Where appropriate, the following information shall also be included:

q. any foreseeable third parties' interests in the patient's genetic information, and the likely consequences of disclosure of the patient's genetic information to those third parties; and

r. the possibility of incidental findings (such as the discovery of parentage discrepancy even though the test is not a parentage test), the likely implications of these findings and how

such findings are to be managed (including whether the patient will want to know such findings).

20.5 The manner in which pre-test genetic counselling was provided and conducted shall be properly documented.

21. Consent for level 3 genetic tests

21.1 Consent for all **level 3 genetic tests** is **mandatory** and shall be obtained by the ordering doctor from

a. the patient if he/she is an adult with mental capacity;

b. in the case of a patient who is a minor, the appropriate person(s) with the authority to make decisions for the said minor; or

c. in the case of a patient who is an adult who lacks mental capacity, the appropriate person(s) with the authority to make decisions on behalf of the adult who lacks mental capacity under the Mental Capacity Act (Cap. 177A).

21.2 If the ordering doctor delegates the consent taking to another team member (who shall be from the same healthcare institution), the ordering doctor must ensure that consent for the level 3 genetic test has been taken in accordance with paragraph 21.3. The licensee and the ordering doctor shall still remain responsible for the safety and welfare of the patient and the quality of the consent taken.

21.3 For level 3 genetic tests, at the minimum, the following categories of information shall be appropriately communicated, explained and documented in the process of obtaining consent for each genetic test:

a. a general description of the genetic test and the purpose of the test;

b. the genetic testing procedure, including the type of sample required, its cost, and other reasonably foreseeable risks, discomforts or inconveniences to the patient arising out of the genetic test;

c. the effectiveness and limitations of the genetic test (e.g. analytical sensitivity and specificity);

d. the foreseeable outcomes of the test and their interpretations, including the discussion on the institutional and laboratory policies on the return of incidental and/or secondary findings, and how incidental and/or secondary findings should be handled;

e. any foreseeable consequences to the patient arising out of the genetic test, such as psychological stress, impact on insurability and employment, and implications on family members;

f. the turn-around time of the genetic test and how the results will be disclosed to the patient and/or person giving consent;

g. the option to withdraw from genetic testing before the completion of the test, or to postpone the receipt of test results;

h. the person or categories of persons or organisations to whom the test results may be disclosed (e.g. those involved in the care of the patient);

i. the extent to which information and records identifying the patient will be kept private and confidential (refer to paragraphs 22 and 37);

j. a statement that no tests other than those authorised will be performed;

k. an acknowledgement that the patient and/or other individual giving consent has had the opportunity to discuss his/her concerns with the genetic test during pre-test genetic counselling with appropriately trained personnel (see paragraph 19);

l. the name and signature of the individual being tested or the individual who is legally authorised to give consent (see paragraph 21.1);

m. the name and signature of the registered medical practitioner or the delegated team member taking the consent;

n. the date of the consent;

o. any further use and management of the patient's genetic information *(including the use and management of the genetic information after death, where possible);* and

p. any further use, management and disposal of the patient's samples *(including the use, management and disposal of the samples after death, where possible).*

The documentation of consent shall also contain the following if applicable:

q. a statement indicating that the remaining unused portion of the sample may be stored for validation, process development, and/or quality control studies. The retention period and storage location of the unused portion of the sample shall be clearly specified;

r. a separate consent form drafted in accordance with the requirements set out in the Human Biomedical Research Act and all other applicable laws, regulations, licensing terms and conditions, directives and guidelines, if the samples are to be stored for current or future research purposes; and

s. the mode of communication of the genetic test results and post-test genetic counselling to the patient.

22. Disclosure of level 3 genetic test results

22.1 The results of level 3 genetic tests shall be disclosed and explained to:

a. the patient if he/she is an adult with mental capacity;

b. in the case of a patient who is a minor, the appropriate person(s) with the authority to make decisions for the said minor; or

c. in the case of a patient who is an adult who lacks mental capacity, the appropriate person(s) with the authority to make decisions on behalf of the adult who lacks mental capacity under the Mental Capacity Act (Cap. 177A)

by the ordering doctor or a team member who is supervised by the ordering doctor. This communication shall be properly documented.

23. Post-test genetic counselling

23.1 It is mandatory to offer post-test genetic counselling for all level 3 genetic tests, by explaining the availability, indications and benefits of post-test genetic counselling, and the potential consequences if post-test genetic counselling is not taken up. The post-test genetic counselling (where provided) shall be conducted and documented by appropriately trained personnel (refer to paragraph 19) and shall follow the requirements set out in paragraph 23.

23.2 Post-test genetic counselling shall be provided to and conducted in a manner appropriate to the needs and comprehension of:

a. the patient if he/she is an adult with mental capacity;

b. in the case of a patient who is a minor, the appropriate person(s) with the authority to make decisions for the said minor; or

c. in the case of a patient who is an adult who lacks mental capacity, the appropriate person(s) with the authority to make decisions on behalf of the adult who lacks mental capacity under the Mental Capacity Act (Cap. 177A).

23.3 At the minimum, the following components of post-test genetic counselling shall be discussed and documented for each genetic test:

a. the results of the genetic test and the interpretation of these results;

b. the implications of the test results to the patient and his/her family members;

c. where the patient is found to have a condition or genetic variant/change, the treatment and management options of the condition or genetic variant/change, and their potential outcomes. Where there are no treatment options for the patient's condition or genetic variant/change, there should be a discussion on whether there are any alternative procedures or treatments available, and the potential benefits, risks and limitations of such alternatives;

d. any psychological, social and ethical issues or concerns;

e. requirement or obligation to disclose the test results to a third party (if any);

f. the protection of the patient's privacy and confidentiality in relation to his/her genetic test results; and

g. where relevant, the consideration for testing of family members' carrier status and/or variant status for confirmation of the patient's condition:

(i) For autosomal dominant (AD) conditions, testing for parental variant status should be offered to determine the origin of the variant (i.e. de novo, inherited, germline mosaicism);

(ii) For autosomal recessive (AR) conditions, testing for parental carrier status should be offered to determine the phase of the variants;

(iii) For X-linked conditions, testing for parental variant status should be offered (i.e. for X-linked recessive conditions, maternal testing should be considered; for X-linked dominant conditions, testing of both parents should be considered) to determine the origin of the variant (de novo, inherited from mother, germline mosaicism); and

(iv) For variant of uncertain significance (VUS), testing of family members may be considered if the results will help to interpret the variant or reclassify the variant.

23.4 The manner in which each post-test genetic counselling was provided, conducted, and communicated shall be properly documented.

23.5 If the genetic test was a screening test for a condition or genetic variant/change, a confirmatory diagnostic test shall be offered as soon as medically/clinically possible after a positive screening test result.

PART F: CLINICAL LABORATORY GENETIC/GENOMIC TESTING (LGT) SERVICES

24. General principles of LGT services

24.1 All clinical laboratories providing LGT services shall be licensed under the PHMC Act.

24.2 LGT services shall only be provided to:

a. a licensed local healthcare institution and/or registered medical practitioner; or

b. an overseas healthcare facility.

24.3 Any clinical laboratory seeking to provide LGT services shall **notify** MOH of such LGT services it intends to provide, and furnish MOH with any other information related to the LGT services, in accordance with MOH's requirements and any other conditions as may be prescribed by MOH. In addition, any clinical laboratory providing level 3 genetic tests **must be accredited by a laboratory accreditation body** approved by MOH stated in **Annex D** and only offer clinical genetic tests that fall within the scope of the accreditation.

