REPORT OF THE SUBCOMMITTEE ON GENETIC LABORATORY SERVICES

to

THE NATIONAL TASK TEAM ON THE TRANSFORMATION OF LABORATORY SERVICES

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MEDICAL GENETIC LABORATORY SERVICES

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EXECUTIVE SUMMARY

Medical Genetics is an emerging field of endeavour in South Africa where due to lack of resources including funding, personnel and equipment, development of laboratory and clinical services have been limited. In the past decade, the service capability of both clinical and laboratory genetic components has declined. After consultation, discussion and investigation at the request of the National Health Task Team on Transformation of Laboratory Services, the ad-hoc sub-committee of medical genetic laboratory services determined that the most significant source of funding for these services was universities, research grants and privately generated funding sources. Recommendations on the functioning of a Medical Genetics Advisory Board for both the public and private sector medical genetic laboratory services for the provision of antenatal, neonatal, and postnatal tests have been made. In addition, special consideration is recommended for the support of Medical Faculties with a potential for developing genetic services. The inclusion of medical genetic laboratory services in the NHLS is considered by the subcommittee and the majority of senior medical genetic personnel to be an opportunity for reversing the trends of the past, and allowing future development which should ensure equitable access of the community to these services.

2. INTRODUCTION

The Minister of Health, Dr. Nkosazana Zuma, established a Task Team on the Transformation of Laboratory Services, chaired by Prof. S. Kallichurum, to advise her on how best to restructure laboratory services with the following elements in mind:

(a) to establish an efficient, cost-effective and financially self-sustaining public entity that is governed nationally;

(b) decentralised operational management to be delegated to the provincial level;

(c) the coordination and integration of national reference laboratory services countrywide to ensure a coherent response to the demands of the National Health System.

(d) the definition of the role of academia in human resource development [teaching, training, research and service development] and the expansion of the service to ensure equity in access to quality and cost-effective laboratory services.

On the 29th January 1999 an ad hoc subcommittee was convened, comprising of Prof. T. Jenkins, Dr. B. Madolo and Prof. A. Christianson (Chairperson), to investigate genetic laboratory services in South Africa, under the following terms of reference.

(a) to explore and investigate the workload, staffing structures, facilities and the cost/budget for running these laboratory services.

(b) to advise the task team on the need or not of their continuation as National Reference Laboratories.

(c) to advise the task team on the possibility of placing these laboratories under one roof to coordinate and integrate their services, if necessary.

After perusal of documentation supplied to the subcommittee and discussions with Mr. VR Mabope, (Chief Director: National Health Systems), Mr. M. Conradie, (Director: National Health Laboratory Services), and Prof. S. Kallichurum, the terms of reference supplied were directed towards the three functional arms of the proposed National Health Laboratory Services (NHLS) namely:

(i) National Reference Laboratory Services
(ii) Clinical Diagnostic Laboratory Services
(iii) Research and Development, Teaching and Academia

A process of consultation was undertaken with senior members of the country's medical genetics fraternity and other interested parties, who are presently either involved in the delivery of medical genetics laboratory services and research, or are developing such capability (Annexure A). Limitations in the time available did not allow for an in-depth investigation of all the options available and the complete distillation of ideas for the incorporation of the country's present medical genetics laboratories into the NHLS. Therefore, this report constitutes a point of departure, and should the broad principles developed in this document be acceptable, further consultation and negotiations with the relevant parties will be a necessity to facilitate their refinement and implementation.

The majority of persons consulted expressed a willingness, and a desire, to be part of a unified National Health Laboratory Service to ensure the future regulation and coordination of genetic laboratory services in South Africa. Where reservations were expressed, the overriding concern was for further clarification of the details for the proposed incorporation and functioning of the academic laboratories with the NHLS.

