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IARC MEDIUM-TERM STRATEGY AND IMPLEMENTATION PLAN FOR 2010–2014

Introduction

1. The burden of cancer is rising markedly worldwide with estimates indicating that there will be double the current number of new cases per year by 2030. The majority of the increase is expected in low- and middle-income countries where health services are least able to meet the impending challenge. If left un-addressed this rise in cancer cases will create enormous hardships at the economic, social and personal levels.

2. The International Agency for Research on Cancer (IARC) must orientate its activities over the next two decades such that it can best contribute to combating the projected increase in the global cancer burden. It should make its contribution in a way that is consistent with its Statute, plays to its strengths as an international organization and makes most effective use of its partnerships nationally and internationally. In this context the Agency will continue to prioritize interdisciplinary work and has a particular focus on low and middle-income countries. At the core of its function is the generation of evidence, through the conduct of novel research, which informs strategies for cancer prevention and control.

3. Past experience at the Agency in developing the evidence-base for cancer prevention has demonstrated the long lead time needed for planning, piloting and implementing effective prevention strategies as well as the considerable resources needed to achieve such aims. In developing its strategy the Agency must focus its research but also seek to maximize its resources from Participating States and extra-budgetary contributions in order to advance its plans with urgency.

4. The Agency's tasks are stated in its Statute in which the guiding principle is to promote international collaboration in cancer research. Specifically, the Statute of IARC states its role as:

- Planning, promoting and developing research in all phases of the causation, treatment and prevention of cancer;
- Collection and dissemination of information on the epidemiology of cancer, on cancer research and on the causation and prevention of cancer throughout the world;
- Studies on the natural history of cancer;
- Education and training of personnel for cancer research.

5. Given that the Statute remains largely unchanged after forty-five years it is remarkably well adapted to the cancer research needs of the future and the following principles will inform the medium-term strategy of the Agency.

6. First, the Statute places **emphasis on research**, thus distinguishing the Agency from other international cancer organizations that focus on developing policy and advocating change towards effective cancer control. This distinction establishes the basis of the complementary relationship with the World Health Organization (WHO), where the research conducted by the Agency (e.g. in tobacco prevention) can be translated by WHO into advice and policy. Close collaboration with WHO is indeed a feature of the current strategy. *The Agency will continue therefore to devote its resources to research and the generation of new information that provides the evidence-base for cancer prevention and control.*

7. Second, the Statute highlights **collaboration in research**. Collaboration is increasingly important for a number of reasons: the need for large multi-centre international studies to identify risk factors; to understand the consistency of effects in different populations; and to ensure efficiencies and economies of effort in times of limited resources. *Creating added value by promoting cooperation among the international cancer research community will be a strong feature of the Agency's activities.*

8. Third, the Statute highlights the **interdisciplinary research** conducted by IARC. Since its inception the Agency has pioneered the integration of laboratory sciences and population-based research. This approach has never promised as much as in the current era where a new understanding of the complexity of carcinogenicity combined with technological advances promises a level of refinement of measurement not previously available to epidemiology. *Understanding mechanisms of carcinogenesis and the translation of this knowledge to both identifying the causes of cancer and providing the scientific rationale for its prevention will characterize the future work of the Agency.*

9. Fourth, the Statute makes clear the **worldwide mandate** of the Agency permitting a collective response from Participating States for support in areas of the world where resources for cancer research are limited. The Agency has unprecedented collaborative networks and a strong reputation in low- and middle-income countries. Indeed, it is in these latter countries that a majority of the increased global cancer burden is anticipated in the coming two decades. These are also precisely the regions where the health services are currently least equipped to face this challenge and where research into causes and prevention of cancer is often under-resourced. Thus a particular emphasis of the Agency in low- and middle-income countries is a feature of the medium-term strategy. These qualities combined with its mandate mean *IARC will play a leading role in conducting and supporting research in the regions where it is most needed in the coming years.*

10. Fifth, the inclusion of **education and training** as one of the four highlighted aspects of the Agency's mission is vital, providing as it does the opportunity to build a new generation of cancer researchers worldwide with the motivation and skills to tackle the global cancer burden. *The Agency will place renewed emphasis on this task drawing on partnerships where appropriate and using modern technology to transfer its knowledge base to the individuals and organizations where it will have most impact.*

11. With this background, a number of areas of activity at the Agency can be considered core to the strategy and these are introduced below. These core activities are priority areas for support from the regular budget. Further details are provided in relation to the structure of the Agency, under each research Section in the Annex to this document. In presenting a strategy, however, it is also important to maintain the flexibility to respond to emerging priorities and new findings during the period covered.

12. Whilst developing the strategy, a number of areas of research were identified which will not receive emphasis. Whilst "treatment" is included in the Statute, it will not be a priority area. The Agency will not have major initiatives on the development of new therapeutic agents for example. However, as noted below (paragraph 40), advances in understanding the molecular basis of cancer means that there are less distinct borders between studies of the causes of cancer and prognosis. Thus on occasion research findings will have implications for how a cancer patient may respond to therapy or be susceptible to relapse, for example, and this may lead to beneficial collaborations with specialized researchers in these areas. In terms of the "natural history of cancer" the Agency will seek to elucidate the genetic and environmental origins of cancer and the underlying mechanisms but will not search for new high penetrance genes or conduct fundamental mechanistic studies in isolation of an understanding of the causes of cancer at a population level.

Resources

13. The strategy presented presupposes a continued balance between regular budget and extra-budgetary resources whereby the latter comprise around 30% of the total available funding. The current strategy can not be realized with contributions from Participating States alone. Currently the majority of extra-budgetary funds are obtained from four sources, namely the National Institutes of Health, USA; the European Union; governmental and charity sources in France and from Foundations, notably the Bill and Melinda Gates Foundation.

14. In its future strategy the Agency will also explore with Participating States the possibility to compete for national funding sources, in collaboration with or independently of national research organizations. Other sources of international support will also be actively explored. At the same time funding will only be sought for projects which fall within the strategy, to avoid a dependence on external funding leading to a donor-driven research agenda.

15. The Agency strategy also depends on the recruitment of high quality staff. Emphasis will be placed on effective presentation and advertisement of posts internationally, including in Participating States, in order to attract the best quality people to IARC.

16. The distribution of resources by area, including staffing, are outside the scope of this document but are available through the detailed Project Abstract Sheets and the biennial budget documents of the Agency.

Core activities

Describing the global cancer burden

17. The Agency aims to be the definitive international point of reference for collection, quality control, processing and statistical analysis of reliable cancer incidence, mortality, survival and prevalence information. This is a vital function in order to provide the full range of information needed at national and regional level to support cancer control programmes. It is recognized that currently, for many regions and countries, very limited data are available and estimates involve extrapolation from other geographical locations and/or by basing incidence estimates on mortality.

18. The Agency will strengthen its efforts to expand the coverage, continuity, and quality of cancer registration, particularly in regions where data are lacking, through provision of training, setting standards and quality control. Where population-based cancer registration is not feasible in the short-term, alternative approaches to exploring cancer occurrence will be developed. Expected outcomes of this part of the strategy include an increase in the current coverage of the world population in future volumes of Cancer Incidence in Five Continents (CI5C); establishment of regional reference centres for cancer registration in Africa, Asia and Latin America; provision of structured training programmes in cancer registration and new estimates of the global cancer burden with forward projections. These activities will also provide a platform for studies of cancer risk factors and a basis for preventive interventions and targeted screening programmes.

19. It is increasingly recognized that a full understanding of cancer trends within a population requires information on survival and prevalence alongside incidence and mortality estimates. Accordingly the Agency will seek to expand its inclusion of these metrics in its publications and participate in relevant international collaborations (EUROCARE, CONCORD, Cancer Survival in Developing Countries) and also play a role in methodological development.

20. Improved accessibility to the information generated will be a further priority, including increasing the use of electronic provision. Specifically the strategy foresees the release on the IARC website, with a user-friendly interface, of CI5C as well as Childhood Cancer volume 3. The Agency will continue to provide the focus for the International Association of Cancer Registries and the European Network of Cancer Registries and seek to integrate its activities with other regional and multi-national cancer registry networks. The WHO, the Clearing House for a broad range of international health statistics, is also engaged in estimating the global burden of disease. IARC and WHO will, therefore, work together to improve the quality and consistency of their methods for generating disease burden estimates.

21. The *WHO Classification of Tumours* series (WHO "Blue Books") is vital in terms of standard-setting for cancer registration and hence the quality and utility of data obtained from cancer registries. The Blue Books are also of great importance in disease classification in clinical practice. The series is remarkable for the contribution it has made improving the standardization of the histological classification of tumours. IARC has been responsible for the "Blue Books" since the 3rd edition and the Agency will now place priority on providing support to increase the rate of production of the 4th series.

