

**DIRECTOR'S RESPONSE TO THE SECTIONS OF
NUTRITION AND METABOLISM (NME) AND
EARLY DETECTION AND PREVENTION (EDP) REVIEWS,
HELD AT IARC IN JANUARY 2013**

1. A number of responses have followed from the peer-review for both the Section of Nutrition and Metabolism (NME) and the Section of Early Detection and Prevention (EDP). These are detailed below by Section and, where appropriate, by Group.

RESPONSE TO THE REVIEW OF THE SECTION OF NUTRITION AND METABOLISM¹

2. Overall, the work of the Section was highly rated. A number of recommendations were directed to the Section overall and these are dealt with first, followed by any remaining points relevant to one of the Groups within the Section.

3. The Review Panel recommended the Section to develop a process for prioritizing research topics and to develop a strategy focused on areas of greatest expertise and unique strengths. There was also recognition of the additional opportunities to bring together the different disciplines across the Section and at the Agency.

4. In response NME has established a strategy to align priorities and goals, to better conceptualize, plan and integrate future projects. Major projects are focused on areas of expertise, integrating detailed dietary assessment, nutritional epidemiology and biomarkers as well as statistical analysis of multidimensional data. Examples of this approach include the work by NEP and BMA on metabolomics/lipidomic studies of liver, breast and pancreatic cancers and of NEP and DEX in assessing correlations between obesity measures and circulating fatty acids, as well as more generally on evaluation of exposure assessment, validity of dietary measurements, and measurement error correction procedures on EPIC data.

5. Major grants have been obtained to pursue this integrated approach (National Cancer Institute [INCa], France; World Cancer Research Fund). Regular scientific discussion and administrative meetings have been established within NME and its Groups resulting in a greater level of communication, awareness and collaboration between NME staff. In addition, a major part of the NME strategy, as exemplified by the leadership of multicentre projects, is to establish

¹ BMA = Biomarkers Group (Head, Dr Augustin Scalbert);
DEX = Dietary Exposure Assessment Group (Head, Dr Nadia Slimani);
NEP = Nutritional Epidemiology Group (Head, Dr Isabelle Romieu);
NME = Section of Nutrition and Metabolism (Head, Dr Isabelle Romieu).

and build upon collaborations, both internally (ongoing projects with ENV, EGE, GEN, MMB²), as well as internationally.

6. The Scientific Council supported efforts of the Section to phase in studies in low- and middle-income countries (LMICs). This work has begun in a number of areas. For example, DEX has established a network of nutrition research centres in Africa while NEP has collaborations on multicentre studies of breast cancer in Latin America and South Africa, as well as studies on early markers of metabolic disorders in Latin America.

7. The Scientific Council highlighted the need to bring the latest understanding of the biology of cancer to bear on the research programme to maximize the likelihood that the relationships investigated are causal and so that the outcomes can be fed back into cancer biology studies. NME is increasingly using this approach. Examples include the study of the metabolism of fatty acids in the onset of breast cancer and the involvement of metabolic and genetic factors in the etiology of colorectal cancer.

8. The Review Panel recommended to develop partnerships with WHO/HQ and other international organizations and to seek resource mobilization for this work through WHO. DEX has prepared a comprehensive document "Towards a global nutrition surveillance for risk assessment, research and prevention" which has been identified as a priority for IARC-WHO collaboration within the context of the Global Action Plan (2013–2020) on noncommunicable diseases (NCDs). This is under consideration by IARC and WHO.

9. In Europe, DEX has successfully expanded the national network of users of the EPIC-Soft dietary methodology to include Austria, Malta, and Serbia. For Africa, FAO expressed a strong interest to collaborate with IARC and WHO on the implementation of a pan-African monitoring survey, as well as the African Nutrition Leadership Program (ANLP) and the African Nutrition Society (ANS). In addition, a symposium devoted to the DEX African initiative (AS-PADAM project) has already been agreed for the 2014 African Nutrition Conference.

10. Biostatistical resources are progressively expanding, particularly from grant funding, to conduct methodological research. Overall, computing facilities and bioinformatics resources are growing at IARC and the NME Section is benefitting from these developments.

11. The Scientific Council noted the value in expanding the postdoctoral training programme and maintaining appropriate mentoring and professional development. These are areas of priority across the Agency, supported by the ETR Group, notably through the creation over the last year of the Early Career Scientist Association, which has a strong focus on career development. Within NME efforts to strengthen support to postdoctoral trainees has involved development of internal group seminars and literature review exercises as well as statistical training. As suggested by the Scientific Council, opportunities for junior staff to work across Groups are considered as a part of the overall project planning.

² EGE = Epigenetics Group (Head, Dr Zdenko Herceg);
ENV = Section of Environment and Radiation (Head, Dr Joachim Schüz; Deputy, Dr Ausra Kesminiene);
ETR = Education and Training Group (Head, Ms Anouk Berger);
GEN = Section of Genetics (Head, Dr Paul Brennan);
MMB = Molecular Mechanisms and Biomarkers Group (Head, Dr Jiri Zavadil).