3. SITUATIONAL ANALYSIS

The relationship of genetics to Mankind dates back to man's efforts at animal husbandry. However, it was not until the beginning of the present century that Human and then Medical Genetics (i.e. genetics related to health and disease) became a subject for systematic research which could then be translated into service. For the first half of the Century these efforts were mired in the morass of eugenics and social Darwinism which led to the "murderous science" of Nazi Germany. From these beginnings arose the principles of Medical Genetics as practised today, wherein clinical and laboratory medical genetic service and research are inextricably linked, with the ultimate purpose of providing people with the right to genetic screening and full non-directive counselling, with the choice of accepting or rejecting either.

Therefore the present, and for the foreseeable future, intimate relationship between clinical governance and laboratory services in Medical Genetics will need to be maintained, when considering the development of future medical genetic laboratory services. The numerous ethical, legal and social issues that such services encounter can be appropriately and concomitantly addressed with the rendering and

development of the services. Furthermore this will facilitate the access of the community to medical genetic services.

3.1 The History of Medical Genetics in South Africa

The history of Medical Genetics in South Africa, was chronicled in a seminal article by Jenkins (J Med Genet.,1990). The process, that took place almost entirely in academic units, mirrored to a large extent medical genetic developments in industrialised nations. However, it was severely limited by lack of resources in terms of finances, personnel and equipment. Despite this, a capability was developed that had a strong laboratory base that was utilised mainly for research, and to a lesser extent service. The clinical component of this development lagged significantly behind the laboratory development and in consequence the ability to deliver a medical genetic service to the community at large was severely limited. In essence, medical genetic services until 1990 were largely limited to people in the middle and upper socio-economic classes and those in urban areas.

Since 1990 a significant effort has been made by the academic units to redress this imbalance. It has however continued to be hampered by the continued lack of resources and a non-recognition of the significant role that medical genetics is beginning to play in South Africa and will play in medicine in general in the future.

With respect to the lack of resources, the situation can be considered to have deteriorated since 1990.

3.2 The need for Medical Genetic services in South Africa

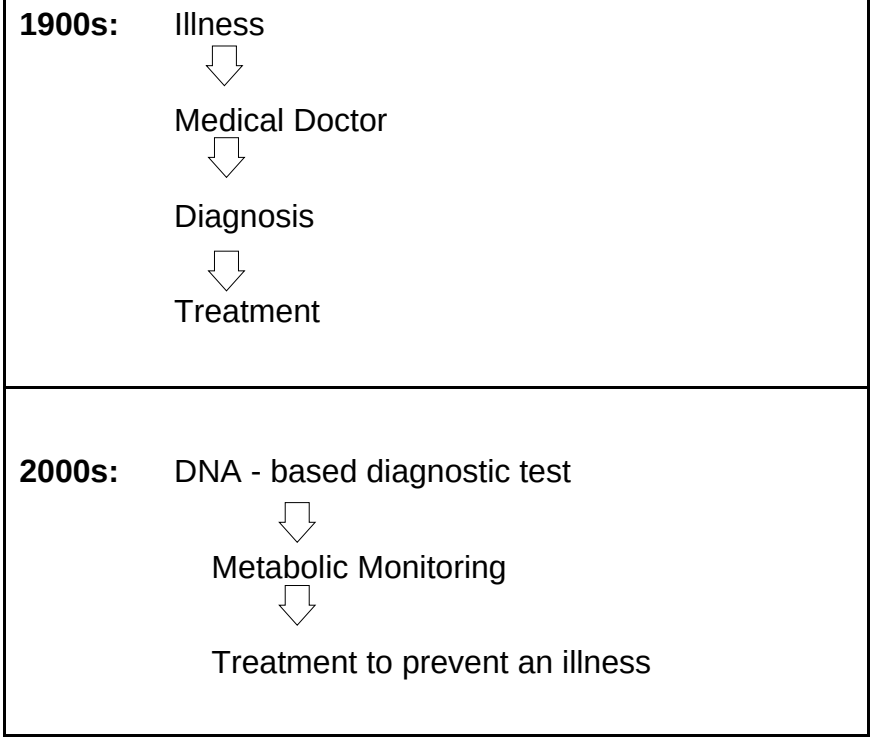
The need for medical genetic services, laboratory and clinical, has not been previously recognised in South Africa. However, the country is presently entering a stage of "epidemiological transition" where, with improving socio-economic circumstances the infant, and children under 5 years, mortality rates are decreasing and longevity is increasing. As a consequence, an increasing proportion of infant mortality and morbidity will in future be due to genetic disorders and birth defects to the extent that they will assume public health significance. Simultaneously, due to increased longevity and social changes associated with urbanisation and modernisation, the prevalence of many genetically determined common multifactorial diseases, including cancer, diabetes, hypertension, stroke and mental disorders will increase. Finally, late onset genetic disorders will also begin to be diagnosed in increasing numbers.

