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# DRAFT IARC MEDIUM-TERM STRATEGY 2016–2020, INCLUDING IMPLEMENTATION PLANS

## Mission and Vision

1. The International Agency for Research on Cancer (IARC) was created to galvanize international collaborative efforts to combat cancer – in the words of the original French proponents – to be an agency engaged in "the fight for life". From this ideal emerges the mission of the Agency: to reduce the burden of cancer worldwide, through the conduct of research.

2. The overarching vision for IARC, in addressing its mission, is to conduct cancer research to inform cancer prevention. This vision includes describing the burden, understanding the causes, evaluating interventions and their implementation and promoting the translation of knowledge into action through provision of an enhanced evidence-base for prevention.

3. IARC occupies a unique position as a top-ranked international research institute which is also a part of the United Nations (UN) family. This powerful combination creates opportunities and impact which are not replicated anywhere else. Within this context, IARC conducts research relevant to public health, outside the constraints of national settings, and ensures its work contributes to the "public goods" available for cancer control globally. The research findings of IARC thus enable policy- and decision-makers, from within governments, international and non-governmental organizations, to base decisions on the most reliable scientific evidence available.

4. To fulfil its vision, IARC generates new evidence both through the conduct of inter-disciplinary research projects and through the collation, analysis and evaluation of data as part of independent expert review. It is both generator and interpreter of data in order to enable evidence-based best practice. This integrated approach requires a core complement of outstanding scientists, both to perform research in cooperation with national researchers and to attract the best scientific experts worldwide to participate in its authoritative reviews.

5. The Agency has a global mandate, permitting key questions to be addressed in the most informative setting. This approach recognizes that high-quality research conducted in different parts of the world is of benefit both to IARC Participating States and other countries worldwide. In taking this approach, IARC also synergizes with and enhances national programmes in cancer research. The inherent collaborative nature of IARC leads to a sharing of knowledge and expertise, resulting in a unique contribution to capacity building of cancer research worldwide.

## Scope and purpose

6. This document presents the Medium-Term Strategy (MTS) to fulfil the mission and vision of IARC over the period 2016–2020. The strategy includes both the principles which guide the Agency in the selection of its activities and the values which underpin that work. The unique place and relevance of IARC is considered within the broader international landscape of cancer research and control and the increasing political focus on noncommunicable diseases (NCDs) following the UN resolution in September 2011.

7. The MTS drives the selection of activities described in the associated Implementation Plan (see Annex 1) which, in turn, is translated into specific Projects with assigned resources as detailed in the Programme and Budget, adopted on a biennial basis. Although reflecting the inherent open-ended nature of science, the Implementation Plan details where possible, measurable expected outcomes of the research and related activities. The research work of the Agency as a whole is continuously monitored by the Agency's Scientific Council and IARC Sections also undergo in-depth peer-review by external scientists on a five-year cycle.

8. IARC's organizational structure is arranged in scientific Sections (see Annex 2) to deliver staff management, career development and accountability for resource utilization, but a majority of its research activities are performed collaboratively across Sections. The cross-cutting nature of the research is represented in the Project Tree (see Annex 3) a logic framework linking the strategic goals of IARC, as set out in the MTS, with its projects and the participating research Sections as presented within the biennial Programme and Budget.

9. In summary, the MTS provides a bridge between the mission and vision for IARC on the one hand and the shape of the Agency's programmatic activities on the other. It is part of a longer-term strategy developed in the previous MTS (2010–2015), which included a period of major rearrangement of the organizational structure, reorientation of the scientific activities and recruitment of scientific leaders to enable this new strategy. However it is noteworthy that the current MTS is more focused and integrated with specific areas of increased emphasis, notably on describing the cancer burden, evaluating preventive interventions and bringing the advances in molecular sciences into epidemiological studies.

## A unique, global role

10. A defining feature of IARC is its position within the UN family and, more specifically, its unique place as the autonomous, specialized cancer agency of the World Health Organization (WHO). This status facilitates research at country-level, elevates the impact of its work and provides a platform for the translation of research findings through to public health recommendations, guidelines and policy. This goal of seeing research translated through to policy is a guiding principle of the new MTS. The international status of IARC means it can provide independent scientific evidence, free from the political pressures frequently faced at national level. Its position and outstanding reputation also provides an opportunity for global shaping of research priorities in the area of cancer prevention.

11. IARC is an organization in the right place at the right time, with a governance structure which permits it to respond quickly to emerging opportunities. Reflecting the changing demographics of population aging and growth, the global cancer burden is projected to increase from 14.1 million new cases per year in 2012 to 21.7 million by 2030, with the greatest increases in low- and middle-income countries (LMICs)[1]. The demographic changes are combined with a transition from infectious diseases to NCDs, partially reflecting the additional effects of tobacco and alcohol consumption, increases in obesity, decreased physical activity, changes in diet, urbanization and increases in environmental pollution. A growing sensitivity at the political level to such changes has translated into the WHO-led Global NCD Action Plan 2013–2020[2], which recognizes cancer as a major health priority for all world regions.

12. The growing international focus on NCDs offers timely opportunities for IARC's research to make a difference at policy level, including in close strategic cooperation with the WHO. In general terms IARC generates key research evidence in relation to the burden, causes and prevention of cancer and this research assists the WHO and other international and national authorities in developing evidence-based policies and guidelines. IARC does not make policy but enables others to do so, on the basis of sound science.

13. In relation to addressing the NCD agenda, IARC has defined, in cooperation with WHO, three principal areas where it will contribute: cancer surveillance, nutrition surveillance, and cervical cancer control. A WHO-IARC Liaison Officer has been assigned to support joint planning, implementation and evaluation across WHO HQ, Regional and Country Offices, in conjunction with the IARC Special Advisors on NCDs and on Cancer Control. IARC also works on common areas with other UN agencies, notably the International Atomic Energy Agency (IAEA – Programme of Action for Cancer Therapy). IARC has positioned itself as a member of the UN Inter-Agency Task Force on NCDs in order to ensure it can provide added value as part of the cross-agency planning.

14. NCDs are recognized as a barrier to sustainable human development, as emphasized at the Rio+20 Conference in the recommendations for the post-2015 Sustainable Development Goals[3]. Global solutions to these shared problems will require international cooperation. There are many national academic and public health organizations which now place priority on global health, but few of these are focused on cancer and none are a part of the UN. Therefore, with its international status, scientific expertise, collaborative networks and high-regard in the global cancer community, IARC is uniquely placed to make an important contribution in the coming decade through to the 2025 target date, set by the World Health Assembly to reduce premature NCD mortality by 25%.

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[1] Ferlay J, Soerjomataram I, Ervik M, Dikshit R, Eser S, Mathers C, Rebelo M, Parkin DM, Forman D, Bray, F. GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11 [Internet]. Lyon, France: International Agency for Research on Cancer; 2013. Available from: http://globocan.iarc.fr, accessed on 08/08/2014.

[2] World Health Organization. "Global action plan for the prevention and control of noncommunicable diseases 2013-2020." (2013) WHO Press, Geneva. Available from: http://www.who.int/nmh/events/ncd_action_plan/en/

[3] The Future we want. 'Rio+20' United Nations Conference on Sustainable Development. Resolution adopted by the United Nations General Assembly on 27 July 2012. Available from: http://www.uncsd2012.org/thefuturewewant.html

## Making resources count

15. Under the current configuration of scale and resources the Agency is not in a position to respond to all the demands and research opportunities presented to it. The MTS provides a rationale for the difficult choices of prioritization and is realistic, taking account of the overall resource constraints and the balance between the regular budget, coming from assessed contributions on Participating States (PS), and extra-budgetary sources. The Agency will encourage new PS to join, particularly those from geographic regions currently under-represented and where cancer burden is increasing most rapidly. IARC's research focus is directly relevant to cancer control in these regions. Additional assessed contributions from new PS will be used preferentially to enable expansion in relevant areas such as cancer registration, prevention and early detection in addition to capacity building.

16. The regular budget is prioritized to specific programmes and to maintaining the core personnel within Sections, to enable them to develop collaborative projects with national partners and to attract extra-budgetary resources. Specific areas prioritized on the regular budget include the provision of global cancer statistics, the Monographs evaluation of carcinogenic agents and the provision of training. Available resources are aligned with the new priorities detailed in the MTS 2016–2020, with increases for prevention and implementation, cancer surveillance, the biobank, training and to the area of communication and dissemination, compared to the MTS 2010–2015.

17. The strategy assumes IARC will maintain its current level of competitive grant awards, recognizing increasing competition internationally and the limited number of funding sources that are open to the Agency. IARC seeks extra-budgetary resources only in line with the MTS; this is ensured by the required clearance from the Director of all external applications for funding. The Agency will continue to exercise great caution in any interactions with the private sector in order to maintain its independence. IARC will seek to expand bilateral partnerships with individual PS, foundations or non-profit organizations to finance specific priority areas.

18. The strategy envisages IARC continuing to conduct the majority of its activities in collaboration with national scientists, bringing significant added value and cooperation to international cancer research. It is noteworthy that each of the sources of extra-budgetary contributions to research successfully won by IARC provide considerable added value to the assessed contributions from PS.

## Principles underpinning priorities

19. Overall, IARC's activities are focused on areas where it can benefit from its international status, independence, expertise, reputation and networks either to address questions that cannot be easily addressed nationally, or to conduct research that can be better achieved internationally. IARC therefore does not simply perform research that is not done elsewhere (an "institute of the gaps") but uses its strengths to complement and reinforce national efforts. Increasingly IARC's activities are informed, albeit not prescribed, by the critical questions faced by countries in their cancer control planning, yielding direct support to policy planning at a

national level. The main principles and features underlying the prioritization of IARC's activities are outlined briefly below.

20. IARC has a strategy focused on **prevention** recognizing that in face of the global trends, no country can treat its way out of cancer and that prevention is essential but relatively neglected compared to treatment and disease management. Prevention research is broadly defined in this strategy to encompass descriptive epidemiology of cancer occurrence; analytical epidemiology of cancer causes; evaluation of preventive interventions; and operational or implementation research to ensure translation through to practice. In contrast, the Agency does not conduct research to develop novel therapies or perform related clinical trials, which are better suited to large clinical cancer centres. The randomized trials the Agency conducts are focused on community-based interventions in collaboration with strong networks of national experts.

21. IARC is an initiator and catalyst for international **collaboration and partnership** across countries and organizations. IARC is well-suited to lead, coordinate and participate in multi-centre, transnational studies, providing informed, independent oversight to complex projects and facilitating the sharing and collation of both data and biospecimens. IARC has made major contributions in this way in the past in many areas such as passive smoking, diet, radiation, genetics and occupational exposures. This role is particularly valued where the research topic is sensitive or controversial at national or international level. The approach also lends itself well to the study of rarer cancers and those mainly affecting under-privileged populations. Here the ability to collaborate across centres and countries may be the only effective way to proceed. International cooperation through strategic partnerships also promotes the use of IARC's findings in development of public health recommendations and policies, including through partnerships with the WHO and other UN organizations; regional cancer networks; networks of cancer professionals; and national and international non-governmental organizations.

22. IARC has a **worldwide mandate**, which permits the study of a problem wherever it can best be addressed. This presents an opportunity to provide valuable information for cancer control across different settings. For example, methodology and scientific expertise in high income countries (HICs) can be adapted and applied to appropriate research projects and cancer control strategies in LMICs. The conduct of research in LMICs can fill important knowledge gaps with local application but also in turn cast light on questions relevant in HICs, for example in identifying human carcinogens from high exposure settings or better understanding of cancer disparities in vulnerable populations. This unique, global view represents a creative approach to generating evidence for cancer prevention with worldwide application.

23. From its inception the Agency has taken an **inter-disciplinary approach** with contributions from epidemiology, biostatistics, laboratory sciences and, increasingly, bioinformatics. This breadth and depth of expertise in-house allows IARC to remain abreast of advances in cancer research, something of vital importance when assessing diverse types of data in the critical evaluations referred to above. The Agency also achieves its inter-disciplinary approach by bringing together the required skill sets in conjunction with national research

teams. This integrated approach, in which IARC has been a pioneer, also builds on improved knowledge of the molecular basis of cancer and the associated technological and analytical advances, to provide unprecedented insights into etiology, prevention and early detection. The application of molecular science to improve the evidence-base for cancer prevention is at a particularly exciting stage and the Agency will use its position to compare and contrast the molecular characteristics of cancers and precancerous lesions from different geographic regions, providing important insights into the extent to which findings on the molecular basis of cancer etiology, early detection, prevention and treatment can be generalized and applied in different populations.

24. The Agency will develop **research platforms** to underpin collaborative research. Notably, the Agency will support large-scale epidemiological studies with rich associated data-sets and biological specimens. IARC has particular opportunities via long-term collaborative projects with national partners, which have established unique cohorts and other epidemiological studies in different parts of the world. IARC will promote international biobanking, providing support for biobank development in LMICs and will expand the IARC Biobank (IBB), promoting wider access to collaborators. At the same time, IARC can assist national collaborators in launching local studies of high scientific merit, targeted to address important questions and raise awareness about particular challenges nationally or regionally.

25. **Developing research capacity** permeates the activities of IARC. On-the-job training occurs naturally through the conduct of joint studies. IARC also brings collaborators from HICs into new international research networks enhancing future cooperation, not necessarily directly involving the Agency itself. This role in capacity building and promotion of networks is targeted to areas of IARC expertise and, in a more structured form, comprises courses and fellowships. The strategy involves increasing cooperation with other national and international partners, to deliver a broader training programme, with much of it provided on a regional basis and increasingly using eLearning.

26. The Agency will continue to collate, analyse, evaluate, and disseminate information on the occurrence, causes and prevention of cancer for the benefit of the wider cancer community. IARC has an outstanding role in this respect, is widely referenced and is not duplicated elsewhere. This **provision of public goods** includes the IARC Monographs, GLOBOCAN, Cancer Incidence in Five Continents (CI5), the Handbooks of Cancer Prevention, the WHO Classification of Tumours, etc. Confidence in such outputs is founded on three pillars: research excellence, international status and independence. IARC will continue to assess new opportunities for similar roles, for example the development of risk factor databases, while maintaining a balance between conduct of novel research and the development and maintenance of these datasets.

27. The activities of IARC lead naturally to **support for cancer control planning**. IARC will help ensure the most reliable and up-to-date evidence is available for planning, in cooperation with a wealth of different partners, but will also contribute relevant information through its own activities. Examples include the development of cancer registries, adaptation of research tools for risk factor surveillance (e.g. for diet or carcinogenic infectious agents) and the conduct of

operational or health systems research in order to identify the supports and barriers to successful implementation of cancer control activities, e.g. for early detection or screening.

### Values underpinning action

28. IARC occupies a privileged and highly influential position as the cancer agency of the WHO and with this profile comes responsibility. Consequently, the way in which IARC conducts its research is equally important to the research itself, not least because of the trust placed in the organization by its collaborators and the reciprocal reliance of IARC on collaborators to fulfil its mission. IARC aims at the highest standards of conduct, founded on a number of values, namely **honesty, integrity, independence, courtesy** and **generosity**. These values, combined with excellence in scientific quality and effectiveness in its mission, are fundamental to the credibility and authority of IARC in its leadership role in cancer research and control worldwide.

29. Transparency is required of all public institutions, but honesty goes further. Transparency requires information to be made available; honesty requires information to be explained with its caveats, complexities and subtleties, thus building a greater degree of trust in the organization.

30. Integrity requires the focus of IARC to be maintained on its public health mission, avoiding being deflected from its primary purpose by secondary concerns. Integrity also implies the organization will honour its commitments and adhere to its values throughout its full range of activities.

31. The growing challenge of conflict of interest in scientific research only serves to highlight the value of IARC's independence. The Agency must exhibit its independence from conflicts of interest or, where these may exist or be perceived, be prepared to explain how such risks or their consequences are addressed in the face of vested interests of all types.

32. Courtesy and generosity are values which characterize the relationships both within IARC, among its personnel, and outside with scientists, study participants, civil society groups, government representatives, international and national agencies and the general public. Courtesy implies that all those who interact with IARC are treated with politeness and in a fair manner. Generosity derives from the privileged position of IARC and its personnel, translating to a sharing of knowledge, credit and resources with collaborative partners, transcending self-interest at the individual or organizational level.

33. It is in combining a clear set of **principles and values** that the Agency is able to define its mission and vision and from here derive its strategy and subsequent programmes and projects. This combination provides the basis for the unique contribution IARC is able to bring to international cancer research and control.

## Cancer research for cancer prevention

### Evolving priorities

34. In comparison to the MTS 2010–2015, the new strategy places more emphasis on a number of defined areas. The first is estimating the global, regional or national cancer burden using data on the magnitude of risk associated with defined factors and the projected impact of interventions. These analyses will integrate economic and health considerations to maximize the relevance to national policy decisions. The second is bringing the latest knowledge on carcinogenesis into the evaluations of carcinogenicity, cancer prevention and tumour classification as well as into research on the causes of cancer. This latter initiative is reflected in the resources assigned to laboratory sciences and the biobank being more closely aligned with the priority exposures and cancers being evaluated in epidemiological studies. The third is evaluating interventions and their implementation, with a shift from research on efficacy in community-based randomized trials towards observational studies of effectiveness at a population level. This development is reflected in new areas of implementation and operational research, particularly targeting initiatives which integrate and synergize with national programmes. The work on prevention and implementation will have a focus on LMICs but will equally address populations in HICs where there are disparities among vulnerable groups, including by age, gender, ethnic group or socio-economic strata.

35. The following three sections of the document describe the major areas of research activity.

### Describe the occurrence of cancer

36. Increasingly the necessity and value of cancer registration are recognized. The accurate quantification of cancer burden in a population is a keystone for both cancer research and cancer control. Without this knowledge governments are hampered in making sound, prioritized investment in cancer services. The growing emphasis on “big data” serves to highlight the benefits of linking registries with other datasets, for example on risk factors, socio-economic status, screening programmes, drug treatment, etc. Similarly, registries can be linked to information at the molecular level available through comprehensive profiling (“omics”) approaches, pathology services and biobanks.