IARC Monographs

22. The IARC Monographs have an international reputation for evaluation of evidence regarding the causes of cancer through its Working Groups, which bring together the expertise of international experts and IARC scientists from across the Agency. Identification of risk factors is fundamental to cancer prevention and the conclusions of the Monographs are used by national health agencies to develop approaches for preventing exposure to known and suspected carcinogens.

23. Major expected outcomes of the IARC Monographs are the production of two to three volumes per year with each volume appearing within one year of the Working Group meeting and publication of summaries of each Monograph in The Lancet Oncology immediately following the meetings.

24. In developing its activities the IARC Monographs will increasingly consider information on mechanisms of carcinogenesis in its evaluations, including concordance between animal and human data, and explore how it can provide more quantitative information on the carcinogenicity of a given exposure, where data permit it, to help inform risk assessment and risk management. In relation to these objectives, major outcomes from the strategy will be two key publications on "Tumour Concordance between Humans and Experimental Animals" and "Mechanisms Involved in Human Carcinogenesis" which will help in the development of future approaches to evaluations. Finally the strategy will yield a plan for the future of the Monographs programme in terms of its involvement in quantitative risk assessment.

Cancer etiology

25. Cancer etiology represents one of the largest areas of activity in the Agency, both in terms of scope and resources, with contributions from, and collaborations between research Sections across the organization. The environment (defined in its broadest sense to include lifestyle, nutrition and occupation, in addition to physical, chemical and biological factors) plays a role in the overwhelming majority of cancers and consequently, at least in principle, the majority can be prevented. However, despite advances in identifying a number of major human carcinogens there remain a significant proportion of cancers for which the etiology is unclear.

26. The challenges are many, including the changing patterns and scale of cancers in low- and middle-income countries and the interplay between genetic background and environment, which is only beginning to be explored. In many national research settings cancer research funding tends to be more orientated towards treatment than identifying causes. These considerations point to the need for the Agency to continue to focus on the causes and prevention of cancer. IARC has a unique combination of strengths and expertise to provide leadership into this research area.

27. Well-designed large, population-based international surveys, like the IARC HPV Surveys, can provide much needed maps of the distribution of known cancer risk factors and, hence, help predict future cancer trends. In addition to specific descriptive studies designed to obtain such information, some survey data may also be obtained in the context of research projects or as an adjunct to activities aligned with cancer registries. This activity will be valuable in assessing

impact on cancer risk on a regional level in conjunction with the WHO emphasis on monitoring exposure to known risk factors.

28. The study of cancer etiology in the current Agency strategy has a number of characteristic approaches, which draw on the interdisciplinary expertise, and applies these to priority areas in relation to risk factors and specific cancer sites. These characteristics are described briefly below.

29. First, the study of etiology will draw on resources of large population-based cohorts (including EPIC) and multi-centre case:control studies including support to international consortia. New opportunities are emerging with adult cohorts in low- and middle-income countries (e.g. Russian Federation, Iran and India). However, the strategy foresees not only the study of risk factors in relation to exposure in adult life but aims to describe the role of early life exposure on subsequent cancer risk through access to a number of mother:child birth cohorts worldwide. To support this strategy the Agency is collaborating with the International Children's Cancer Cohort Consortium.

30. The Agency does not have the resources to establish major new cohorts and thus emphasis is placed on opportunities to provide leadership and expert support to existing cohorts and in promoting multi-centre studies. In addition, it is recognized that the study designs the Agency adopts will reflect the logistics of a given situation; for example, in some low- and middle-income countries difficulties of follow-up may make the conduct of cohort studies unfeasible.

31. Second, the strategy involves emphasis on the causes of cancer in low- and middle-income countries. These are areas of the world where the Agency has strong, established collaborations and where the capacity to conduct research by national scientists can be strengthened by international cooperation. The Agency will work through research collaborations at the national level but also seek partnerships with other international organizations. For example, the Agency will participate actively in the African Organization for Research and Training in Cancer (AORTIC) to develop a cancer research agenda for Africa.

32. Third, the approach to cancer etiology is characterized by a major emphasis on translation of the latest advances in knowledge of mechanisms of carcinogenesis into biomarkers which can be applied into epidemiological studies. This strategy demands close interaction between the Agency's laboratory scientists, biostatisticians and epidemiologists, reflecting the inherent inter-disciplinary nature of much research at the Agency. The etiologic studies will use biomarkers to improve exposure assessment, define susceptibility and classify disease. Such biomarkers will also serve to address the biological plausibility of putative exposure-disease associations and be used as endpoints in pilot intervention studies. Therefore the development of epidemiological studies which have associated biobanks will be a priority.

33. This type of translational research from laboratory to population draws its strengths from integrating mechanistic research within large molecular epidemiology programmes. There is thus continuity between this priority area and the subsequent one on "Mechanisms of Carcinogenesis". The strategy will have a focus on elucidating gene-environment interactions by combining large-scale genetic studies (such as genome-wide association studies) with detailed assessment of exposure to environmental risk factors. In recent years, the availability of novel

technologies to assess environmental exposure, based on "omics" technology, mass spectrometry and nuclear magnetic resonance, has opened new possibilities for addressing etiological risk factors with unprecedented detail. In addition, advances in understanding mechanisms of carcinogenesis are opening new avenues of research on the way in which exposures affect cancer risk, for example, through epigenetic alterations.

34. In the field of infections and cancer, accurate biomarkers already exist for a number of chronic infections strongly associated with cancer (e.g. HBV, HCV, and HIV) thus allowing efficient study of the probability of developing pre-cancerous and cancerous lesions in infected individuals according to the presence of different risk modifiers. Better biomarkers of chronic carriage are, however, required for some important cancer-related infections (e.g. HPV, Helicobacter species, EBV) and, most important, to allow the exploration of still unknown associations between infections and additional cancers.

35. In general, biomarker validation and translation into epidemiological studies requires well-designed pilot studies in humans and adaptation of the biomarkers to the type of biospecimens available in biobanks with the requisite high-throughput. The capacity of IARC in this area of translational research will be increased by additional resources within existing Sections, including the Section of Mechanism of Carcinogenesis (assessment of exposures, biomarkers of early disease) and the section of Nutrition and Metabolism by creation of a Biomarkers Group. Expected outcomes in the next five years will include new biomarkers measured by assays applicable to biobank samples.

36. Priority will be placed on understanding the role of infections, nutrition and metabolism (including obesity) and the interaction between environmental risk factors and genetic susceptibility. These areas are supported by the Sections of Infections, Nutrition and Metabolism, Environment, Mechanisms of Carcinogenesis and Genetics and place emphasis on collaborations between laboratory scientists, epidemiologists and biostatisticians in interdisciplinary studies.

37. Major expected outcomes from the cancer etiology studies include an improved understanding of: the role of HPV (mucosal and cutaneous types) in cervix, skin and other cancers; the impact of HIV on cancer risk; the etiology and prevention of liver, oesophagus and nasopharyngeal cancer in low- and middle-income countries; the causes of childhood cancer including evaluation of radiation sensitivity following exposure in childhood and *in utero*; the genetic and environmental causes of kidney and melanoma skin cancer; the mechanisms by which diet and nutrients affect cancer risk and the role of early life exposures, including diet, in susceptibility to cancer later in life, occupational risk factors for lung cancer and the joint effects of tobacco smoking and occupational carcinogens.

Mechanisms of carcinogenesis

38. The period of the current medium-term strategy has witnessed significant advances in understanding mechanisms of carcinogenesis. In particular comprehension of the structure of the genome and the importance of epigenetic alterations (methylation, histone modifications, microRNAs) in the development of human cancer reveal new ways in which the environment

may interact with cells to increase cancer risk. The potential reversibility of epigenetic changes offers interesting opportunities for intervention.

39. As described in "Cancer etiology", the above insights into the genome and the epigenome will result in novel endpoints in carcinogenesis, with an opportunity to translate these into methods applicable to population studies. This line of research also helps elucidate the interaction between environmental and genetic or other host factors in the development of cancer. In this context the Agency will increasingly focus its genetics research on functional genomics in order to build on the knowledge gained from genome-wide association studies. Specifically this approach is designed to elucidate the pathways involved in carcinogenesis and the functional impact of specific genetic variants on cancer risk; the interaction between low penetrance alleles with environmental factors will be a feature of the work, as well as the identification of genetic and epigenetic changes affecting cancer stem cells.