25. Personnel

25.1 The **licensee shall appoint a clinical laboratory director** of LGT services in its clinical laboratory, who shall be any of the following:-

a. a registered medical practitioner who has relevant qualifications or training in molecular genetics, biochemical genetics or cytogenetics, and has **at least 5 years** of relevant working experience in molecular genetics, biochemical genetics or cytogenetics in a clinical laboratory;

b. a doctoral scientist who has relevant qualifications or training in molecular genetics, biochemical genetics or cytogenetics, and has **at least 5 years** of relevant working experience in molecular genetics, biochemical genetics or cytogenetics in a clinical laboratory;

c. a person with a degree in medicine who has relevant qualifications or training in molecular genetics, biochemical genetics or cytogenetics, and has **at least 5 years** of relevant working experience in molecular genetics, biochemical genetics or cytogenetics in a clinical laboratory;

d. a person with a Master's degree in molecular genetics, biochemical genetics or cytogenetics, and has **at least 10 years** of relevant working experience in molecular genetics, biochemical genetics or cytogenetics in a clinical laboratory;

or

e. is otherwise approved by DMS.

25.2 The licensee shall appoint a **person(s) to manage** its clinical laboratory (equivalent to the "laboratory manager"), who shall be:-

a. a person who has a degree in medicine or a basic degree in a relevant science subject, and has **at least 5 years** of relevant working experience in a clinical laboratory; or

b. is otherwise approved by DMS.

25.3 The licensee shall staff its clinical laboratory with at least **one trained person**. A "trained person" is a person:-

a. who has had **at least 3 years** of relevant working experience in molecular genetics, biochemical genetics, or cytogenetics in a clinical laboratory, and at least:

(i) a diploma in medical laboratory technology or an equivalent qualification; or

(ii) a basic degree in a relevant science subject; or

b. is otherwise approved by DMS.

25.4 The licensee may employ persons with the qualifications listed at paragraph 25.3a, but who does not have **at least 3 years** of relevant working experience. Such persons shall work under the close supervision of:

a. A trained person (per paragraph 25.3);

b. The person appointed to manage the clinical laboratory (per paragraph 25.2); or

c. The clinical laboratory director of the clinical laboratory providing LGT services (per paragraph 25.1).

25.5 No person shall be involved in the conduct of LGT services (including handling samples) unless he/she is a person described in paragraphs 25.1, 25.2, 25.3 or 25.4.

25.6 The licensee shall keep and maintain the job descriptions, qualification(s) and training records of all its clinical laboratory personnel involved in the conduct of LGT services.

26. Clinical laboratory records

26.1 The licensee shall ensure that the records of all specimens received, tests conducted and test results of its clinical laboratory are kept and maintained in accordance with the PHMC Act, its Regulations, and all other licensing terms and conditions, directives and guidelines that may be issued by DMS/MOH. These records shall include, but are not limited to:-

a. relevant medical records of patients (e.g. clinical diagnosis and history of test requests);

b. all test request forms;

c. records of samples (including receipt and disposal records);

d. all signed consent documents required under this Code of Practice;

e. test reports (including reports for outsourced tests);

f. preventive maintenance, monitoring and calibration records of equipment;

g. validation records of all tests (e.g. analytical validity of LDTs, modifications to commercial *in vitro* diagnostic tests);

h. valid copies of the accreditation certificates (with scope of accreditation) of overseas clinical laboratories if samples were sent overseas for testing or examination (where applicable);

i. Quality Control (QC) records (internal QCs and Proficiency Testing/External Quality Assessments (EQAs), inter-laboratory comparisons where applicable);

j. evaluation records of internal and external QC measures, including findings and any preventive and corrective actions taken to address deficiencies; and

k. all relevant approvals from the appropriate authority if samples are stored and used for research purposes after testing (where applicable).

27. Sample and information requirements to conduct the genetic test

27.1 The licensee shall ensure that robust protocols are put in place for genetic tests conducted by its clinical laboratory, including on the samples required, the accompanying information required, specimen collection, sample handling and transport so as to prevent wrong collection,

mislabelling, contamination, alteration or loss of specimens. These protocols shall be set out in writing and a copy shall be made available at the clinical laboratory premises at all times.

27.2 The licensee, clinical laboratory director and all employees of the clinical laboratory shall strictly adhere to the above-mentioned protocols.

27.3 The licensee shall ensure that all healthcare institutions, overseas healthcare facilities and/or registered medical practitioners that have requested for the LGT services of its clinical laboratory are informed of the requirements needed to conduct the genetic tests (e.g. patient and/or family information required, samples required, and requirements as regard to sample collection, handling, transportation and documentation).

27.4 The licensee shall ensure that its clinical laboratory only provides LGT services to requests which are accompanied by details of the registered medical practitioner (i.e. name, Medical Council Registration (MCR) number, designation, specialty and phone number), healthcare institution and/or overseas healthcare facility (i.e. name, address and phone number) which have requested for the LGT service.

28. Facilities

28.1 The licensee shall equip its clinical laboratory with adequate facilities for the proper and efficient performance of all categories of examinations which it is licensed to undertake, and for its functions to be performed with accuracy, timeliness and safety.

29. Quality control and quality assurance

29.1 As a quality control measure, the licensee shall ensure that its clinical laboratory maintains a quality assurance manual which shall include the following information:

a. objectives of the clinical laboratory;

b. list of all diagnostic services provided by the clinical laboratory;

c. current organisational chart;

d. the clinical laboratory's policies, workflows and work processes;

e. the clinical laboratory's performance outcomes, including the speed and accuracy of its diagnostic reporting;

The licensee shall also ensure that its clinical laboratory has the following programmes in place, and that the performance of these programmes are recorded in the quality assurance manual:

f. quality assurance programmes, including regular reviews of policies, work processes and overall clinical laboratory performance; and

g. continuing educational programmes for staff.

29.2 The licensee shall ensure compliance with all quality control measures and quality assurance activities listed under paragraph 29.1.

30. Commercial genetic tests

30.1 Prior to its clinical laboratory using any commercial genetic test to provide LGT services, the licensee shall ensure that the test and all related equipment/medical devices have been registered with the Health Sciences Authority (HSA), if subject to HSA's regulatory controls.

30.2 The licensee shall first ensure the analytical validity of each commercial genetic test, before its clinical laboratory uses it in clinical practice.

30.3 The licensee shall furnish MOH Inspectors/Investigators with supporting validation data for its commercial genetic test(s) upon request and/or during inspection.

30.4 The licensee shall ensure that its clinical laboratory does not use any commercial genetic test in respect of which the analytical and clinical validity of the tests have yet to be established.

31. Laboratory-developed genetic tests (LDTs)

31.1 Prior to using any LDT to provide LGT services, the licensee shall ensure that its clinical laboratory establishes the analytical validity (e.g. specificity, accuracy, precision, analytic sensitivity, interferences, reportable range, etc.) and clinical validity of the LDT. The licensee shall ensure that its clinical laboratory takes into account the intended clinical purpose of a genetic test when establishing the analytical validity of that test.

31.2 The licensee shall first ensure the analytical and clinical validity of each LDT, before its clinical laboratory uses it in clinical practice.

31.3 The licensee shall furnish MOH Inspectors/Investigators with supporting validation data for its LDTs upon request and/or during inspection.

31.4 The licensee shall ensure that its clinical laboratory does not use any LDT genetic tests in respect of which the analytical and clinical validity of the tests have yet to be established.

32. Pre-analytical procedures

32.1 The licensee shall ensure that its clinical laboratory has appropriate procedures in place for the receipt, acceptance and rejection of genetic samples. These procedures shall be set out in writing.

32.2 The licensee shall ensure that the disposal of all rejected specimens are properly documented in the patient report and/or quality management records of its clinical laboratory.

32.3 The licensee shall ensure that its clinical laboratory has appropriate procedures in place for specimen preservation and storage before testing. These procedures shall be set out in writing.

32.4 The licensee shall ensure that its clinical laboratory has appropriate procedures in place to prevent specimen loss, alteration, or contamination. These procedures shall be set out in writing.