37. Unfortunately, many countries have either poor quality cancer surveillance data or no data at all, with large disparities evident between the HIC and LMICs. For optimal cancer planning, data are required on the rates of incidence, survival, mortality and prevalence within the population. Novel statistical approaches are allowing more sophisticated and informative ways of analysing data on cancer occurrence. IARC will make more use of alternative ways to assess burden, e.g. Disability-Adjusted Life Years (DALY) or Global Disability-Adjusted Life Expectancy (DALE) in order to better translate findings through to strategies for cancer control.

38. While at the national level cancer statistics are a vital component for cancer control, there are also wider benefits. For example, geographic and temporal variations stimulate new hypotheses about the underlying causes of the observed differences, and ultimately provide the basis for new prevention strategies. Registries are used to capture confirmed cancer cases in research projects, e.g. cohort studies. In addition, they provide population-level data to assess

the effectiveness of preventive interventions. The Agency has expertise and a long track-record in cancer registration and the associated area of descriptive epidemiology. The future strategy will focus on the following main axes.

*Technical support to cancer registration*

39. Recognizing the importance of high quality cancer registration and the current lack of data in many countries, the WHO NCD Global Monitoring Framework included cancer incidence (by type of cancer, per 100 000) as one of its key indicators. The Agency has an ambitious plan to address the current shortcomings in quality and coverage of cancer registration worldwide through its multi-partner collaborative project, the Global Initiative for Cancer Registry Development (GICR). GICR will create and develop IARC Regional Hubs as resource centres to provide technical and scientific support, training and advocacy to registries in a given region. This work will proceed within the context of IARC's participation in the UN Inter-Agency Task Force on the Prevention and Control of NCDs.

40. A notable feature of IARC's approach is that it does not simply utilize data acquired by cancer registries but works alongside national staff to improve the quality, coverage and analytical capacity of their registries. This approach, not replicated elsewhere, establishes a relationship of mutual benefits and trust out of which strong, long-standing collaborations have emerged.

*Provision of global cancer indicators*

41. IARC is the definitive reference source for global cancer indicators. Data for preparation of these indicators will be collected and analysed through close cooperation with cancer registries worldwide, in conjunction with the International Association of Cancer Registries. Information will be presented in accessible formats suitable for decision-makers, scientists, civil society and the lay public. The Cancer*Mondial* website will be transformed into the "Global Cancer Observatory", a database and comprehensive analytical tool providing the definitive online resource for both global and national cancer statistics constructed from core publications including: CI5, GLOBOCAN, and the International Incidence of Childhood Cancer (IICC). IARC will continue to document and improve the range and quality of data on cancer survival outcomes in LMICs through the SURVCAN project given survival outcomes are major indicators of the health systems efficiency in early diagnosis and prompt care.

42. IARC will seek to enhance the validity of estimates of cancer burden in GLOBOCAN. Longer-term projections will be made of trends in cancer burden, based on demographic changes. Present data sources and methods utilized in estimating incidence and mortality at the national level will be reviewed to explore a more unified modelling framework, including provision of measures of the reliability of the estimates.

43. IARC will engage in research to draw more value from the available data and provide additional tools for cancer control planning. Notably, there will be a focus on indicators which recognize cancer as a chronic disease, including: DALE, DALY, cancer prevalence (with longer follow-up to 10 years post-diagnosis), and estimates of the economic impact. Geographic and temporal cancer patterns will also be assessed in relation to indicators of human development

and socio-economic inequalities as well as public spending on health. This work enables far greater insight into the marked disparities in cancer burden falling on vulnerable groups within HICs, including indigenous peoples, immigrant populations and socio-economically disadvantaged groups.

*Descriptive cancer epidemiology*

44. IARC will produce a series of estimates of population attributable fractions (PAF) for major risk factors as well as for specific geographic regions to assist national decision-makers in setting priorities for cancer prevention. The Agency will further expand analyses to model the impact of various cancer control measures on burden at the national, regional and international level over extended time periods, taking account of economic as well as health impacts.

45. The Agency will engage with leading experts to ensure access to and use of latest statistical methodologies and data presentation tools. The International Descriptive Epidemiology Advisory (IDEA) Group will be a nominated panel of external experts (3–4 persons) whose main aims are to: provide a platform for discussion of recent and planned projects and provide expert opinion on future direction and content; and to help identify leading individuals and institutions as potential collaborators in specific areas of future research.

46. A key feature is the interface with other Sections, with expertise in the development of PAF (e.g. obesity, alcohol, tobacco and other carcinogenic agents identified through the Monographs) and evaluation of the impact of interventions (e.g. tobacco control, vaccinations, screening and early detection programmes). In this way the data coming from IARC's core research areas will inform and shape such estimates. In some areas IARC will also generate data on risk factor prevalence which will provide the basis for the PAF; examples include prevalence of human papillomavirus (HPV) and *H. pylori* infections as well as information on dietary patterns. IARC will explore the opportunity and value of expanding this activity more formally to provide "exposure registries" covering common risk factors across different geographic regions. This would include assembling or linking to data available from multiple sources (e.g. WHO STEPS) to provide added value and avoid duplication of effort.

*Providing an international standard classification of human tumours*

47. The WHO Classification of Tumours ("Blue Books") series is an essential tool in pathology and clinical oncology, epidemiology and cancer registration and highly valued worldwide as an authoritative resource. Increasingly molecular classification is used to tailor treatments to individual tumour profiles, and etiological studies will need to study subjects by more precise disease definitions to identify risk factors which may only be relevant to a distinct sub-set of tumours. IARC will therefore continue to produce the WHO Classification of Tumours series, incorporating the latest knowledge about molecular characteristics of cancer. The series will also maintain different levels of characterization to ensure the publications retain relevance in various resource settings where the degree of sophistication to analyse tumour specimens differs markedly.

48. In summary, the field of cancer surveillance is in a dynamic phase where the Agency makes an unprecedented contribution. It has major value in its own right but also acts as a foundation to work on the causes and prevention of cancer.

## Understand the causes of cancer

49. Identifying the causes of cancer is crucial for prevention. The Agency will address specific etiologic hypotheses through epidemiological and laboratory research and evaluate the evidence for the carcinogenicity of different agents through its world-renowned Monographs programme.

50. Estimates vary, but in developed countries up to 50% of cancers could be prevented if the current knowledge about causes was translated into effective interventions; a major part of the future strategy is focused on addressing the challenge of translation from knowledge to action. However, these estimates also serve to emphasize the significant proportion of cancer for which causes remain ill-defined and indicate that identification of additional causes is challenging given the presumably complex mechanisms or combinations of exposures involved. Therefore IARC will invest major efforts to understand cancer etiology worldwide. This will include not only individual risk factors but combinations of exposures, potentially occurring consecutively or simultaneously, and combinations of exposures and genetic susceptibility. As well as population risks, uncovering such complex cancer profiles may permit future identification of high-risk individuals or groups within a population through prediction algorithms.

*Priority cancers and risk factors*

51. Cancers contributing a significant public health burden, either on a global or regional scale, are a priority. In this regard there are cancers where the proportion of cases explained by known risk factors is limited (e.g. prostate, brain, pancreas, kidney, testis, nasopharynx, gallbladder and haematological cancers) and others where established risk factors in one region may contribute less elsewhere (e.g. breast, oesophagus, oropharynx and colorectal cancers).

52. Another criterion in priority setting is the value brought through international cooperation, either to provide enough subjects for study in the case of rarer cancers (e.g. childhood cancers and sarcomas), or to permit comparisons of striking international variations in incidence (e.g. testis, oesophagus) or risk factors. The Agency is also well-placed to conduct etiologic studies in different populations to provide evidence of consistency in observed associations.

53. For cancers where much is already known about etiology, the Agency will orientate its future effort more towards early detection and prevention, for example in the cases of lung, liver, stomach, oral cavity and cervix cancer.

54. Research will continue on defining the cancer burden associated with risk factors such as tobacco, alcohol, infections, environmental contaminants, radiation, occupation and diet. However, cancer etiology is complex and most often multi-factorial. Therefore, the Agency will not limit itself *a priori* to defined exposure categories but will consider the full breadth of influences on cancer development when planning and designing its studies, from the social determinants (“causes of the causes”) through to endogenous and metabolic factors, such as the microbiome, reflecting the broad concept of the exposome.

55. IARC will also continue to explore how germ-line genetic variation influences cancer etiology by investigating the nature of genetic susceptibility, how it modulates the effects of known environmental and lifestyle factors and indicates novel agents via the identification of interactions.

*Design and methodology*

56. Despite significant progress in understanding etiology, epidemiology has been hampered by difficulties in accurately measuring exposure and in defining periods in the life-course when exposure is most relevant. These difficulties remain true, for example for diet, overweight and physical inactivity as well as for environmental chemicals such as pesticides or endocrine disruptors. In seeking to reduce exposure misclassification and related measurement uncertainties IARC will increasingly draw on new technologies (e.g. "omics", biosensors, geographic information systems, mobile communication technologies) and more sophisticated modelling, for example, based on environmental monitoring data.

57. Emphasis will be placed on large, collaborative projects, most frequently multicentre and transnational in design. Notably a number of major cohorts and multicentre case-control studies will be maintained as platforms for research (e.g. the European Prospective Investigation into Cancer and Nutrition, EPIC). The Agency will also seek to collaborate with national partners on the increasing number of open access cohorts (e.g. UK Biobank) to complement IARC-led projects. Further opportunities will be sought to develop platforms in LMICs where the Agency has already a number of ongoing large population-based studies of different design (e.g. Central Europe, India, Iran, Latin America, the Russian Federation and South Africa). Priority will be placed on studies which have associated biospecimens as well as accurate clinical and outcome information.

58. As mentioned above, the timing of a given exposure may play an important role in influencing risk. Measuring these temporal relationships provides not only evidence for causality but may also indicate the most effective point for intervention. The Agency will partially address this by extending its research to encompass birth cohorts through existing international consortia. The biological consequences of early life exposures will be addressed using biobanks associated with these cohorts to provide mechanistic support for exposure-disease associations.

59. IARC will continue to develop and expand its expertise in biostatistics and capacity in bioinformatics, both in-house and through external collaboration. As data sharing across the scientific community increases, there is a wealth of complex *in silico* data (genomic or other) that the Agency can draw upon and complement data generated from IARC-led studies. To adapt and adopt relevant strategies suited to IARC's specialized applications, the Agency will maintain expertise both on the underlying statistical principles and the informatics tools used to implement them, as well as enhancing its collaborations with centres having greater bioinformatics capacity.

*New insights from molecular science*

60. Laboratory science offers many remarkable opportunities to study cancer etiology. On the one hand these include direct application in epidemiology, for example, to improve measurement of exposure, genetic susceptibility and the classification of tumours. On the other hand complementary perspectives are provided through elucidation of underlying mechanisms of carcinogenesis, from experimental models, molecular endpoints in observational studies or following interventions. In this regard IARC is able to consider, in a fresh way, how factors such as diet, metabolism, physical inactivity, alcohol, obesity, chemical pollutants, radiation, genetic

susceptibility etc. act through a wide variety of mechanisms, some of which (e.g. epigenetic deregulation) emerged in recent years.

61. Genomic studies are demonstrating that environmental and lifestyle exposures result in specific patterns of somatic alterations in tumours. The Agency will use experimental models to compare and contrast molecular alterations following carcinogen exposures to those observed in human tumours and precancerous lesions. In addition to comparing the patterns of alterations, their biological consequences will be studied in specific cases were the functional relevance is pivotal to understanding risk at the population level.

62. The somatic alterations in a tumour or pre-cancerous lesion also influence the prognosis of the patient, including the risk of progression and response to therapy. Thus molecular signatures can be used as tools to explore the link between exposures, molecular alterations and prognosis. The exponential increase in the capacity to sequence genomes may also allow the detection of lesions before they become symptomatic, via sequencing of easily accessible biospecimens for minute amounts of tumour DNA. The Agency will seek to apply the advances mentioned above to identify molecular events ("drivers"), which differentiate early stage lesions by their risk of progression to malignancy. The aim is not to have major programmes on biomarker development. Rather it is to evaluate, in the context of IARC's international studies, how biomarkers may permit the triage of early lesions which have different risk of progressing to frank malignancy, thus transforming the balance between benefits and harm associated with the screening and early detection in cancers such as breast or prostate.

63. There is an important global perspective to this molecular research, which is of central relevance to IARC's involvement. Specifically, to describe the degree of international variation in these patterns of molecular alteration, consequent to geographic heterogeneity in exposures, and to define to what extent biomarkers of early detection and new targeted therapeutic agents are going to be generalizable across different populations worldwide.

*Expert evaluations of human carcinogens*

64. The IARC Monographs represent an unparalleled foundation for policymakers when seeking to minimize the risks associated with exposure to carcinogenic agents. Consequently the Monographs are widely used in national policy and guideline development and represent another unique, highly valued contribution from the Agency, reflecting their remarkable credibility and authority in evidence interpretation. The Monographs are also a stimulus to new research in the Agency and outside as gaps in evidence emerge from the expert evaluations conducted.

65. From its own research and through wide consultation, the Agency will continue to define the priorities for the evaluation of agents in the Monographs programme. The programme will further evolve through the inclusion of quantitative data where it is available; through increasing use of complex (e.g. "omics") datasets on mechanisms; increased standardization when incorporating such data into evaluations; and expansion of online and web-based tools to ensure maximum dissemination and accessibility.

## Evaluate and implement cancer control strategies

66. The purpose of understanding the cause of a disease is to intervene at a point along the causal pathway in order to reduce morbidity and mortality. In the past IARC has conducted research on interventions, but more emphasis has been placed on identifying risk factors. The current strategy drives a greater integration and smoother transition between the two. The work on prevention will extend beyond demonstration of the efficacy of interventions to the evaluation of effectiveness in demonstration programmes or routine health services. This implies the recruitment of new skills in implementation research.

67. Particular research gaps exist in LMICs which, if adequately addressed, should explain and help reduce cancer disparities between the developed and developing countries. Such research will equally contribute to improving outcomes among disadvantaged and vulnerable populations in HICs or provide information difficult to obtain in HICs. An example being alternatives to mammography-based screening, where data from LMICs on the effectiveness or otherwise of approaches like clinical breast examination may contribute to the debate on screening modalities in HICs. This cross-talk also creates excellent opportunities for research methodologies and expertise in HICs to be transferred to LMICs through collaborative studies, in so doing increasing capacity in the latter countries.

*From efficacy to effectiveness*

68. The conduct of large-scale community-randomized intervention trials is complex and expensive. IARC has had major success in this area supported by large competitive research awards (e.g. Bill and Melinda Gates Foundation for cervical cancer screening or HPV vaccination) or through collaboration with national partners, where projects are largely financed nationally (e.g. *H. pylori* eradication within the Korean stomach cancer screening programme). IARC will continue to seek opportunities in priority areas, but cannot support such high-cost studies on its regular budget.

69. It is evident that the demonstration of efficacy of a preventive intervention in a trial setting is insufficient to assess its impact on disease burden when scaled-up to the population level. Factors such as restricted health systems, cultural or economic barriers are often neglected, contributing to a failure to realize the benefits of earlier research. The Agency will expand the scope of its prevention research to investigate the operational factors which support or impede the implementation of primary and secondary prevention strategies.

70. Emphasis in primary prevention will be placed on vaccines (Hepatitis B virus (HBV), HPV) or eradication (*H. pylori*) of infectious agents as well as the impact of policy, behavioural and educational interventions on tobacco, alcohol and obesity control. For the infections, reduced prevalence will be assessed through population prevalence surveys, which are also valuable in modelling projections of the impact of exposures and interventions. For secondary prevention the Agency will evaluate screening for cancers of the cervix, breast, colorectum and oral cavity.

71. As new findings arise from the etiologic and screening/early detection research, additional opportunities to evaluate primary and secondary interventions are expected to emerge, for example, in relation to diet, obesity, chemical contaminants, radiation, etc. or the early detection of lung, prostate, head and neck, ovarian and other cancers.

*Implementation research priorities*

72. Implementation research has a broad scope and IARC has to be selective, focusing on where it can add value and build on its strengths. Consequently, the Agency will consider primarily the role of health systems in the delivery of the types of interventions described above, where it already has expertise. Taking this approach IARC can build on a solid foundation of ongoing work on the efficacy of preventive interventions, but extend the work to identify factors affecting effectiveness and the successful implementation and scale-up of programmes. This research draws heavily on local collaboration and health systems infrastructure and thus allows IARC to build cost-effective projects into national programmes during demonstration or pilot phases.

73. As part of NCD prevention and control initiatives, there is increasing integration of certain basic cancer interventions within primary care services. These include early detection tests (e.g. visual screening for cervical cancer; clinical breast examination), recognition of cancer symptoms and referral of individuals to secondary care for diagnosis and treatment. Some LMICs have made significant efforts in this direction and IARC will explore opportunities for ecological studies to evaluate the impact of interventions on early detection and improved survival.

74. Implementation can be context-specific and therefore the selection of study sites is an important consideration. While many of the lessons learned in health systems settings in LMICs will be relevant to other countries in similar regions, projects will be selected in light of their potential to be generalized. In addition, integration with IARC's work in cancer registries will help inform study site selection, to permit the longer-term impact of interventions to be followed, providing analyses not only of changes in incidence but also survival and prevalence where appropriate.

*New insights from molecular science*

75. Prevention research will develop via a more extensive interface with the laboratories at the Agency. As research reveals the underlying biological pathways perturbed in carcinogenesis it is possible not only to ask which environmental or lifestyle exposures drive those changes, but also how different interventions may modulate those pathways and offer opportunities for prevention. This encourages smaller-scale, short-term intervention studies to assess the potential to modulate critical biological pathways as measured by metabolomics, epigenomics and transcriptomics. This research may also lead to intermediate endpoints for longer-term intervention studies. The Agency will prioritize interventions involving lifestyle changes, particularly diet and physical activity, rather than opportunities afforded via chemoprevention.