40. The genetic alterations in human tumours are providing a mechanistic link between etiology and therapy, traditionally seen as two ends of the cancer research spectrum. Advances in molecular genetics mean the genetic profile of the tumour may now reveal both its etiology (e.g. *TP53* mutations spectra) and its susceptibility to therapy. Some of the biomarkers derived in this context may also be valuable as prognostic indicators. Thus whilst the Agency will continue to focus on causes and prevention, the characterization of human tumours will lead to interesting opportunities for early detection of cancer and a new understanding of the factors affecting prognosis and survival of cancer patients.

41. The major expected outcomes in this area are: to contribute to understanding the etiopathogenesis of oesophageal and liver cancer in low-income, high-incidence regions; development of a mechanistic understanding of the contribution of newly identified genetic loci from genome-wide association studies to carcinogenesis; to understand the impact of specific environmental exposures, including nutrition, in early life and adulthood on epigenetic changes; to develop plasma-based biomarkers of mutations and epigenetic changes in order to monitor exposures to risk factors and to predict the development of common cancers.

Cancer prevention

42. The Agency will place emphasis on research into the effectiveness of intervention strategies and how these can be best implemented at the population level in particular socio-economic and cultural environments. This work will be relevant to WHO in terms of the development of public health policy and practice. The Agency will expand its range of skills to include scientists with expertise in behavioural epidemiology and health services research and seek external collaboration with internationally recognized experts in these and related disciplines. This type of partnership is essential to understand communication issues in the local context for the successful design of effective public health programmes.

43. Priority areas for prevention will include evaluation of health promotion programmes, for example, with respect to modification of lifestyle, avoidance of tobacco, dietary advice, the effects of obesity and physical exercise etc., and population level interventions such as vaccination programmes and screening. In relation to infections the Agency has particular strengths in HPV and cervical cancer, which is a priority, as well as the opportunity to complete

the Gambia Hepatitis Intervention Study (GHIS) to evaluate the effectiveness of HBV vaccination on liver disease and liver cancer. The latter study will be supported through to completion of its principle aims, namely to evaluate the impact of vaccination on chronic liver disease and hepatocellular carcinoma. The strategy includes investment to appoint a hepatologist to be based in The Gambia in order to provide leadership in the final phase of the project. Furthermore, through its contribution to better understanding the risks for hepatocellular carcinoma and the clinical presentation of the disease in West Africa, this study will provide a framework to develop recommendations and guidelines for effective reduction of the burden of liver cancer in high-incidence areas of Africa.

44. Cancer screening will include considerations of quality assurance and will be focused not only on high-income countries, notably in Europe, but also low- and middle-income countries. The synergy between cancer registries and the evaluation of screening programmes is envisaged as a key strength. Finally, cancer screening is a complicated process that requires quality assurance as much as high population coverage. There is clear demand for an international clearing house for guidelines, quality assurance and monitoring of screening implementation. IARC is already active in this field but has a possibility to increase its role substantially.

45. Major expected outcomes are: evaluation of a two-dose HPV vaccination regimen compared to the current standard three-dose regimen; provision to decision makers in developing countries with operational, efficacy and safety data to make an appropriate, evidence-based HPV vaccination policy; evaluation of the long-term protective efficacy of Hepatitis B vaccine against chronic liver disease and liver cancer in a high-risk context; cost-effectiveness assessment of trials; guidelines used by governments and regulatory agencies as documented in official sources and in peer-reviewed reports; changes in health care utilization and health outcomes resulting from implementation of guidelines.

Education and training

46. The Agency will place more emphasis on developing an integrated and expanded programme of education and training coordinated by a senior professional staff appointment. The activities will include the strengthening of the Fellowships Programme with an expanded remit. Encouraging young scientists from high-income countries to devote a career to international cancer research can complement the direct training of researchers from these latter regions. Emphasis in regard to expansion will be on post-doctoral training rather than pre-doctoral, the former being in general better suited to the Agency's profile. Increased extra-budgetary sources of funding for fellowships will be sought as will cooperation with UICC and other bodies as well as with Participating States. Sponsorship of named fellowships will be pursued as long as there is no compromise of the peer-review process or undue constraint on the research topics, which must be in line with the IARC strategy. Any proposed support from Foundations would only be accepted following discussion with the Governing Council Chair.

47. Training courses will be matched to the Agency's core competencies in cancer registration, cancer epidemiology, molecular epidemiology and cancer screening and early detection. As well as developing its own courses IARC will seek partnerships with other providers in order to

maximize its contribution without duplication of effort and resource. When appropriate the use of multi-lingual technical material and distance learning methods will be employed. IARC will continue to make its courses available predominantly without fees.

48. In contrast to many other educational programmes the IARC approach is seen as contiguous with its research activity. By maintaining active working relationships with past fellows, course attendees etc., IARC can greatly improve their subsequent opportunities for conducting high-quality research. For example, IARC post-doctoral fellowships include support to students upon return to their home countries to help them establish cancer research projects targeting the most important local needs often in collaboration with IARC; cancer registration training frequently leads to increased capacity in registries that contribute to the Agency's collation of global cancer data; and training in screening techniques is applied in subsequent research projects.

Common resources

49. There are a number of skills and resources that provide support across the Agency's activities. The strategic approach to the provision of these is outlined briefly below.

Biostatistics

50. The Agency requires competencies in advanced statistical methodology and bioinformatics. This is vital to exploit fully the range of opportunities offered by the large databases held at IARC. There is however a required balance between methodological research and the application and support to studies across the Agency. To achieve this implies both a strong professional grouping in-house and access to external collaboration. The opportunity to conduct methodological research is considered important in recruiting top-quality biostatisticians.

51. In order to provide the above balance the Agency has established a Biostatistics Group, which comprises scientists from different research Sections. This Group thus differs in concept from the Section/Group structure, in that it does not involve line management. However, a budget is assigned to the Group Head for implementation of cross-cutting activities and initiatives (for example, training, consultants and seminars). In addition, the work plans for each biostatistician will include specific objectives and assigned time for each Group member to work on methodological projects.

52. This recognized grouping in Biostatistics will also result in a focus for more junior members (post-doctoral fellows, students, support staff) of the Agency involved in biostatistics and bioinformatics as well as more general associated issues such as database management. In relation to bioinformatics, the Agency will rely on external collaboration through universities and research institutes but will invest in-house in expertise to ensure an effective communication with external experts and some core support to Agency scientists.

IARC Biobank

53. The development of collections of well-annotated human biological specimens is a strategic activity for IARC that contributes to exploration of the complex relationship between the environment and cancer. The IARC Biobank provides an infrastructure for such collections and a laboratory platform for quality control, specimen processing (including DNA extraction) and distribution. The Biobank also represents a resource for the wider international cancer research community. The Agency has good relationships through established networks of biobanks and will continue to lead initiatives for developing internationally accepted standards and guidelines for biobanking through a Biobank Steering Committee (BSC).

54. The IARC Biobank has specimens from about 800 000 subjects recruited in studies around the world. This represents some 8 million individual samples, making it one of the largest biobank resources dedicated to cancer worldwide. About half of these specimens (4 million, 300 000 subjects) are from EPIC, but IARC also maintains several large-scale cohorts, case-control and case-series studies including the Siberia cohort (150 000 subjects), the GEMINI cohort of Northern Iran (50 000 subjects), major collections on infection and cancer (180 000 subjects) and large collections related to international studies on lung, head and neck, liver, oesophageal cancers and lymphoma. In addition, IARC has developed a repository of lymphoblastoid cell lines from cancer prone subjects from around the world (2500 cell lines), as well as many smaller collections valuable for specific studies. A reorganization of all archives of biological materials is nearing completion and this will improve accessibility to IARC scientists and external collaborators.

55. The Agency has responded to the importance of this area by strengthening the management and governance structure to be led by a dedicated professional staff scientist, supported by a technical team. The new structure will permit further implementation of the Laboratory Information Management System which has been developed to catalogue and track bio-specimens during processing and distribution to partner laboratories.

Laboratory Support Services

56. IARC will continue to seek partnerships with centres of expertise in areas of specialized technology e.g. nuclear magnetic resonance (applied to metabonomics), in order to avoid duplication or over-specialization. At the same time in order to attract the best laboratory scientists and fulfil its research objectives, the Agency needs to invest in equipment and high quality facilities in core areas of laboratory science such as molecular and cell biology, immunoassays, high performance chromatography, mass spectrometry, microscopy etc. Priorities for future investment will include next-generation DNA sequencing to provide relatively inexpensive, genome-wide sequence readout as an endpoint to applications ranging from polymorphism discovery, DNA methylation profiling, mutation mapping, chromatin immunoprecipitation to microRNA discovery as well as mass spectrometry to permit analysis of exposure biomarkers. A prime consideration prior to purchase of major equipment items is the opportunity to outsource or collaborate as an alternative to in-house investment.