Biomarkers Group (BMA)

12. The Review Panel recommended giving priority to completion of “proof-of-principle” work which would demonstrate the value of metabolomics for nutritional epidemiology and also to clarify the Group's Unique Selling Point. To address this, the Group has focused on development of exposome-wide association studies to identify novel risk factors for defined cancer sites (colorectal, breast and liver) and exposures (diet, hormones) of major interest for NME.

13. The Review Panel also recommended further developing collaborations for intervention and feeding studies. Different projects based on small scale intervention studies have been initiated to identify novel biomarkers of dietary intake (collaborations with the National Cancer Institute, USA; University College Dublin, Ireland and University of East Finland) and environmental pollution (collaboration in the EU-funded EXPOsOMICS consortium).

14. The opportunity to link metabolomics data to other omics approaches has been developed with Groups at IARC. Specifically, EGE and BMA participate in the same EXPOsOMICS consortium and will jointly analyse the epigenome and metabolome in several cohorts and intervention studies aimed at improving exposure measurements to environmental pollutants. Funding has also been applied for NME to combine metabolomic and epigenetic data in a project centred on adiposity and breast cancer risk.

15. The Scientific Council recommended utilization and cooperation in light of metabolomic resources available in the USA and elsewhere. This is an integral part of developments in BMA where active collaborations have been established with other leading metabolomics facilities (Universities of Alberta, California Berkeley, California Davis and Imperial College London). BMA recently organized the First International Workshop on the Food Metabolome and Dietary Biomarkers which gathered 50 experts from various countries in Glasgow (4–5 July 2013).

Dietary Exposure Assessment Group (DEX)

16. Following the Review, DEX is now focusing on the development and implementation of its dietary assessment methodologies. As recommended, DEX is working with other IARC Groups to support its activities: ITS³, for implementation of the web-research infrastructure; ETR for establishing an e-training platform to be linked to the research infrastructure; and COM, for the development of a dedicated website. In addition, DEX will establish collaborations with McGill University (Montreal, Canada) and INSA (Informatics Department; Lyon, France) to strengthen its IT activities.

17. The Review Panel noted the value in linking state-of-the-art assessments of physical activity to research on energy balance/obesity. These areas are now encompassed in collaborative research projects and networks including at the European level in DEDIPAC (Determinants of Diet and Physical Activity) and a DEX-led research proposal on “Obesity and risk of cancer” in the large EU-USA Consortium (CHANCES project). The Group is collaborating on a similar topic with experts from the Queens University Belfast (UK), the German Cancer Research Centre-DKFZ (Germany) and Wageningen University (Netherlands).

³ ITS = Information Technology Services (Head, Mr Philippe Damielcki);
COM = Communications Group (Head, Dr Nicolas Gaudin).

Nutritional Epidemiology Group (NEP)

18. The Scientific Council encouraged a leading role for NEP in EPIC. NEP is now working with all EPIC centres to coordinate and carry-out the centralization at IARC of follow-up lifestyle exposure data, which will be available to all EPIC researchers within and outside IARC; the Agency is also coordinating the process of an updated disease end-point follow-up. Further support for the centralization of data from EPIC centres has been obtained and two database managers will be hired to finalize the task. In addition, the Agency has assigned Dr Paul Brennan (Head, GEN) to the EPIC Steering Committee to ensure a broader participation from IARC in this key project.

19. The Scientific Council recommended careful consideration of the opportunity cost of diversifying into research on healthy ageing and to seek out appropriate expertise and collaborations. The Agency will maintain its cancer focus as a part of healthy ageing, but has an opportunity to integrate this with collaborative efforts on the wider topic of NCDs. For example, this is a part of the strategic direction of EPIC, with NEP collaborating as a work package leader on a major EU-project on healthy ageing (CHANCES project). Over the last year NME invited Dr Parminder Raina, PI of the Canadian Longitudinal Study on Healthy Ageing to IARC as a Visiting Scientist to increase collaborative expertise. Future developments will build on the strength of the EPIC cohort to evaluate multi-morbidity, covering most frequently occurring NCDs, in line with the "25 by 25" UN recommendations on reducing premature mortality from NCDs.

20. The Scientific Council asked the Group to consider whether it is timely to devote resources to epigenetic measurements and to establish good collaborative links within and beyond IARC. As mentioned above, the Group is collaborating closely with EGE at IARC (e.g. breast cancer epigenetic studies; birth cohort) and with external experts with dedicated laboratories and methodologies (e.g. Purdue University, USA; collaboration on liver cancer epigenetics).

RESPONSE TO THE REVIEW OF THE SECTION OF EARLY DETECTION AND PREVENTION⁴

21. The work of the Section was highly rated and the importance of this area of research to the Agency was strongly supported.