Epidemiological transition occurred in industrialised nations earlier this century and is presently taking place in many developing nations in the Middle East, Latin America

and in China. It has been considered to begin when the infant mortality rate drops below 40/1000 live births an eventuality that is possible in South Africa within the next 5 to 10 years. The rapid recent development of medical genetic technology has also resulted in new approaches in Medicine (Figure 1). The future thus holds significant challenges with respect to the development of medical genetic technological capability for all laboratory services, but especially for a nascent NHLS as envisaged for South Africa.

FIGURE 1: 21st Century Medicine

A "paradigm shift" in medicine is occuring



3.3 Finances:

Available sources of funding for medical genetics in South Africa, vary widely amongst the different academic departments undertaking such work.

The Universities in which all of the departments/divisions of Medical Genetics are situated, make a considerable contribution in terms of staff salaries providing accommodation, and capital for equipment and consumables. Research funding from the university and from national and international sources has played a significant role in the viability of these departments. Monies generated by units

offering their services to patients in the private sector has become a major source of ongoing income, especially in some of the departments. To varying degrees these funds have been vital for the maintenance of these departments over the last decade especially with respect to employing staff and purchasing equipment. Funding from public sources for staff salaries, equipment and consumables has been available from Provincial Departments of Health, but this has been severely eroded in recent years. Some funding has been provided by the Genetic Services Subdirectorate of the National Department of Health; payment for certain tests, on a fee for service basis, for patients in the public health sector has been made from this fund. Access to this source of money has however, recently become restricted.

An effort was made to assess the cost effectiveness of the laboratory services in the different departments. Due to limitations in time, the complexity of the funding structures in the various departments and because of the practice of cross subsidisation between clinical and laboratory research and service, this was not possible.

What needs to be noted, however, is that despite continuing and increasing limitations in financial resources the academic departments of medical genetics at the Universities of Cape Town, Stellenbosch, Free State, the Witwatersrand/ South African Institute of Medical Research (SAIMR), MEDUNSA and Pretoria have managed to provide a limited, albeit diminishing service, and continue to do effective research. A research capability has also developed at the University of Natal Medical School and in the committee's opinion, the Faculty appears to be rapidly developing the ability to develop a medical genetic service. The University of Transkei has also initiated a molecular research initiative. This is limited and needs to be nurtured.

3.4 Personnel:

Almost without exception the permanent staff complement of the established medical genetics departments/units/laboratories has diminished over the last decade. In the case of MEDUNSA this has been to the point of bringing the unit's continued existence into question. In other centres it has resulted in loss of service capability and it has placed great strain on their ability to maintain standards. It has certainly resulted in their inability to deliver their services to the community at large. Thus, at present, equity and access to medical genetic services for the majority of the population remains an unachievable goal.