57. There are a number of specialized resources and support services (e.g. health and safety, washing, sample shipment) used by each of the laboratory groups in the Agency. In order to ensure the integrated development of these areas, the Laboratory Steering Committee (LSC) now oversees the core support services and sets priorities for investment, in line with the IARC medium-term strategy, through advice to the Director. Health and safety matters are overseen by the Occupational Heath and Safety Committee, which includes representatives of all categories of staff and of the administration as well as the IARC physician. A new professional scientist post has been created to manage on a day-to-day basis the Laboratory Support and Biobank Group (LSB) covering the activities described in this and the preceding section.

Communication

58. The preparation and dissemination of scientific information is one of the prime objectives of the Agency. The Agency aims to communicate its findings from population-based research, cancer registration activities, IARC Monograph evaluations, WHO Classification of Disease, working groups etc. The Agency findings are mainly targeted to the scientific community, regulatory bodies, governments and professional associations. There will be a specific onus on communication with Participating States. Nevertheless as a publicly funded body the Agency also has a responsibility to translate its activities into formats which are informative for the international press and public. This type of communication will be limited to research findings. More general information to lay audiences on cancer as a disease and its treatment is better handled either by national bodies (government, charities or foundations for example) or by international advocacy organizations such as the International Union Against Cancer.

59. The Agency will review its current approach to communications during the first part of the current strategy period and evaluate the need for change in relation to its mission. This exercise will result in an explicit IARC Communications Strategy.

60. Dissemination of information is through paper publications and increasingly the web, media reports, etc. The Agency will develop ways of making available the widest range of cancer data through its publications programme and its web platform. The IARC website will ensure greater visibility of research output from various large internal sub-sites such as the Monographs databases, the cancer incidence and mortality databases, the IARC TP53 mutation database and new databases in the fields of genetics and epigenetics; dissemination will also include tools and methodologies, e.g. the development of an EPIC-soft web-based methodological platform for dietary assessment. The IARC web team supports Research Sections/Groups and ensures an institutional/corporate identity, clearly representing the Agency’s mission, values and strategy.

61. The inflow of information is central to scientists' research, and the library services ensure an appropriate bibliographic resource for all. The library will provide user-centred collections, resources and services in a hybrid library environment: physical and virtual, local and remote, print and electronic.

62. A new Advisory Committee on Publications will guide the Agency throughout the strategy period in establishing a prioritized publication plan, focusing on outputs not provided from other sources (e.g. Cancer Registration: principles and practice).

63. Coordination with WHO will be a feature of the Agency's approach to communication at different levels. Improved processes for planning of press releases and other communication initiatives will be sought with WHO in the context of a two-way exchange. WHO Press is the exclusive partner for dissemination of Agency publications and this demands an active dialogue concerning the preparation and marketing of IARC publications to maximize dissemination. A new financial agreement regarding the flow of income from book sales to the Governing Council Special Fund has been agreed for 2010. Income from sales will be directed to the support of IARC publications.

Management and monitoring

64. The Agency has established a management structure that provides clear lines of responsibility and accountability as well as an opportunity for all working at the Agency to have a voice. The Senior Leadership Team (SLT) comprises the Director, Director of Administration and Finance, Head of Communications and all Section Heads. This committee serves to advise the Director on scientific strategy, priorities for resource utilization and management issues. The IARC Operational Team (IOT) is chaired by the Director of Administration and Finance and comprises the Heads of Support Services, Head of Communications and one Head of Section. This committee seeks to implement the decisions of the SLT and to raise points for consideration by the SLT.

65. From 2008 IARC began to implement financial and management procedures in order to comply with International Public Sector Accounting Standards (IPSAS) by 2010. The procedures should be modern and sound and responsive to a research environment whilst also being transparent to Participating States. The euro, in which 80% of the IARC expenditure is incurred, will be used as the currency of reference and the SAP management system will be upgraded and design errors corrected. The presentation of the medium-term strategy and budgets by Section will enable Participating States to more clearly see the link between activity and resources. IARC now makes all its Governing Council and Scientific Council documents (apart from peer-review documents) openly available via its website.

66. The Agency will continue to seek competitive, extra-budgetary sources of funding to complement its income from Participating States. It is recognized that the ability to attract extra-budgetary funding is one indicator of research quality. Whilst no cap will be set on the proportion of overall financing from such sources, the Agency will only request funds for projects that contribute to the development of the Agency's mission.

67. The scientific structure is organized by Sections (see Organizational Chart at the end of the Annex), which are in turn comprised of one or more Groups. Each Section and Group has a Head with a clearly defined set of responsibilities. Sections and Groups may be altered to adapt to changing priorities. Cooperation between Sections is encouraged and enabled by presence of all Section Heads on the SLT and various initiatives that cut across the organizational structure (see Common Resources).

68. In the strategy the research is presented for each Section and Group, in order to provide clear specific aims, approaches and expected outcomes (see Annex). Each Section will be subject to peer-review by the Scientific Council on a five-year cycle. Based on the most recent cycle of reviews and the stage of development of the various Sections the following schedule is envisaged, subject to agreement by the Council:

Year	**Sections**	
2010	Genetics	
2011	Cancer Information	Environment
2012	Early Detection and Prevention	Nutrition and Metabolism
2013	Molecular Pathology	IARC Monographs
2014	Mechanisms of Carcinogenesis	Infections and GHIS

69. The overall performance against the medium-term strategy will be measured against a set of Key Performance Indicators (KPIs) agreed by the Governing Council.

70. The Annex which follows describes the activities in each of the scientific Sections of the Agency.

Annex

Section of Cancer Information (CIN)

Relevance to IARC mission

The provision of data on cancer incidence, mortality, survival, and prevalence and the estimation of geographic and temporal trends are a core activity of the Agency. These data are essential to cancer control programmes worldwide and provide a foundation for studies of cancer etiology and prevention. Innovation is needed to improve the range, timeliness and presentation of cancer information as well as exploring new statistical approaches and methodologies. The Agency will actively support the collection of cancer information through cancer registries and place effort on making the information increasingly accessible to a variety of users.

Specific aims:

1. **Increase in geographical coverage and the continuity of collection of data on cancer incidence, particularly in low- and middle-income countries;**
2. **Improvements in the timeliness and accessibility of Cancer Incidence in Five Continents (CI5C) and Childhood Cancer database;**
3. **New up-to-date estimates of the global burden of cancer in order to improve prevention and cancer control.**

Major approaches:

1. Support to cancer registries, especially in low- and middle-income countries through collaboration with the local governments, WHO regional offices and non governmental organizations; creation of regional reference centres for training in cancer registration in Africa, Asia and Latin America; production of technical material in English, French and Spanish to reduce language barriers.

2. Establish a permanent editorial board and secretariat at IARC in collaboration with IACR and ENCR and other registry networks. Create an on-line data upload facility (bilingual) to ensure more timely updates of the IARC database and easier access for the contributors and users of cancer information.

3. Develop standardized methods to estimate cancer incidence, mortality, survival and prevalence in the world in collaboration, where appropriate, with international advisory groups and WHO.

4. Assist in the development of cancer prevention policies in different WHO Regions to geographical specificities in cancer pattern.

Expected outcomes:

Increased coverage of the world population in CI5C; regional reference centres for cancer registration in Africa, Asia and Latin America; regular training courses and release of multi-lingual technical material; distance learning materials for cancer registration, data analysis and

CanReg5 software; collaboration with IACR, ENCR and IAEA (PACT project) to avoid data inconsistencies and duplication of effort; release of CI5C volume X (print and electronic formats) in 2012; release of CI5C volumes I-IX, the new CI5C volume X and Childhood Cancer volume 3 on the IARC web site; new estimates of the global cancer burden and future projections using updated GLOBOCAN data.

Section of IARC Monographs (IMO)

Relevance to IARC mission

The first step in cancer prevention is to identify the causes of human cancer. The IARC Monographs fit with the mission of cancer prevention by reviewing, evaluating and assessing the evidence on causes of cancer, which can then be the subject of efforts by national health agencies to prevent exposure to known and suspected carcinogens. The Section works in close relation with external *ad hoc* Advisory Groups to ensure that the topics of new Monographs reflect current research and public health priorities. The development of Monographs is a highly integrating activity within IARC that draws expertise from every area of research developed by the Agency.