32.5 The licensee shall ensure that at least two (2) unique identifiers are maintained for each specimen throughout the entire testing process, and when transferring the specimen to another clinical laboratory.

32.6 The licensee shall ensure that a traceable system is set up for its clinical laboratory to positively identify all patient specimens, specimen types, and aliquots through all phases of the genetic tests such as specimen receipt, nucleic acid extraction, nucleic acid quantification, hybridisation, detection, documentation, and storage.

32.7 The licensee shall ensure that the procedures prepared by its clinical laboratory are validated and subject to appropriate quality control processes.

32.8 The licensee, clinical laboratory director and all employees of the clinical laboratory shall strictly adhere to the requirements and procedures set out in paragraph 32.

33. Analytical procedures

33.1 The licensee shall ensure that all commercial *in vitro* diagnostic (IVD) tests carried out by its clinical laboratory are performed in accordance with the manufacturer's instructions.

33.2 If its clinical laboratory decides to deviate from the manufacturer's instructions when performing IVD tests, the licensee shall ensure that its clinical laboratory validates and documents this deviation.

33.3 The licensee shall ensure that all LDTs carried out by its clinical laboratory are performed in accordance with methods that have been properly validated by the clinical laboratory.

33.4 The licensee shall ensure that quality control measures (including EQAs) are put in place for every type of genetic test performed at its clinical laboratory. The list of agencies that may endorse and/or provide EQAs is listed at **Annex E.**

33.5 When EQAs are not available, the licensee shall ensure that its clinical laboratory regularly participates in alternative methods of quality control measures (e.g. inter-laboratory comparison) in relation to the genetic tests it performs.

34. Post-analytical procedures

34.1 The licensee shall ensure that its clinical laboratory has proper quality control processes in place to ensure that accurate results are produced before it is allowed to report such results as being clinically significant. If it is not practicable to do so, the licensee shall ensure that this result is reported as unconfirmed.

34.2 The licensee shall ensure that its clinical laboratory develops a written Standard Operating Procedure (SOP) on the return of incidental and/or secondary findings to the requesting healthcare institutions, overseas healthcare facilities and/or registered medical practitioners. In developing the SOP, proper consideration shall be given to factors such as the predictive value, actionability of the incidental and/or secondary findings and patient's consent.

34.3 The licensee, clinical laboratory director and all employees of the clinical laboratory shall strictly adhere to the requirements and procedures set out in paragraph 34.

35. Genetic test reports

35.1 The licensee shall ensure that all genetic test reports from its clinical laboratory are timely, accurate, concise, comprehensive, and communicate all essential information to enable effective decision-making by healthcare professionals. The licensee shall also ensure that these reports may be easily interpreted by healthcare professionals who are not geneticists.

35.2 The licensee shall ensure that all genetic test reports from its clinical laboratory use applicable internationally accepted terminology and nomenclature, including for identification of reference sequences (where applicable).

35.3 The licensee shall ensure that all genetic test reports from its clinical laboratory state, in simple terms, the method and scope of the analysis performed.

35.4 Where the test or examination to which the genetic test report relates has been outsourced to another accredited clinical laboratory, the licensee shall ensure that the report states clearly the name and address of the clinical laboratory which performed the test or examination, and that it is accompanied by the original copy of the report from the clinical laboratory which performed the test or examination.

35.5 The licensee shall ensure that at the minimum, genetic test reports from its clinical laboratory includes the following information:

a. identification that unequivocally links the report to the patient;

b. the name and contact information of the referring registered medical practitioner and the

referring healthcare institution/overseas healthcare facility;

c. the indication for testing and specific medical information where it is relevant to the interpretation of the test result;

d. the primary sample type;

e. the date of receipt of the sample;

f. the name and location of clinical laboratory(ies) involved in the preparation of the report, including any referral clinical laboratory(ies) which performed the actual testing on the sample;

g. information on the test performed and the methodology used (e.g. the gene/s name, genetic locus/loci, the reference sequence used, test limitations);

h. the test result;

i. an interpretation of the test result (this shall also reflect the predictive value of the test where appropriate);

j. clinical recommendations with regard to drug interactions and toxicity for test reports of level 1 genetic tests listed in Annex B and for all pharmacogenetic test reports;

k. the contact information of the licensee's clinical laboratory;

l. the date of issue of the report;

m. the identity of the individual approving the report; and

n. the signature of the clinical laboratory director. If the clinical laboratory director does not meet the criteria stated in paragraph 25.1a, he/she should, where possible, co-sign the report with an appropriately qualified/trained registered medical practitioner.

Where appropriate, the genetic test report shall also include the following information:

o. a recommendation for genetic counselling by appropriately trained personnel;

p. implications of the test result to the patient's other family members; and

q. recommendations for follow-up testing and/or management.

35.6 The licensee shall ensure that its clinical laboratory has received the patient's signed consent form, and that consent had been obtained from the patient in accordance with the requirements set out in paragraph 21, prior to the issuance of **level 3 genetic test results**.

35.7 Where applicable, the licensee shall ensure that its clinical laboratory stores and uses its patient's samples (including all genetic materials derived from the samples) after testing in accordance with what was authorised by the patient, and in compliance with all prevailing laws and regulations.

35.8 The licensee shall ensure that there are protocols in place in its clinical laboratory to ensure the confidentiality of the patient's genetic information (refer to paragraphs 22 and 37).

35.9 The licensee shall ensure that all protocols listed under paragraph 35.8 are fully complied with.

PART G: GENERAL REQUIREMENTS

[Explanatory Note: Part G applies to both the provision of CGT and LGT services.]

36. Outsourcing of test/examination to any foreign (overseas) clinical laboratories

36.1 The licensee shall ensure that only evidence-based test(s) or examinations are outsourced to foreign (overseas) clinical laboratories ("FCL").

36.2 If any specimens are to be sent from its healthcare institution to an FCL for testing or examination, the licensee shall ensure that:

a. the FCL is accredited by an accreditation body listed in **Annex F**;

b. only tests or examinations covered within the scope of the FCL's accreditation as referred to in paragraph (a) above are performed at the FCL;

c. the specimen sent to the FCL is of sufficient integrity to allow the FCL to meet the necessary standards;

d. all essential and relevant elements necessary for the FCL to perform its testing or examination accompany the patient sample during transfer to the FCL;

e. genetic test reports from the accredited FCL meet the requirements stated in paragraph 35; and

f. the test results from the FCL are provided to the requesting registered medical practitioner.

37. Confidentiality

37.1 The licensee shall ensure that its healthcare institution has a system in place to ensure that patients' genetic information remain confidential, through the implementation of adequate safeguards (administrative, technical and physical).

37.2 The licensee shall ensure that the confidentiality system and safeguards implemented under paragraph 37.1 are fully complied with.

37.3 The licensee shall ensure that the genetic test results and/or genetic information of its patients are not disclosed to any third parties (including family members) without prior consent from:-

a. the patient if he/she is an adult with mental capacity;

b. in the case of a patient who is a minor, the appropriate person(s) with the authority to make decisions for the said minor; or

c. in the case of a patient who is an adult who lacks mental capacity, the appropriate person(s) with the authority to make decisions on behalf of the adult who lacks mental capacity under the Mental Capacity Act (Cap. 177A).

38. Documentation

38.1 The licensee shall ensure that it properly keeps and secures its documentation in relation to the provision of CGT and LGT services. This documentation includes the documents set out in this Code of Practice.

39. Records

39.1 The licensee shall ensure that all relevant medical records of patients are kept and maintained in accordance with the requirements set out under Regulation 12 of the PHMC Regulations, the MOH Guidelines on the retention period of medical records and other directives or guidelines as may be issued from time to time on this matter.

39.2 The licensee shall ensure that all records of consent with regard to level 3 genetic tests are appropriately documented and maintained.

