



STANDARDS
MALAYSIA

SKIM AKREDITASI MAKMAL MALAYSIA (SAMM)
LABORATORY ACCREDITATION SCHEME OF MALAYSIA

STR 2.8 - SPECIFIC TECHNICAL REQUIREMENTS FOR ACCREDITATION OF CYTOGENETICS TESTING

Issue 3, 26 April 2017
(Amd. 1, 3 November 2017)
(Supplementary to MS ISO 15189)



JABATAN STANDARD MALAYSIA
Department of Standards Malaysia

TABLE OF CONTENTS

	Page
1 Introduction	1
2 Scope of accreditation	1
3 Terms and definitions	1
4 Management requirements	2
5 Technical requirements	2
5.1 Personnel	2
5.2 Accommodation and environmental conditions	3
5.3 Laboratory equipment, reagents, and consumables	4
5.4 Pre-examination processes	4
5.5 Examination processes	4
5.6 Ensuring quality of examination results	6
5.7 Post-examination processes	7
5.8 Reporting of results	7
5.9 Release of results	8
5.10 Laboratory information management	8
Appendix 1	9
References	10
Acknowledgements	11

SPECIFIC TECHNICAL REQUIREMENTS FOR ACCREDITATION OF CYTOGENETICS TESTING

1 Introduction

- a) This document describes the minimum specific technical requirements to be complied by any cytogenetics testing laboratory that wishes to be accredited by Standards Malaysia.
- b) This document shall be read in conjunction with MS ISO 15189 Medical Laboratories - Requirements for Quality and Competence and other specific criteria documents published by Department of Standards Malaysia (Standards Malaysia).

Note: Other accreditation criteria include SAMM Policies, Specific Criteria 2 and relevant Specific Technical Requirements documents.

- c) The clause numbers in this document correspond to those in the standard which require elaboration.

2 Scope of accreditation

The areas for accreditation of Cytogenetics Testing include the following:

- 2.1 Constitutional Cytogenetics (Prenatal & Postnatal)
- 2.2 Cancer Cytogenetics
- 2.3 Fluorescence In Situ Hybridisation (FISH)

3 Terms and definitions

- 3.1 Analyse - To evaluate each chromosome in a cell, either by comparing the homologues band for band through the microscope, on a high-resolution digital display, or by using photographs.
- 3.2 G-banding - A technique that, following various pretreatments of chromosome preparations and staining with Giemsa (or similar) stain, produces characteristic alternating dark and pale bands along each chromosome. G-banding is the standard technique for chromosome identification in human cytogenetics.
- 3.3 Count - To enumerate the number of chromosomes in a cell. The chromosomes need not be banded. A count should include comment on any obvious structural aberrations.
- 3.4 Karyotype - To arrange the banded chromosomes of a single cell in the standard arrangement (International System for Human Cytogenetics Nomenclature, ISCN). The

arrangement may be achieved by physically cutting up a photograph or by using an image analysis system.

3.5 Score - To enumerate the presence or absence of a specific cytogenetics feature.

4 Management Requirements

As in the standard MS ISO 15189 and Specific Criteria 2 (SC 2).

5 Technical Requirements

5.1 Personnel

5.1.2 Personnel qualifications

(a) **Cytogeneticist** shall be a person with appropriate qualification and experience who will be responsible for the overall directions and control of the laboratory and provision relevant to the laboratory operation. Such qualification and experience would be:

- i) A qualified pathologist registered with the Malaysian Medical Council with postgraduate/subspecialty qualification in cytogenetics recognised by the Government of Malaysia and/or registered with the National Specialist Register; or
- ii) A medical practitioner registered with at least four (4) years experience in laboratory cytogenetics; or
- iii) A scientist with a Doctorate of Philosophy in a subject relevant to the field of genetics/human genetics with at least one year experience in laboratory cytogenetics; or
- iv) A scientist with a Masters of Science Degree in a subject relevant to the field of genetics/human genetics with at least three (3) years experience in laboratory cytogenetics; or
- v) A scientist with a Bachelor of Science Degree or equivalent qualification in a subject relevant to the field of genetics/human genetics with at least seven (7) years experience in laboratory cytogenetics.

(b) Scientist

A scientist shall be a person with minimum Bachelor of Science or Biomedical Science Degree or equivalent qualification and experience relevant to the laboratory operation to directly supervise diagnostic work in the cytogenetics laboratory.

(c) **Technologist**

A medical laboratory technologist shall be a person with at least a Diploma in Medical Laboratory Technology or equivalent and has undergone supervised training in laboratory cytogenetics.

5.1.3 Job descriptions

Workload

- (a) Cytogenetics is currently a labour intensive field, but with increasing automation, the staff to workload ratio may be affected. The number of specimens processed will depend on the other duties among staff members, such as the experience of that person, the degree of laboratory automation and the complexity of the analyses.
- (b) The following ranges can be considered as a basis for calculating annual workload per staff:
- i. 250 - 350 lymphocyte cultures; or
 - ii. 150 - 250 bone marrow cultures; or
 - iii. 250 - 350 prenatal cultures; or
 - iv. 400 - 500 metaphase/interphase fluorescence in situ hybridisation (FISH) tests; or
 - v. 150 - 220 specialized FISH tests (e.g. multiple subtelomere); or
 - vi. 50-100 solid tissue FISH (e.g. paraffin-embedded tissues).