Specific aims:

1. **To evaluate in the IARC Monographs the scientific evidence concerning environmental factors of public health importance;**
2. **To consider the relevance of experimental models through comparison between tumours in experimental animals and humans in relation to the same exposure;**
3. **To review mechanisms of human carcinogenesis and the use of mechanistic data, including biomarkers, in carcinogen evaluation;**
4. **To investigate the possibility of providing quantitative estimates of carcinogenic risks to humans.**

Major approaches:

1. Convening international, interdisciplinary Working Groups to develop two or three volumes of *Monographs* each year reviewing all pertinent epidemiological studies of cancer and cancer bioassays in experimental animals, plus representative studies on mechanisms of carcinogenesis.

2. Reviewing the Working Group's final text and tables for scientific accuracy and clarity and edit the Monograph for publication in book and electronic formats.

3. Working Groups to develop scientific publications on *Tumour Concordance between Humans and Experimental Animals* and on *Mechanisms Involved in Human Carcinogenesis*.

4. Convening an *ad hoc* Advisory Group that includes specialists in quantitative risk assessment to advise on how to develop estimates of the cancer risks posed by agents evaluated in recent Monographs. Advice will be sought as to the needs of national health agencies and research organizations, the types of risk estimates that IARC might develop, and the process for doing so.

Expected outcomes:

Production of two to three *Monograph* volumes per year; priority agents include mobile phones, motor vehicle emissions, polyomaviruses, asphalt/bitumen, and acrylamide; publication of summaries of each *Monograph* in *The Lancet Oncology* immediately following the meetings and of full *Monographs* within one year of the Working Group meeting; an *ad hoc* Advisory Group meeting to recommend priorities for future review (2013); IARC Publications on *Tumour Concordance between Humans and Experimental Animals* (2012) and *Mechanisms Involved in Human Carcinogenesis* (2013); a decision and plan for the future of the *Monographs* programme in terms of its involvement in quantitative risk assessment.

Section of Mechanisms of Carcinogenesis (MCA)

Relevance to IARC mission

The overall aim of the Section is to contribute to cancer prevention and control through a better understanding of mechanisms of carcinogenesis. The Section works closely with epidemiology groups, particularly in relation to the biobank opportunities, in selecting its priority areas. These include investigating interactions between the environment, the genome and the epigenome. In collaboration with epidemiology groups, the Section develops translational studies on biomarkers of effects of environmental exposures and biomarkers of early cancer, focusing on cancers such as hepatocellular carcinoma (HCC), squamous cell carcinoma of the aero-digestive tract (SCC) and breast cancer, which are common in low-income countries. This involves the development and coordination of international consortia (e.g. International Liver Cancer Study, http://ilcs.iarc.fr/). Another focus is to develop functional genomic studies to explore the involvement of genetic loci identified by genome-wide association studies, in collaboration with the GEN Section. The role of the Section in database development and maintenance is restricted to areas where there is a strong associated research activity at the Agency.

Molecular Carcinogenesis Group (MOC)

Specific aims:

1. **To understand the interplay between mutagenesis and biological selection in shaping patterns of mutations in cancer-related genes;**
2. **To characterize the carcinogenic mechanisms underlying the involvement of loci identified by genome-wide association studies;**
3. **To identify and validate molecular markers for early detection and prognosis of HCC and SCC in areas of high incidence;**
4. **To disseminate molecular cancer epidemiology information through public databases.**

Major approaches:

1. Sequencing of oncogenes and tumour suppressor genes in defined case-series of HCC and SCC (*TP53, RAS, EGFR, CCNB1, CDKN2a, PTEN* and *TP63*).

2. Assessing the contribution of germline *TP53* mutations to cancer burden in low-income countries.

3. Developing organotypic cultures for functional genomic studies on dysfunctional oncogenes/tumour suppressors.

4. Performing translational studies on DNA and proteins from plasma/serum and other bodily fluids as sources of biomarkers for early detection.

5. Developing an open-access, web-based database of *TP53* mutations.

Expected outcomes:

Identification of the formation and biological selection of cancer-causing mutations with a focus on SCC of the oesophagus, breast and HCC in low-income, high-incidence regions; development of molecular understanding of the contribution of newly identified genetic loci such as CHRNA genes on chromosome 15q to carcinogenesis; identification of plasma DNA and protein markers useful for predicting the development of common cancers such as HCC or breast cancer. Dissemination of knowledge on mutation patterns through the IARC TP53 mutation database, the largest single-locus mutation database (http://www-p53.iarc.fr).

Epigenetics Group (EGE)

Specific aims:

1. **Analyse epigenetic profiles (focused on DNA methylation and microRNAs) in specific human cancers;**
2. **Identify risk factors in the environment, diet and lifestyle associated with epigenetic changes;**
3. **Assess the impact of nutrition and early-life exposure on epigenetic states and cancer susceptibility during childhood and adulthood;**
4. **Conduct mechanistic studies aiming to discern the mechanisms by which epigenetic modifications dictate cancer development, progression and metastasis;**
5. **Develop epigenetic methods applicable to biobanks associated with population-based and prospective studies (mother/child cohorts).**

Major approaches:

1. Analysis of DNA methylation and microRNA expression profiles in human cancer and surrogate tissue using new technologies in high-throughput (pyrosequencing) and genome-wide (Illumina arrays) settings.

2. Establishment of cost-effective tools for screening of biological samples (including body fluids) for biomarker discovery, validation and application to cohort studies with associated biobanks.

3. Performing mechanistic studies on cell lines to investigate the role of specific molecules that mediate epigenetic mechanisms.

4. Development of models for inducible inactivation of specific genes in normal and cancer cells (including siRNA and Cre-loxP approaches).

Expected outcomes:

Identification of epigenetic profiles in specific human cancers and epigenetic events associated with specific risk factors; identification of the impact of nutrition and early-life exposure on epigenetic states and cancer susceptibility in the context of epidemiological studies; improved understanding of epigenetic mechanisms underlying critical cellular processes and cancer development and progression; establishment of methods with sufficient sensitivity and specificity for the detection of DNA methylation changes in bodily fluids.

Section of Molecular Pathology (MPA)

Relevance to IARC mission

The Section studies the molecular basis of human tumours, in particular brain tumours, which pose a significant challenge due to poor prognosis and the paucity of information on etiology. Combined epidemiological and genetic studies are best suited to advance knowledge of this tumour. The Section's expertise in the molecular cancer pathology is essential to successfully leading the WHO Blue Book project. The WHO Blue Books are internationally recognized as the gold standard for tumour classification, and have established a uniform nomenclature for human tumours worldwide.

Specific aims:

1. **To assess risk and prognostic factors, including genetic alterations, for brain tumours and to identify causes of brain tumours particularly in children;**
2. **To provide a histological and genetic tumour classification, through the WHO Blue Books, that reflects recent advances in histopathology and cancer genetics, and which is accepted and used worldwide.**

Major approaches:

1. Population-based study of glioma patients in Switzerland, including collection of information on radiotherapy and concurrent chemotherapy treatment; correlation of histologically recognized phenotypes with genetic and expression profiles in brain tumours collected at a population level with excellent clinical data; international consortium for rarer brain tumours, such as low-grade gliomas in order to collect a large number of cases; genome-wide approach to screening for genetic alterations.

2. Working Groups, consensus and editorial meetings and consultancies to complete the 4th edition of the World Health Organization (WHO) *Classification of Tumours* Series (WHO Blue Books) (12 volumes, 10 remaining to be completed); liaison with WHO Press to ensure accessibility of the series worldwide, and translations (provided that these are of high quality); WHO Working Group to meet whenever a new WHO Blue Book is published, to decide whether additional ICD-O morphology codes are necessary for emerging tumour entities; diagnostic pathways for developing countries (for inclusion in the WHO Blue Books) using algorithms which allow a reliable diagnosis for major tumour types.

Expected outcomes:

Population-based study of glioma patients established; International consortium established for low-grade gliomas; increased frequency of publications of volumes in the 4th series of the WHO Blue Books; improved accessibility and utility of WHO Blue Books worldwide including low- and middle-income countries.

Section of Infections (INF)

Relevance to IARC mission

Known infectious agents are important causes of human cancer, being responsible for about 20% of cases worldwide and these are largely preventable. In addition, new associations between chronic infections and cancer are likely to exist and to be identified in the future. IARC gives particular priority to the most vulnerable populations in less developed countries where the infection-attributable cancer burden is largest. The Section comprises both laboratory and epidemiology groups working in an integrated manner.

Infections and Biology Group (ICB)

Specific aims:

1. **Modulation of innate immunity by oncogenic infectious agents;**
2. **Impact of oncogenic mucosal HPV type variants in the progression of cervical diseases;**
3. **Role of novel potential oncogenic viruses, i.e. cutaneous HPV types and polyomaviruses, in human cancer;**
4. **Novel assays for detection of infectious agents in human specimens.**

Major approaches:

1. Study the mechanisms underlying the viruses-mediated deregulation of the innate immunity (aberrant expression of key effectors i.e. Toll-like receptors) using biological and biochemical approaches.

