

## **ACCEPTANCE OF GRANTS AND CONTRACTS AND RETURN OF INTEREST INCOME TO GRANTS**

### **1. Post facto reporting**

The Governing Council is invited to note the post facto reporting of grants and contracts accepted by the Director over €100 000 per annum, including sums passed to third parties, as detailed below.

### **Section of Cancer Information (CIN)**

#### **1.1 Project title: The Evolution of Cancer in Ageing Societies: An International Perspective**

Three theories have been proposed to explain the dynamics of ageing populations: compression of morbidity, expansion of morbidity, and dynamic equilibrium. Yet, these theories have never been applied to understand the evolution of cancer, a disease that occurs primarily at old age. Using global databases, we will assess the population impact of changes in longevity and duration of morbidity among patients with cancer. By assessing cross-country variation over time and cancer site we will assess influence of health care system and distribution of risk factors on healthy life years among cancer patients after diagnosis. We hypothesize that increases in life expectancy after cancer diagnosis have primarily led to expansion (longer time spent with disease before death) rather than compression of years lived with illness and disability. Life table analysis weighted for severity of cancer types to derive disability-adjusted life expectancy will be used to assess the evolution of cancer in ageing societies. This is the first study to apply the dynamics of ageing population theories to unravel how cohorts of cancer patients can be expected to evolve after survival. The study will also provide an important base for applying these theories in the ageing theories in general and to solve health care issues pertinent to this frail population.

Donor: European Commission, Directorate General for Research (EC DG RTD), Belgium

Duration: 24 months

Funds for IARC: €201 932 (US\$ 268 170)

Funds for partners: -

Total: €201 932 (US\$ 268 170)

**Partners: n/a**

## **Office of the Director (DIR)**

### 1.2 Project title: **Global Initiative for Cancer Registry Development in Low- and Middle-Income Countries and Biobank initiative in Low- and Middle-Income Countries**

As part of its remit, IARC promotes and enables the continued expansion and improvement in the extent and quality of cancer registration in Low- and Middle-Income Countries (LMICs). To ensure the appropriate capacity and expertise relative to the scope and ambition of the undertaking, a key instrument is the development of a number of regionally-based resource centres (IARC Regional Hubs for Cancer Registration) in Africa, Asia and Latin America. With IARC maintaining a coordinating role, the aim of such Hubs is to provide the necessary support, advocacy, consultancy and training for those working in the field of population-based cancer registration within these designated regions.

The Regional Hub in Izmir, Turkey is one of a number of hubs to be established. The hub will serve to provide administrative and technical support to the delivery of training, as the focal point of the registry community in the region, responding to initial queries and liaising with IARC to assess and identify priorities and needs. Activities include the technical support to registries regarding: population-based registration methods, coding and classification; installation, data management, quality control and data analysis using CanReg5; support to quality assurance and publication of data.

The IARC "Biobank Network and Cohort building" (BCnet) project will create an opportunity for LMICs to work together in a coordinated and effective manner and jointly address the shortfalls in biobanking infrastructure and other shared challenges including, ethical, legal, and societal issues. IARC will partner with international societies and organizations to promote cancer control in LMICs through educational and methodological support towards building and developing sustainable research infrastructures for cohorts and biobanking facilities.

The project will be launched in 2013, with an International Working Group meeting at IARC. The Working Group consisting of experts in biobanking and network partners from LMICs will define the specific aims and objectives for the network and identify short- and long-term goals.

Donor:	National Institutes of Health (NIH), USA
Duration:	12 months
Funds for IARC:	€169 650 (US\$ 225 000)
Funds for partners:	-
Total:	€169 650 (US\$ 225 000)
<b>Partners:</b>	<b>n/a</b>

## Office of the Director (DIR)

### 1.3 Project title: **Enhanced exposure assessment and omic profiling for high priority environmental exposures in Europe**

This project aims to predict individual disease risk related to the environment, by characterizing the external and internal exposome for common exposures (air and drinking water contaminants) during critical periods of life, including *in utero*. A large amount of health data is now available from longitudinal cohorts in both children and adults, with detailed information on risk factors, confounders and outcomes, but these are not well linked with environmental exposure data. The exposome concept refers to the totality of environmental exposures from conception onwards, and is a novel approach to studying the role of the environment in human disease. This project will move the field forward by utilizing data on individual external exposome (including sensors, smartphones, geo-referencing, satellites), and internal exposome measured with omic technologies in an agnostic search for new and integrated biomarkers. These tools will be applied in both short-term intervention studies and long-term longitudinal studies in humans. The ultimate goal is to use the new tools and biomarkers in risk assessment and in the estimation of the burden of environmental disease. This multidisciplinary proposal combines: (i) development of a general framework for the systematic measurement of the internal and external exposome in Europe in relation to air and water contamination, as a way to reduce uncertainty in risk assessment and to address the effects of mixtures and complex exposures, (ii) evaluation of key physiological changes and health outcomes in short-term and life-course studies associated to environmental exposures and (iii) evaluation of the burden of disease in the European population, based on state-of-the-art assessment of population exposures.