40. Specimen collection, handling and transport

40.1 Where a licensee outsources its CGT and LGT services, the licensee shall ensure that the referring healthcare institutions, and/or registered medical practitioners requesting for the services are informed of the outsourcing, and of the testing clinical laboratories' requirements for the conduct of the genetic tests (e.g. sample type, collection, handling and transport, and patient and/or family information) and abide by these requirements.

40.2 The licensee shall ensure that it provides clear and appropriate instructions to patients who collect their own samples.

41. Direct-to-consumer (DTC) genetic testing

41.1 CGT, LGT and CG services shall only be provided to consumers by licensed healthcare institutions in accordance with this Code of Practice. CGT, LGT and CG services shall not be offered or provided by manufacturers or suppliers of genetic tests directly to consumers (being any patient or other member of the public) in any circumstances, whether or not for a fee or other reward.

Annex A

COMPARISON OF THE REQUIREMENTS FOR THE 3 LEVELS OF GENETIC TESTS

Requirements	**Level 1 genetic tests**	**Level 2 genetic tests**	**Level 3 genetic tests**
Consent	**Mandatory**; Follow current clinical practice standards applicable to any other diagnostic procedure.		**Mandatory**; Follow requirements in paragraph 21 of the COP.
Pre-test counselling	**Mandatory**; Provided by the ordering doctor (i.e. registered medical practitioner who ordered the genetic test(s)) as per current clinical practice standards applicable to any other diagnostic procedure.		Not applicable
Post-test counselling	**Mandatory**; Offered to the patient after the results of the genetic test(s) are known and where provided, conducted by the ordering doctor as per current clinical practice standards applicable to any other diagnostic procedure.		
Pre-test genetic counselling*	Not applicable	**Can be offered** if there is a reasonable chance of a level 2 genetic test revealing a germline variant/change.	**Mandatory**
Post-test genetic counselling*	Not applicable	**Highly recommended** for results that have implications other than drug dosing and/or if the individual is found to be at risk of having a germline variant/change.	**Mandatory** to offer

*Pre-test and post-test genetic counselling shall be conducted and documented by appropriately trained personnel (refer to paragraph 19) and shall follow the requirements set out in paragraphs 20 and 23 respectively.

Levels of genetic test	Examples of tests
Level 1	A. Examples of biochemical genetic tests • Tests involving the analysis of the **quantity** of protein/metabolite e.g. amino acids, organic acids, carnitine and acylcarnitines, acylglycines, glycosaminoglycans, glycoproteins, cerebrospinal fluid (CSF) neurotransmitters • Tests involving the analysis of the **structure** of protein/metabolite e.g. determination of transthyretin (TTR) protein structure in plasma using mass spectrometry (test for transthyretin-associated familial amyloidosis) • Tests involving the analysis of protein **activity** e.g. enzymes such as galactose-1-phosphate uridyl transferase (GALT) enzyme activity (test for galactosemia), biotinidase enzyme activity (test for biotinidase deficiency (BIOT)), α-glucosidase enzyme activity (test for Pompe disease (glycogen storage disease type II)) B. Haemoglobin electrophoresis for detecting haemoglobinopathies C. Tissue typing for transplant D. Blood typing; work up for transfusion reactions E. Tests approved for classification as level 1 genetic tests by DMS in Annex B
Level 2	• Epidermal Growth Factor Receptor (EGFR) variant testing in lung cancer tissue for the sole purpose of predicting sensitivity or resistance to targeted therapy in lung cancer • KRAS variant testing in colorectal cancer tissue for the sole purpose of predicting sensitivity or resistance to targeted therapy in colorectal cancer • Fluorescent-in-situ hybridisation of tumour/cancer tissue for gene amplification of gene variants/changes for the sole purpose of predicting sensitivity or resistance to targeted therapy in colorectal cancer • NGS based gene panel for somatic gene variants/changes in tumour/cancer tissue for the sole purpose of predicting sensitivity or resistance to targeted therapy e.g. Acute Myeloid Leukemia gene panel • Tumour microsatellite instability (MSI) tests, tumour next-generation sequencing (NGS) tests and tumour immunohistochemical (IHC) tests for mismatch repair (MMR) proteins that may potentially reveal germline variants/changes but where further tests would be needed for the diagnosis and/or confirmation of the germline variant/change/condition e.g. testing for TP53 variants in ovarian cancer tissue

Levels of genetic test	Examples of tests
Level 3	• Tumour MSI tests, tumour NGS tests and tumour IHC tests for MMR proteins that predominantly investigate variants/changes that are invariably/almost certainly germline, and where these variants/changes have risks of identifying a hereditary cancer syndrome (i.e. a single gene disorder predisposing to cancer) e.g. testing for BRCA1 variants in breast or ovarian cancer tissue • Prenatal QF-PCR Aneuploidy • Non-invasive Prenatal Screening (NIPT) • NGS based NIPT • MS-PCR for Prader Willi syndrome, Fragile X syndrome • Karyotyping (prenatal, postnatal) for constitutional/germline abnormalities • Chromosomal microarray analysis (prenatal, postnatal) for constitutional/germline abnormalities • Uniparental disomy (UPD) analysis • Gene sequence analysis for a germline variant(s)/change(s) • Gene deletion/duplication analysis for a germline variant(s)/changes(s) • Fluorescent-in-situ hybridisation for constitutional/germline abnormalities • NGS based gene panels for constitutional/germline abnormalities e.g. identification of gene variants/changes associated with Hypertrophic Cardiomyopathy (HCM) • Whole exome sequencing (WES) for germline genetic variants/changes • Whole genome sequencing (WGS) for germline genetic variants/changes

Annex B

LIST OF GENETIC TESTS APPROVED FOR CLASSIFICATION AS LEVEL 1 GENETIC TESTS BY DMS (PURSUANT TO PARAGRAPH 4.2e)[2] [3]