The loss of qualified laboratory staff is most notable in Cytogenetics, which

constitutes the backbone of medical genetics laboratory services. Work in this field is labour intensive and specialised. Without cytogenetics any chance of expanding the prenatal diagnostic services in South Africa will be severely compromised. The field has also become important in the diagnosis and treatment of cancer, especially haematological malignancies. Thus the situation at the MEDUNSA laboratory which has lost 5 of their original staff of 8, and where a suitably qualified person cannot be found to fill a vacant senior post, must be a warning of the impending dissolution of this type of service. This situation is similar in other academic centres which have markedly reduced service capacity. An urgent need therefore exists to ensure posts are opened for the training and placement of cytogeneticists, if the existing limited service is to be maintained and then ultimately expanded.

The situation in the field of molecular genetics on superficial examination appears not to be as critical (Annexure B). The laboratory service demand is lighter than in cytogenetics and research staff also undertake service or diagnostic work. Nevertheless, a serious shortage of qualified staffing in this field exists and it is compounded by the fact that, when individuals obtain Masters and Doctoral degrees they move out of the country because of the lack of suitable positions available in South Africa.

3.5 Equipment:

There is a core of appropriate equipment that can be used simultaneously for service and research in most of the established Medical Genetic departments / units and laboratories. Much of this equipment has been purchased, and is maintained, from university, research and privately generated funding. Other sources of similar equipment will also exist in academic departments and laboratories outside the field of medical genetics, as in the cases of the Universities of Natal and the Transkei, the Natal Blood Transfusion Service and the Laboratory of Tissue Immunology at the University of Cape Town. More comprehensive investigation of the extent of this source of equipment and its potential usage for the NHLS will need to be undertaken in the future.

3.6 Comment:

South Africa, at the present time can be considered to have the greatest capability in the field of medical genetics in sub-Saharan Africa. However, the situation with respect to finances, personnel and equipment and its uses for both service and

research is finely balanced and in danger of being further seriously eroded unless immediate steps are taken to remedy the situation.

The possibility for the incorporation of medical genetic laboratories into the NHLS is seen by many as an ideal opportunity to reverse the trends of the past. The proposals documented below would enable the field of medical genetics to initially stabilise and then grow to meet the demands of the next century, in an environment that has appropriate regulation, auditing and accounting. However, this document deals mainly with medical genetic laboratory services, which as noted above, cannot be dissociated from clinical genetic services. The latter are in an even more parlous state than that existing in medical genetic laboratory services. If they are not simultaneously developed, equitable access of the community at large to even the most basic medical genetic care, will not become a future reality.

4. PROPOSAL FOR THE INTEGRATION OF MEDICAL GENETIC LABORATORIES INTO THE NHLS

This will be discussed under the headings given to the subcommittee of

1) National Reference Laboratory
2) Clinical Diagnostic Laboratory Services
3) Research Development, Teaching, Training and Academia

4.1 NATIONAL REFERENCE LABORATORY (NRL)

The committee was persuaded that for Medical Genetics service to function efficiently, a NRL was necessary, but that it should function as a national advisory body for medical genetics laboratory services. It would be directly responsible to the NHLS Board, funded by that Board, and be responsible for nationally organisable tasks. It would undertake the requisite research and development and then place proposals for policy before the NHLS Board (Figure 2). Because the NHLS Board falls under the direction of the National Ministry of Health, the Medical Genetics Advisory Board could be utilised for similar functions related to medical genetics for the National Department of Health.

Medical Genetic Advisory Board (MGAB)

Proposed composition:

- 4 people in Medical Genetics (Clinical and laboratory based)

- Deputy Director: Human Genetics, National Department of Health
- One person qualified in Law and/or Ethics

The chairperson could either be nominated by the NHLS Board, or elected by the members of the MGAB and would report to the NHLS board. The MGAB would meet on a 3 to 4 monthly basis, and may co-opt national, and if necessary international, expertise to assist in the performance of its task.

Secretariat

A secretariat based at the SAIMR, Johannesburg would be employed to administer and co-ordinate the functions of the MGAB.