Donor:	European Commission, Directorate General for Research (EC DG RTD), Belgium
Duration:	48 months
Funds for IARC:	€980 152 (US\$ 1 261 457)
Funds for partners:	€7 768 477 (US\$ 9 998 039)
Total:	€8 748 629 (US\$ 11 259 496)

#### **Partners:**

Imperial College of Science, Technology and Medicine (IMPERIAL), UK €1 246 767 (US\$ 1 604 591)  
Universiteit Utrecht (UU), Netherlands €1 361 304 (US\$ 1 752 000)  
Fundacio Centre de Recerca en Epidemiologia Ambiental (CREAL), Spain €1 185 106 (US\$ 1 525 233)  
Universiteit Maastricht (UM), Netherlands €1 444 272 (US\$ 1 858 780)  
Ethniko Idryma Erevnon (EIE NHRF), Greece €372 360 (US\$ 479 228)  
Schweizerisches Tropen und Public Health Institut (Swiss TPH), Switzerland €482 417 (US\$ 620 871)  
King's College London (KCL), UK €632 318 (US\$ 813 794)  
Genedata AG, Switzerland €461 380 (US\$ 593 797)  
The Regents of the University of California (UC), USA €245 451 (US\$ 315 895)  
University of Bristol (UNIVBRIS), UK €77 830 (US\$ 100 167)  
Centre de Recerca I Innovacio de Catalunya (CRIC), Spain €259 272 (US\$ 333 683)

## **Section of Environment and Radiation (ENV)**

### 1.4 Project title: **Research into cancer risks related to exposure to radiation**

The present proposal of four subprojects has been prepared to address specific questions related to exposure to low dose protracted ionizing radiation and cancer risks. Project 1 partially supports the further follow-up of an existing cohort of workers in nuclear power plants and will expand the previous follow-up to the extent that the results will be based on twice as many cancer deaths as before, providing a clearer picture of the overall cancer risk and risks by subtypes of cancer, exposure time periods or age at exposure. Project 2 partially supports better dosimetry for an ongoing project on diagnostic computer tomography scans and cancer risk in children, which, given the increased amount of use of such examinations, is key to radiation protection in children. Project 3 is a pilot study in an under-investigated setting in South Africa with uranium contaminated air, soil and water from mine tailings from the gold mining. Project 4 uses data collected in a multinational brain tumour study in adults to investigate the risk in relation to diagnostic radiation exposure.

Donor: Ministry of Health, Labour and Welfare (MHLW), Japan

Duration: 12 months

Funds for IARC: €220 080 (US\$ 276 135)

Funds for partners: -

Total: €220 080 (US\$ 276 135)

**Partners: n/a**

### 1.5 Project title: **Reviewing the cancer burden related to environmental carcinogens exposure in Qatar**

The deliverable of the project is a risk characterization of environmental risk factors and their related cancer burden in Qatar. This approach involves hazard assessment (identification of known carcinogens relevant to the population of Qatar), dose-response assessment (describing the levels of exposures and their relation to magnitudes of risk) and exposure assessment (data collection of exposure distributions in Qatar). IARC has large experience in this approach and can utilize various sources of information and procedures for related purposes; for instance, the hazard assessment will be based on the IARC monographs that is a work of reference for many health authorities around the world.

As a start, the project supervisors and the lead scientist of the project will visit Qatar to introduce the approach and to make the necessary contacts to assess the relevant information from inside the country. During the course of the review, one staff member of the project will regularly visit Qatar to continue data collection on exposures. A final meeting with all stakeholders will be held at the end of the project.