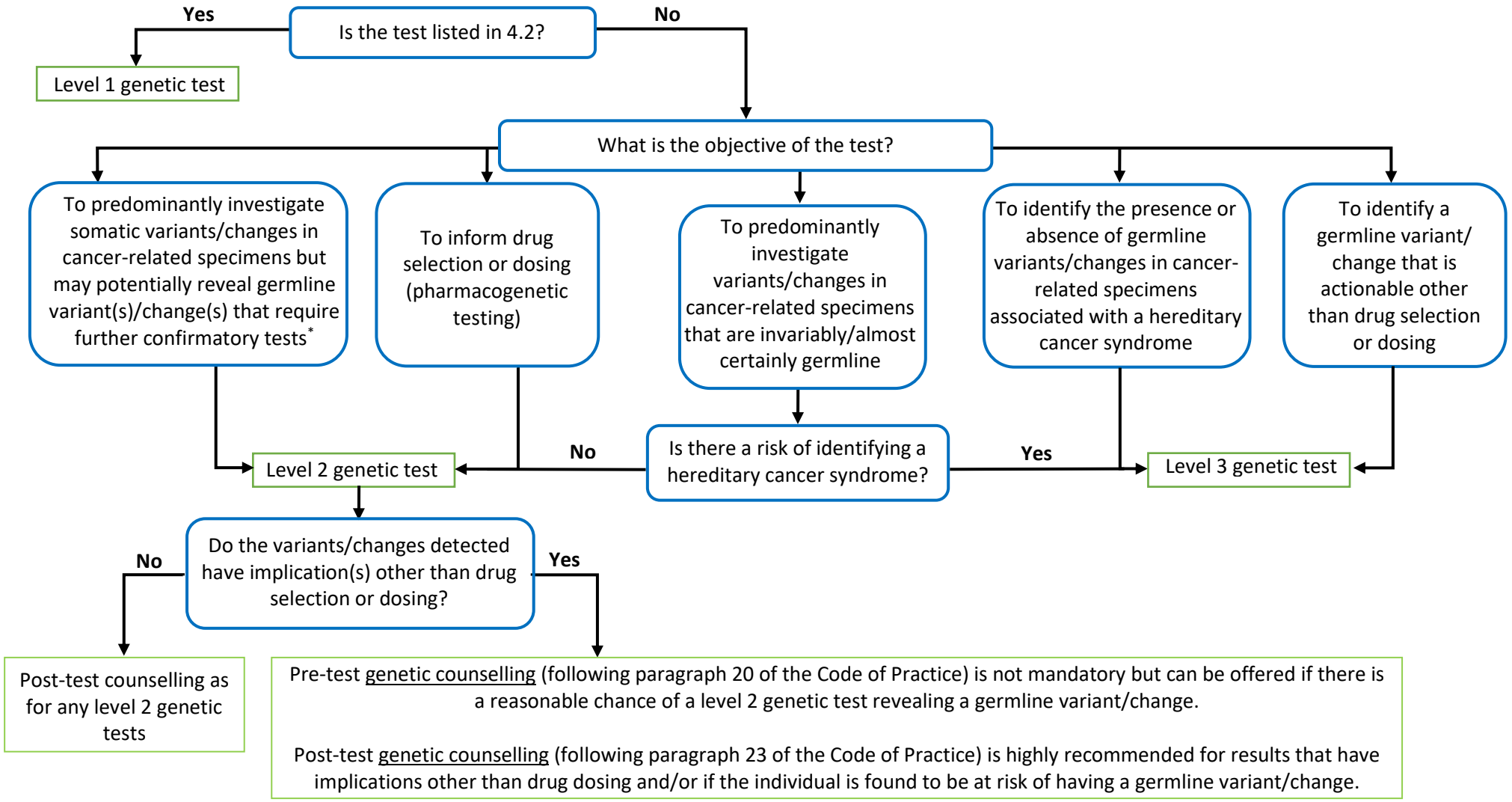
As stipulated in paragraph 35.5j, clinical recommendations with regard to drug interactions and toxicity should be included for test reports of level 1 genetic tests listed below.

Gene(s)/Variant(s) Tested	Examples of indications for which gene(s)/ variant(s) are tested	Examples of drugs that gene(s)/ variant(s) are tested to inform
VKORC1, CYP4F2 and CYP2C9	Thromboembolic/excessive clotting disorder Anticoagulation	Warfarin
TPMT, *NUDT15*	Autoimmune disorder Inflammatory disorder Cancer	Thiopurines (azathioprine, mercaptopurine and thioguanine)
UGT1A1	Cancer	Irinotecan
*HLA-B*5701*	HIV	Abacavir
*HLA-B*5801*	Gout, hyperuricemia	Allopurinol
*HLA-B*1502*	Epilepsy	Carbamazepine, phenytoin
HLA-B27	Juvenile Arthritis (ERA)/autoimmune disorder/allergy	Sulphasalazine
HLA-DQ2	Risk of celiac disease	
HLA-DQ8	Risk of celiac disease	
CYP3A5	Need for immunosuppression e.g. post-transplant	Tacrolimus
CYP2C19	Major depressive and anxiety disorders	Citalopram, Escitalopram
	Coronary heart disease	Clopidogrel
	Invasive fungal infections	Voriconazole

[2] Clinical Pharmacogenetics Implementation Consortium (CPIC) Guidelines (2020). Retrieved from https://cpicpgx.org/guidelines/.
[3] Dutch Pharmacogenetics Working Group (DPWG) Guidelines (2020). Retrieved from https://www.knmp.nl/patientenzorg/medicatiebewaking/farmacogenetica/pharmacogenetics-1.

Gene(s)/Variant(s) Tested	**Examples of indications for which gene(s)/ variant(s) are tested**	**Examples of drugs that gene(s)/ variant(s) are tested to inform**
CYP2C19 and CYP2D6	Major depressive disorders	Amitriptyline
CYP2D6	Major depressive and anxiety disorders	Fluvoxamine, Paroxetine, Nortriptyline
	Pain management	Codeine, Tramadol, Oxycodone
	Suppression of nausea and vomiting	Ondansetron, Tropisetron
	Cancer	Tamoxifen
*CYP2C9, HLA-B*1502*	Epilepsy	Phenytoin
SLCO1B1	Lipid lowering	Simvastatin
Actionable PGx Genotyping Panel *(CYP3A5, CYP2C9, CYP2C19, CYP2D6, CYP4F2, NUDT15, TPMT, VKORC1, SLCO1B1, HLA-B*1502, HLA-B*5701, HLA-B*5801)*	Pre-emptive genotyping that provides an assessment for genes with strong drug gene associations	Multiple
DPYD	Cancer	5-fluorouracil chemotherapy

DECISION MATRIX TO DISTINGUISH AMONG THE VARIOUS LEVELS OF GENETIC TESTS



*Performing diagnostic and/or further confirmatory testing to differentiate between somatic and germline origin is not mandatory. Where relevant, such diagnostic and/or further confirmatory testing should be offered to the patient, and as such testing is voluntary, the patient's consent should be required before proceeding.

Annex D

LIST OF APPROVED LABORATORY ACCREDITATION BODIES FOR LEVEL 3 GENETIC TESTING

1 College of American Pathologists (USA)

2 Deutsche Akkreditierungsstelle (DAkks) (Germany)

3 Singapore Accreditation Council-Singapore Laboratory Accreditation Scheme (Singapore)

4 United Kingdom Accreditation Service (formally known as Clinical Pathology Accreditation) (UK) – *on a case-by-case basis*

** The list of accreditation bodies may change over time.*

** Licensees shall engage the respective accreditation bodies directly on the scope of accreditation.*

Annex E

LIST OF AGENCIES THAT ENDORSE AND/OR PROVIDE EXTERNAL QUALITY ASSESSMENT SCHEMES (EQAS)

The following information aims to **guide** healthcare institutions in complying with the Private Hospitals and Medical Clinics Regulations (see Regulation 52(2)(a)) by listing agencies/bodies which provide External Quality Assessment Scheme (EQAS). The list is non-exhaustive and healthcare institutions may have EQAS performed by other agencies/schemes.

1 Overseas Agencies

a) American Association of Blood Banks (USA)
b) Centers for Disease Control and Prevention (USA)
c) Centers for Medicare & Medicaid Services (USA)
d) College of American Pathologists (USA)
e) Medical Laboratory Evaluation Program (MLE)
f) National Association of Testing Authorities (Australia)
g) National External QA Scheme (UK)
h) National Pathology Accreditation Advisory Council (Australia)
i) National Serology Reference Laboratory (Australia)
j) Public Health Laboratory Service (UK)
k) Royal College of Pathologists (Australia)
l) United Kingdom Accreditation Service (formally known as Clinical Pathology Accreditation) (UK)
m) World Health Organization (excluding WHO collaborating centres in Singapore)

2 National Proficiency Testing Schemes

In addition, all clinical laboratories providing specialised tests (e.g. HIV, malaria parasite) listed in the Fifth Schedule to the PHMC Regulations are required to participate in the respective National Proficiency Testing Schemes provided by the following local bodies:

a) Blood Services Group (Centre For Transfusion Medicine)
   Health Sciences Authority
   (National Proficiency Testing for ABO/Rh Testing)
b) National HIV Reference Laboratory
   Department of Pathology
   Singapore General Hospital
   (National Proficiency Testing for HIV Testing)
c) Central Tuberculosis Laboratory
   Department of Pathology
   Singapore General Hospital
   (National Proficiency Testing for AFB [Smear])
d) National Malaria Reference Centre
   National Public Health Laboratory

Ministry of Health

(National Proficiency Testing for Malaria Parasite Testing)