76. As touched on earlier, the somatic alterations and genetic variants being identified in tumours and circulating tumour DNA in body fluids may also permit the early non-invasive detection of cancer, thus providing new avenues for using genomics within secondary prevention programmes. In addition, many IARC studies of etiology collect data on patient prognosis and outcome, permitting evaluation of exposures and biomarkers as prognostic indicators. These latter findings may in turn inform tertiary prevention strategies in cancer patients.

*Expert evaluations of preventive interventions*

77. The IARC Handbooks of Cancer Prevention are widely respected and used as a foundation for protecting populations against disease. However, many topics were evaluated more than a decade ago, and new data from screening programmes and opportunities for primary prevention warrant a critical reappraisal. Therefore, in analogous fashion to the IARC Monographs, the Agency will use its convening role to produce specific, evidence-based recommendations on successful prevention strategies through this series.

78. The Handbooks programme will provide a vital resource for policymakers in setting cancer control strategies and will benefit from the expertise and experience of the Monographs programme. Future priorities will be shaped by expert consultation, and interventions for consideration will include preventive agents (e.g. NSAIDs, vitamin D and sunscreens), personal behaviours (e.g. weight control and physical activity) and early detection/screening (e.g. breast, cervix, oral cavity, prostate, lung, colorectal, ovarian and skin cancers).

## Increase the capacity for research

### Increase human resources for cancer research

79. Without trained cancer researchers in LMICs, research programmes in these countries will be constrained and the agenda will tend to be driven by those from outside. IARC will therefore continue its mandate to build a new generation of researchers to reinforce cancer research worldwide. Three principal features will characterize the Agency's activities: post-doctoral and other professional training; training courses in areas of core competencies; and the integration of training in the context of collaborative research projects with individuals and organizations.

80. IARC will continue its post-doctoral training programme, guided by the IARC Post-doctoral Charter. The Agency will seek to expand the number of post-doctoral trainees with a particular emphasis on those from LMICs and from IARC PS, funded via bilateral agreements. Relatively less emphasis is placed on pre-doctoral training, other than from French institutions or through bilateral partnerships with designated national centres where an integrated PhD training programme can be assured.

81. In parallel, more flexible approaches to further professional development will be introduced, targeting early career scientists and other public health professionals, including shorter fellowships for focused training periods. The Agency will continue to host top international cancer researchers as Senior Visiting Scientists to contribute to the Agency's programmes and build international collaborations, and to offer Expertise Transfer Fellowships allowing scientists to visit and transfer technology and expertise to LMICs.

82. IARC will bring its learning and training resources closer to their target audiences by developing eLearning materials and initiatives. The Agency website will be upgraded to provide a single online entry point to all related training resources and opportunities. Online courses will be developed in order to expand the audience of existing courses; eLearning materials will be produced and made available in English and other languages including French, Spanish and

Russian. In addition to current courses provided in the areas of cancer registration, cancer epidemiology and early detection, more specific and advanced courses will be developed in the areas of core competencies of the Agency. In line with the expansion of implementation research, the Agency will evaluate the needs for capacity building in the necessary research skills in this domain and consider partnerships which could deliver the required training in LMICs.

83. The training programme at IARC will remain closely linked to the research activities with many of the trainees also part of research projects. In this manner the training provided at IARC is often a catalyst to scientific collaborations that are maintained far beyond the training period itself. It is worth noting that as a consequence of the collaborative nature of IARC's work many links are made via the Agency between scientists in HICs, including PS, and those in LMICs thus further promoting opportunities for capacity building.

### Laboratory and computing services

84. IARC's activities in laboratory science, epidemiology, biostatistics and bioinformatics require specialized support. The Agency will therefore maintain in-house capacities and competencies in order to deliver the required substantive support in these critical areas.

85. In respect to laboratory equipment, IARC's strategy requires regular upgrade of key apparatus, particularly in the "omics" domains, and in turn this enables recruitment of leading molecular researchers. In order to maximize efficiency in-house, common platforms and facilities will be created and managed centrally. At the same time, IARC has a policy of strategic partnerships with centres of expertise to avoid duplication or unnecessary over-specialization. This is particularly true of research institutes in Lyon, where IARC cooperates closely with the Centre Léon Bérard, the University Claude Bernard Lyon 1, the Ecole Normale Supérieure, the ProfileXperts Genomics Platform, the Platform for Experimental Biology on Mice and the European Centre for High-Field Nuclear Magnetic Resonance, in the areas of DNA sequencing, metabolomics, bioinformatics and access to experimental animal facilities with imaging.

86. In parallel to the laboratory equipment, the Agency will ensure appropriate IT infrastructure to permit the efficient analysis of large complex datasets, storage of the unprecedented volume of data generated, and opportunities noted above for research using record linkage. Emphasis will also be placed on data security and confidentiality, particularly noting the responsibility of custodianship of information from collaborators from across the world.

### Biobank

87. The availability of well-annotated human biological specimens is a foundation to studying the causes and prevention of cancer. IARC's priority will be biobanks derived from population-based studies rather than the systematic collection of clinical series of tumour specimens. The IARC biobank (IBB) is therefore developed as an integral support to the research programme. Indeed, many of IARC's research studies rely on access to existing biospecimens stored within

the IBB, which houses over 7 million samples from more than 50 countries; IBB is thus one of the largest and most varied biobanks worldwide dedicated to cancer research.

88. The value of biospecimens comes through utilization and therefore IARC will continue to provide greater access to the IBB resources through collaborative research projects. This will be based on the new IARC Sample Access Policy, along with tools to increase visibility of the different collections to potential collaborators. In addition, the IBB will provide services to IARC scientists and collaborators in sample retrieval, DNA extraction and shipment according to international protocols and guidelines.

89. IARC will expand the IBB through collections coming from its own collaborative studies. However, a strategic opportunity comes from the increasing cooperation with LMICs where support and advice on best biobanking practice and secure storage of biospecimens present challenges. IARC is prioritizing two activities in response. The first is to act as custodian for duplicate storage of collections from LMICs where local facilities may be currently unable to ensure the long-term security of samples. This is reflected in the new IARC building design which foresees capacity for expansion of the IBB with improved state-of-the-art automated storage to facilitate sample tracking and retrieval and the rationalization of space.

90. The second activity concerns capacity building in biobanking. Within the biobank networks in HICs (e.g. the Biobanking and Biomolecular Research Infrastructure – European Research Infrastructure Consortium, BBMRI-ERIC) the Agency is focusing on supporting cooperation between those biobanks linked to large population-based cohorts, where epidemiological data and samples are available from both cancer cases and controls; this focus is designed to underpin the etiological research of IARC and its collaborators. At the same time biobanking is an increasingly sophisticated area with detailed protocols and governance, but with a need to adapt best practice to circumstances where resources are more limited. IARC has a major role to play in this adaptation by using its participation in leading biobank networks to develop international guidelines and protocols for biobanks in LMICs. This will include the physical collection and management of biospecimens but also support in relation to the ethical and legal aspects to protect study participants while avoiding unnecessary barriers to international research cooperation. To address these issues, IARC has established the LMIC Biobank and Cohort Building Network (BCNet) in partnership with other organizations, particularly the US-NCI/Centre for Global Health. The network will provide education and training as well as bilateral support to individual countries for establishment of a biobank.

## Strategic leadership

*Internal leadership and evaluation*

91. The Agency is organized in Sections and constituent Groups (see Annex 2) each with a defined set of responsibilities, assigned budget, specific aims, approaches and expected outcomes (see Annex 1). The Agency's Section/Group structure evolves to meet changing priorities, with Groups formed or disbanded as priorities change. While the Section structure provides clear lines of responsibility and accountability throughout the organization, a majority of the programmatic activity is delivered across Sections as detailed under "Scope and Purpose",

and illustrated in the Project Tree (see Annex 3). The Project Tree permits IARC management to plan, assign and monitor the alignment of resources with identified priorities and to make strategic investments accordingly.

92. The Agency has a participative leadership which permits rapid decision-making and enables timely responses to emerging opportunities and priorities. The Director works closely with the IARC Senior Leadership Team (made up of the Director, all Section Heads, Director of Administration and Finance, Head of Communications and Special Advisors) to develop priorities for research and administrative change. Research priorities are further considered through in-house discussions and, where appropriate, consultation with external experts via creation of IARC *ad hoc* working groups. IARC organizes research retreats on specific topics and will create "Cancer Teams" comprised of scientists (senior and early career) from across the Agency to work together on different aspects of a given cancer or risk factor. The Cancer Teams will provide specific research plans including requests for resource mobilization. The Director will use the Director's Development Provision to support identified opportunities. Particular priority will be given to projects which add value by drawing on existing epidemiological platforms and bio-specimen resources.

93. Sections are subject to peer-review by the Scientific Council on a five-year cycle. In line with advice from the IARC governing bodies, this remains the primary mechanism of evaluating activities in relation to the MTS, including informing decisions to cease certain activities or programmes and reinforce others. IARC also presents specific projects to the Scientific Council for review. The IARC Director reports on an agreed set of Key Performance Indicators on an annual basis to the Governing Council.

94. It is noteworthy that a majority of IARC projects are conducted with extra-budgetary funds won through competitive processes subsequent to peer-review. Within the Implementation Plans, metrics and milestones are provided where possible. At the same time the Agency will seek to ease the weight of formal reporting to its governing bodies, elements of which currently add little to the quality of activities and consume considerable resources.

*Enable and support the efficient conduct and coordination of research*

95. The support structures of the Agency are engaged in enabling the efficient conduct and coordination of research to ensure management according to the highest international standards; funding requirements are met and available resources are used in accordance with appropriate accounting standards; strategic investments are made to support emerging research opportunities and to enhance and safeguard the operation of the scientific research platforms; and the organizational culture and systems support a healthy and motivating work environment.

96. The current strategy follows concentrated effort over five years to put in place efficient, effective and transparent systems with the aim of best supporting the research Sections in implementing their activities. These successes and the increasing cooperation and integration between the scientific and administrative parts of the Agency form the basis to four main priority areas.

97. First, the Agency will work with the French authorities, the Governing and Scientific Councils and the Agency personnel in the design and construction of a new IARC building in Lyon to provide suitable premises for the forthcoming decades. The current target move date is during 2019.

98. Second, the Agency will continue to improve the management of its finances and support the delivery of its scientific activities through administrative service provision, including procurement, contract management, recruitment and payments. Efforts will continue on the streamlining of processes and on ensuring the appropriate capacities are in place for efficient delivery of the scientific programme, while also ensuring application of the prevailing UN rules and regulations including public sector accounting standards.

99. Third, the Agency will position itself to attract a broader portfolio of resources to support its scientific activities. Particular focus will be on identifying and pursuing bilateral agreements for funding, including from governments interested in IARC's work within the global NCD Action Plan. Efforts will continue to attract additional PS and, in coordination with WHO legal advisors, on how to leverage resources and collaborations with non-state partners.

100. Fourth, the Agency will continue to ensure a work culture that encourages exploring new approaches and opportunities. In work climate surveys, particular emphasis has been placed on communications among personnel with different levels of responsibility and on improved opportunities for career advancement. IARC will work to ensure an atmosphere of recognition and workplace satisfaction for all personnel. Specifically, platforms will be put in place to support colleagues in developing skills to meet the changing needs of the Agency and satisfy personal aspirations. Work will continue with WHO on its reform process and interactions with the International Civil Service Commission and the broader UN family on ensuring that new staff-benefit structures, policies and regulations are well-suited to IARC's priorities for attracting and retaining the best personnel in all areas.

*Communication and dissemination*

101. To underpin its leadership role and ensure maximum dissemination of its findings IARC has transformed its communication strategy. Key aims are improved access to IARC publications through collaboration with scientific information providers, and the creation of an integrated, feature-rich web platform to support the dissemination of publications, notably prioritizing e-publications for viewing across digital devices. The Agency will provide access to interlinked online resources and databases by integrating IARC web resources, web-based cancer databases, and online publications.

102. A more proactive media presence has been developed including prioritizing effective information-flow to key stakeholders in IARC PS. IARC's media strategy will also result in consistent, accessible messages to the general public about the potential of prevention and early detection. These changes are supported by a restructured Communications Group around four themes of Knowledge Management and Publications; Media; Web; and Editing and Translation, with additional investment in each.

103. Through these initiatives the Agency aims to achieve wider international awareness among researchers, health professionals and laypersons as a source of accurate information as well as for its central role in coordinating and conducting international research. As penetration into LMICs with medium-speed internet connections remains variable, this particular challenge will be considered throughout implementation of the digital platform. Alongside a new knowledge dissemination platform, IARC will implement a marketing strategy to exponentially expand its reach to a wider range of audiences.

*Global leadership in cancer prevention*

104. IARC is a global leader in cancer research and has a strategic aim to use its position to promote cancer prevention among governments, funders, health professionals, scientists and the general public. This will be achieved through a number of strategic partnerships at different levels.

105. First, IARC will provide leadership to cancer control planning within the Global NCD Action Plan and thus contribute to the post-2015 sustainable development agenda. IARC's participation in the UN Inter-Agency Task Force on NCDs is a core element of this strategy, with the Agency having assigned roles in cancer and risk factor surveillance as well as cervical cancer control. Through close cooperation with WHO, IARC will contribute tools and expertise in cancer registration, nutritional surveillance and early detection and screening to support WHO Member States in addressing the NCD Global Monitoring Framework.

106. Second, IARC is aligning itself with regional cancer control priorities via strategic partnerships to ensure both that IARC's priorities are informed by knowledge from these partners and that its findings are effectively disseminated in return. Key partners include: the WHO Regional Offices, regional cancer networks (e.g. Red de Institutos Nacionales de Cáncer in Latin America; the Asian National Cancer Centres Alliance; the Gulf Centre for Cancer Control and Prevention); professional networks (e.g. International Association of National Public Health Institutes) and collaborative research organizations (e.g. the BBMRI-ERIC and the Global Alliance for Genomics and Health); as well as non-governmental organizations (e.g. Union for International Cancer Control) and collaborative networks (e.g. International Cancer Control Partnership). IARC will partner in the dissemination of information and data (e.g. the Cancer Atlas with the American Cancer Society) and in shaping the international research agenda towards existing gaps in cancer prevention with, for example, the International Cancer Funders Group (NCI, USA, INCa, France and Cancer Research UK). Indeed one of the outcomes of the Monographs and Handbooks on Cancer Prevention is the identification of gaps in research to be addressed by IARC and cancer research organizations worldwide.

107. Third, IARC will work with WHO on coordinating respective methodologies in order to streamline the transition from IARC's scientific review processes (including the IARC Monographs and Handbooks of Cancer Prevention) through to the guidelines and recommendations developed by WHO. IARC will complement its Monographs and Handbooks with the timely publication of IARC Working Group Reports evaluating the current state of the science in areas critical for public health (e.g. e-cigarettes); recent examples have included *H. pylori* eradication for stomach cancer prevention and alternative endpoints for new HPV vaccines.

108. Fourth, IARC will use its status as the cancer research agency of WHO to promote cancer prevention among the scientific community, funders, policymakers and the general public as a key element of global cancer control. This theme will be developed through the flagship 2016 IARC Scientific Conference on "Global cancer occurrence, causes and avenues to prevention". The Agency will explore areas where regional or global alliances may be forged to promote the cause of cancer prevention, including the possibility of a global alliance for cancer prevention across different non-private sector actors. IARC has recently coordinated the European Code against Cancer and will evaluate with other partners, notably WHO and regional cancer networks, whether a similar approach should be taken in other regions of the world.

**Annex 1 – Implementation Plan**

**Annex 2 – IARC organizational structure**

**Annex 3 – IARC Project Tree[4]**

[4] Provided as a separate file; if you wish to print Annex 3, please do so in A3 format.