Donor: Supreme Council of Health (SCH), Qatar

Duration: 9 months

Funds for IARC: €198 209 (US\$ 257 414)

Funds for partners: -

Total: €198 209 (US\$ 257 414)

**Partners: n/a**

### **Infections and Cancer Epidemiology Group (ICE)**

1.6 Project title: **Monitoring HPV vaccination and HPV screening programmes to promote sustained implementation in low- and middle-income countries**

Reliable evaluation of programme effectiveness is crucial for building and optimizing effective cervical cancer prevention services. This proposal aims to provide timely high-quality data on human papillomavirus (HPV) vaccine effectiveness in two early and successfully introducing low- and middle-income countries (LMICs), namely Bhutan and Rwanda. It also aims to strengthen HPV-based screening programmes in these same two model settings, both to offer more immediate benefit to older women, and to allow long-term vaccine impact assessment. The data generated from this project is expected to facilitate introduction of these successful programmes into other LMICs.

Donor:	Bill and Melinda Gates Foundation (BMGF), USA
Duration:	60 months
Funds for IARC:	€1 794 945 (US\$ 2 199 688)
Funds for partners:	-
Total:	€1 794 945 (US\$ 2 199 688)
<b>Partners:</b>	<b>n/a</b>

### **Nutritional Epidemiology Group (NEP)**

1.7 Project title: **Biomarkers of B vitamins, epigenome, genetic polymorphisms, and breast cancer risk in the European Prospective Investigation into Cancer and Nutrition (EPIC) Study**

Breast cancer is the most frequent cancer among women worldwide. International variation in incidence rates indicate that environmental and lifestyle factors, particularly diet, are likely to play an important role in breast cancer etiology. Epidemiological studies on the association between folate (vitamin B9) intake, originating mainly from green leafy vegetables and fruits, and breast cancer risk have not provided consistent results, and the WCRF report concluded that the epidemiological data for an association between folate and breast cancer risk was too limited to allow conclusions to be reached. Issues that require further consideration include genetic background, and interaction between folate and alcohol intake. Indeed, the heterogeneous findings regarding the association between folate and breast cancer risk may reflect the importance of effect modifiers, such as polymorphisms in genes involved in folate metabolism, particularly methylenetetrahydrofolate reductase (MTHFR), a key enzyme residing at a critical metabolic branch point in folate metabolism. Alcohol consumption may also modify the association between folate intake and breast cancer risk. Folate-breast cancer risk association may also differ according to estrogen and progesterone receptor status of tumours.

The role of epigenetic changes as a crucial mechanism deregulating a wide range of key cellular processes has emerged in many cancer types, including breast cancer. Various dietary regimes, lifestyle and endogenous factors are suspected to contribute and modulate susceptibility to breast cancer through epigenetic mechanisms. However, studies in human populations are far from conclusive.

This project has specific objectives i) to analyse the association between plasma concentrations of folate as well as other B vitamins, as biomarkers of dietary intakes, and breast cancer risk according to alcohol intake, estrogen and progesterone receptor status, and genotypes of the *MTHFR* 677C>T and 1298A>C in the EPIC study; ii) to analyse the DNA methylome and identify differential DNA methylation in white blood cells of breast cancer cases and matched controls using a genome-wide approach, and iii) to determine the effect of vitamins B on the DNA methylome in white blood cells. The results of this study will contribute to scientific evidence for appropriate public health and prevention strategies aimed at reducing breast cancer incidence, and will be especially valuable in the ongoing discussions, in many countries, concerning folic acid fortification.

Donor: Institut National du Cancer (INCa), France  
Duration: 36 months  
Funds for IARC: €650 000 (US\$ 841 969)  
Funds for partners: -  
Total: €650 000 (US\$ 841 969)

**Partners:**

Cancer Research Centre of Lyon (CRCL), France  
Institut National de la Santé et de la Recherche Médicale (INSERM), France

**Prevention and Implementation Group (PRI)**

1.8 Project title: **Multicentric study of cervical cancer screening and triage with human papillomavirus testing**

Cervical cancer remains a serious public health problem, with more than 500 000 new cases and nearly 250 000 deaths occurring every year, particularly in developing countries where almost 90% of cases occur. Cytology based cervical cancer screening programmes have successfully reduced cervical cancer incidence in developed countries but, with few exceptions, not in developing countries. Programmes using cervical cytology, which detects cellular changes indicating cervical intraepithelial neoplasia or cancer, are very complex to implement properly and the method has limited sensitivity and low reproducibility, which imposes the need for repeating tests frequently. This results in high cost and logistic complications which hamper the implementation and success of cytology-based screening programmes in developing countries.

Currently, there are several laboratory tests for detection of cervical HPV infection which have high sensitivity and are highly reproducible. These tests are now being used or considered to replace cervical cytology for primary screening because of their high sensitivity to detect cervical cancer precursors; high reproducibility; capacity to detect more disease at an earlier stage; and because their high negative predictive value allows extension of the screening interval, with consequent savings that can compensate the possibly higher cost of the test compared to cytology.