Functions of the MGAB

The MGAB would have responsibility for the research and development of proposals for policy with respect to:

i) the development of standards for laboratories involved in the provision of service in medical genetics.

ii) the development of a system of laboratory quality control and proficiency testing.

iii) quality assurance and laboratory licensing which would take place outside the auspices of this body.

The policies set by the NHLS board, including quality control, proficiency testing, quality assurance and licensing should apply to all laboratories (public and private) that perform genetic testing in the country. In addition, patients having genetic tests should be provided with genetic counselling. As a general rule for each genetic test, at least one counselling session should occur. Test results often have implications for other family members and therefore issues of confidentiality also need to be carefully addressed. The provision of laboratory services must therefore be linked with the clinical/counselling genetic services thus enabling the patient to make informed reproductive health and management choices.

The principles for the provision of medical genetic services are similar to those of HIV. Preventive measures may be taken, there is a need for pre and post test counselling, the calculation of risk, and the management of psychosocial aspects.

iv) The determination of NHLS research and service priorities for genetically determined conditions and birth defects. To undertake this, it would be necessary for the MGAB, through The Secretariat, to maintain a surveillance system.

A centrally regulated genetics laboratory service with support from the national health system will allow access to (i) data on patients requesting genetics tests, (ii) clinical data on patients for whom no laboratory test may be offered. The information can be processed in a unit where expertise on the analysis of genetic conditions would be required. The processed information can then be forwarded to the Health Systems Research Unit in the Department of Health and to Service managers in the various provinces; as well as to the NHLS board and the PBEs (Figure 3).
The raw data collected from the laboratory and the clinics needs to be handled so that it would not be possible to identify individual patients (including patients with rare conditions) and therefore these data cannot be made part of the routine reporting process.

(v) make recommendations to the NHLS board on the allocation of research funds. It would also be appropriate for the MGAB to maintain a system of review of research protocols, for NHLS priorities, using national and international experts.

vi) address ethical and administrative issues in medical genetic services (laboratory and clinical) as the need arises. This would include issues such as pre-implantation diagnosis, cloning, and the release of genetic information to third parties (eg insurance companies and employers).

vii) develop policy proposals for the establishment of genetic laboratory services in under served areas where and when appropriate e.g. KwaZulu-Natal, Eastern Cape and the Northern Province.

viii) co-ordination of medical genetic laboratory service to minimise unnecessary duplication of genetic tests for rare conditions. This would include the collaboration with overseas laboratories for those rare tests that are not done in South Africa.

ix) setting fee structures for laboratory services

(x) other tasks as directed by the NHLS board

The MGAB should be seen as a body that bears responsibility for policy development, with respect to the regulation, auditing and accounting of medical genetic laboratory services. This body will therefore require an appropriate constitution and mandate.

4.2 CLINICAL DIAGNOSTIC LABORATORY SERVICES

Presently almost all diagnostic laboratory tests in the field of medical genetics (molecular DNA testing, metabolic tests, and cytogenetic tests) are undertaken in academic centres. The continued maintenance of these services in the proposed NHLS would thus fall under the auspices of the Provincial Business Entities (PBE). As the majority of these tests are specialised it would be prudent to suggest that a national grid of "referral laboratories" is developed to undertake this testing as discussed below (Figure 4).

4.2.1 SPECIALISED REFERRAL LABORATORIES

Molecular DNA Testing

Several laboratories presently provide molecular DNA diagnostic services for an array of conditions (Annexure B). To date informal agreements between these laboratories has, to some extent, ensured that each test offered is only undertaken at one laboratory unless the prevalence of the condition or other reasons dictate otherwise. The MGAB would oversee the coordination of this policy. As noted above there are exceptions to this "rule" and the future involvement of such tests in the field of common multifactorial diseases will require the timeous development of appropriate policy.

The positioning, rationalisation and regulation of molecular DNA technology for three special applications requires consideration.