Annex F

LIST OF APPROVED LABORATORY ACCREDITATION BODIES

Healthcare institutions intending to outsource tests to a foreign clinical laboratory must ensure that the foreign clinical laboratory providing the tests has been accredited by an accreditation body approved by the Director of Medical Services (see Regulation 55 of the Private Hospitals and Medical Clinics Regulations). The list of approved laboratory accreditation bodies is as follows:

1 American Association of Blood Banks (USA)

2 American College of Radiation Oncology (USA)

3 American College of Radiology (USA)

4 American Society for Histocompatibility and Immunogenetics (USA)

5 American Society of Crime Laboratory Directors/Laboratory Accreditation Board (USA)

6 College of American Pathologists (USA)

7 Danish Accreditation [DANAK] (Denmark)

8 Dutch Accreditation Council [Raad voor Accreditatie] (The Netherlands)

9 Foundation for the Accreditation of Cellular Therapy (USA)

10 International Accreditation New Zealand (New Zealand)

11 National Association of Medical Examiners (USA)

12 National Association of Testing Authorities (Australia)

13 National Pathology Accreditation Advisory Council (Australia)

14 Singapore Accreditation Council-Singapore Laboratory Accreditation Scheme (S'PORE)

15 Swiss Accreditation Services (Switzerland)

16 Taiwan Accreditation Foundation (Taiwan)

17 The Joint Commission (USA) (formally Joint Commission on Accreditation of Healthcare Organizations)

18 United Kingdom Accreditation Service (formally known as Clinical Pathology Accreditation) (UK)

FAQS ON THE CODE OF PRACTICE ON STANDARDS FOR THE PROVISION OF CLINICAL GENETIC/GENOMIC TESTING SERVICES AND CLINICAL LABORATORY GENETIC/GENOMIC TESTING SERVICES ("STANDARDS")

Scope and Interpretation of the Standards

Q1:	**Do the Standards apply to organisations or services that offer genetic testing from overseas?**
A:	The Standards are relevant for all healthcare institutions licensed under the Private Hospitals and Medicine Clinics Act (PHMCA) in Singapore. This includes hospitals, medical clinics, and clinical laboratories. The Standards also outline requirements for the outsourcing of tests or examinations to overseas clinical laboratories (please see paragraph 36).
Q2:	**Do the Standards apply to genetic research?**
A:	The Standards do not apply to genetic testing conducted solely for research, education or any other non-clinical purposes (please see paragraph 1.3). Genetic research which would be considered "human biomedical research" under Section 3 of the Human Biomedical Research Act (HBRA), will be regulated under the HBRA.
Q3:	**Do the Standards apply to clinical laboratories licensed under the PHMCA that provide Clinical Laboratory Genetic/Genomic Testing (LGT) services to support clinical trials (in particular, to decide patient eligibility in the trials)?**
A:	Genetic tests carried out to determine patient eligibility for clinical trials that have clinical implications on patient management are within the scope of the Standards. The Clinical Genetic/Genomic Testing (CGT) and LGT services provided should therefore meet the requirements set out in the Standards. Where samples are sent to the PHMCA-licensed clinical laboratory from overseas, the clinical laboratory may only provide LGT services to overseas healthcare facilities, in accordance with the Standards (particularly, the applicable requirements set out in Part F and G of the Standards).
Q4:	**Is Preimplantation Genetic Diagnosis (PGD) covered under the Standards?**
A:	The Standards do not apply to PGD (please see paragraph 1.3). MOH is currently developing a set of requirements which will apply to Preimplantation Genetic Testing/Screening/Diagnosis services.
Q5:	**Can a solo registered medical practitioner who is running his/her own medical clinic provide Clinical Genetic Testing Services?**
A:	The Standards do not preclude a solo registered medical practitioner, with his/her own medical clinic licensed under the PHMCA, from providing CGT services. The medical practitioner should satisfy the requirements (including the competency requirements) stipulated in the Standards.

Q6:	**What is the definition of the term "clinical laboratory"?**
A:	"Clinical laboratory" carries the same definition as in Section 2 of the Private Hospitals and Medical Clinics Act.
Q7:	**What does "in-house" mean, in relation to laboratory-developed tests (LDT)?**
A:	"In-house" means the development, validation and use of LDT within a PHMCA-licensed clinical laboratory (i.e. not supplied to an external party/facility). If an LDT is made available for use in or sale to other laboratories, it will no longer be exempted from pre-market registration and approval will be required from the Health Sciences Authority under the Health Products Act (Medical Devices Regulations).
Q8:	**How should records be maintained in order to support the management and/or use of genetic information?**
A:	Licensees shall keep and maintain proper medical records in accordance with the requirements set out under: (i) Regulation 12 of the PHMC Regulations (ii) MOH Guidelines on the retention period of medical records and (iii) Other directives or guidelines as may be issued from time to time on this matter.
Q9:	**How should genetic information and/or samples be managed and/or used after death?**
A:	As a good clinical practice, registered medical practitioners should ensure and carry out the discussions on (i) further use and management of genetic information, and (ii) further use, management, and disposal of samples after death with patients undergoing clinical genetic services, in accordance with the clinical practice standards applicable to any other diagnostic procedure (e.g. Singapore Medical Council Ethical Code and Ethical Guidelines, Intestate Succession Act and Application of Muslim Law Act). Where possible, proper documentation on the patients' consent and decision for the management and/or use of genetic information and disposal of samples after death should be properly maintained within the patients' medical records.

Incidental and Secondary Findings

Q10:	**How should incidental and/or secondary findings from CGT services be managed?**
A:	With respect to level 3 genetic tests, there should be a discussion on the institutional and laboratory policies on the return of incidental and/or secondary findings during pre-test genetic counselling and/or consent taking (paragraphs 20.4f and/or 21.3d) and the patient's consent should be sought on how incidental and/or secondary findings will be handled (paragraph 21.3d). With respect to level 1 and 2 genetic tests, the possibility of incidental and/or secondary findings is generally low and the consequences of the incidental and/or secondary findings are generally viewed to have less wider implications. As such, registered medical practitioners providing counselling and consent should follow the clinical practice standards applicable to any other diagnostic procedure.

	Taking into account the above discussions with the patients on the policies regarding the return of incidental and/or secondary findings, registered medical practitioners should then order the appropriate genetic tests to support their patients' needs. Clinical laboratories providing level 3 genetic tests should have a written Standard Operating Procedure (SOP) with regard to: 1) whether they will offer to report incidental and/or secondary findings and communicate the policy clearly to their clients *(i.e. doctors ordering the tests);* 2) if they will offer to report incidental and/or secondary findings, they should include an option for the patient to opt in or opt out of being informed of incidental and/or secondary findings; and 3) they should report according to the patient's option on whether to be informed of incidental and/or secondary findings. Also see paragraph 34.2 of the Standards: *34.2 The licensee shall ensure that its clinical laboratory develops a written Standard Operating Procedure (SOP) on the return of incidental and/or secondary findings to the requesting healthcare institutions, overseas healthcare facilities and/or registered medical practitioners. In developing the SOP, proper consideration shall be given to factors such as the predictive value, actionability of the incidental and/or secondary findings and patient's consent.*

<u>Competency Requirements of the Ordering Doctor for Level 2 and 3 genetic tests</u>

Q11:	**With respect to the Standards (paragraphs 9.3 and 14.4), what is meant by** **(a) Relevant qualifications or training** **(b) Relevant working experience**
A:	(a) Examples of "relevant qualifications or training" would include courses on genetics related topics such as <u>genetic counselling</u> and non-invasive prenatal testing (NIPT). It also includes completion of online modules, attendance at genetics related seminars and workshops. (b) Working experience should be either 2 years full-time or a cumulative equivalent (e.g. part-time basis over a period of 4 years, so long as it is the cumulative equivalent of 2 years full-time working experience). As part of the inspection process, licensees would be asked to produce documentation to support the competency requirements of the ordering doctors. Whilst the Standards do not "prescribe or hard-code" the type of qualifications, training or working experience, the onus would be on both the licensee and the ordering doctor to ensure that the provision of the clinical genetic tests are within the limits of the ordering doctor's competencies. This is so that patients will receive appropriate and good quality care and that ordering doctors practise within their scope of competencies. MOH is also working on developing guidelines to aid in the determination of competencies required for the provision of the level 2 and level 3 genetic tests. Further details will be shared when ready.