This multicentre study aims to evaluate different methods, including visual inspection with acetic acid, cytology and novel molecular techniques for triage of HPV positive women, to recommend screening approaches in different settings that are able to detect most CIN3+ lesions with the least referral and treatment at acceptable cost. Additionally, the study will create a biobank that will allow evaluation of future techniques for triage of HPV positive women.

Donor:	World Health Organization (WHO), Geneva, Switzerland
Duration:	12 months
Funds for IARC:	€119 550 (US\$ 150 000)
Funds for partners:	-
Total:	€119 550 (US\$ 150 000)
<b>Partners:</b>	<b>n/a</b>

## 2. **Prior approval**

The Governing Council is invited to consider, for approval, projects submitted over €500 000 per annum, excluding sums passed on to collaborating institutions, and projects that require more than €100 000 per annum, excluding the principal investigator's staff costs, from the IARC regular budget, as detailed below.

### **Genetic Cancer Susceptibility Group (GCS)**

#### 2.1 Project title: **Translation of Genetic, Epidemiological and Tumour cell findings in Hodgkin lymphoma and EBV stratified Risk groups (TOGETHER)**

The aim of this project is to comprehensively characterize genetic, environmental, somatic and functional aspects of the complex natural history of classical Hodgkin lymphoma (cHL) to improve clinical management and develop prevention strategies. cHL has been an enigma since its first description in 1832 and is one of the commonest malignancies of young adults. Despite treatment success, a proportion of patients die of their disease and many survivors develop serious long-term side-effects from aggressive treatment. To improve patient care a complete understanding of its pathogenesis is urgently needed. cHL has a clear heritable component and the etiology involves at least one infectious agent, Epstein-Barr virus (EBV), detected in 30% of the cases. The established etiological heterogeneity combined with the unusual pathology of cHL tumours underscores the need for access to well-characterized cases, appropriate biological materials and innovative use of modern genomic techniques to disentangle the factors involved in this relatively rare disease.

TOGETHER assembles world-leading experts in cHL epidemiology, virology, tumour biology and genetics to achieve a step change in our understanding of cHL pathogenesis. State-of-the-art genomics techniques and novel analytical tools will be used to further define host genetic susceptibility; identify critical somatic aberrations present in tumour cells; and search for the elusive viral agent in the subset of cHL not caused by EBV. Functional studies will be performed to analyse biological and immunological mechanisms underlying genetic susceptibility and

tumour cell aberrations. Findings will be analysed with respect to tumour heterogeneity and clinical outcome using a uniquely large, extensively characterized cHL patient cohort. The anticipated advancement in the understanding of cHL pathogenesis will significantly improve clinical management and prevention strategies for cHL and related diseases.

Donor: European Commission, Research Executive Agency (EC REA), Belgium  
Duration: 72 months  
Funds for IARC: €3 436 690 (US\$ 4 557 944)  
Funds for partners: €10 958 725 (US\$ 14 534 118)  
Total: €14 395 415 (US\$ 19 092 062)

**Partners:**

University Medical Center Groningen (UMCG), Netherlands €3 797 116 (US\$ 5 035 963)  
Statens Serum Institut, Denmark €3 464 334 (US\$ 4 594 607)  
University of Glasgow, United Kingdom €3 697 275 (US\$ 4 903 548)

**Infections and Cancer Epidemiology Group (ICE)**

2.2 Project title: **Infections in Cancers among the Immunosuppressed**

A large and globally informative assessment of all infections present in cancers of the immunosuppressed is proposed. The majority of cancer types known to be caused by viruses (Kaposi Sarcoma (KS), Hodgkin and Non-Hodgkin lymphoma, and cancers of the liver, cervix, vulva, vagina, penis, anus and oropharynx) are increased among the immunosuppressed. Skin and lip cancers are also greatly increased, as are, more moderately, cancers of the oesophagus, stomach, intestine, larynx, lung, melanoma, kidney, bladder, conjunctiva, non-KS sarcomas, multiple myeloma, and leukaemias. Severe immunosuppression in high-resource countries is mostly in conjunction with organ transplantation, whereas in Africa it is mostly caused by Human Immunodeficiency Virus (HIV). This project will provide an update of global estimates of cancer relative risk in the immunosuppressed, including which infections these cancers may contain. Combining excellence in global cancer epidemiology, registry linkages, biobanks, microbiological analyses, pathology, bioinformatics, biostatistics, and functional molecular studies, will allow an unbiased assessment of infections that may be present in some 6000 cancers identified using: i) linkage of nationwide hospital and cancer registries with biobanks in the Nordic countries; ii) cohorts of transplant-recipients and HIV-infected individuals in Australia; and iii) a large series of HIV-infected cancer patients in South Africa. The presence of infections will be assessed in tissue specimens using high throughput sequencing and multiplexed PCR. The study will provide a comprehensive atlas of infections in cancers of the immunosuppressed and help prove the causality of the observed associations.