5.2 Accommodation and environmental conditions

5.2.1 Laboratory and office facilities

The laboratory shall have spaces allocated for processing and analysis of the different types of specimen and also a dedicated area for FISH work.

5.3 Laboratory equipment, reagents and consumables

5.3.1 Equipment

- a) Incubator: Prenatal and non-prenatal samples shall be incubated separately to minimise the risk of microbial cross-contamination.

- b) Biosafety Cabinet: Appropriate biosafety cabinets should be used for the containment of biological materials.
- c) Image Capture System: All image capture systems should be maintained regularly with software upgrades.
- d) Critical equipment shall have a system to monitor breakdown or downtime of machine when necessary.

5.4 Pre-examination processes

As in MS ISO 15189.

5.5 Examination processes

5.5.1 Selection, verification and validation of examination procedure

5.5.1.1 Cultures

- a) Prenatal cultures
 - i) Prenatal specimens such as Amniotic fluid, Chorionic villi (CVS) and Percutaneous Umbilical Blood Sampling (PUBS) should be processed under sterile conditions using appropriate aseptic cell culture techniques.
 - ii) Each prenatal specimen shall be divided and cultured in two separate incubators and maintained with independent cell culture media and other reagents.
 - iii) All cultures should be retained until the final results are released.
 - iv) For chorionic villus specimens, careful examination should be carried out to reduce the risk of maternal cell contamination (villi free from maternal decidua, blood vessels and unidentified tissue). All CVS shall include analysis of long-term cultures.
 - v) In the presence of fetal chromosome abnormality, where parental studies are required, it is recommended that these studies should be carried out in the same laboratory as the prenatal sample.
- b) Postnatal cultures
 - i) If possible, each postnatal specimen such as peripheral blood and fetal blood should be established in two independent cultures.

- ii) When appropriate and upon request, molecular analysis/FISH is recommended to supplement cytogenetics analysis.
- c) Bone marrow cultures
 - i) In bone marrow cultures, the likelihood of obtaining high-quality results should be optimised by using direct, short-term and synchronised cultures. Where necessary, suitable mitogens or growth factors may be used.
 - ii) Processing of specimens for hematological malignancy shall be consistent with the reason for referral or presumed clinical diagnosis.

5.5.1.2 Banding

- a) Karyotyping should be carried out using a G-banding technique.
- b) A standardised method for assessing banding quality should be used, with an agreed minimum standard that may vary depending on the reason for referral. Refer **Appendix 1**.
- c) Copies of the most recent International System for Human Cytogenetics Nomenclature (ISCN) shall be available.

5.5.1.3 Chromosome analysis

- a) The laboratory shall have written protocol for the analysis criteria. In general, a minimum of 5 banded cells should be fully analysed and an additional 10 cells should be counted for all cases.
- b) For cancer cytogenetics, if no chromosomal abnormality is found in the first five cells analysed, then a further five cells are to be fully analysed and an additional 10 cells should be counted.
- c) In the presence of aneuploidies/polyploidies/structural abnormalities, all cells should be analysed.
- d) If clinically relevant mosaicism is suspected, examination (counting and/or analysis) of at least 30 cells is recommended to exclude mosaicism of 10% at the 0.95 confidence level.
- e) Mosaicism or clonality can be confirmed by FISH analysis if suitable probe is available.

- f) Each case should be analysed by two independent cytogenetics personnel. A cytogeneticist should check and verify each case by analysing every chromosome, either by direct microscopy, photographs or digital images.

5.5.1.4 FISH

- a) If a cytogenetics laboratory is performing FISH on paraffin-embedded tissues (FFPE) or blastocyst/embryo biopsies, the laboratory shall have sufficient technical skills, expertise and collaborative/supervisory arrangements to perform and fully interpret the findings.
- b) Sufficient numbers of metaphases, interphases or nuclei shall be analysed to ensure the statistical validity of the result and the signals shall be scored by a second reviewer (signals must be scored by 2 independent analyses).

5.5.2 Measurement of uncertainty

The laboratory shall have documented procedure for uncertainty of measurement in FISH study with quantitative result.

5.6 Ensuring quality of examination procedures

5.6.1 General

The laboratory shall monitor the success rate of acceptable performance:

- | | |
|---------------------------------|-----|
| i) Amniotic fluid specimens | 99% |
| ii) Chorionic villi specimens | 98% |
| iii) Peripheral blood specimens | 98% |
| iv) Bone marrow specimens | 85% |

5.6.2 Quality control

5.6.2.1 General

The laboratory shall set, monitor and maintain laboratory quality control procedure.

5.7 Post-examination processes

5.7.1 Review of results

- a) All analysis shall be reviewed and validated by a second competent individual.
- b) All results and reports shall be checked and authorised before release.
- c) A minimum of 2 karyotypes/images shall be printed and archived.