Q12:	**Can genetic counsellors order Clinical Genetic Tests?**
A:	The role of genetic counsellors is to provide genetic counselling. Ordering of clinical genetic tests and interpretation of test results for the diagnosis and management of patients should be done by registered medical practitioners with the appropriate competencies as stipulated in the Standards, so as to safeguard patients' safety and welfare.
Q13:	**A level 1 genetic test ordered by a General Practitioner uncovers an uncommon genetic disorder. Who should the patient be referred to?**
A:	If any level 1 genetic test uncovers an uncommon genetic disorder, the patient should be referred to a registered medical practitioner with the relevant qualifications/training and experience to diagnose/manage that genetic disorder.
Q14:	**Are General Practitioners (GP) allowed to order single gene tests?**
A:	Depending on the intent of the test, the specimen and genes/variants tested, a single gene test could fall into any one of the three levels of genetic tests specified in the Standards. (Please also refer to the decision matrix in **Annex C** of the Standards.) All registered medical practitioners (including GPs) can order level 1 genetic tests. Only registered medical practitioners who meet the competency requirements as stipulated in the Standards can order level 2 and level 3 genetic tests.

Classification of Clinical Genetic Tests

Q15:	**Would MOH provide an exhaustive list of Clinical Genetic Tests for each level (tier)?**
A:	The Standards acknowledge the rapid developments in the field of genetics and genomics, and are therefore not intended to be overly-prescriptive. Rather, the Standards are drafted with the intention of allowing flexibility to adapt to developments in the field of genetics and genomics within reasonable regulatory boundaries. At present, the 3 levels of genetic tests have been tiered according to the **impact of the tests to the patient and his family,** including the follow-up management required, the risk of inappropriate ordering of genetic tests and the predisposition to wrong interpretation of test results. For greater clarity, a decision matrix has been provided in **Annex C** of the Standards as a guide to the classification of genetic tests.
Q16:	**Are all Next Generation Sequencing (NGS)-based tests classified as level 3 genetic tests?**
A:	The classification of genetic tests is not based on technology but rather on intent of ordering of the test. Therefore, not all NGS-based tests are necessarily classified as level 3 genetic tests. Please refer to the decision matrix provided in **Annex C** of the Standards as a guide to the classification of genetic tests. NGS-based tests that predominantly investigate somatic variants/changes but may potentially reveal the presence of germline variants/changes, and where further tests would be needed for the diagnosis and/or confirmation of the germline variant/change/condition, are classified as level 2 genetic tests. NGS-based tests that predominantly investigate variants/changes that

	are invariably/almost certainly germline, and where these variants/changes have risks of identifying a hereditary cancer syndrome, are classified as level 3 genetic tests. However, all genetic tests that sequence and report the whole genome [whole genome sequencing (WGS)] and/or whole exomes [whole exome sequencing (WES)] are classified as level 3 genetic tests. Genetic tests which involve WGS and/or WES, <u>but report only the specific gene panels as requested by the ordering doctor</u> will be classified according to the decision matrix in **Annex C**.
Q17:	**How can we determine if a genetic test has been approved by the Director of Medical Services (DMS) as a level 1, 2 or 3 genetic test?**
A:	**Annex B** of the Standards lists the genetic tests that have been approved for classification as level 1 genetic tests (as per paragraph 4.2e). Licensees will be notified through eLIS of any updates to **Annex B**. Similarly, licensees will be updated through eLIS of any tests which have been approved for classification as level 2 or 3 genetic tests by DMS (under paragraphs 9.2d and 14.2e).
Q18:	**Why is immunohistochemical screening considered a genetic test given that it assesses protein expression?**
A:	Protein expression is determined by genes. Hence, protein expression reflects gene activity and function. **<u>Example</u>** If an immunohistochemical test is designed with the primary purpose of determining changes that are somatic e.g. HER2/neu staining, this is considered to be a level 2 genetic test (see **Annex C**). This includes tests that may potentially reveal germline variants/changes but where further tests would be needed for the diagnosis and/or confirmation of the germline variant/change/condition. If an immunohistochemical test <u>predominantly</u> investigates variants/changes that are invariably/almost certainly germline, and where these variants/changes have risks of identifying a hereditary cancer syndrome (i.e. a single gene disorder predisposing to cancer), this is considered to be a level 3 genetic test (see **Annex C**).

<u>Minors</u>

Q19:	**How do you determine if a minor has sufficient understanding and intelligence to provide consent?**
A:	The ordering doctor can establish the minor's level of maturity and understanding through the following (refer to Section C6.4 of the Singapore Medical Council's Handbook on Medical Ethics): (i) using simple language and/or pictures, drawings and diagrams, and/or (ii) having minors repeat and/or articulate their interpretation of the information presented, their decisions and reasons behind them. The ordering doctor could repeat the steps above (if time permits) to check for consistency of the minor's understanding and decision. When in doubt about whether a minor has the necessary level of maturity and understanding,

	the ordering doctor should consider obtaining an opinion from an appropriate colleague such as a child psychiatrist, psychologist or counsellor.

Counselling and Genetic Counselling

Q20:	**What is the difference between "counselling" and "genetic counselling"?**
A:	In this COP, "counselling" is used generically to refer to a process of providing professional assistance and guidance to individuals in resolving personal, social or psychological problems and difficulties. This is distinct from "genetic counselling", which is used specifically to refer to the process of advising individuals and families affected by or at risk of genetic disorders to help them understand and adapt to the medical, psychological and familial implications of genetic contributions to specific health conditions.
Q21:	**Is counselling mandatory for level 1 and 2 genetic tests?**
A:	Yes, the registered medical practitioner who orders the level 1 or 2 genetic test must counsel the patient before doing the genetic test as part of standard patient care. The registered medical practitioner shall also offer post-test counselling to the patient after the results of the level 1 or 2 genetic test are known. The patient can refuse to attend the post-test counselling. The elements of pre-test genetic counselling (paragraph 20.4 of the Standards) and post-test genetic counselling (paragraph 23.3 of the Standards) for level 3 genetic tests can be considered and where relevant, be discussed with the patient during counselling for level 1 and 2 genetic tests. Pre-test genetic counselling is not mandatory but can be offered if there is a reasonable chance of a level 2 genetic test revealing a germline variant/change that has wider implications than drug dosing/selection (e.g. the risk of having a hereditary cancer syndrome); and if provided, shall be conducted and documented by appropriately trained personnel (per paragraph 19.1) and shall follow the requirements set out in paragraph 20. (*Please also see paragraphs 8.4 and 13.5 of the Standards)* Post-test genetic counselling is highly recommended for any abnormal level 2 genetic test that has implications other than drug dosing and/or if the individual is found to be at risk of having a germline genetic variant/change/condition; and if provided, shall be conducted and documented by appropriately trained personnel (per paragraph 19.1 of the Standards) and shall follow the requirements set out in paragraph 23 of the Standards.
Q22:	**Can pre- and post-test counselling for level 1 and level 2 genetic tests be outsourced?**
A:	Pre-and post-test counselling for level 1 and level 2 genetic tests may be outsourced to suitably qualified healthcare professionals. "Suitably qualified healthcare professionals" referred to in paragraphs 8.5 and 13.7 of the Standards may include registered nurses. However, the licensee and the ordering doctor remain responsible for the safety and welfare of the patient and the quality of the counselling. *"Registered nurse" means a person registered as a nurse under the Nurses and Midwives Act.*