2. Prospective and case-control studies in geographically and ethnically diverse populations to determine the role of HPV natural variants in cervical carcinogenesis.

3. Search for the presence of cutaneous HPV types and polyomaviruses in human cancer specimens and characterization of their biological properties by *in vitro* and *in vivo* models.

4. Development of Multiplex PCR associated to APEX or Luminex technologies with specific or degenerate primer sequences for the detection of infectious agents suspected to play a role in human cancer (i.e. emerging agents such as Merkel cell polyomavirus) in different types of biological samples.

Expected outcomes:

Improved understanding of the mechanisms of persistence of infectious agents in the host during the process of carcinogenesis and identification of possible tools to restore the normal regulation of the innate immunity; clarification of the cancer risks associated with different mucosal HPV variants and with cutaneous HPV types and polyomavirus infection; new sensitive and specific methods for detection of infectious agents.

Infections and Epidemiology Group (ICE)

Specific aims:

1. **Reasons and implications for the lack of decrease in HPV prevalence in middle-aged women in some regions of the world with high cervical cancer incidence;**
2. **Spectrum of cancers associated with moderate levels of immunosuppression in HIV-infected people receiving combined anti-retroviral therapy (cART);**
3. **Temporal trends in HCV-associated hepatocellular carcinoma and the most important routes of HCV acquisition in less developed countries;**
4. **Role of *Helicobacter* species other than *H. pylori* and *Salmonellae* in cancer of the gallbladder and biliary tract.**

Major approaches:

1. Follow-up studies of HPV infection in women in sub-Saharan Africa, Asia, and Latin America merging more research-oriented studies with larger demonstration programmes of screening and HPV vaccine monitoring in collaboration with the EDP Section.

2. Record-linkage studies of cancer excess in people with HIV/AIDS (in Europe and selected less developed countries) and follow-up studies of cART recipients in sub-Saharan countries.

3. Reviews of hospital records of hepatocellular carcinoma patients and case-control studies in countries like Mongolia, Pakistan, and China where limited data suggest that HCV prevalence is rising and dual infections with HBV and HCV are extremely frequent.

4. Case-control studies of prevalence *Helicobacter* species and *Salmonellae* in tissue-biopsies and bile of patients with cancer of the gallbladder and biliary tract and patients who undergo cholecystectomy for other causes. Pilot study in France, and then expansion to countries at high-risk for cancer of the gallbladder and biliary tract (Chile, Pakistan, India, and Eastern Europe).

Expected outcomes:

Identification of relative and attributable risks for the characteristics under study; international comparisons of infection prevalence; strategies of cancer prevention in HIV-positive individuals; extrapolation from HIV-infected people to other conditions, where moderate levels of immunosuppression may be present.

Section on Environment (ENV)

Relevance to IARC mission

Environmental exposures are a key to human cancer causation, encompassing many known risk factors including tobacco smoking, alcohol drinking, occupational exposures, environmental pollutants, radiation, as well as a wide range of emerging sources of concern that the Section needs to be able to respond to. IARC is well placed to address important questions of environment and cancer risk because of its ability to coordinate large-scale studies, which take advantage of heterogeneity of cancer and cancer risk factors across human populations including those in low- and middle-income countries. IARC can also integrate epidemiological and biological techniques, including the use of biomarkers. Studies of the effects of ionizing radiation are important for elucidating mechanisms of carcinogenesis and can provide the scientific basis for radiation protection of the general public, patients and occupationally exposed populations. In particular, uncertainties persist with regard to the health consequences of low doses and low dose rates, and host factors that can modify radiation-related cancer risk.

A new Head of Section will be appointed in 2010 with the flexibility to set more specific priorities within this research area.

Lifestyle and cancer Group (LCA)

Specific aims:

1. **Evaluation of the risks from environmental risk factors (defined in its broadest sense to include personal exposures, occupational, physical, and chemical);**
2. **Production of the Handbooks on Tobacco Control;**
3. **Production of a Handbook on the public health aspects of alcohol and cancer.**

Major approaches:

1. Analytical epidemiological studies of environmental risk factors using various established studies such as the Iranian (Golestan) cohort on oesophageal cancer; the Russian asbestos cohort study; the analysis of existing datasets (for example, INCO; ARCAGE) and new pooling projects (SYNERGY) to study environmental and occupational risk factors (e.g. diesel engine exhaust, carbon black, etc.).

2. Case-control studies of tobacco-related cancer and joint effects of tobacco and other environmental carcinogens, uncommon tobacco and tobacco-related products such as betel quid and khat in countries where they are widely used.

3. Pooled analyses on alcohol drinking and cancer risk in consortia of case-control and cohort studies; evaluations of whether compounds other than ethanol and specific exposure circumstances (e.g. "binge" drinking, consumption of home-made spirits) and gene-alcohol interactions contribute to the carcinogenicity of alcoholic beverages; the role of alcohol on lung cancer in never smokers.

4. Working group meetings and literature collation; collaboration with WHO Tobacco Free Initiative for Tobacco Control Handbooks. Production of handbook on public health aspects of alcohol and cancer, in collaboration with WHO.

Expected outcomes:

Computation of relative risks and attributable risks for the exposures in the various etiologic studies; a Working Group meeting on pesticides, farming and cancer; two Handbooks on Tobacco Control: 4th Handbook on effectiveness of taxation policies and the 5th Handbook on effectiveness of tobacco product labelling policies; a Handbook on alcohol and cancer.

Radiation Group (RAD)

Specific aims:

1. **Radiation risks from medical diagnostic exposures in childhood;**
2. **Effects on cancer incidence and mortality of protracted exposure to low-dose radiation in occupational settings;**
3. **Evaluate factors (age, lifestyle, genetic make-up) that affect individual sensitivity to radiation and how they modulate radiation-related cancer risk.**

Major approaches:

1. International cohort study (retrospective and prospective) of children with CT scans and interventional cardiology procedures.

2. Follow-up of the International Collaborative Study of Cancer Risk among Radiation Workers: extended mortality and dosimetry information for workers in the study.

3. Integrated epidemiological/biological studies (e.g. molecular epidemiology study of papillary thyroid carcinoma in young people following the Chernobyl accident); study of influence of genotype and lifestyle on the radiation-associated breast cancer; follow-up of the IARC European Childhood Leukaemia-Lymphoma Study (ECLIS).

Expected outcomes:

More precise and reliable direct estimates of the effects of low radiation doses and exposure to internally incorporated radionuclides and mixtures of radiations; evaluation of radiogenicity of slowly progressing malignancies and radiation sensitivity following exposure in childhood and *in utero*; improved understanding of gene-radiation interactions.

Section of Nutrition and Metabolism (NME)

Relevance to IARC mission

Diet and nutrition are important cancer risk factors in the developed and developing world, although the role of specific nutritional factors and their mechanisms of action remain poorly understood. Overweight and obesity represent a global epidemic whilst physical inactivity and energy imbalance are increasingly recognized as important determinants of cancer risk. In low- and middle-income countries the incidence of chronic disease is increasing rapidly but the role of diet is far less studied. In addition, although fetal life and early infancy appear to have a major influence on health in later years, the role of nutrition during pregnancy on later cancer risk is poorly understood.

There is an urgent need for a better understanding of the underlying mechanisms whereby foods and nutrients may impact cancer causation, development and survival. Future research will include the role of micronutrient deficiency as well as over-nutrition and energy balance on markers of cancer risk and development as well as gene-nutrient interactions. The overall goal of this Section will be strengthened by close collaboration amongst its Groups. Translation of findings into public health recommendations and the development of cancer prevention strategies will be emphasized.

Nutritional Epidemiology Group (NEP)

Specific aims:

1. **To evaluate the association between diet, nutrition, physical activity, energy imbalance and obesity with cancer risk in high- and middle- to low-income countries using cohort and case-control designs, or human intervention studies;**
2. **To elucidate the relationship between levels of biomarkers of nutrition (including food contaminants), hormones and related biomarkers, with cancer risk and intermediate end-points;**
3. **To better understand how early exposures during fetal and early life may affect the risk of cancer later in life;**
4. **To support the coordination of the EPIC network.**

Major approaches:

1. Investigate the role and mechanisms of action (e.g. through use of metabolomics and other "omics" and biomarker technologies) of diet, nutrition, physical activity, obesity and hormones in cancer risk and intermediate endpoints using cohorts in high- (e.g. EPIC) and low- and middle-income (e.g. Mexico) countries.

2. Collaborate with and support the development of new cohort studies in low- and middle-income countries, in particular in India and Africa, to further evaluate how changes in diet and lifestyle affect the risk of cancer.