Paternity Testing

With the new laws presently in place for child maintenance and support the need for paternity testing has increased. Presently this is undertaken by several laboratories in academic departments, some blood transfusion services, and in private practice. This includes three separate laboratories in Cape Town. This situation requires further investigation with a view to rationalisation and regulation.

Forensic Molecular DNA Testing

There is currently a proposal that the South African Police Services Forensic Science Laboratory develops a "DNA criminal intelligence database". There are many legal and ethical issues involved in the use of DNA molecular technology for forensic purposes.

The control of the use of this technology by the SAPS raises further ethical and legal considerations. It is therefore suggested that serious consideration be given to placing the laboratory services involved in this work under the NHLS and thus subject to the regulations developed for all medical genetic laboratory services.

Pre-implantation Genetic Diagnosis

This is a field of endeavour which is developing in South Africa, particularly in private practice. Its regulation is considered to be a matter of urgency.

Metabolic Disease Testing

Presently there is only one laboratory, in the Department of Biochemistry, University of Potchefstroom, that specialises in the laboratory diagnosis of metabolic disorders. There are however other laboratories which do have capability in the field, providing a limited service. The inclusion of the services of the University of Potchefstroom laboratory into the NHLS is desirable, and the need for a second such facility may need to be investigated in the future.

4.2.2 REFERRAL LABORATORIES

Cytogenetic Testing

As stated previously this forms the backbone of current medical genetic laboratory services and is used for prenatal diagnosis of birth defects, postnatal diagnosis of birth defects, and in the diagnosis and management of malignancies, particularly haematological cancers. There are cytogenetic laboratories in six academic centres, the Blood Transfusion Service in Durban and a provincial laboratory in Potchefstroom (Annexure C). Laboratories are also functioning in private practice. Two laboratories are situated in the Western Cape (Universities of Cape Town and Stellenbosch) and three in Gauteng (SAIMR / University of Witwatersrand, MEDUNSA, University of Pretoria) and one at the University of the Free State. For the present these laboratories should take responsibility for providing services to their particular PBE. To ensure other Provinces have access to cytogenetic laboratories, it is suggested that the Eastern Cape and Northern Cape (south half centred on Springbok) are aligned to the Western Cape PBE; the Free State PBE covers the Northern Cape (northern half centred on Kimberley) and the Gauteng PBE provides services for Mpumalanga, the North West and the Northern Provinces.

4.2.3 GENERAL PATHOLOGY LABORATORY

Maternal Serum Screening

The development of antenatal care services may lead to the future possibility of maternal serum screening for alpha feto protein or possibly the Triple Test to screen for Down syndrome. Such testing would occur in a general chemical pathology laboratory. However issues related to the ethics and administration of such testing, including counselling, would bear consideration by the MGAB as in essence they are tests for birth defects.

Neonatal Screening

Inherited errors of metabolism do not presently constitute a known significant public health problem in South Africa. However with the advancement of transitional epidemiology this situation will change and the necessity for neonatal screening will evolve. Like maternal serum screening this may be undertaken in a general chemical pathology laboratory but raises ethical and administrative issues that fall within the ambit of medical genetics.

New Developments

It can be anticipated that testing for certain genetically determined disorders will become simpler and less expensive in the future. Again, although the testing may be under taken in a general pathology laboratory, issues related to their appropriate usage will bear consideration by medical geneticists.

4.2.4 SPECIAL CONSIDERATIONS

University of Natal

The present situation in KwaZulu-Natal requires special consideration. The University of Natal Medical Faculty has on a research basis developed some molecular DNA testing capacity. From discussions with a wide range of interested parties in the Faculty of Medicine, including the acting Dean, Prof J Moodley, it is obvious that a collective will has developed there to establish a medical genetics capability. This coincides with the building of a quaternary care Academic Hospital with accommodation and facilities potentially available for this development.