# DRAFT IARC Medium-Term Strategy for 2016–2020

## Annex 1: Implementation Plans

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## Section of Cancer Surveillance (CSU)

### Relevance to IARC mission

The major focus of the CSU Section is directly or indirectly linked to the pursuit of global cancer surveillance, an area increasingly prioritized in international and national political and research agendas. Work centres around the systematic and ongoing collection, analysis, interpretation and dissemination of information on the global burden of cancer for cancer control purposes, in keeping with a primary aim of the Agency in describing the occurrence of the disease. There are essential overlaps in three cyclical areas of activity that are key to the Agency's medium-term strategy:

1) Dissemination of global indicators: the compilation, estimation and reporting of cancer statistics generated through flagship projects and databases including *Cancer Incidence in Five Continents* (CI5), GLOBOCAN, *International Incidence of Childhood Cancer* (IICC) and the WHO mortality databank. Reporting is via a progressively interactive and user-friendly online interface and through dissemination in peer-reviewed journals;

2) Cancer Registry collaboration: the longstanding and mutually supportive relationship with cancer registries worldwide remains vital to the Agency in improving the availability, validity, and timeliness of cancer data at the national, regional and global level. Through the *Global Initiative for Cancer Registration Development* (GICR), CSU supports the planning and development of population-based cancer registries (PBCR). Regional Hubs are being established to expand localised and targeted support to countries in defined regions via technical guidance, training and advocacy, as well as assistance to registries to enhance networking and research capacity;

3) Dissemination of descriptive epidemiologic research: this includes reports on incidence, mortality, prevalence and survival, as well as innovative research that examines indicators that highlight cancer as a major cause of premature death, as a barrier to old age, and as a chronic condition linked to socioeconomic transition;

### Specific aims:

1. **To be the definitive reference source in the provision of global cancer statistics, in adults, children and adolescents.**
2. **To provide measurable improvements in the coverage, quality and capacity of cancer registries in LMICs through the operationalization of the GICR, and in particular through the development of Regional Hubs, offering increasingly localised support across LMI regions.**
3. **To conduct descriptive epidemiological research, with an increasing focus on research that directly responds to the NCD and sustainable development agenda.**

**Major approaches:**

1. **Global cancer indicators: development and dissemination.** The major requirement is innovation in dissemination of our global statistics via the development of the Global Cancer Observatory (GCO). The GCO will include an innovative and user-friendly interface that provides timely information on a broad range of instructive indicators, developed from our major projects and databases:
    a. GLOBOCAN 2015. This will be completed in parallel with b. and c. (see below) in order to build up national estimates of incidence, mortality and prevalence. Other developments will include more relevant measures of prevalence and indicators linked to disparities and inequalities, as well as an expansion of cancer sites available. Measures of validity and reliability will be provided via our collaboration ICE and with the University of Washington.
    b. Cancer Incidence in Five Continents Volume XI (CI5-XI). CI5-XI will compile cancer incidence from registries worldwide for the period 2008-2012. In addition to the traditional sites and histological subtypes, new groupings based on the TNM classification are envisaged. To ensure rapid progress and to unite efforts, editorial collaborations with the International Association of Cancer Registries (IACR) and the Regional Hubs will be fostered.
    c. Cancer Survival in Countries in Transition (SurvCan-3). Survival comparisons will be based on cancer patients diagnosed 2003-2007 followed up until end-2012. The focus continues to be registries in LMICs including the provision of guidance on methods to ensure complete follow-up. Survival estimates from 50 registries will be compared with selected high-income countries used as regional comparators for benchmarking.
    d. International Incidence of Childhood Cancer (IICC-3). A collaborative network of general and paediatric registries has been developed through IICC-1 and IIIC-2 collaboration. The third volume compares cancer incidence in children and adolescents 1990–2008. A review of CSU's childhood cancer programme will assess prospects for building on IICC-3 including: i) the global description of childhood cancer incidence for specific cancer types; ii) trend analyses of childhood cancer incidence spanning the three volumes of IICC and iii) equivalent comparisons of childhood cancer survival.
2. **Cancer registry support and development**. Through the GICR and collaborations with the IACR, direct liaison with registries is critical for CSU in advancing cancer registration worldwide. The provision of technical guidance, training and advocacy will increase the availability of high quality data for national cancer control planning purposes in LMICs and provide essential data for research. Linking in with the global political NCD agenda, the GICR is a multi-partner initiative coordinated by IARC providing measurable improvements in the coverage, quality and networking capacity of cancer registries in LMICs. There are four elements of coordination and governance to ensure the GICR becomes fully operational:
    a. Developing IARC infrastructure. International leadership is needed from IARC to support training and site visits to targeted countries. As part of research capacity-building exercises, research studies including 'first reports' across countries and regions will be developed.

b. Developing infrastructure at the Regional Hubs. To steadily increase Hub capacity for the delivery of training, support and advocacy, three-year action plans are being developed at each Hub. These will identify priorities and assess present and future resource needs in fully developing local expertise.
c. Escalating support to targeted countries. The project initially identified 24 countries in four Hub regions capable of sustaining PBCR development via site visits/recommendations, follow-up and CRAs. The target is to be working in 50 countries in support of registration by 2018.
d. Building GICR Partner relations. Each GICR Partner has a critical role in coordinating their cancer surveillance objectives under the GICR umbrella. Strategic linkages will be fostered with input from all partners.

There are additional, related, approaches in support of registration including: the development of training materials for distance learning and associated courses; further development of the CanReg5 software and data quality software; support for revision/updating of ICD-O-3 and in field-testing of the cancer chapter in ICD-11; close cooperation with the IACR, including revision of international standards in coding, classification and registration practices (cf. IARC Technical Report No. 43).

3. **Descriptive epidemiology of cancer: core activities and innovation.** The recognition that NCDs are set to become prime causes of morbidity and mortality worldwide has led to increasingly demand for research that supports future planning and documents the evidence base for cancer prevention and control. The planned programme includes dissemination of routine studies as well more cutting-edge projects that directly tap into the evolving NCD and cancer agenda:

   a. Global surveillance linked to supporting current and future cancer strategies aimed at reducing the burden. To highlight need for cancer planning, future baseline estimates will provide medium-term predictions according to demography and risk changes.
   b. Cancer as a chronic disease. Inequalities in diagnosis and treatment increase disparities in premature mortality and quality of life. CSU aims to estimate globally: (i) disability-adjusted life years, healthy life expectancy and disability-adjusted life expectancy; (ii) longer duration prevalence, assigning survivors to different phases of care.
   c. Quantification of different risk factors and interventions to assess potential for prevention, including: (i) population attributable fractions for key risk factors and for selected countries/regions; (ii) assessment of the long-term impact of selected interventions and (iii) estimation of productivity loss from premature cancer mortality.
   d. Cancer and socioeconomic transition. The aim is to explore trends in cancer incidence and mortality against levels of indicators of human development and spending on health care.
   e. Trends in Cancer Incidence and Mortality Volume 2. Using temporal data from ten consecutive volumes of CI5, and the WHO mortality and the internal GLOBOCIM databases, CSU will update the seminal 1993 IARC Scientific Publication with a comprehensive and systematic assessment of cancer incidence and mortality trends for 27 cancers 1960–2010 across five continents. The emphasis is on detailed tabular and graphical descriptions of the secular changes, including age-period-cohort analyses.

f. Descriptive studies at the global and regional level. Using the databases within the GCO, studies will describe and elucidate the global patterns and trends by cancer type. Priorities include promotion of the synergistic aspects of incidence, mortality and survival, with examples, and an international assessment of the "war against cancer".
g. Childhood cancer. Based on IICC, a comprehensive publication series on global childhood cancer burden/trends by tumour will be developed, including survival studies.

**Expected outcomes:**

1. Six IARC Regional Hubs established in Africa, Asia and Latin America, the Caribbean and the Pacific Islands; measurable improvements in the coverage, quality and national networking capacity of PBCR in 50 LMICs by 2018.
2. Launch of the *Global Cancer Observatory* providing a broad range of instructive indicators developed from the major projects and databases 2014-18 including IICC-3 (scheduled Dec. 2016), CI5 XI and SurvCan-3 (Dec. 2017), and GLOBOCAN 2015 (Dec. 2017).
3. Descriptive studies of incidence, mortality, prevalence and survival by place and time, augmented by applied research studies providing the evidence base for global cancer planning, through novel indicators of relevance to cancer control.

## Section of IARC Monographs (IMO)

### Relevance to IARC mission

The mission of IARC is the global control of cancer, with emphasis on primary and secondary prevention, which is the most effective response to the rising burden of cancer, particularly in low- and middle-income countries where health services are least able to meet the impending challenge.

The first step in cancer prevention is to identify the causes of human cancer and what works in cancer prevention. In accordance with one of its fundamental missions the Agency prepares and distributes authoritative information on the causes and prevention of cancer throughout the world. The *IARC Monographs* are the authoritative reference for cancer causing agents, and the *IARC Handbooks of Cancer Prevention* establish what works in primary and secondary cancer prevention.

The availability of an international consensus from an independent, specialized agency provides an authoritative basis for national decision-making, and facilitates national recommendations. National and international health agencies use the *IARC Monographs* to guide and support their actions to prevent exposure to known, probable, and possible carcinogens and the Handbooks to plan interventions aiming at primary and secondary prevention of cancer. In this way, the *Monographs* and the *Handbooks of Cancer Prevention* together contribute to cancer prevention and the improvement of public health.

**Specific aims:**

1. **To critically review and evaluate the published scientific evidence on carcinogenic hazards to which humans are exposed, including chemicals, complex mixtures, physical agents, biological agents, occupational exposures, and personal habits.**
2. **To critically review and evaluate the published scientific evidence on preventive effects that could be employed in cancer control, including preventive activities and agents (e.g. weight control and physical activity, aspirin, sunscreens), and cancer screening (e.g. for cancers of the cervix, colon, prostate, and lung).**

**Major approaches:**

1. IARC convenes an international, interdisciplinary Working Group of expert scientists to develop each volume of *IARC Monographs*. Agents are selected for evaluation based on (1) evidence of human exposure and (2) some evidence or suspicion of carcinogenicity. Agents and exposures can be re-evaluated if significant new data become available. IARC selects experts for the Working Group based on their knowledge and experience and absence of real or apparent conflicting interests. The *Monographs* are developed over a two-year period (from announcement of topics on the Monographs' website to publication of the full-text Monographs) and evaluations are finalized during an 8-day meeting whose objectives are peer review and consensus. Each Monograph consists of a comprehensive, ***critical review*** and summary of the scientific literature (published articles, articles accepted for publication, and publicly available documents from government agencies). Before the meeting, each member of the Working Group writes a portion of the critical review. At the meeting, four subgroups (exposure, cancer in humans, cancer in experimental animals, and mechanistic and other relevant data) review these drafts and develop consensus subgroup drafts. The Working Group meets in plenary session to review the subgroup drafts and develop a consensus ***evaluation.*** After the meeting, IARC scientists review the final draft for accuracy and clarity prior to editing, formatting, and publication. A short summary of the outcome is published in The Lancet Oncology.
2. To further increase transparency and efficiency in the *Monographs*, IMO will implement new tools for systematic review, standardizing literature searches and creating databases of information on study designs and results. The Monographs will also implement quantitative risk characterization progressively over the next five years. Mechanistic data are contributing increasingly to the final overall evaluation of carcinogenicity. IMO will build on insights from the Volume 100 Workshops on Tumour Concordance and Mechanisms of Carcinogenesis and develop guidance to the interpretation of high-throughput "omics" data, by selecting a few model agents with extensive omics data and more traditional data on mechanisms, for evaluation in forthcoming Monographs meetings.

3. To stay at the forefront in identification of cancer hazards and preventive agents IMO will continue to organize scientific workshops on topics related to cancer hazard identification and cancer prevention (e.g. the role of mutations in germ cells and the subsequent risk of cancer), and initiate and collaborate in research projects pertinent to the Monographs programme.
4. IMO will further enhance the dissemination of Monographs evaluations with the development of a user-friendly and searchable internet database of Monographs results, interlinked with IARC databases on tumour pathology (WHO 'Blue Books'), cancer incidence and mortality (GLOBOCAN), preventive agents and actions (IARC Handbooks of Cancer Prevention) and other major IARC databases, and external databases, such as the WHO International Classification of Diseases (ICD-11) and the US NLM ChemID. Together with the stronger focus on online publication and ePUBs, and coupled with new 'print-on-demand' options, the print run will be further reduced. In collaboration with national cancer institutions efficient means of translation into major other languages will be made available.
5. The *IARC Handbooks of Cancer Prevention* provide the same rigorous evaluation process as the *IARC Monographs*, with evaluations on the scientific evidence on preventive agents and primary and secondary interventions. A short summary of the evaluations will be published in the *New England Journal of Medicine*. The process of selection of expert scientists, drafting of reviews, convening the Working Group and producing the ***critical review*** and ***evaluation*** are analogous to the Monographs. Agents are selected for evaluation based on (1) potential public health relevance and (2) some evidence of preventive effects. Agents and exposures can be re-evaluated if significant new data become available.
6. IMO will develop a sustainable series of *IARC Handbooks of Cancer Prevention* with topics on primary and secondary prevention, with one meeting per year. Regarding preventive activities and agents, topics may include updates and re-evaluations of weight control and physical activity, as well as aspirin and sunscreens. Potential new topics ready for first-time evaluations include vitamin D and vitamin B. In terms of screening, cervical cancer screening merits re-evaluation and consideration of new approaches such as HPV testing, particularly in low- and middle-income countries, as well as implementation of screening in the context of HPV vaccination. First-time evaluation of cancer screening for cancers of the colon, prostate, and lung are additional potential topics.

**Expected outcomes:**

1. Two to three IARC Monographs meetings a year resulting in the evaluation of high priority agents (such as acrylamide, aspartame, Bisphenol A and some pesticides).
2. Organization of scientific workshops on topics related to cancer hazard identification and cancer prevention and presentation of the findings in scientific journals or IARC publications.
3. A series of new *IARC Handbooks of Prevention*, publishing one Handbook per year.

## Section of Mechanisms of Carcinogenesis (MCA)

### Relevance to IARC mission

Improving the knowledge of mechanisms of carcinogenesis linked to environmental and lifestyle exposures provides a foundation for studies of cancer etiology, carcinogen evaluation and cancer prevention, the core activities of IARC. The main objective of the Section is to identify molecular mechanisms by which such exposures induce genetic and epigenetic alterations and affect molecular pathways critical for cancer, thus enhancing the evidence base for cancer prevention. Emphasis is placed on relevant events that precede or drive tumour initiation and progression. Key MCA strategies include innovative research, development of (epi)genomic and screening methodologies and bioinformatics resources applicable to experimental models and biobanks associated with population-based and epidemiology studies. MCA also contributes to translational studies, through the discovery of mechanism-based biomarkers of exposure, early detection, and risk stratification.

MCA applies state-of-the-art molecular/cell biology and functional genomic tools, building on the most recent knowledge of the cancer (epi)genome, genomic databases and new bioinformatics tools. The demand for faster, affordable and less labour-intensive strategies is increasingly met by several emerging technologies that have demonstrated the capacity of delivering next-generation solutions for robust and cost-effective (epi)genome analysis. Therefore, the development of (epi)genomic and profiling methodologies, as well as bioinformatics tools applicable to human cancers and experimental models remains an essential part of the MCA strategy.

The above developments constitute an exciting opportunity to identify and characterize the key molecular pathways underpinning carcinogenesis that are expected to enhance understanding of cancer etiology and identification of prevention opportunities. The application of *omics* approaches, brought about by the advent of less costly profiling technologies, and access to large population-based studies raise the opportunity of identifying novel biomarkers and testing the “exposome” concept, a new initiative aiming to describe the breadth of carcinogenic exposure throughout the lifecourse, and open up avenues to prevention, risk stratification and intervention.

MCA studies are interdisciplinary in nature and the synergistic collaborations with other IARC laboratory-based scientists and epidemiologists as well as external groups advance major IARC programmes. The Section comprises two groups: the Molecular Mechanisms and Biomarkers Group (MMB) and the Epigenetics Group (EGE), both of which work in close collaboration to create synergies and better exploit and further expand unique research tools and expertise.

## Molecular Mechanisms and Biomarkers Group (MMB)

**Specific aims:**

1. **To build the evidence-base for cancer prevention by elucidating the mechanistic roles of molecular alterations in carcinogenesis associated with specific environmental and lifestyle risk factors.**
2. **To develop biomarkers, screening methods and bioinformatics resources applicable to population-based as well as mechanistic studies of cancer risk and carcinogen impact.**

**Major approaches:**

1. Systematic screens for molecular alterations linked to carcinogens, using cell models, human tumours and bioassays (with IMO, EGE, GCS, BST). Advanced laboratory techniques (e.g. genome editing) will address mechanistic roles of specific alterations. Applying *omics* to studies of tumour etiology and recurrence in urological, liver, breast and ovarian cancers.
2. Developing informative biomarkers of exposure and carcinogenesis utilizing/supporting translational and epidemiology studies in high-risk regions; application to body-fluid nucleic acids (e.g. cfDNA, ncRNA from plasma, urine). Devising carcinogen signature assays in readily available samples (FFPE, plasma). Updating IARC TP53 database by integrating mutational, clinical, demographic and lifestyle data and developing a database of mutation signatures. Developing open-source bioinformatic tools for somatic alteration analyses.

**Expected outcomes:**

1. Novel molecular signatures of specific exposures and identification of affected cellular pathways in the action of those exposures relevant to carcinogen evaluation and classification in the *IARC Monographs* Programme.
2. Provision of new biomarkers of exposure, pre-cancerous or early-stage events, predictive of tumour development and recurrence for employment in epidemiological studies. Regular annual releases of the IARC TP53 database updates, together with timely releases of dedicated open-source, user-friendly tools for analyses of complex molecular alterations data. A database of mutational signatures will be established within 1-2 years as a new long-term resource.

## Epigenetics Group (EGE)

**Specific aims:**

1. **To provide critical insights into mechanisms of carcinogenesis relevant to studies of cancer etiology and prevention through the identification of epigenetic alterations and molecular pathways deregulated by specific carcinogenic agents.**
2. **To identify epigenetic biomarkers of exposure, early detection and risk stratification and contribute to the characterization of key components of the exposome.**
3. **To develop epigenomic and profiling strategies, and bioinformatics tools, applicable to population-based cohorts, epidemiology and carcinogen evaluation.**

**Major approaches:**

1. Mechanistic studies of functionally important epigenetic "driver" genes ("epidrivers") and molecular pathways altered by specific carcinogenic agents (with a focus on non-genotoxic epigenetic agents), using in vitro models (human and mouse immortalization models) and state-of-the-art approaches, epigenome-wide shRNA library knockdown screens, (epi)genome editing, and functional genomics (collaboration with MMB and IMO).
2. Using cutting edge epigenomics, population-based cohorts (EPIC), and innovative bioinformatics tools, investigate epigenomic profiles of specific cancers and surrogate tissues and identify signatures of cancer risk and exposures (focus on breast and liver cancer, with NEP and GCS). Using cord blood samples from a consortium of international birth cohorts (I4C), analyse the epigenome and contribute to the characterization of the fetal exposome linked to childhood cancer (with MMB, GCS, MBA, ICB, and BST).
3. Developing pipelines for methylome-wide profiling and targeted epigenetics in high-throughput settings and robust bioinformatics analysis to facilitate identification of causal pathways linking exposures, exposome measures or early mechanistic effects to cancer. Developing epigenetic assays to be incorporated into carcinogen evaluation.

**Expected outcomes:**

1. Identification and functional characterization of epigenetic driver events and molecular pathways deregulated by specific carcinogenic agents to advance knowledge of mechanisms of carcinogenesis and underpin studies of cancer etiology and prevention.
2. Identification of epigenetic signatures in specific cancers (breast, head and neck, liver, and childhood), and surrogate tissues contributing to an understanding of etiology and development of epigenome-based biomarkers of cancer risk and mechanism-based biomarkers of exposures. Availability of novel biomarkers of childhood cancer risk and clues to causation, providing an improved evidence-base for prevention that recognises the importance of life-course events.