22. The Review Panel indicated that the overall recommendations made for the Section as a whole also applied to the individual Groups. These referred to perceived needs for: review of the overarching strategy for the Section; a decision concerning the model for acquiring the skills necessary to pursue a programme of research in implementation science; and continuing the dialogue with junior staff to further improve possibilities for professional development.

23. The above points were partly linked to the anticipated retirements of two of the three Group Heads in late 2014 and early 2015 and to new opportunities in implementation research. Specifically, points were raised about the degree to which the Section will truly address the

⁴ EDP = Section of Early Detection and Prevention (Head, Dr R. Sankaranarayanan);
PRI = Prevention and Implementation Group (Head, Dr Rolando Herrero);
QAS = Quality Assurance Group (Head, Dr Larry von Karsa);
SCR = Screening Group (Head, Dr R. Sankaranarayanan).

latter area, one the Review panel strongly supported, and also about new skills, e.g. health economics, policy research and behavioural science, needed for EDP to fulfill its potential. In this context also, the Scientific Council noted the requirement for additional support from the regular budget.

24. Future developments in EDP have been extensively considered since the Scientific Council last year. The Director invited Professor David Hill, a behavioural scientist and former UICC President, who has conducted implementation research, to spend several months at the Agency assessing the current activities and major opportunities. This resulted in in-house consultations, discussion groups and an extensive report made available for discussion by the IARC Senior Leadership Team. The Director has followed with more detailed planning discussions with the leaders within the Section.

25. A number of conclusions have been drawn from this process. The Section will continue its current activities in primary and secondary prevention (including screening, early detection, vaccination and eradication and quality assurance), particularly in LMICs where some of the important lessons from high income countries, e.g. on quality assurance, can be applied. The best opportunities in implementation research involve quantitative analyses of interventions in routine health services, in collaboration with national partners building on and improving existing skills and research collaborations. Despite the further constraints on the regular budget, additional resources will be needed for EDP in order to bring new and essential skills to the Section, in particular in implementation research and health economics whilst maintaining key elements of the current research programmes. While there are many research opportunities in LMICs, there are also related research areas of relevance to the IARC mission in the high-income countries, e.g. international comparisons of performance of cancer screening programmes, and development and evaluation of training in programme implementation. These opportunities will also be considered in the overall research portfolio of the Section.

26. Given current resources and skills, in the short-term the Agency would be likely to make less impact through investment in research into areas that are completely new to its expertise, for example, research into behavioural change e.g. in physical activity or weight loss, or more qualitative approaches. Where these skills are needed for specific research projects they would be sought through collaboration with centres of expertise.

27. Given the timescale for departure of senior staff and the need for careful planning, the process of transition will be developed over the coming year in close consultation with the scientific leadership and staff of the Section. During this process the Section leadership will continue the dialogue with junior staff to strengthen the possibilities for professional development.

Prevention and Implementation Group (PRI)

28. The Review Panel considered valuable the current and future work proposed by PRI on HPV vaccination, particularly the evaluation of alternative schedules in collaboration with the USA NCI, as well as the new initiatives to evaluate alternatives to triage HPV positive women in the context of HPV-based screening programmes. Similarly the proposed work on worldwide molecular epidemiology of *Helicobacter pylori* and its eradication were considered of potential importance for the future development of gastric cancer control programmes. The Group continues to work intensively in the above-mentioned projects and is envisioning an extension of its scope to include implementation research in the context of ongoing studies.

Quality Assurance Group (QAS)

29. The Review Panel recommended continuing the quality-assurance guideline work and considering expanding efforts to include LMICs; promoting and facilitating international comparisons of cancer screening performance; and strengthening research activities. In response to these recommendations, QAS is continuing work on the EU guidelines for quality assurance in breast cancer screening. It has completed piloting the first intensive training course of the European Schools of Screening Management (ESSM) in planning, implementation, quality assurance and evaluation of population-based screening programmes. It has also initiated collaborative projects with central Asian republics in evaluation and implementation of cancer screening and early detection.

Screening Group (SCR)

30. The Scientific Council noted the great majority of the intervention trials were based in India and stated that "having multiple countries involved would enhance the generalizability of the findings and experience gained in implementing the studies". There are a number of significant factors in the choice of India for these trials, including the required access to substantial health care resources through local government and the presence of population based cancer registries for passive follow-up of large trials (more than 800 000 participants). For example, the direct cost of all the four randomized trials with follow-up ranging from 10–15 years was less than 4 million US\$.

31. At the same time the Screening Group works extensively in other populations, notably on assessment of cancer screening in Bangladesh and Thailand; technical support to scaling up screening and treatment in Angola, Congo, Guinea, Mali and other African countries; provision of technical support to cervical screening training initiatives in Bangladesh, Guinea, Brazil and Peru; the evaluation of alternative breast screening technologies in China and Thailand; and a large scale colorectal cancer screening demonstration project in Thailand. These collaborations have been continued and demonstrate the feasibility of applying the principles tested and validated in trials in India to different settings.