3. Evaluate the effects of maternal nutrition on child's nutritional status and biological and metabolic profiles as predictors of disease status at different stages of life through existing mother:child birth cohorts.

4. Evaluate the potential interactions between dietary intake, physical activity and obesity on genetics and epigenetic phenomena and the risk of cancer.

5. Explore the relationship of food contaminants and cancer and evaluate low-technology interventions to modulate micronutrient content or reduce toxin (e.g. aflatoxins) contamination.

Expected outcomes:

Increased knowledge and dissemination of information on cancer risks associated with dietary habits, physical activity and obesity in both high- and low- to middle-income countries; collaboration in international projects and inter-disciplinary initiatives to better understand the impact of complex and rapidly changing dietary exposures and hormone levels on metabolomic profiles and cellular mechanisms involved in the development of cancer; recommendations to identify susceptible subjects and define effective prevention strategies.

Dietary Exposure Assessment Group (DEX)

Specific aims:

1. **To improve the accuracy, understanding and interpretation of (changes in) dietary exposure in relation to cancer in the context of international studies;**
2. **To develop, validate and disseminate standardized dietary methodologies relevant to international studies;**
3. **To provide nutritional cancer research findings of relevance to international public health nutritional recommendations and guidelines for cancer prevention.**

Major approaches:

1. Implementation of a comprehensive web-based platform, the EPIC-soft Methodological Platform, for use and dissemination of a standardized 24-hour dietary recall methodology.

2. Development of new dietary tools, including standardized nutrient databases, a data entry version of EPIC-soft and EPIC-soft country-specific versions for use in international nutritional studies.

3. Monitoring of changes in dietary exposure (including biomarkers) in existing/new cohorts and population-based nutrition monitoring surveys, using a common bridging dietary methodology and focusing particularly on populations in rapid nutritional transitions (e.g. Eastern countries, developing countries).

4. Development, application and dissemination of new methodologies to analyse dietary patterns (particularly nutrient and biomarker patterns) to be used in international descriptive and diet-disease association studies and for deriving public health nutrition recommendations and guidelines.

Expected outcomes:

Improved dietary exposure assessment using a combination of dietary and biomarker data; provision of standardized methodologies and data to monitor rapid dietary changes; new knowledge on dietary patterns and their associations with cancer and other intermediate end-points; improved evidence-base for international public health nutritional recommendations and guidelines.

Biomarkers Group (BMA)

Specific aims:

1. **To develop new biomarkers to improve assessment of diet, physical activity and exposure to environmental risk factors including food contaminants;**
2. **To increase the application of biomarkers to large cohort and case-control studies as well as to the investigation of small-scale dietary interventions in humans;**
3. **To establish a metabolomic research capacity in collaboration with external partners;**
4. **To better understand the mechanisms by which biomarkers of diet, food contaminants and hormones affect cancer and intermediate endpoints at cellular and physiological levels.**

Major approaches:

1. Developing a laboratory platform for high sensitivity detection of biomarkers of exposure using relevant analytic tools including mass spectroscopy, gas and liquid chromatography, and immuno-detection methods.

2. Promoting integration between research on mechanisms of carcinogenesis in the IARC laboratories, biomarker discovery, and translational research in molecular epidemiology.

3. Collaboration in local and international projects on mechanistic approaches of the impact of dietary exposures, physical activity, energy balance and hormone levels on cancer risk.

4. Establishing a strong partnership between IARC biomarker laboratories and external partners for profiling metabolic variations in relation to nutrition and physical activity.

Expected outcomes:

Setting up of new methods for the measurements of relevant biomarkers and application to epidemiological studies; application of metabonomics to original, descriptive and experimental research on phenotypic and metabolic nutrition profiles; provide new insight into the role of diet at the cellular and physiological levels.

Section of Genetics (GEN)

Relevance to IARC mission

The work in the Section addresses the key role of environmental and lifestyle risk factors and their interplay with genetic background in population-based studies. Studies include a focus on low- and middle-income countries through partnerships and collaborations with researchers in these regions. An additional focus on cancer outcome may elucidate approaches for the early detection of cancer and help evaluate prevention strategies.

Genetic Epidemiology Group (GEP)

Specific aims:

1. **To understand the genetic epidemiology of lung and upper aero-digestive tract cancers;**
2. **To elucidate how genes are involved in the development and progression of kidney cancer;**
3. **To investigate the genetic epidemiology of EBV related cancers in diverse populations;**
4. **To explore the etiology of rare childhood cancers.**

Major approaches:

1. Coordinating large case-control studies in high-risk populations including central Europe (for lung cancer) and Asia/Latin America (head and neck cancers); leading international consortia to develop pooled genome-wide data analyses and conduct replication studies; incorporating multiple cohort studies (e.g. EPIC, CONOR, Epihealth Russia) to investigate biomarkers related to risk.

2. Incorporating kidney cancer cases and controls from large cohort studies; genome-wide association studies to identify gene loci associated with disease onset and outcome; whole genome sequencing to identify sporadic mutations associated with disease onset.

3. Coordinating and supporting epidemiological studies of naso-pharynx cancer (NPC) in south East Asia (Malaysia and Thailand); linkage analysis of multi-case families; analysis of EBV infection in NPC and its correlation with susceptibility and outcome; genome-wide association studies of Hodgkin's lymphoma.

4. Developing an international framework for large-scale etiological studies on childhood cancers, including retinoblastoma, Wilms tumour, rhabdomyosarcoma, neuroblastoma and hepatoblastoma.

Expected outcomes:

Identification and elucidation of common gene variants associated with lung cancers, as well as head and neck cancer, and their interaction with known environmental risk factors; discovery and verification of germ-line and sporadic genetic events associated with onset of kidney cancer;

development of an extensive biorepository of kidney cancer cases for prognostic studies; identification of rare and more common genetic variants associated with NPC and Hodgkin's lymphoma; evaluation of a large international pilot study into rare childhood cancers.

Genetic Susceptibility Group (GCS)

Specific aims:

1. **To identify (rare) intermediate-risk sequence variants that contribute to breast, kidney and lung cancer;**
2. **To develop an international large-scale molecular epidemiology study on cutaneous malignant melanoma for determining the full frequency spectrum of genetic variations associated with individual susceptibility, including stage and disease outcome;**
3. **To maintain and to further develop the genetic platform and related LIMS to support IARC large-scale genomics projects.**

Major approaches:

1. The discovery of uncommon-to-rare genetic risk variants is achievable using a case-control mutation screening approach. Observed sequence variants are ranked from most likely neutral to most likely pathogenic using bioinformatics approaches and statistical tests of association.

2. By combining case-control genotyping, case-control mutation screening, genotype-based tests of differential expression, expression profiling studies and bioinformatics, we will carry out an integrative analysis of genetic alterations implicated in the development of several cancers.

3. Developing collaborations with other IARC groups to carry out mutation screening, array-based genomics and transcriptomics analyses. Evaluating mutation-screening capacity through next-generation sequencing technologies. Expanding workflows and LIMS capacity to new applications.

Expected outcomes:

Identification and elucidation of rare intermediate-risk genetic variants associated with susceptibility to melanoma, kidney and breast cancer, and tobacco-related cancers and their interaction with known environmental risk factors will contribute to a better understanding of the etiology of these cancers. Identification of susceptible individuals may aid early detection and prevention of the disease in populations at risk. The study on melanoma will complete findings from family-based studies and genome-wide association studies, and will reveal new candidate genes that may significantly modify the risk due to *CDKN2A* alleles in high-risk families, or the risk associated with exposure to sunlight, in the general population.

Biostatistics Group (BST)

The Biostatistics Group (BST) is managerially linked to the Section of Genetics but its role is across the Agency.

BST aims at selecting or developing statistical methodology in order to enhance the research of other groups within the Agency. This reflects the key nature of biostatistics in the conduct of high-quality cancer research. The Group also has the aim of developing best practice in relation to biostatistics, bioinformatics and database management at IARC. It provides a professional setting for the biostatisticians working across the Agency and a basis for external collaborations.

Specific aims:

1. **Development and refinement of bioinformatic and biostatistical methods for analysis of genetic and environmental data;**
2. **Investigation and validation of multivariate data reduction techniques for metabolomics and nutrition studies;**
3. **Continued support for the use of basic statistical methods by investigators within other groups;**
4. **Development of a professional environment for development of biostatistics at the Agency including training, coordination of methodological research and professional development.**

Major approaches:

1. New and continuing collaborations with existing groups.

2. Develop collaborations with external groups who have specialist expertise, i.e. for metabonomics and bioinformatics.

3. Seek to determine optimal available methods or develop new methodology where nothing suitable exists.

4. Coordination of PMDS for biostatisticians across Sections; seminar series, invitation of consultants; training opportunities.