3. Development of epigenomic methodologies, profiling strategies and related bioinformatics tools will enable multidisciplinary studies on cancer etiology and prevention, with the focus on cancers for which much remains to be discovered with respect to disease causation (breast and childhood cancer). The development of epigenetic assays will facilitate evaluation of new carcinogens (such as endocrine disruptors, phytoestrogens, nano particles, pesticides), and incorporation of epigenetic data into carcinogen evaluation by the *IARC Monographs* Programme. Testing these and other agents known to act through non-mutational mechanisms and classified by IARC as probably carcinogenic or possibly carcinogenic to humans (Groups 2A and 2B), may reveal new "epigenetic carcinogens".

## Section of Molecular Pathology (MPA)

### Relevance to IARC mission

The Section of Molecular Pathology (MPA) conducts original research to elucidate the molecular basis and genetic pathways of human neoplasms, and to identify molecular markers for tumour diagnosis/classification and tumour progression. Genetic studies are carried out using tumour samples from patients with excellent clinical data which have been collected at a population level, to provide unique data combining the pathology, genetics, clinical features and epidemiology of tumours. The main focus is on brain tumours, a relatively under-researched cancer where little is known about the etiology and where molecular genetics is already transforming tumour classification and consequently the clinical management of the disease. MPA's research program is a key element of IARC's goals of elucidating the mechanisms of carcinogenesis which help understand the etiology and prognosis of cancer. MPA also provides histology services (embedding, cutting sections, and staining, including immunohistochemistry) to all IARC research groups.

MPA is responsible for the publication of the World Health Organization (WHO) Classification of Tumours Series (WHO Blue Books). We work with internationally recognized pathologists from around the world to reach consensus regarding tumour classification. Without clearly defined diagnostic criteria, epidemiological and clinical studies are difficult to conduct. The WHO Blue Book projects therefore contribute to the IARC's mission of monitoring global cancer occurrence, understanding causes and evaluating prevention. Most human tumours have been diagnosed and classified based on histological features; more recently, molecular markers are increasingly being used to define disease entities, taking advantage of rapid progress in understanding of the genetics of human neoplasms. Expertise in pathology and genetics in human tumours is essential to successfully carry out the WHO Blue Book projects.

### Specific aims:

1. **To provide genetic information that will be used as the basis for future molecular diagnosis and classification of human tumours, to identify genetic markers for prognosis and novel treatment strategies, and to use genetic data to provide new clues to understand the etiology of human tumours.**

## 2. The objective of the WHO Classification of Tumours is to provide a uniform nomenclature and diagnostic criteria of human cancers that is accepted and used worldwide.

### Major approaches:

1. Histopathology will be compared with genetic / epigenetic / gene expression profiles of human tumours in particular brain tumours, in order to provide information which is essential for molecular diagnosis and tumour classification. This will include next-generation sequencing to identify genetic markers that reliably define tumour entities and those that predict tumour progression. We also plan to identify novel germline mutations in families with clustering of nervous system tumours. These studies will be carried out using a large number of brain tumour samples with excellent clinical data collected at the population level in the Canton of Zurich, Switzerland (987 cases diagnosed between 1980–1994 and 264 cases between 2005–2009) as well as low-grade diffuse gliomas (approx. 400 cases) collected through international collaboration.
2. MPA is the initiator and coordinator, with Series Editors, Volume Editors, and Contributors, to maintain the highest scientific quality and consistency of the WHO Classification and WHO Blue Book styles throughout the series. We collaborate with Series Editors to select Volume Editors based on their excellent scientific quality, international recognition, and mainstream opinions regarding tumour classification. In collaboration with Volume Editors, MPA ensures that the book structure closely reflects the draft of the 4$^{th}$ edition of the WHO Classification. MPA prepares an online submission system, which serves for submission of text, figures and tables, and for editing. MPA organizes the Consensus and Editorial conferences, to ensure that controversial issues are resolved by consensus, new disease entities and changes of terminologies are approved, and that these decisions are reflected in the book text. The IARC Section of Cancer Surveillance (CSU) and MPA organize the IARC/WHO Committee of the ICD-O, to assign new ICD-O codes for any new disease entities proposed. MPA ensures that the histology figures presented in the books are of the highest scientific quality.
3. In liaison with WHO Press, Geneva and the IARC Communications Group (COM), MPA ensures the worldwide distribution of WHO Blue Books (print, e-books, PubCan website). In order to deal with rapid progress in genetics of human neoplasms, we plan to increase the speed of revisions of WHO Classification to every 5-6 years.

### Expected outcomes:

1. Provision of evidence to support molecular diagnosis and tumour classification of brain tumours to be included in the next Edition of the WHO Classification of Tumours and genetic data which provide clues to the etiology of this tumour type.
2. International recognition of the WHO Classification of Tumours Series as the gold standard for tumour diagnosis and classification, which are accepted and used by pathologists, clinicians, cancer registries, epidemiologists, and cancer researchers worldwide.

## Section of Infections (INF)

### Relevance to IARC mission

INF includes two groups (ICB and ICE) with defined specific aims and methods but which work together in numerous projects and participate in multi-disciplinary collaborations both in-house and outside. The overarching objective of INF is to improve the epidemiological and biological evidence-base that will inform improved control of infection-related cancers. This requires access to both high quality data and samples from representative or special populations. On account of the high burden of infection-associated cancer in LMICs, many INF studies are based in Africa and Asia. To achieve reliable results, INF constantly tries to expand and improve the quality of laboratory and statistical analyses. The well-established status of IARC as a leading centre for cancer epidemiology means that a wealth of data and biological samples are accessible to INF both from its own studies and from other institutions and international collaborations, especially on cancers of the cervix and of the head and neck.

The main goal of ICB group is to establish a causal role of specific infectious agents in human cancer using two different and complementary strategies: (i) functional studies to characterize the biological properties of specific infectious agents using *in vitro* and *in vivo* model systems; and (ii) epidemiological studies to determine the presence of specific infectious agents in benign and malignant human lesions. The functional studies in the ICB Group are focused on characterizing the ability of viruses to de-regulate cellular pathways involved in the immune response and cellular transformation in order to predict their oncogenic potential. ICB also develops and validates novel detection assays for a broad spectrum of infectious agents, suitable for application in collaborative epidemiological studies.

The primary goal of ICE Group is to help reduce the burden of cervical cancer among women worldwide by promoting HPV vaccination and cervical screening programmes in LMICs. Other associations between viruses and cancer require additional research and better standardized control measures and hence ICE investigates HPV in cancer of the anus and oropharynx, as well as cancers associated with HIV and HCV. ICE is also developing innovative statistical methods to estimate the uncertainty of population-based statistics and cancer fractions attributable to infection. In addition, mathematical models to project the impact of different combinations HPV vaccination and screening on HPV-associated cancer in Europe and LMICs are being produced.

## Infections and Cancer Biology Group (ICB)

### Specific Aims:

1. **To characterize the biological properties of novel oncogenic viruses.**
2. **To develop novel diagnostic tools to facilitate epidemiological studies on infections and cancer, with particular focus on the role of microbiome in virus- and non-virus-induced cancers.**
3. **To elucidate possible cooperation of infectious and environmental agents in human carcinogenesis.**

**Major approaches**

1. The approach is based on the ability of oncogenic and non-oncogenic viruses to promote cellular transformation and alter immune-related pathways, two key events in virus-induced carcinogenesis. Studies are focused on novel members of the polyomavirus family, EBV and mucosal and cutaneous HPV types, with the aims of (i) identifying novel viruses that display oncogenic activities in *in vitro* and *in vivo* experimental models and (ii) discovering novel viral/cellular mechanisms of interaction, with particular focus on epigenetic changes and alterations of cellular gene expression. As *in vitro* experimental models, we will use primary human cells that are the natural hosts of the different oncogenic viruses, e.g. primary B cells for EBV and human keratinocytes for HPV types. Regarding *in vivo* models, in collaboration with the German Cancer Research Center (DKFZ, Heidelberg) we will continue to develop transgenic mouse lines expressing different viral oncogenes in different anatomical regions, using tissue-specific promoters.

2. ICB has developed high-throughput, sensitive assays of infectious agents in small amounts of specimen, including exfoliated cells from different mucosae, urine, saliva, skin swabs and sections of paraffin-embedded tissues which make these assays valuable for epidemiological studies. Assays permit the detection and identification of DNA and RNA from a broad spectrum of infectious agents, including mucosal human papillomavirus (HPV) types (n=21), cutaneous HPV types (n=71), hepatitis B virus (HBV), hepatitis C virus (HCV), HIV, all known human herpesviruses (n=8) and human polyomaviruses (n=12). Future efforts will focus on the generation of novel diagnostic assays for additional infectious agents. Due to the emerging recognition of the importance of the human microbiome, an assay is being developed for the detection of approximately 100 human bacteria that colonize the genital tract, oral cavity and gut, e.g. *Helicobacter pylori*, *Chlamydia trachomatis*, *Helicobacter hepaticus*, *Helicobacter bilis*, *Fusobacterium nucleatum* and *Porphyromonas gingivalis*. The first efforts will be focused on the evaluation of a direct role of bacterial infections in head and neck cancer that are not associated with mucosal high-risk HPV types. We will also determine whether the microbiome via its interaction with the immune system may have an indirect role in carcinogenesis, favouring in the oral cavity the infections of oncogenic viruses.

3. Epidemiological studies of geographic patterns of cancer suggest possible cooperation between infectious agents and largely unidentified environmental factors e.g. Burkitt's lymphoma and nasopharyngeal cancers, both associated with EBV. Our ongoing studies focus on the characterization of cooperative mechanisms in *in vitro* and *in vivo* experimental models between (i) UV irradiation and E6 and E7 oncoproteins from cutaneous HPV types that are suspected to be involved in non-melanoma skin cancer (NMSC), and (ii) the mycotoxin aflatoxin $B_{1,}$ a food contaminant in sub-Saharan regions, and EBV. In future studies, we plan to further dissect these mechanisms and evaluate the impact of additional environmental risk factors in virus-mediated carcinogenesis. These will include how tobacco products may cooperate with HPV oncoproteins to promote the development of pre-malignant and malignant lesions in the upper respiratory tract, and how arsenic, a risk factor of NMSC, could further stimulate the formation of UV-induced skin cancers.

### Expected outcomes

1. Provision of novel insights into the biology and epidemiology of cutaneous HPV types in NMSC, particularly whether these viruses play a key role at the initial stage of carcinogenesis, but not being required for the maintenance of the transformed phenotype of the infected cells ("hit-and-run" scenario).
2. Improved understanding of the low or high transforming activities of different HPV cutaneous types. These findings may permit sub-grouping of the beta HPVs into low- and high-risk types, as for the mucosal alpha HPV types. Such a distinction would greatly facilitate the design of epidemiological studies to evaluate their association with NMSC.
3. Comparative analyses of the biological properties of EBV, polyomaviruses and HPVs will lead to the identification of key properties of oncogenic viruses, which may provide new tools for the evaluation of the oncogenic potential of novel viruses.
4. Delivery of a diagnostic platform to study more than 200 microorganisms in epidemiological studies of infections and cancer. In particular, the bacterial detection assays will be used to evaluate the impact of the microbiome in virus and non-virus-induced cancers.

## Infections and Cancer Epidemiology Group (ICE)

### Specific Aims:

1. **To implement and monitor HPV vaccination and HPV-based screening in low-income countries.**
2. **To understand the spectrum, natural history, and prevention of infection-associated cancers other than cervical cancer.**
3. **To improve statistical methods to estimate infection-associated cancers.**

### Major approaches

1. ICE promptly started monitoring HPV vaccination in Bhutan and Rwanda by repeated performance of HPV prevalence surveys, with the support of the local Ministries of Health and the Bill and Melinda Gates Foundation. Initially, monitoring will target the distribution of HPV types in unvaccinated women, in invasive cervical cancers, and in severe precancerous lesions to serve as a comparison for post-vaccine HPV prevalence. The monitoring of cervical cancer screening includes studies on the feasibility, effectiveness, and cost-effectiveness of shifting from cytology-based to HPV-based screening (in Bhutan) and the gradual implementation of CareHPV-based screening (Rwanda). The validation of self-collected samples and triage methods in HPV-positive women will also be addressed. Finally, a cohort study of women recruited in baseline HPV prevalence surveys is planned in Bhutan and Rwanda.
2. In addition to HPV and cervical cancer, ICE has projects on the natural history and prevention of a broad spectrum of less well-understood cancer-associated viruses in different populations. For oropharyngeal cancer, the focus is on HPV markers, the identification of the

still ill-defined precancerous tonsil lesions, and the relationship between history of tonsillectomy and subsequent oropharyngeal cancer risk. A prospective study of HIV-positive men who have sex with men will evaluate the predictive value of HPV markers on the incidence and regression of high-grade precancerous lesions of the anus. To study cancer in HIV-infected people in the cART era, records from participants in HIV/AIDS registries in Switzerland, Italy, Rwanda, and Uganda will be anonymously linked to cancer registry files. The resulting datasets will produce estimates of cancer incidence and relative risks in HIV-infected people *versus* the general population. Nested case-control studies will focus on the impact of immunodeficiency markers and cART use on cancer risk. Finally, ICE will continue to update information on HCV infection and HCV-related cancer worldwide and to search for opportunities to implement screen-and-treat protocols.

3. Innovative statistical methods are essential to ICE projects. Standard confidence intervals reflect only the random variation in data sources, but are not sufficient for synthetic analyses which combine different sources and forms of data in which sources of information can have a very different reliability. A comprehensive Bayesian approach can tackle the uncertainty due to different quality (rather than quantity) of information sources and extrapolation to populations for whom directly-applicable data is unavailable. Biology-driven statistical modeling of cancer incidence data can disentangle age, period and cohort effects and, hence, the impact of changes in behavior, diagnostic standards, and screening on cancer trends. Mathematical models combining HPV transmission and progression of precancerous lesions will allow the comparison of different cervical cancer prevention strategies (vaccination and screening) in Europe and LMICs. Modelling will be also used to evaluate cost-effectiveness cervical cancer prevention in Bhutan and Rwanda.

**Expected outcomes**

1. Improved understanding of the effectiveness of HPV-based cervical cancer prevention in low-income countries; these data will serve as a model for implementation and be used by WHO to prepare new recommendations for cervical cancer screening and by GAVI to provide advice on the best protocols for HPV vaccination programmes in the poorest countries.

2. Identification of precancerous lesions and relevant HPV markers in the tonsils to improve prevention and treatment of oropharyngeal cancer. Improved understanding of the trade-off between efficacy and safety in the treatment of precancerous anal lesions. Evidence-based national and international recommendations on the expansion cART use at higher CD4+ cell counts for the prevention of cancer in LMICs.

3. Provision of measures of uncertainty for application to future releases of Globocan, and to the estimates of the fraction of cancer attributable to infections. As the primary focus of these projects is methodological, their value to the Agency strategy stretches beyond infection-associated cancers.

## Section of Environment and Radiation (ENV)

### Relevance to IARC mission

The overall objectives of ENV are to investigate environmental, lifestyle, occupational, and radiation-related causes of cancer in human populations. The Section investigates these potentially modifiable factors with the aim of informing primary prevention strategies for cancer, increasing understanding of biological mechanisms of carcinogenesis, and assessing the impact of both biological and social determinants of cancer risks, prognosis and post-diagnosis cancer outcomes. These objectives are achieved through the conduct of collaborative international epidemiological studies including coordination of international consortia or through the initiation of targeted individual analytical epidemiological studies.

ENV's role is in three main areas. Firstly, in settings where levels of exposure to putative or established carcinogens (pollutants, occupational exposure or radiation) are high and research is thus warranted; national research benefits from international collaboration and in particular from the independence of the Agency within the UN family. Secondly, of major relevance is the inclusion of affected but under-researched settings, particularly but not exclusively from LMICs, in the study of modifiable environmental and lifestyle carcinogens. Thirdly, the role of broader social as well as biological factors throughout the course of the disease, from critical time periods in human development to post-diagnostic factors influencing cancer outcome, is not well understood.

Most environmental exposures are ubiquitous and because of this, unravelling the cancer risks even at low doses is important as this may have a large impact on the overall cancer burden. There are several major reasons why the impact of environmental risk factors may have been underestimated up to now. Rather crude exposure assessment and/or dosimetry applied in the past and lack of investigation of the potential of environmental exposures to interact with one another and with endogenous factors could have masked relevant associations. New measurement techniques and advances in cancer biology for detection of biomarkers of exposure as well as biomarkers of effect however allow better characterization of the role of multiple factors and their interactions, dose-response relationships and possibly vulnerable populations. In addition, the majority of previous studies were conducted in rather homogeneous populations of high income countries, so by increasing the geographical and lifestyle diversity, the variability in exposure patterns increases and enables detection of risk factors previously masked by studying somewhat uniform source populations.