Donor: European Commission, Research Executive Agency (EC REA), Belgium  
Duration: 72 months  
Funds for IARC: €6 078 924 (US\$ 8 062 234)  
Funds for partners: €7 713 488 (US\$ 10 230 090)  
Total: €13 792 412 (US\$ 18 292 324)

**Partners:**

Karolinska Institute, Sweden €7 713 488 (US\$ 10 230 090)

### **3. Interest income from grants**

Article 5.6 of IARC Financial Regulations requires that interest earned on the designated voluntary contributions is credited to miscellaneous income. While most donors have accepted this financial regulation, some donors require IARC to place interest earned in the same account as the one in which their contribution is managed either to be used for the project or to be returned to the donor at the end of the project. Such condition is usually included when the contribution agreement is signed. Thus far the Governing Council has considered and exceptionally approved, on a case by case basis, a waiver of Article 5.6 to allow IARC to comply with the donor's regulations as described in Resolutions GC/30/R10, GC/32/R18, GC/47/R6, GC/49/R16 and GC/50/R6.

This has posed some challenge especially when the agreement has already been signed and the donor expects the Agency to comply with the interest income condition prior to the case being considered by the Governing Council. Although such cases remain exceptional, the Agency has been exposed to legal and reputational risk as a consequence.

To mitigate these potential risks, the Secretariat requests the Governing Council for consideration of a standing approval to exceptionally apportion interest earned on designated voluntary contributions to their respective accounts when such requirements are clearly stated in the signed contribution agreements. To ensure the continued oversight of such cases, which are exceptions to the Financial Regulations, the Agency will report to the Governing Council at its annual meeting, the interest income apportioned to those contributions.

IARC continues to enforce Article 5.6 of IARC Financial Regulations and ensure that exceptions to this regulation are strictly controlled.

This request also includes, for the Governing Council's consideration and approval, the interest earned on the following grants/contributions which have been presented to the Governing Council previously but not with respect to the apportion of interest (values presented below are those of the grant, not interest earned). It is noted that the European Commission (Directorate General for Research (EC DG RTD)) has recently changed their financial regulation with regard to the interest income; all new grants signed from 1 January 2013 will not require interest income to be apportioned for the pre-financing portion.

- Grants presented in this document:
  - From the Bill and Melinda Gates Foundation for: Monitoring HPV vaccination and HPV screening programmes to promote sustained implementation in LMICs; US\$ 2 199 688
  - From the European Commission for: The Evolution of Cancer in Ageing Societies: An International Perspective; €201 932
  
- Grants from the European Commission for the following projects (Document GC/54/11 and Resolution GC/54/R10):
  - Scientific and technical support to the European Partnership for Action against Cancer and follow-up of the implementation of the Council Recommendation on Cancer Screening – Revision of the European Code Against Cancer; €524 451

- Scientific and technical support to the European Partnership for Action against Cancer and follow-up of the implementation of the Council Recommendation on Cancer Screening; €775 536
- Role of human papillomavirus infection and other co-factors in the aetiology of head and neck cancer in Europe and India; €1 217 849
- Grants from the European Commission for the following project (Document GC/53/16 and Resolution GC/53/R18):
  - Epidemiological study to quantify risks for paediatric computerized tomography and to optimize doses; €329 094<sup>1</sup>
- Grants from the European Commission for the following projects (Document GC/52/14 and Resolution GC/52/R12)
  - Providing high quality data, information and knowledge in the areas of cancer registration, cancer screening, cancer risk factors and cancer prevention strategies; €799 995<sup>2</sup>
  - IARC International Fellowships Programme; €839 520

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<sup>1</sup> Please note that the budget allocated to IARC was increased from €303 945 to €329 094 in November 2011, after being approved by GC/53 in May 2011.

<sup>2</sup> Please note that the project title was changed from "IARC – DG SANCO cooperation action on policy and epidemiological support II" (as referred to in GC/52 in May 2010) to "Providing high quality data, information and knowledge in the areas of cancer registration, cancer screening, cancer risk factors and cancer prevention strategies".