The committee would strongly recommend that this initiative is supported by the National and Provincial Departments of Health and the proposed NHLS. The development should encompass all aspects of medical genetics, including cyto and molecular genetic laboratories and a clinical genetics service. The placement of the present Natal Blood Transfusion Cytogenetic Laboratory within this complex should be a matter for investigation.

University of the Transkei

In collaboration with the Department of Medical Biochemistry at the University of Cape Town the University of Transkei has initiated a molecular DNA research laboratory. At present this has very limited capability. However, given this Medical Faculty's placement in a community of approximately 4 million people, which it services, the possibility of establishing a cytogenetic laboratory and developing the molecular DNA laboratory should be encouraged.

Cytogenetic Laboratory - North West Province

The cytogenetic laboratory situated at Potchefstroom is considered by the committee to be non-viable and has the added disadvantage of not being associated with a clinical genetics service. It is currently handling fewer than 100 samples per year with a staff complement of one cytogeneticist, and a part-time laboratory assistant.

Its continued existence therefore requires consideration.

4.3 RESEARCH AND DEVELOPMENT, TEACHING AND ACADEMIA

Presently almost all activities in medical genetics in South Africa, including service, research and development, and teaching and training, occur in Academia. Some work, mainly connected with laboratory services, occurs in private practice. The continued undertaking of research and development, and teaching and training, for the foreseeable future, will depend on the academic institutions, and is therefore dependent upon the relationship that will be developed and maintained between them and the proposed NHLS. To date the nature of this relationship has not been determined, and falls outside the ambit of this report. Given the disparity in the way that different medical genetic departments are structured and financed it must be presumed that this future relationship would have to be negotiated with the individual departments, which will be guided in these negotiations by the policies of their parent University.

The exact nature of this future relationship was a concern of many during the consultations of the subcommittee. The manner in which medical genetic departments, units and laboratories are integrated into the NHLS can be expected to have significant consequences for their structure, functioning, staffing and financing. It will thus determine their ability to undertake research, development, teaching and training. It was not possible to discuss specifics related to these issues without having details of the proposed relationship between the NHLS and academic laboratories. Given the precarious situation in medical genetics in South Africa, all of these aspects of academic endeavour will be essential to ensure the continued

viability of medical genetics and will need to be addressed as part of the future negotiations to integrate the academic departments into the NHLS.

4.4 FUNDING

Funding of academic laboratories within the NHLS to undertake service work is an issue that still has to be determined. However this funding would have to be supplied by the PBEs within which the laboratory resided. In addition to the funds necessary to perform the task at hand it is suggested that consideration be given to the allocation of a proportion of the funds generated to bench research and special developments in the laboratories and some form of departmental incentive scheme.

Currently funds for genetic laboratory tests are in the Human Genetics subdirectorate budget. It is recommended that these funds are kept in this subdirectorate until such time as genetic services are developed in all the provinces, and all provinces are able to allocate a portion of their budget to pay for genetic tests. The present situation is that because the provision of genetic services is not seen as a priority, it is difficult in some provinces for clinicians to request genetic tests for their patients.

5. RECOMMENDATIONS

After consultation, discussion and due consideration the subcommittee makes the following recommendations:

1) Medical genetic laboratory services be included in the NHLS.
2) All present academic laboratories involved in service in the field of medical genetics be encouraged to participate.
3) Because of the inseparable link between medical genetic laboratory services and clinical genetic services, these services be combined in the same structure.
4) A National Reference Laboratory, designated in this document as a Medical Genetic Advisory Board be established.
5) A grid of national referral laboratories, be established to offer medical genetic tests to the country.
6) The initiation and development of medical genetic diagnostic facilities, linked to clinical genetic services be established in all Medical Faculties.
7) Paternity testing, forensic molecular DNA testing, and pre-implantation genetic diagnosis fall within the NHLS.
8) That forethought and care is taken when negotiating the entry of the country's medical genetics departments, units and laboratories into the NHLS, to ensure that they can continue to undertake their present role and meet the demands that will arise in the future.

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