### Specific aims:

1. **To study carcinogenic effects of exposure to protracted low doses of ionising radiation.**
2. **To study exposure to non-ionising radiation (electromagnetic fields).**
3. **To study the epidemiology of cancers with yet undiscovered but suspected causes involving environmental, lifestyle or occupational exposures.**

**4. To study unique environmental, lifestyle and occupational exposures in affected but under-researched settings.**

**5. To study lifestyle and environmental determinants of cancer risks, prognosis and cancer outcomes.**

**Major approaches:**

1. Ionising radiation (IR): Medical exposures to IR have roughly doubled over the last two decades largely through the growing use of computed tomography (CT) examinations. Although highly beneficial to the patient, it raised concerns about associated cancer risks, particularly at young ages. ENV initiated a cohort study of 1 million paediatric patients in Europe undergoing CT examinations and is implementing a similar protocol in countries with different public health system and radiation protection culture (e.g. Brazil). Characterization of cancer risks associated with environmental exposures following nuclear accidents or nuclear weapon testing remains controversial and ENV is an established coordinator or collaborator at the main sites, i.e. Chernobyl, Southern Urals, Semipalatinsk (Kazakhstan) and Fukushima. These studies allow direct quantification of cancer risks from low dose IR and include development of innovative methodological approaches to estimate individual radiation doses and related uncertainties, integration – where possible – of biological approaches to understand mechanisms contributing to and modulating radiation carcinogenesis, and address public health concerns in the population.
2. Electromagnetic fields (EMF): It is still an open question whether exposure to EMF is associated with an increased risk of certain cancers. Given the ubiquitous and increasing nature of exposure globally, further research remains justified. Over the past years ENV has developed internationally acknowledged expertise in this area and in this capacity is involved in long term prospective studies of users of mobile phones and other new technologies.
3. Cancers with suggested but as yet unidentified modifiable causes: ENV is studying the descriptive and etiologic epidemiology of the East African oesophageal cancer belt, which has distinct geographical, age and sex patterns suggestive of environmental or behavioural risk factors. ENV established a collaborative platform across affected countries (Esophageal Squamous Cell Carcinoma African Prevention Effort: ESCCAPE). Similarly, a new network of paediatric oncology with 3-5 representative key units per continent was set up to expand childhood cancer research into under-researched regions, in particular to study aetiological hypotheses that have been proposed to explain geographical differences in incidence (GALnet). For testicular cancer, parental or early life exposures appear critical to explain distinct geographical patterns. ENV collaborates in studies investigating the role of parental occupational exposures, especially in relation to pesticide exposures.
4. Targeted research in under-researched settings: Epidemiologic studies on environmental or occupational exposures in relation to current or past industrial activities or on unique behavioural patterns (lifestyle) include: pollutants related to gold mining in South Africa (uranium and heavy metals); chrysotile mining and milling in Southern Urals, Russia; oil and other heavy industrialization in Nigeria; indoor and outdoor air pollution in several East African countries; Khat chewing in Ethiopia and Yemen and other risk factors of oral and

upper digestive tract cancer; pesticide application and other agricultural exposures in multi-centric studies of pesticide applicators and farmers in different countries.

5. Lifestyle and environmental determinants: ENV has a major focus on the epidemiology of breast cancer in Sub-Saharan Africa, including studies of etiology, genetics, barriers to early presentation/diagnosis, treatment and ultimately survival. Research outlined in major approach #3 on oesophageal cancer and childhood cancer will include components investigating how socio-environmental factors influence early detection, prognosis and/or survival to inform implementation of cancer control. Finally, the Agency is requested to assist in the development of recommendations for primary prevention; recommendations are currently being finalized for the EU and are planned to be expanded to other regions of the world.

**Expected outcomes:**

1. A more reliable basis for diagnostic practice and for CT dose optimisation including adaptation of the European Guidelines on quality criteria for CT to paediatric patients, International Commission on Radiological Protection (ICRP) recommendations; long term follow up of this cohort will improve the estimation of life-time cancer risks following exposures early in life. More certainty about the cancer risks associated with low dose IR and insights to mechanisms underlying the biological and carcinogenic effects of low doses.
2. More certainty as to whether long-term exposure to mobile phones or other wireless technologies are associated with an increased risk of cancer; use of this knowledge in the setting of future national and international guidelines.
3. Improved insights into the causes of the oesophageal cancer in East Africa. Better understanding of the worldwide risk patterns of childhood leukaemia and the role of parental occupational exposures on testicular cancer in their sons.
4. Increased awareness and evidence-base for local cancer control among populations not well protected from environmental exposures e.g. environmental pollutants, air pollutants, and uranium, occupational chemical exposures related to heavy industrialization and lifestyle habits (Khat chewing). Provision of relevant data for modification of cancer control on a global scale where new risk factors or dose-response relationships are identified.
5. Identification of factors influencing breast cancer survival, thereby mitigating premature mortality in sub-Saharan Africa, with wider relevance to other LMICs.

## Section of Nutrition and Metabolism (NME)

### Relevance to IARC mission

Diet, nutrition, metabolic/hormonal imbalances, excess energy consumption, obesity, and physical inactivity are thought to be important contributors to increasing cancer incidence rates worldwide. However, the mechanisms of action of these factors remain poorly understood. Overweight and obesity represent a global epidemic contributing to a number of common chronic diseases, including cancer. Concurrently, physical inactivity and energy imbalance are

increasingly recognized as important determinants of cancer risk. In addition, the contributing influence of nutritional transition from traditional to Western-type diets, which is taking place in LMICs (e.g. Latin America, Africa) is far less studied. Major chronic diseases have been linked to factors occurring during the developmental period as suggested by the "fetal programming basis of health and disease" best studied through a life-course approach to understand the role of exposure on epigenetic and gene expression changes. In addition, cancers and other chronic diseases appear to share common risk factors leading to multi-morbidity as age increases, and the role of the complex mosaic of interacting factors including dietary and lifestyle habits, obesity and weight gain, metabolic, genetic and social factors as well as the interaction between NCDs is not well defined.

There is an urgent need for a better understanding of the underlying mechanisms whereby foods, nutrients, physical inactivity and metabolic factors may impact cancer causation and survival, multi-morbidity and interaction with other NCDs. This can best be achieved through the utilization of biomarkers and metabolomics to study cellular, biochemical and physiological changes resulting from specific dietary intakes, physical activity and other lifestyle factors in large epidemiological (cohort and case-control) and intervention studies in human subjects. The overall goals of this Section are strengthened by close collaboration amongst its groups (BMA, DEX, NEP). Provision of science-based evidences to contribute to the translation of findings into public health recommendations, identification of susceptible individuals, and the development of cancer prevention strategies is one of the key aims. Acknowledging the IARC's longstanding experience in this research area, a recent request from WHO emerged to support its global action plans on NCD, through the setting up of a joint IARC-WHO "global nutrition surveillance" initiative (DEX Group), as one of the main worldwide and shared risk factors across NCDs.

### Nutritional Epidemiology Group (NEP)

**Specific aims:**

1. **Evaluate the association between dietary and lifestyle habits, energy imbalance, obesity, metabolic and environmental factors with cancer risk and survival in HICs using cohort studies, and human intervention studies.**
2. **Refine, elucidate and explore underlying mechanisms of the association of dietary, lifestyle and environmental factors with cancer incidence, intermediate endpoints and survival, integrating biomarkers of dietary exposure and metabolism, metabolomics, interaction with genetic polymorphisms and epigenetic effects.**
3. **Evaluate the association of diet, biomarkers of dietary exposure, physical activity, energy imbalance and obesity, and environmental determinants (including biomarkers), with breast and other cancers, intermediate endpoints and survival in LMICs.**
4. **Improve our understanding on the role of exposures during fetal and early life on the risk of obesity, cancer and other chronic diseases later in life.**

## 5. Identify dietary, lifestyle (including weight, weight change, physical activity), social, metabolic and genetic risk factors related to multi-morbidity and longevity across the lifespan and establish integrated risk models of healthy ageing.

**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 (fatty acids, vitamin D, vitamins B, antioxidants, fibre, selenium, polyphenols, alcohol and food contaminants), physical activity, obesity and hormones in cancer risk, intermediate endpoints and cancer survival by exploiting available epidemiologic resources at IARC (e.g. EPIC), enriching existing data bases, collaborating with new cohort initiatives or conducting intervention studies in humans under controlled conditions. The main cancers of interest include colon, breast, liver, pancreas, prostate, gallbladder and billary tract, ovary, endometrium and thyroid (in collaboration with BMA, DEX, MCA, EGE, GEP).
2. Collaborate and support the development of adult cohort studies (e.g. EsMaestras cohort in Mexico) and multi-center case-control studies in LMICs (e.g. in Latin America CAMA and PRECAMA and Africa, SABC), to further evaluate how diet, life style and nutritional transition (micronutrient deficiency and over-nutrition) impact the risk of obesity and specific cancer phenotypes with a major focus on breast cancer (in collaboration with BMA, DEX, ENV, MCA).
3. Partnership with birth cohorts and cohorts of children and adolescents from LMICs undergoing lifestyle transition (e.g. in Latin America, and Africa) to evaluate the role of diet and change in diet, lifestyle and other environmental exposures on the incidence of obesity, metabolic disorders and early markers of cancer risk (including epigenetic phenomena).
4. Use an available cohort study (EPIC) and partner with other large cohorts to identify dietary and life style factors associated with multi-morbidity and healthy ageing including a lifespan approach. A biomarker component (nutritional and metabolic and inflammatory biomarkers, genetic, epigenetic, metabolomics) will be included to increase the understanding of specific mechanisms and pathways involved in multi-morbidity, heathy ageing and longevity (in collaboration with DEX,BMA, GEP, COM).

**Expected outcomes:**

1. Increased knowledge and dissemination of information on cancer risk factors and biological mechanisms associated with dietary habits, physical activity and obesity in both HICs and LMICs.
2. 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.

3. Training of at least 10 health professionals in the field of cancer and nutritional epidemiology, pathology, data analysis in LMICs to strengthen research in understudied populations and support local training ("Train the trainers" approach).
4. Identification of susceptible subjects for the risk of cancer incidence and survival, and multi-morbidity to support screening national programmes. Recommendations for the identification of susceptible subjects and targeting of effective prevention strategies will be provided to National Health authorities through WHO and PAHO.

## Biomarkers Group (BMA)

**Specific aims:**

1. **Develop and identify novel biomarkers of exposure for dietary, environmental and metabolic factors applicable to population-based studies on cancer.**
2. **Develop and implement metabolomic approaches to identify exposures and metabolic phenotypes associated with carcinogenesis.**
3. **Improve understanding of the mechanisms by which diet, food contaminants and hormones affect cancer and intermediate endpoints.**

**Major approaches:**

1. Development and implementation of cutting-edge metabolomic approaches and bioinformatic tools to identify and validate novel biomarkers of exposure to dietary, environmental and metabolic factors (the 'exposome') in pilot intervention and large-scale epidemiological studies (in collaboration with DEX, NEP, ENV, IMO). Development of novel analytical methods based on mass spectrometry to measure targeted fractions of the exposome in cancer epidemiological studies.
2. Application of advanced analytical methodologies (mass spectrometry, gas chromatography, immunoassays) and untargeted and targeted metabolomic approaches to measure the exposome and its fractions in epidemiological and/or intervention studies set up in high and low income countries (in collaboration with NEP, ICE, GEP, EGE). Evaluation of the variability of the exposome. Identification of biomarkers of dietary, environmental, lifestyle and metabolic factors associated to cancer outcomes and intermediate endpoints in exposome-wide association studies.

**Expected outcomes:**

1. Novel biomarkers of exposure for foods (coffee, meats, fruit and vegetables, alcoholic beverages), food constituents (dietary fibers), food contaminants (endocrine disruptors) and other environmental factors, and metabolism (obesity). Development of the Exposome-Explorer database on biomarkers of exposure to cancer risk factors; release of dietary biomarkers component by mid-2016.

2. Robust high-throughput methodologies for measuring the blood and urine exposome and some specific fractions (dietary biomarkers, hormones, endocrine disruptors) for environment-wide association studies.
3. New information on dietary, environmental and metabolic factors predicting cancers (with a special focus on breast, thyroid, colorectum, skin and prostate cancers) providing new insights into the mechanisms of tumorigenesis with important implications for risk prediction and novel prevention strategies.

## Dietary Exposure Assessment Group (DEX)

**Specific aims:**

1. **Set-up a worldwide Nutrition Surveillance to support IARC/WHO action plans on diet-related cancers and other NCDs (IARC-WHO "Global Nutrition Surveillance" joint initiative).**
2. **Conduct targeted research on the main determinants of the global nutrition transition, and more specifically on the role of industrially processed foods on the global disease burden.**

**Major approaches:**

Building on the longstanding dietary research experience of DEX at the international level and following a stepwise strategy, we intend to:

1. Implement the DEX standardized dietary methodology (GloboDiet program and its support e-research infrastructure) in National dietary monitoring surveillance systems (representative sample, N=2000 individuals) in 2 to 4 pilot countries in the 6 WHO regions. A five-step approach will be followed, including 1) the preparation of the GloboDiet country-versions; 2) the validation (incl. feasibility piloting) of these versions; 3) their implementation in the national surveillance system of the selected countries; 4) the broader expansion to other regional countries and development of local hubs; and 5) provision and analyses of standardized dietary data for multiple research, surveillance and prevention purposes. The project will build on a strong internal (CSU, ETR, BMA, NEP, ITS) and external network (WHO, National institutes of health network, FAO, EFSA, ANS).
2. Targeted research to better measure, understand and monitor the global nutrition transition and investigate its (trend) associations with cancer and other NCD, including obesity:

    a. *Holistic measurement of dietary exposures* through more diet-biomarker integrated (e.g. plasma specific biomarker of highly processed foods or other new biomarkers relevant for nutritional surveillance and research) and multivariate approaches (e.g. nutrient patterns).

    b. Targeted projects on *"highly processed foods"* starting from methodological developments to research implementations, with a particular focus on more vulnerable population groups such as "*obese people*", "*children and adolescents*", "*elderly*", "*low economical social*" classes.

3. This research will build on existing dietary exposure and endpoint data (EPIC, BBMRI-ERIC, DEDIPAC, cohorts in LMICs) and new data to be collected through the IARC-WHO "global nutrition surveillance" joint initiative (DEX specific aim 1). This research will be done in close collaboration with partners within (BMA, NEP, CSU, MO) and outside IARC (e.g. GloboDiet consortium, WHO, EPIC, DEDIPAC, WCRF, BBMRI, FAO, cohorts in LMICs).

**Expected outcomes:**

1. Collection and provision of new standardized dietary data as a unique worldwide reference resource for joint research, surveillance and prevention, at the national, regional and international levels (N=25 countries worldwide; N=50 000 individuals, with an advanced "proof of principle" in Europe).
2. Provision of pooled analyses on comparable dietary exposure data worldwide to measure and monitor (trend) associations with cancer and other NCDs across countries and address some diet-related urgent questions, in close collaboration with CSU, WHO and the established networks and consortia.
3. Contribution to a better measurement, understanding and monitoring of the nutrition transition worldwide, through the use of cutting-edge integrated and multivariate diet-biomarker approaches. Provide evidence-base on the association between the global nutrition transition and its main determinants (particularly highly processed foods and its biomarkers) and the global cancer and other NCD burden worldwide.
4. Contribution to knowledge transfer, training and building capacities, and provide the missing frameworks for advancing more concerted research, prevention and policy actions, particularly in LMICs. Increased number of countries implementing the DEX methodologies for which the cost-effectiveness will be systematically measured and continuously improved through "evaluation questionnaires". Presence of regional hubs of the core e-research infrastructure and (e-)training facilities to support the "Global nutrition surveillance initiative" will be implemented locally, once fully developed and tested.
5. Strengthened inter-disciplinary and inter-UN agencies/organizations collaborations on an area of a major research and public health relevance worldwide. This long-term commitment will be strengthened through creation of consortia of National Public Health institutes and other key partners (advanced proof of principle in Europe before expansion to other regions) and strengthened direct collaborations with WHO-HQ, its regional offices and other UN agencies (e.g. FAO), through formalized agreements on the respective tasks and joint expected outcomes.

## Section of Genetics (GEN)

### Relevance to IARC mission

Identifying specific genes and gene variants that contribute to the development of cancer is important for a number of reasons. These include a greater understanding of how environmental/lifestyle factors may exert their effects in combination with genes as well as biological pathways that are involved in cancer. Elucidating germline variation that contributes to cancer relies on the study of populations with accurate evaluation of their lifestyle or environment. Thousands or even tens of thousands of cases and controls are needed to robustly identify new cancer genes and variants. These extremely large studies are beyond any national group making genetics very much an international endeavor, and the GEN section has a key role in initiating, coordinating and facilitating such international collaborative studies. Similarly, these genetic studies require a broad range of interdisciplinary expertise, drawing from the complementary strengths in genetic and lifestyle epidemiology, genetics/genomics, bioinformatics and biostatistics present within the Section's three scientific groups. GEN additionally interacts within other partners across the Agency and extensively externally in order to undertake these comprehensive genetic studies. In line with the Agency strategy, GEN studies involve extensive collaboration with colleagues in low- and middle-income countries, and they include an important focus on the rapidly expanding role for genetics and genomics in cancer prevention.

GEN projects involve extensive field-work in collaboration with external investigators to develop large-scale epidemiological studies with appropriate clinical data and biospecimen collection. This typically occurs within the Genetic Epidemiology Group (GEP), which also performs genome-wide genetic analysis and assesses the existence of gene-environment interactions. The Genetic Cancer Susceptibility (GCS) Group has a focus on identification of uncommon or rare genetic variants that contribute to genetic cancer susceptibility. GCS uses a variety of study designs, including familial and case-control studies, and advanced genomic and bioinformatic techniques. GCS also manages much of IARC's genomics and bioinformatics capability for other IARC scientific groups. The Biostatistics (BST) Group provides the statistical foundation for GEN projects and contributes to the ever-evolving field of bioinformatics.

## Genetic Epidemiology Group (GEP)

### Specific aims:

1. **To identify novel cancer predisposition genes through large scale case-control studies of selected cancers and to understand how specific genes may interact with known or suspected lifestyle or environmental exposures.**
2. **To identify how genomic markers may contribute to the early detection of specific cancers.**
3. **To identify whether germline or somatic (i.e. tumour) variants implicate lifestyle causes of cancer or are associated with clinical outcome.**

4. **To develop, maintain and coordinate large-scale international case-control or cohort studies, along with international consortia, in order to facilitate international genetic epidemiology research.**

**Major approaches:**

1. Development of large-scale international consortia of case-control and cohort studies, specifically for three cancer sites – lung, head and neck, and kidney. Conduct of comprehensive genome-wide association studies for each of these cancers. Study of potential gene-environment interactions including comprehensive evaluation of environmental and lifestyle risk factors, incorporating biomarkers of exposure where appropriate.
2. Extensive evaluation of important risk factors in relevant study populations (with a priority for cohort studies), coupled with large-scale analyses of germline genetic variation using a Mendelian randomization framework to obtain conclusive evidence of causality.
3. Tumour sequencing of selected cancers to identify mutation profiles that may be indicative of specific exposures. Study biomarkers for early detection, including circulating tumour DNA, circulating miRNA profiles and HPV antibodies.
4. Analysis of somatic mutations in tumours using case-control studies or case-series with comprehensive information on risk factors and clinical outcome in diverse populations.
5. Continuing recruitment and follow-up of case-control studies for lung, head and neck and renal cancers, in particular in high-risk regions of central Europe and South America. Coordination of large cohort studies including those in Russia, Iran and Europe.