Expected outcomes:

Established professional grouping of biostatisticians working across the Agency; close cooperation with research Groups and Sections in study design and analysis; appropriate methodologies available to Agency scientists through collaboration with BST.

Section of Early Detection and Prevention (EDP)

Relevance to IARC mission

The Section seeks to provide evidence as to which primary and secondary prevention interventions are appropriate, effective and cost-effective in lowering the burden of breast, cervical, oral, and colorectal cancers globally. This approach includes studying the means to implement integrated and quality-assured interventions in routine settings in different parts of the world. These research topics are in tune with the overall mission of the Agency aiming to reduce cancer burden by prevention. The Agency conducts research to inform cancer prevention policy but does not develop or advocate policies. The IARC mandate extends to investigate how prevention strategies, demonstrated as effective, may be best implemented at a population level. This involves consideration of socio-economics, health service provision, communication and culture, among other factors, and behavioural research.

Screening Group (SCR)

Specific aims:

1. **Immunogenic and cervical cancer preventive potential of "sub-optimal" doses of HPV vaccination;**
2. **Cost-effectiveness of visual inspection, HPV testing and cytology screening approaches for cervical cancer prevention in low-resource settings;**
3. **Role of breast awareness and physical examination of the breast in improving control of breast cancer;**
4. **Understand obstacles to participation in preventive programmes in different populations.**

Major approaches:

1. A multicentre, cluster-randomized clinical trial of 2 versus 3 doses of HPV vaccine (quadrivalent HPV vaccine targeting HPV 16, 18, 6, 11 types or a broader spectrum new generation vaccine) in selected districts in India, during a six-year period (2009–2015), in partnership with national institutions.

2. Calculation of the cost-effectiveness of visual inspection, HPV testing and cytology approaches in cervical cancer screening in limited-resource settings using data from two large cluster-randomized controlled trials from India.

3. Cluster-randomized intervention trials of breast awareness and physical examination in high-risk populations in limited-resource settings. These trials will involve approximately 200 000 women aged 30–69 years randomized to receive physical examination of the breast versus routine care or to receive breast awareness messages versus routine care. Particular attention will be paid to elucidating the cost and effectiveness of diagnostic follow-up and treatment of women with detected breast abnormalities, as well as the cost of appropriate and sufficient quality assurance.

4. Focused behavioural/implementation research will be undertaken in the context of both the above research studies and the existing routine screening programmes in low- and medium-resource countries to elucidate factors associated with satisfactory participation of the target populations and successful implementation of interventions. In particular, this research will take into account the need for balanced information which is understood by the people invited to participate, as well as the potential of inadequate communication to impair participation and compliance with diagnostic and treatment protocols intended for use in large scale early detection and primary prevention interventions in routine health care settings.

Expected outcomes:

Scientific evidence on the efficacy, feasibility, safety and acceptability of two-dose HPV vaccination regimen compared to the current standard three-dose regimen; provision to decision makers in developing countries with operational, efficacy and safety data to make an appropriate, evidence-based HPV vaccination policy; cost-effectiveness assessment of two trials comparing costs of quality assurance of the screening process extending from information and invitation of the target population to diagnosis and treatment, estimation of the cost per life year saved and extrapolation of these results to different developing countries scenarios with similar quality assurance infrastructure.

Quality Assurance Group (QAS)

Specific aims:

1. **Identification of which primary and secondary prevention interventions are acceptable, effective and cost-effective in lowering the burden of cancer at the population level;**
2. **Development of evidence-based recommendations for implementing the above interventions with appropriate quality;**
3. **Recognition of commonalities and differences in the above areas in various cultural, social and economic settings.**

Major approaches:

1. Updating the European Code Against Cancer, which in the next edition will include fundamental messages on primary and secondary prevention.

2. Developing or updating of evidence-based, multidisciplinary guidelines for quality assurance in cancer screening programmes, particularly for breast, cervical and colorectal cancer; and development and piloting of accreditation/certification schemes for services fulfilling the respective guidelines, taking into account the need for monitoring, evaluation and continuous quality improvement.

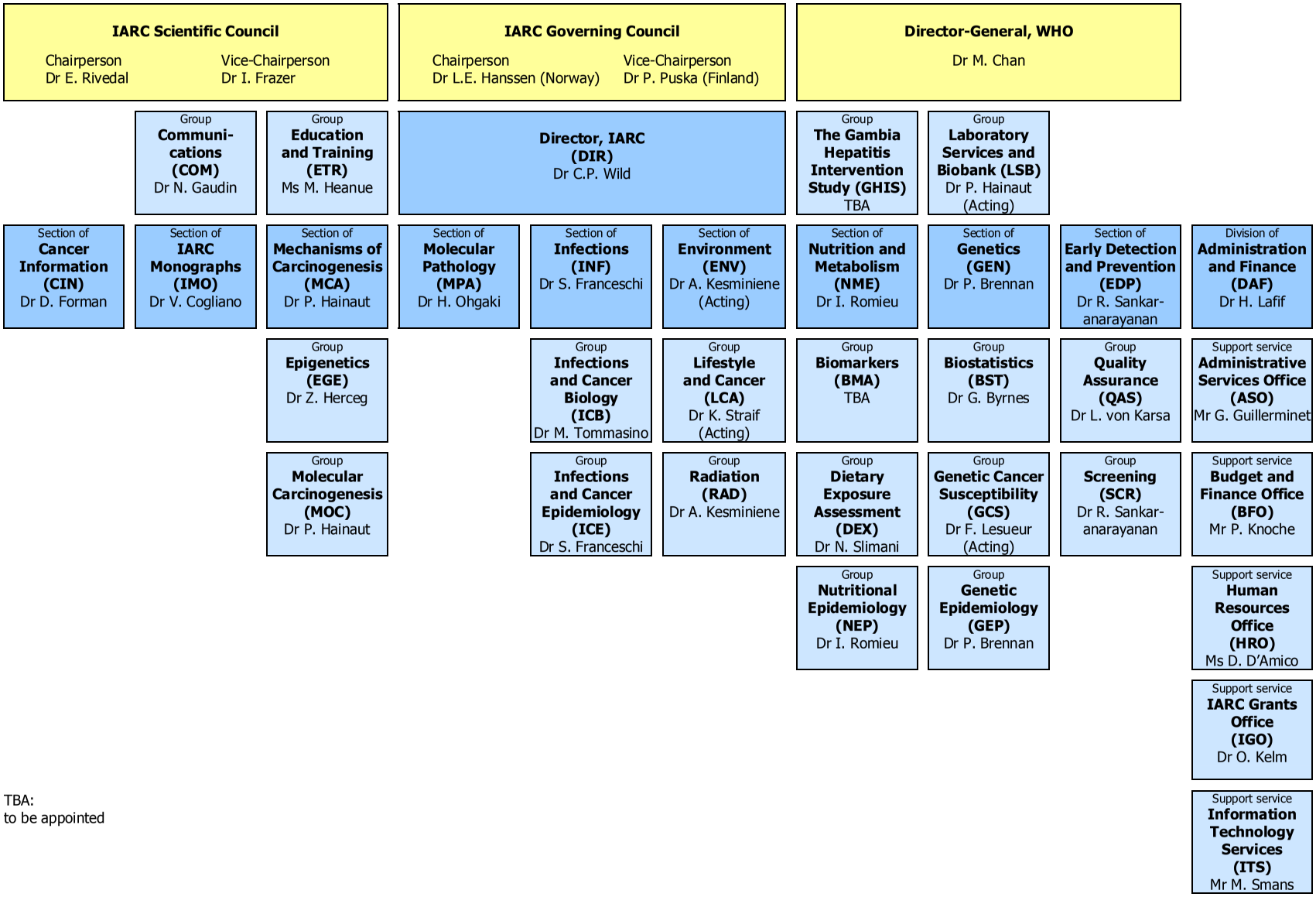
3. Systematic reporting on the performance and impact of cancer screening and complementary primary prevention programmes worldwide.

4. Development of IARC-wide collaboration and international networks (programmes, competence and reference centres) in coordination with WHO to develop guidelines beyond the confines of Europe.

Expected outcomes:

Guidelines used by governments and regulatory agencies as documented in official sources and in peer-reviewed reports; collation and analysis of data from a wide range of sources (cancer registries, vital statistics, screening and vaccination registries); translational research (feasibility planning and testing, piloting, quality assurance and programme rollout); changes in health care utilization and health outcomes resulting from implementation of guidelines.

International Agency for Research on Cancer – World Health Organization – At 6 April 2010



TBA:
to be appointed