5.7.2 Storage, retention and disposal of clinical samples

Storage of the primary specimen and other laboratory sample shall be in accordance with the pathology guidelines of retention period i.e. College of Pathologists, Academy of Medicine Malaysia Guideline on Retention of Pathology Records and Materials.

5.8 Reporting of results

5.8.1 General

5.8.1.1 Reports shall include the following:

- a) Patient details (name, date of birth, gender, age);
- b) Name of requesting clinician and location;
- c) Clinical indication/reason for referral;
- d) Specific studies undertaken (if applicable);
- e) Specimen type;
- f) Date of referral and date of report;
- g) Laboratory/sample identification;
- h) number of cells counted and analysed;
- i) Banding technique applied and resolution level achieved using the International System for Human Cytogenetics Nomenclature (ISCN);
- j) An indication that the result is normal or abnormal (e.g. no abnormality has been detected or abnormality detected or the result is inconclusive);

- k) Where applicable, appropriate interpretative comment / clinical interpretation should be included;
- l) Name and/or signature of the person who validates the report (if applicable);
- m) Name and signature of the authorised person who release the report;
- n) Where applicable, recommendations for further investigations and genetic counselling should be indicated.

Note:

- i) The description of test results shall follow the recent International System for Human Cytogenetics Nomenclature (ISCN).
- ii) All reports shall be checked and authorised by a qualified pathologist.
- iii) In the absence of a qualified pathologist, a cytogeneticist can release the results with the following mandatory remark in the report: "Tests results shown on this report require clinical interpretation and comments by a qualified pathologist."

5.8.1.2 The laboratory should have a written policy for reporting time. Recommended report times (includes all weekends and public holidays) for 90% of the referrals are as stated below:

- i) 28 days for lymphocytes cultures;
- ii) 21 days for bone marrows;
- iii) 7 days for urgent lymphocyte, bone marrow or cord blood cultures;
- iv) 15 days amniotic fluid/CVS; and
- v) 7 days FISH.

5.9 Release of results

As in MS ISO 15189.

5.10 Laboratory information management

As in MS ISO 15189.

Appendix 1**Recommended Minimum Banding Resolution**

The recommended scores given below are defined as the lowest standard acceptable for a given reason for referral without issuing a qualified report.

REASON FOR REFERRAL	BANDING RESOLUTION (bphs)
Routine prenatal diagnosis: e.g. for age or biochemical pre-screens	400
Aneuploidies & known large structural rearrangements	400
Expected small structural rearrangements and their prenatal diagnosis	400
Possible small unknown structural anomalies: e.g. recurrent abortion, dysmorphic features, developmental delay, recurrent or spontaneous miscarriages	550
Microdeletion syndromes	≥700

Adapted from: ASDG, Australian Society of Diagnostic Genomics, Quality Assessment Program – Clinical Cytogenetics, Formerly known as ASoC QAP (2016)

References:

1. National Pathology Accreditation Advisory Council: Requirements for Cytogenetics Testing (Third Edition 2013).
2. E.C.A. Newsletter, General Guidelines and Quality Assurance for Cytogenetics, No 29, January 2012.
3. An International System for Human Cytogenetics Nomenclature (ISCN) 2013.
4. ASDG, Australian Society of Diagnostic Genomics, Quality Assessment Program – Clinical Cytogenetics, Formerly known as ASoC QAP (2016).

Acknowledgements

1. Dr. Zubaidah Zakaria (Chairman) Institute for Medical Research (IMR)
2. Ms. Noraidah Hj. Subakin (Secretary) Department of Standards Malaysia (Standards Malaysia)
3. Dr. Puteri J. Noor Megat Baharuddin Institute for Medical Research (IMR)
4. Prof. Madya. Dr. Rosline Hassan Hospital Universiti Sains Malaysia (HUSM)
5. Ms. Noor Azreena Abd. Aziz Lembaga Penduduk dan Pembangunan Keluarga Negara (LPPKN)
6. Dr. Roziana binti Ariffin Hospital Kuala Lumpur (HKL)
7. Ms. Farah Amalina Mohd Zulkufli Hospital Kuala Lumpur (HKL)
8. Ms. Aminah Mekesat Hospital Kuala Lumpur (HKL)
9. Dr. Saira Bahnu Mohamed Yousoof Subang Jaya Medical Center (SJMC)
10. Mr. Mohammad Zarizi bin Abd Ghani University Malaya Medical Centre (UMMC)
11. Dr. Ilunihayati Ibrahim Hospital Raja Perempuan Zainab II (HRPZ II)
12. Dr. Hanita Othman Pusat Perubatan UKM (PPUKM)
13. Prof. Madya Dr. Salwati Shuib Pusat Perubatan UKM (PPUKM)
14. Ms. Fariza Wan Abdullah Department of Standards Malaysia (Standards Malaysia)
15. Ms. Rohasmizah Ismail Department of Standards Malaysia (Standards Malaysia)
16. Ms. Siti Norehan Ishak Department of Standards Malaysia (Standards Malaysia)
17. Ms. Norsheda Mohd Bahari Department of Standards Malaysia (Standards Malaysia)