**Expected outcomes:**

1. Completion of large international genome-wide association studies, and identification of novel genetic loci for lung, head and neck, and renal cancers.
2. Further elucidation of non-genetic risk factors for these cancers including nutritional and infectious agents, and how they interact with genetic factors.
3. Identification of high-risk groups for both cancer onset and poor outcome.

## Genetic Cancer Susceptibility Group (GCS)

**Specific aims:**

1. **Identify high impact genes involved in susceptibility for lung, head and neck (including nasopharyngeal), and renal cancers, as well as lymphomas, using sequencing and imputation techniques.**
2. **Investigate somatic events associated with environmental and lifestyle exposures and how they relate to germline variation to influence cancer etiology.**

**3. Develop laboratory methods and analysis to evaluate the potential of circulating biomarkers for early detection of cancer.**

**4. Develop, adapt and optimize genomic and bioinformatic techniques to suit the GCS Group, the GEN Section and the wider needs of the Agency.**

**Major approaches:**

1. Use next generation sequencing to investigate the contribution of uncommon genetic variation to cancer susceptibility. Validate and explore findings using larger scale targeted sequencing in cases and controls selected within the GEN biorepositories or through imputation techniques within the large GWAS resources available to the GEN Section.
2. Explore how genetic susceptibility may be mediated by considering the relationship between gene expression levels (eQTL) and somatic mutations (number or types of mutations). GCS also develops novel analytical methods using both somatic and germ-line events to further enhance susceptibility gene discovery.
3. Investigate genetic susceptibility to nasopharyngeal cancer, interactions with environmental exposures, Epstein-Barr virus and tumour biology across populations and ethnicities.
4. Develop laboratory protocols and bioinformatics analysis for the evaluation of novel non-invasive biomarkers for early diagnosis of cancer, such as ultra-deep next generation sequencing to detect circulating tumour DNA or gene expression profiling of exosomal RNAs from plasma samples.
5. Develop semi-automated workflows for tailored, flexible and cost-effective genomic analysis of IARC's large, heterogeneous sample collections. Provide bioinformatics capacity, ensuring that necessary computing resources and analytical protocols are available for genomics analysis. Incorporate quality control measures throughout these processes to ensure high data quality. These facilities are made available to IARC scientific groups through the Genetics Platform (GSP). Working closely with various IARC committees (Laboratory Steering Committee [LSC] and Bioinformatics Steering Committee [BISC]) and scientific groups, GCS also coordinates the development of genomic and bioinformatics capacity of the Agency.

**Expected outcomes:**

1. Through the identification and description of genes involved in cancer susceptibility, contribute to the elucidation of cancer etiology and their potential for risk prediction with a specific focus on lung and head and neck tumours.
2. Develop and apply genomics techniques for identification of circulating genomic biomarkers including circulating tumour DNA, and test their utility for early detection of cancer. Specific cancers of interest will include lung, head and neck, kidney, pancreas and bladder cancers.
3. Facilitate access to genomics and bioinformatics expertise in the Agency, foster collaborations between IARC groups.

## Biostatistics Group (BST)

**Specific aims:**

1. **Assure the legitimacy of statistical procedures used to minimize mistaken inferences, while optimizing power and precision by helping choose appropriate statistical tools.**
2. **Work in close collaboration with investigators in GEN and other Sections to guide study design and sequencing strategies to optimize information collection relative to specific hypotheses.**
3. **Seize opportunities to fill methodological gaps revealed through analyses undertaken in GEN.**

**Major approaches:**

1. Propose, evaluate and refine methods for variant calling in the non-standard circumstances that arise in non-standard contexts such as heterogeneous tissue, circulating tumour or cell-free DNA.
2. Develop, refine and adapt methods for recognizing signatures of toxins or carcinogenic mechanisms in whole-genome or whole exome sequence, arising from small samples and potentially non-human experimental sources.
3. Respond to day-to-day needs of biological researchers seeking to relate cellular features to epidemiological observations of outcomes or exposures.

**Expected outcomes:**

1. Collaboration within GEN and with other Sections resulting in improved methodology and analyses. Progress will be made in emerging areas of cross-species genetic signatures, linking tumour and germ-line sequence data, and circulating DNA.

## Section of Early Detection and Prevention (EDP)

**Relevance to IARC Mission**

The Section of Early Detection and Prevention (EDP) is responsible for evaluating specific prevention and early detection interventions for major cancers such as breast, cervix, large bowel, head and neck, and stomach among others and for documenting the results in terms of their feasibility, safety, acceptability, efficacy and cost-effectiveness in collaboration with national investigators in different countries, particularly in low- and middle-income countries (LMICs). The broad objectives of the research studies are to inform and guide development of rational public health policies in the context of overall cancer control initiatives, and to catalyze the development, implementation and scaling-up of population-based prevention and early detection programs with inbuilt quality assurance, monitoring and evaluation mechanisms, particularly in public health services in LMICs. The Section is involved in investigating the means and outcomes of implementing effective prevention and early detection strategies including

screening and early diagnosis initiatives in routine health services. It undertakes assessment of current prevention and early detection initiatives in suitable health service and academic platforms in LMICs and recommends priority actions to improve the implementation and outcomes of such interventions.

The Section provides technical support to national governments in LMICs for on-going and planned population-based prevention and screening programmes and stresses the importance of linking early detection services with good quality treatment and follow-up care in order to realize the full potential of early detection in reducing cancer deaths and in improving quality of life, in addition to cost savings, in the overall context of cancer control programmes. The research projects from the Section are implemented through appropriate national institutions and national health service platforms in order to promote development of prevention and early detection services and local capabilities and capacity as a positive sequel to research. The Section performs situational analysis of cancer prevention and early detection interventions in the context of NCD and national cancer control programmes in LMICs with various international partners and provides recommendations for improving primary prevention and early detection interventions in response to the national cancer control needs.Considerable importance is given to the development of training materials and training of service providers as master trainers in the context of the research initiatives to induce a cascading effect on the development of trained human resources for cancer prevention and early detection in LMICs. These activities are in tune with the overall mission of the Agency aiming to reduce cancer burden.

## Prevention and Implementation Group (PRI)

### Specific aims

1. **To evaluate new cancer preventive strategies, with particular emphasis on the use of new technologies, including molecular markers.**
2. **To engage in research on methods to implement existing strategies taking into account the social, economic and cultural differences.**
3. **To collaborate with decision makers to implement already available preventive interventions against cancer, particularly in LMICs where the need is highest.**
4. **To foster technology transfer and generate educational processes for clinicians, public health decision makers and the public, to make sure the available technology is put in place where it is most needed.**

### Major approaches

1. Population-based randomized clinical trials to evaluate safety and efficacy of primary preventive interventions against HPV-related cancers. A large randomized clinical trial of the bivalent HPV vaccine (PEG) is underway in Costa Rica in collaboration with the US National Cancer Institute. High efficacy of the vaccine has been demonstrated against vaccine-type HPV infection or lesions of the cervix, vulva, anus and oral cavity. Further follow-up will provide information on safety, immunogenicity and efficacy up to 15 years after vaccination.

2. Randomized trials to evaluate safety and efficacy of primary preventive interventions against gastric cancer. Two randomized clinical trials of Helicobacter pylori eradication are underway in Korea and Latvia. The study in Korea (HELPER) will recruit 12 000 subjects 40-64 years old participating in the Korean National Gastric Cancer Screening Program. Subjects will be screened for *H pylori* and randomized to eradication therapy or placebo and actively followed for 10 years to determine efficacy of the intervention for gastric cancer prevention, in addition to its safety, adverse consequences, feasibility and cost effectiveness. The study in Latvia (GISTAR) plans to recruit 30 000 subjects aged 40-64 years old randomized to screening with *H pylori* and pepsinogen test or to no intervention. In the intervention group, those with abnormal pepsinogen will be referred to endoscopy for appropriate management and follow-up and those with *H pylori* will be treated. Follow-up will continue for 15 years to investigate the utility of this screening approach to reduce gastric cancer incidence and mortality.

3. Evaluation of efficacy, safety and implementation approaches for screening interventions in large scale population studies. A screening trial to investigate triage alternatives for HPV positive women in the context of HPV-based programmes is being conducted among approximately 50 000 women 10 Latin American countries (ESTAMPA). The study will evaluate the performance of visual, cytologic and molecular tests for prediction of advanced cervical cancer precursors.

4. Multi-centric population-based studies to investigate prevalence and determinants of cancer risk factors in high- and low-incidence areas of specific cancers (e.g. stomach) The ENIGMA study will consist of a series of population-based prevalence surveys of *H pylori* infection in subjects 1-69 years old. Random samples of defined populations (700 in each site) with high- and low-incidence of gastric cancer will be recruited to investigate possible bacterial, host or environmental explanations for the differences in incidence, estimate future gastric cancer incidence and determine antibiotic resistance patterns. In some areas treatment will be offered and it will be possible to investigate feasibility and acceptability of *H pylori* eradication at the population level.

5. Collaboration with policy makers and clinical groups in the establishment and improvement of cancer prevention interventions, particularly the establishment of HPV-based organized screening programmes. The role of PRI is mainly focused on advocacy, participation in development of procedures and guidelines, training and impact assessment of the interventions.

### Expected outcomes

1. Confirmation of the long-term efficacy and safety of the bivalent vaccine against HPV infections at different anatomic sites; used by WHO to update its recommendations and used by other international organizations, professional organizations and national governments in setting guidelines for and implementing integrated vaccine and screening policies for cervical cancer prevention.

2. Definition of the potential population impact of population screen-and-treat programmes of Helicobacter pylori eradication to prevent gastric cancer, including clarification of target

groups, feasibility and safety of the intervention and the potential role of biomarkers for risk-stratification for Helicobacter pylori screen and treat; used by WHO and its regional and country offices, UICC, professional organizations and national governments to develop guidelines and implementing gastric cancer control programmes.

3. Definition of the safest and most cost-effective triage methods for HPV positive women in the context of screening programmes based on HPV testing. The results are expected to be used by WHO, international alliances such Cervical Cancer Action-Coalition to stop cervical cancer (CCA), UICC, and national governments and professional organizations as a major resource for development and implementation of evidence-based cervical cancer screening policies and training initiatives in LMICs by national and provincial governments.
4. Clarification of the yet unexplained extreme regional variations in gastric cancer incidence, development of predictive models of future gastric cancer incidence around the world and definition of H pylori treatment regimes for different geographic regions on the basis of antibiotic resistance patterns. The results may be used by the WHO, professional organizations and national and regional governments to establish gastric cancer control programmes.
5. Improvement of cervical cancer control programmes in low- and middle-income countries with reductions in incidence and mortality.

## Screening Group (SCR)

**Specific aims:**

1. **To evaluate optimum screening tests, screening frequencies, methods and treatment modalities for cervical intraepithelial neoplasia (CIN) in preventing cervical cancer in LMICs.**
2. **To evaluate the efficacy of less than 3-doses of HPV vaccination in preventing persistent vaccine-targeted HPV infection and cervical precancerous lesions.**
3. **To evaluate the value of clinical breast examination (CBE), breast awareness linked with diagnosis and treatment and alternative and affordable imaging modalities in early detecting and reducing breast cancer mortality in LMICs.**
4. **To evaluate the means and effectiveness of scaling up colorectal cancer screening with faecal immunochemical blood test (iFOBT or FIT) screening and triaging of screen positive persons by colonoscopy through routine health services in middle-income countries.**
5. **To provide technical support and conduct operational research in implementing cancer screening and early diagnosis programmes in the context of noncommunicable diseases (NCDs)/cancer control initiatives in LMICs.**

**Major approaches**

1. Long-term (10 or more years) population-based follow-up studies involving more than 200 000 women positive or negative on human papillomavirus (HPV) testing, cytology screening and visual inspection with acetic acid (VIA) screening and of more than 3000 women with CIN treated by different modalities permits estimation of cervical cancer incidence reductions in these different subgroups by linking with cancer registries. The value of cytology, HPV genotyping and VIA triage of HPV positive women in the early detection and prevention of cervical cancer is evaluated in a cluster randomized trial in India and in a cross-sectional study in Thailand.
2. The efficacy of 1-, 2- and 3-doses of HPV vaccination in inducing immunogenicity and preventing vaccine-targeted and non-targeted HPV infection and CIN is being investigated in a multicentre follow-up study involving 17 700 girls in India.
3. A cluster randomized trial in India involving 120 000 with 12-year follow-up is examining the impact on breast cancer mortality of 3 rounds of CBE screening followed by triage of CBE positive women by triple diagnosis (physician CBE, diagnostic imaging and fine needle aspiration cytology (FNAC/excision biopsy) compared to breast awareness messages and improved access to diagnosis and treatment from routine health services. This study also evaluates the value of FNAC, triple diagnosis and alternative imaging modalities based on near infrared and breast tissue elasticity in the early diagnosis of breast cancer. The value of breast awareness in improving early diagnosis is also evaluated in a 30 000-person cohort study in a health maintenance organization in Mumbai, India. Patterns of care for breast cancer management will be addressed in the context of these studies. The accuracy of near infrared imaging and breast tissue elasticity in detecting early breast lesions will be evaluated in cross-sectional studies. Cost-effectiveness of the different interventions will also be addressed.
4. Long-term (5 or more years) population-based follow-up of people screened with FIT is being carried out in the population of Lampang Province in Thailand. The documentation of CRC incidence and recurrence rates will permit evaluation of the negative predictive value and effectiveness of 5-yearly FIT screening and triaging of screen positive persons by colonoscopy in populations with intermediate incidence rates of CRC. Operational research involving scaling up of FIT screening in 5 provinces of Thailand will be analysed. Cost-effectiveness of FIT screening will also be evaluated.
5. Technical support is provided in implementing a nationwide VIA screening programme in Bangladesh, state-wide VIA screening, breast cancer screening with CBE and oral visual screening in Tamil Nadu state, India, and HPV testing based cervical screening in 5 provinces of Thailand. Technical support for early detection and treatment of cervical cancer in selected health service platforms is provided in Angola, Mali, Morocco, Guinea and Republic of Congo and in HIV care platforms in Botswana. Technical support in situational analysis of prevention and early detection and recommendations to improve these interventions in the context of national cancer control programmes is being provided in a number of LMICs. Operational research to implement cancer prevention, early detection and treatment services and to improve health service capacity in cancer care is being planned in

Timor-Leste. Training manuals for breast, cervix, colorectal and oral cancer screening are being revised.

**Expected Outcomes:**

1. Clear recommendations on resource stratified, feasible and effective screening and treatment strategies of CIN for prevention of cervical cancer will emerge that may be used by the WHO and its regional and country offices, other UN agencies such as UNFPA, World Bank, international alliances such CCA and UICC, and national governments and health care regulatory and financing authorities in countries and professional organizations as well as by international cancer control consultations such as those by IAEA/PACT. These findings will be a major resource for development and implementation of evidence-based cervical cancer screening policies and training initiatives in LMICs by national and provincial governments.
2. Clear recommendations on the value of a single and two-dose HPV vaccination in preventing cervical cancer will be obtained and the optimum integration of HPV vaccination and low-intensity HPV screening for cervical cancer prevention in LMICs will be clarified. These findings may be a valuable resource for organizations such as the WHO, Revolving Fund of PAHO, other UN agencies such as UNFPA and UNICEF, World Bank, international alliances such as GAVI Alliance, CCA and UICC, professional organizations and national governments in setting guidelines for and implementing integrated vaccine and screening policies for cervical cancer prevention.
3. An understanding of the impact and cost-effectiveness of systematic CBE screening and breast awareness linked to early diagnosis will underpin the development of breast cancer control policies in LMICs. The value of alternative imaging modalities, fine needle aspiration cytology and triple diagnosis in breast cancer early diagnosis will be established. These results may be used by WHO and its regional offices, organizations such as the Breast Health Global initiative (BHGI) and UICC, professional organizations such as AORTIC, international cancer control consultations such as those by IAEA/PACT and reviews by Cochrane Collaborations to catalyse breast cancer early detection policies in low- and middle-income countries.
4. Factors important in the implementation of CRC screening and colonoscopy triage will be established. The experience gained in Thailand will be useful to scale up screening and treatment in other middle-income countries. The utility and safety of 5-yearly FIT screening in middle-income countries will be clarified. The findings may be used by WHO, UICC, IAEA PACT missions and national governments in MICs in evolving public health policies of colorectal cancer screening.
5. Considerable operational research experience in assessing, evaluating and improving cancer prevention and early detection programmes in routine health services in LMICs will be accrued. These skills will empower IARC as major resource within WHO for planning, monitoring, implementing and evaluating cancer control initiatives in LMICs. IARC will be a major resource for training materials, training programmes for master trainers in cancer screening and in implementing cancer programmes linking early detection with treatment in LMICs.

## Director's Office

A number of Groups within the Director's Office provide support for the Scientific Groups, specifically the Laboratory Services and Biobank; the Education and Training Group and the Communications Group. These support structures are also informed in their activities by committees comprised of personnel across the Agency. These include the Laboratory Steering Committee, the Biobank Steering Committee and the Advisory Committee on Publications.

The three Groups have specific aims and expected outcomes in line with the MTS and providing support to the planned activities of the scientific Sections of the Agency.