Q23:	**Why is there a requirement of 2 years' relevant working experience before a qualified genetic counsellor is able to provide genetic counselling?**
A:	The skills required to conduct proper genetic counselling are varied. As such, at least 2 years of relevant working experience in clinical genetic counselling is needed to ensure that an individual has gained enough knowledge and experience to execute and conduct proper genetic counselling. This relevant working experience may be acquired either locally or overseas.
Q24:	**Can registered nurses provide genetic counselling for level 3 genetic tests?**
A:	A registered nurse can provide genetic counselling for level 3 genetic tests if he/she meets the criteria set out in paragraph 19.1 of the Standards. In particular, we wish to point out that where a registered nurse does not meet the criteria set out in paragraphs 19.1(a) of the Standards, he/she would still be able to provide genetic counselling as a "suitable professional", under paragraph 19.1(d), and under the direct supervision of a person who meets the criteria set out in paragraphs 19.1(a), (b) or (c) of the Standards.
Q25:	**Can pre- and post-test genetic counselling for level 3 genetic tests be outsourced?**
A:	Pre-test and post-test genetic counselling for level 3 genetic test may be outsourced to appropriately trained personnel (as referred to in paragraph 19 of the Standards). However, the licensee and the ordering doctor remain responsible for the patient's safety and welfare, and the quality and outcome of the counselling.
Q26:	**Is post-test genetic counselling mandatory for level 3 genetic test results which are negative?**
A:	It is mandatory to offer post-test genetic counselling for all level 3 genetic test results, by explaining to the patient why post-test genetic counselling is needed and the potential consequences if post-test genetic counselling is not taken up, even for level 3 genetic tests which are negative. The patient can refuse to attend the post-test genetic counselling. The post-test genetic counselling *(where provided)* shall be conducted and documented by appropriately trained personnel (refer to paragraph 19 of the Standards) and shall follow the requirements as set out in paragraph 23 of the Standards.
Q27:	**Should post-test genetic counselling be conducted in one sitting or over a few visits?**
A:	Genetic counselling may be conducted over one or a few visits at the discretion of the appropriately trained personnel.

Consent

Q28:	**Is consent mandatory for level 1 and 2 genetic tests?**
A:	Yes, consent for level 1 and 2 genetic tests must be obtained. Please see paragraphs 8.2 and 13.3 of the Standards. When obtaining consent for level 1 and 2 genetic tests, the elements of consent for level 3

	genetic tests (paragraph 21.3 of the Standards) can be considered and where relevant, be discussed with the patient.
Q29:	**Is there a prescribed consent form for level 3 genetic tests?**
A:	A consent form is not prescribed in the Standards but the required information that should be communicated, explained and documented when obtaining consent for level 3 genetic tests is set out in paragraph 21 of the Standards.
Q30:	**Can the taking of consent be delegated to a team member?**
A:	The taking of consent may be delegated to a team member who is from the same healthcare institution. The ordering doctor is to ensure that consent is taken in accordance with the requirements set out in the Standards. The licensee and the ordering doctor remain responsible for the safety and welfare of the patient and the quality of the consent taken.

Clinical Laboratory Genetic Testing services

Q31:	**Is the onus on clinical laboratories to ensure that ordering doctors satisfy the required competency requirements?**
A:	The onus is NOT on the clinical laboratories to ensure that the ordering doctors satisfy the competency requirements. Nevertheless, clinical laboratories should have processes in place to ensure that the clinical genetic test is ordered by a licensed healthcare institution, overseas healthcare facility and/or registered medical practitioner. Also see paragraph 27.4 of the Standards. *27.4 The licensee shall ensure that its clinical laboratory only provides LGT services to requests which are accompanied by details of the registered medical practitioner (i.e. name, Medical Council Registration (MCR) number, designation, specialty and phone number), healthcare institution and/or overseas healthcare facility (i.e. name, address and phone number) which have requested for the LGT service.*
Q32:	**Would MOH provide recommended ranges for analytical performance expectations (specificity, accuracy, precision, analytical sensitivity, interferences, reportable range, etc.) for commercial genetic tests?**
A:	As per paragraph 30.1 of the Standards, prior to its clinical laboratory using any commercial genetic test to provide LGT services, the licensee shall ensure that the test and all related equipment/medical devices have been registered with the Health Sciences Authority (HSA), if subject to HSA's regulatory controls. Only evidence-based test(s) or examinations are allowed. The Standards acknowledge the rapid developments in the field of genetics and genomics and is not meant to be overly-prescriptive. Therefore, the licensee is to ensure that the analytical validity of commercial genetic tests is established before they are made available for use in clinical practice.
Q33:	**Does the genetic test report need to be signed by a medical practitioner?**
A:	No, the genetic test report shall be signed by the clinical laboratory director or his authorised representative, who shall be suitably qualified.

	If the clinical laboratory director does not meet the criteria stated in paragraph 25.1a of the Standards, **where possible**, the report shall also be co-signed by an appropriately qualified/trained registered medical practitioner (as referred to paragraph 25.1a of the Standards).
Q34:	**Where a clinical laboratory licensed under the PHMCA outsources tests/ examinations to another clinical laboratory, can the clinical laboratory make changes to the report received from the laboratory that conducted the test?**
A:	Per PHMC Reg. 54(3)(b), the report shall be accompanied by the original copy of the report of the clinical laboratory which performed the test or examination. Amending original reports is therefore not allowed.
Q35:	**As for the competency requirements in paragraphs 25.1(a), (b), (c) and (d) of the Standards, does the clinical laboratory director need relevant qualification or training in ALL 3 of the disciplines (molecular genetics, biochemical genetics or cytogenetics)?**
A:	No. The clinical laboratory director will only need relevant qualifications or training in any ONE of the following disciplines - molecular genetics, biochemical genetics or cytogenetics, AND at least 5 years (as per paragraphs 25.1(a), (b) and (c) of the Standards) or 10 years (as per paragraph (d) of the Standards) of relevant working experience in any one of the disciplines. Furthermore, the relevant working experience must be acquired in a clinical laboratory.
Q36:	**Are clinical laboratories allowed to provide laboratory genetic testing services to overseas healthcare facilities through a middleman?**
A:	Paragraph 24.2 of the Standards state that LGT services shall only be provided to (i) a licensed local healthcare institution and/or registered medical practitioner; or (ii) an overseas healthcare facility. Therefore, where the request for an LGT service is done through a middleman, the initial request must still originate from an overseas healthcare facility. As part of the inspection process, the clinic laboratory may be required to produce the necessary documentation to show that the LGT service was requested from an overseas healthcare facility, even if directed through a middleman.

General Requirements

Q37:	**What should licensees do when a rare genetic test needs to be ordered, that is neither available locally nor in foreign clinical laboratories accredited by a MOH-approved accreditation body in Annex F?**
A:	Licensees may write in to eLIS@moh.gov.sg.
Q38:	**Are Direct-To-Consumer (DTC) tests for nutrigenomics, lifestyle and ancestry genetic testing allowed?**
A:	Clinical genetic tests shall not be offered or provided by manufacturers or suppliers directly to consumers (please see paragraph 41 of the Standards).

	Nutrigenomics, lifestyle and ancestry genetic tests, which are NOT used for clinical applications, do not fall under the scope of the Standards. These are considered as 'low risk' to consumers and may be offered directly to consumers as 'recreational or for non-clinical' purposes. MOH will be issuing a guidance document for the providers of non-clinical genetic testing to outline good practices for providers offering non-clinical genetic testing in Singapore to ensure the safety, welfare and privacy of the consumers. Further details will be shared when ready.