## Laboratory Services and Biobank (LSB)

### Relevance to IARC mission

The main activities of the Laboratory Services and Biobank Group (LSB) are operational, safety and quality control in relation to laboratory services, and the management of the IARC Biobank (IBB), to enhance IARC's role in international cancer research. LSB also works in supporting the establishment and upgrading of biobanks in LMICs.

The following activities are key to the Agency's Medium-Term Strategy:

a. **Management of the IBB and pre-analytical processing services** – by providing a safe and secure environment for IARC's resources, catering for the increasing demand on biospeciment storage, and providing services in sample retrieval, DNA extraction and quantification and shipment.
b. **Development of biobanks in LMICs** – through the Biobank and Cohort building Network (BCNet), IARC provides expert advice and training in biobanking to promote the establishment and improvement of institutional and national biobanks amongst the members of the network. Through collaboration with other networks and societies, the BCNet provides links between LMICs and the international community to facilitate research collaborations.
c. **Provision of laboratory support to IARC research Sections** – by monitoring the common laboratory platforms including equipment, implementing and monitoring good laboratory practices, and providing advice and training on laboratory health and safety for staff and newcomers.

### Specific aims:

1. **To maintain and manage the IBB according to international guidelines and principles and provide high-quality samples for research.**
2. **To support the increase in biobanking and access to quality biological samples and associated data available for research both in and from LMIC settings.**
3. **To support common laboratory research platforms and maintain state-of-the art facilities and standard practices through the implementation and monitoring of equipment, facilities and standard operating practices.**

**Major approaches**

1. **Maintain and manage the IBB**. The major requirements are to provide a safe and secure environment for existing and new biological samples; to introduce standard systems of collecting and archiving samples with associated data including data on sample quality; to provide a complete catalogue of stored samples; to manage the use of samples through the sample access procedure and to introduce new services in the pre-analytical platforms, e.g. DNA extraction from dried blood spots and tissue samples.

    a. Developing and expanding IARC infrastructure: the storage space and facilities to accommodate new samples need to be expanded together with the extension of the automatic freezer monitoring systems.
    b. The adoption of a minimum data set will provide the tool for collecting standard data on sample collections through the completion of specially designed forms to provide relevant information.
    c. Organize the reception and distribution of biological samples to and from IARC to ensure that the resources are managed and used efficiently through the established sample access policy thus contributing to supporting scientific research collaborations.
    d. Introduce new technologies to upgrade and provide new services in areas such as DNA extraction from small sample volumes and from samples other than whole blood.

2. **Collaboration with the international community and LMICs to increase biological resources available for cancer research.** The development of a catalogue of biobank resources in LMICs will provide a useful new platform for research. This will be done in conjunction with conducting education and training programmes and providing access to biobanking Standard Operating Procedures (SOPs) for sample collection and management including ethics, legal and social issues in LMICs.

    a. Build LMIC biobanking infrastructure: develop and share templates of regulatory documents on ethical, legal and social issues for LMIC biobanking, e.g. access policy and informed consent and SOPs for the collection and management of quality biological resources.
    b. Build BCNet partner and member relationships. The cataloguing programme will provide the platform for resource sharing, increasing the visibility of available biological material and promoting research collaborations.
    c. Develop close links with the international community and LMICs to increase biological resources available for cancer research. In collaboration with Centre for Global Health, NCI, USA and other biobanking organizations, networks and societies, implement development and training programmes to establish and upgrade biobanking infrastructure in LMICs.
    d. As a member of Biobanking BioMolecular Resources Research Infrastructure Consortium (BBMRI-ERIC), provide a link with the European biobanking community to access services and platforms to improve the level of LMIC biobanking.

3. **Manage the IARC common laboratory research platforms.** Monitor common equipment and services to ensure that the facilities are fit for purpose. Maintain a safe environment for staff and ensure that personnel receive up-to-date instruction and information on health and safety at work.
    a. Develop the IARC laboratory infrastructure, by implementing maintenance and upgrade schedules for equipment. In collaboration with the Laboratory Steering Committee, identify new technologies and equipment investment required to maintain a high quality laboratory research platform.
    b. Support laboratory groups by providing services to better answer their needs, developing Good Laboratory Practices, implementing SOPs as a tool to better control experimental protocols and to enhance safer and harmonized working conditions in the laboratories, thus improving the quality of experimental research.
    c. Provide regular safety briefings to newcomers and refresher courses for laboratory personnel on safe work practices and new procedures and regulation.

**Expected outcomes:**

1. Establish an 'IARC minimum dataset' to improve the quality of data and information on samples stored in the IBB and maintain an up-to-date catalogue of IARC biological resources.
2. Launch the revision of the IARC green book 'Common Minimum Technical Standards and Protocols for Biological Resources Centres Dedicated to Cancer Research' by 2017.
3. Following the launch of the BCNet catalogue in 2015, at least 50% of the 16 BCNet founding members will provide data for the online catalogue by 2016.
4. Ongoing improvement to the IARC laboratory services platform, with continued participation in the discussion and planning for the 'Nouveau Centre' project, in particular contributing to the development of the biobank and laboratory facilities.

## Education and Training Group (ETR)

### Relevance to IARC mission

For five decades as a core statutory function of the Agency, the IARC's Education and Training programme has made a substantial contribution to the development of human resources for cancer research in many countries. Two main lines of activities have been developed: the provision of training through the award of fellowships and participation in collaborative research projects; and the delivery of training courses, basic and advanced. The programme has in turn contributed to the shaping of the Agency's research strategy and to widening the network of collaborators as well as to the promotion and enhancement of IARC's reputation and standing worldwide as an international organization.

The mission of ETR is to coordinate the various IARC training initiatives and promote them both internally and externally.

**Specific aims:**

1. **To provide early career scientists with training at IARC in those aspects of cancer research related to IARC's mission, in order to build a new generation of cancer researchers and reinforce cancer research worldwide, especially in LMICs.**
2. **To attract top international cancer researchers to IARC to spend various periods of time contributing to the Agency's programmes and making IARC an ideal environment for education, training and exchange.**
3. **To develop new opportunities at IARC for further professional development for early career scientists and other public health professionals in order to support and promote the development of cancer research and prevention.**
4. **To bring IARC learning and training resources closer to their target audiences, by developing eLearning material and initiatives.**
5. **To stimulate research in cancer epidemiology, as well as enhance cancer surveillance, detection and prevention by developing individual and institutional expertise in areas of IARC competence through training courses.**

**Major approaches:**

1. **Early Career Scientists.** The Postdoctoral Fellowships will be further developed in order to offer 15 new awards each year for postdoctoral scientists to be trained at IARC. The current funding sources and partnerships will be maintained. The current model of bilateral agreements will be expanded and new models explored.

   The Post-doctoral Charter will continue to be implemented and developed, including the organization of generic courses, in order to optimize the training environment and enhance career prospects for all postdoctoral scientists.

   Current links with universities will be strengthened and new partnerships developed, to ensure that IARC is officially recognized as a host institute for PhD and master students.

   Support will be provided to the 'Early Career Scientist Association' (ECSA) so that opportunities for training, career development and social activities are promoted for early career scientists, and that ongoing dialogue is maintained between them and the IARC management.

   Efficient administrative management of all early career and visiting scientists benefitting from the IARC Research Training and Fellowship Programme will continue to be ensured.

2. **Senior Scientists.** The Senior Visiting Scientist Award will be continued with two to three Awards offered each year to top researchers to work at IARC on a collaborative research project. The Expertise Transfer Fellowship will be further promoted to ensure one award is offered each year, enabling an experienced investigator to spend 6–12 months in a host institute in a LMIC in order to transfer knowledge and expertise in a research area relevant to the host country and related to the Agency's programme.

3. **Short-term fellowships.** Fellowships for short stays at IARC (3–4 months) will be established in order to transfer specific skills and develop research capacity in the home institution. Such fellowships will be based on the model developed with the Union for International Cancer Control (UICC), which allows one participant from the Summer School to return to IARC to receive further training. Other models, such as "Sandwich Fellowships" between home institutions and IARC will be explored.

4. **eLearning.** The ETR website will provide an IARC online learning platform, providing a single entry point to all IARC Education and Training initiatives, with information about the calendar of planned events, application forms, learning and training resources, links to reference materials, etc. Specific fund-raising activities will be carried out in order to customize and set up existing Learning Management Systems to develop a dedicated platform for activities in this area as well as to produce and publish eLearning material in English and other languages.

   An IARC webinar series will be set up, building on certain seminar cycles currently organized at IARC. The sessions will be recorded and material posted on the site for free access. The target will be to organize four events per year.

5. **Courses.** The Summer School consists of a series of training modules offered each year at IARC. Emphasis has been on providing training in epidemiology, with modules on cancer registration, descriptive and analytical epidemiology. Advanced modules will be developed in areas of IARC competence, including exploring new opportunities in the area of implementation research.

   Partnerships will be set up in order to run online courses expanding the target audience of existing IARC courses, such as the "Introduction to Cancer Epidemiology" module of the Summer School. The priority will be to develop online courses in languages other than English.

   In its function to oversee the portfolio of IARC Education and Training initiatives, ETR will continue to monitor the provision of courses initiated by IARC scientific Sections. According to the needs, ETR will also collaborate with Sections for the design, development, organization and/or evaluation of education and training materials, courses or programmes.

**Expected outcomes:**

1. IARC Fellowships awarded to early career and visiting scientists.
2. IARC online learning platform set up.
3. Courses organized and documented in areas of IARC competence.
4. Partnerships set up in order to develop relevant education and training programmes.

## Communications Group (COM)

### Relevance to IARC Mission

The effective communication and dissemination of IARC's research is central to the Agency's mission. To ensure a global approach to knowledge dissemination, the Communications Group (COM) builds on existing external networks with WHO staff in HQ and the Regions and with various organizations (UICC, national and regional cancer institutes and centres, etc.), and on links with all IARC Sections. COM is responsible for presenting a coherent image of all aspects of IARC's work to the scientific community, policymakers, funders, the media, and the general public, thus ensuring IARC's reputation as an authoritative and unbiased source of information. COM accomplishes these overarching goals through activities in the following areas: 1) the Knowledge Management Centre, comprising the library and publications programme, 2) editing and translation, 3) public and media relations, and 4) web services. With its strategic planning exercise in 2012–2013, COM articulated as its focus the transition from print-based to digital publishing.

### Specific Aims

1. **Broadly disseminate both open access and fee-based IARC publications and provide greater access to audiences in LMICs while continuing to ensure a revolving fund from sales of publications to sustain the publications programme.**
2. **Establish a unified, online platform for IARC knowledge and information that meets users' needs and industry standards for digital publishing.**
3. **Establish digital publishing and revenue models for the WHO Classification of Tumours series and other publications.**
4. **Raise awareness of IARC's work and mandate in the media and general public and ensure a consistent and clear brand image.**
5. **Advance and promote IARC's high-level research profile by providing timely and accurate cancer research information via the web.**

### Major Approaches

1. A wide range of activities is needed to support the goal of broad dissemination. For scholarly journal articles authored by IARC staff, this requires internal organization and training in the form of open access policy monitoring and supporting IARC scientists in negotiating author copyright transfer agreements. Engagement of external partners will be required for increased dissemination of IARC-produced books and publications. COM will continue to establish relationships with reputable organizations to make IARC content accessible to the widest audience possible: in July 2014 IARC became a participating publisher in HINARI, a programme set up by WHO together with major publishers to enable institutions in LMICs to gain access to one of the world's largest collections of biomedical and health literature. Monographs and other freely available IARC-produced books and series will be deposited in the USA National Library of Medicine's PubMed Bookshelf and other similar repositories as appropriate. COM will cooperate with scholarly information aggregators and vendors in order

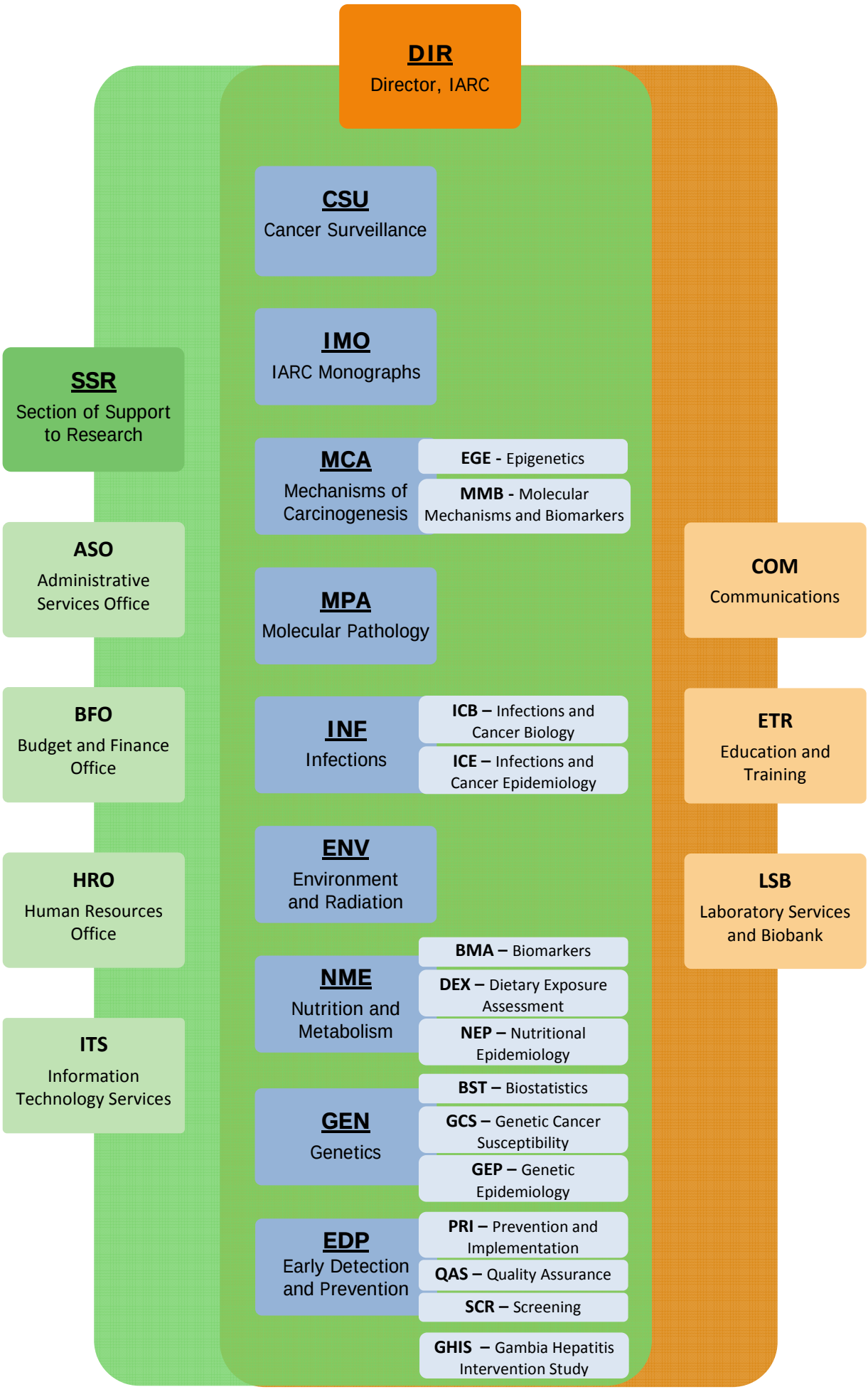
to facilitate access by academic institutions, hospital libraries, research centres, and other target audiences.

2. A significant technology investment is required to enhance the value and visibility of IARC's publications and meet the expectations of an audience well-versed in scientific, technical, and medical (STM) online content. PubCan is an online database currently under development that brings together IARC publications content in a dynamic and cross-searchable format. It consists of three key components: the ICD-O-3 codes online, Monographs content, and WHO Classification of Tumours (Blue Books) content. PubCan aligns closely with COM's digital publishing strategy, and the vision for this database is the ability to offer IARC's readership an integrated and intuitive platform for timely, authoritative, and compelling content, both open access and fee-based. COM's role will be to launch and stabilize the platform over the period covered by the MTS.
3. The WHO Classification of Tumours (Blue Books) series is a key reference title in diagnostic pathology and the primary revenue generator among IARC publications. As IARC transitions from a print-based to a digital publishing model, the Blue Books require particularly thoughtful planning. The development of technical and e-commerce infrastructure, a key objective, must reflect an approach to pricing and distribution that balances IARC's reliance on revenue, for the sustainability of Blue Books and COM activities, with affordability by LMICs and IARC's overarching support of open access. As with the goal of broadly disseminating IARC's publications, the transition of Blue Books to online publication and sales will require IARC to develop a range of new activities to establish and maintain the necessary infrastructure. Having sole responsibility for the distribution of Blue Books in electronic formats will require COM to learn quickly about digital distribution, but will provide the advantage of connecting more immediately with IARC's target audiences.

### Expected Outcomes

1. Launch and stabilization of an integrated, feature-rich web platform for IARC publications that brings IARC in line with current STM publishing practices and standards.
2. Increased availability of IARC-authored scholarly journal articles, either immediately upon publication with payment of article processing charges, or via self-archiving of manuscripts.
3. Availability of IARC fee-based titles for free or at low cost by LMICs through IARC's participation in the HINARI programme of WHO.
4. Establishment of technical and business infrastructures to support electronic distribution of IARC publications to both individuals and institutions.
5. Increased visibility of IARC's work through publications and journals, and also among the general public and media through media coverage, media activities, and press conferences.
6. Maintenance of a strong network of contacts with key mainstream and specialized media.
7. Set-up of Drupal Content Management System (CMS) for new IARC websites (dynamic content). Migration of previous IARC websites (static content) to an instance of the CMS.
8. Harmonized editorial, translation, and production processes and workflows, to ensure that publications are prepared efficiently and the highest standards are applied.

## SC/51/12 – Annex 2: IARC Organizational Chart

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