

ACCEPTANCE OF GRANTS AND CONTRACTS

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 Surveillance (CSU)

1.1 Project title: Capacity Assessment and Training, Mentorship and Publications for the Regional Cancer Registries Programme in East Africa

Nested within the Global Initiative for Cancer Registry Development (GICR), a multi-partner initiative coordinated by the International Agency for Research on Cancer (IARC) to provide measurable improvements in the coverage, quality and networking capacity of cancer registries in low- and middle-income countries (LMICs), IARC seeks to collaborate with the East, Central and Southern Africa Health Community (ECSA-HC).

The aim of the project is to support the sustainable expansion of registries to increase their availability, quality and use in selected East African countries including Burundi, Kenya, Rwanda, Tanzania and Uganda.

IARC will coordinate and deliver cancer registry support tailored to the needs of each of the five target countries. The approach will be to develop local capacity by involving experts to provide structured learning, reference materials and on-going guidance.

Donor: World Bank (WB), United States of America through East, Central and Southern Africa Health Community (ECSA-HC), Tanzania

Duration: 13 months

Funds for IARC: €163 100 (US\$ 202 609)

Funds for partners: *to be decided*

Total: €163 100 (US\$ 202 609)

Partners:

African Cancer Registry Network (AFCRN), United Kingdom

Section of Early Detection and Prevention (EDP)

Prevention and Implementation Group (PRI)

1.2 Project title: **Preparation and implementation of pilot screening programmes for breast cancer at the regional level in order to implement population-based screening of the disease throughout the Republic of Belarus**

This project aims to set up a pilot programme for breast cancer screening in the Republic of Belarus. It will be delivered through the following steps of implementation:

- 1) The Programme Management Team will be set up to coordinate all work at the planning and test research stage, pilot phase and the stage of introduction of activities under the breast cancer screening programme. In addition, the technical and organizational infrastructure will be developed to allow screening of breast cancer in the Republic of Belarus in an efficient way. The main elements of this infrastructure are the breast screening register, supported by IT systems to manage the service for breast cancer detection, monitoring, evaluation and other aspects of professional and technical quality assurance, and modified protocols for cancer registries.
- 2) The programme staff and stakeholders involved in the planning stage of research, test and pilot phase will be trained in the coordination and delivery of breast cancer screening.
- 3) Test research will be conducted and the results used to inform the provision of services for breast cancer detection in the large-scale pilot phase of the project.
- 4) A plan and corresponding information materials will be developed for the test stage and the pilot project and used to raise awareness amongst stakeholders, to invite the target group and improve communication to achieve high participation in the screening programme.
- 5) A pilot programme for breast cancer screening will be implemented based on the results of the test research. The results of the pilot programme will be used to inform the introduction of activities of the breast cancer screening programme and will serve as basis for national authorities to make a final decision about commencement of the gradual introduction of activities to achieve full coverage of the target population at the national level.

Donor: World Health Organization, Regional Office for Europe (WHO/EURO), Denmark

Duration: 36 months

Funds for IARC: €325 316 (US\$ 370 098)

Funds for partners: -

Total: €325 316 (US\$ 370 098)

Partners: n/a

1.3 Project title: **Prevention at Primary Care Level**

PAPRICA is a three-year project originally funded by the French National Cancer Institute (l'Institut National du Cancer – INCa) that started in March 2016. The goal of this project is to test whether an educational intervention at the level of general physicians in Lyon, aimed at improving their knowledge and competency around Human Papillomavirus (HPV) vaccination, would increase the number of vaccinated young girls in Lyon. As outlined in the original project description, the larger context of this project is to verify whether an innovative educational intervention is able to reinforce the French general physicians' role as key players in primary care prevention. This approach is encapsulated in the title of the project, "Prevention at Primary Care Level".

In this respect, the project PAPRICA can be seen as aiming to establish a platform for prevention education targeting general physicians, with the intent to positively impact public health in France. The first phase of the project envisaged a pilot of the platform using one subject, notably HPV vaccination, with the aim to increase coverage of vaccination, which remains very low in France. Should the platform prove to be efficacious in transmitting information and knowledge, it is envisaged to first extend PAPRICA to other towns in France and second to use it for targeting other public health issues, such as breast cancer screening, colorectal cancer screening and others.

The current, complementary funding, from the Métropole de Lyon serves to reinforce PAPRICA's scientific team knowledge and expertise in the field of social psychology and interventional research. At the same time it also serves to extend PAPRICA's network and federate collaboration around IARC in the Auvergne-Rhône-Alpes region.

Donor:	Métropole de Lyon, France through Le Cancéropôle Lyon Auvergne Rhône-Alpes (CLARA)
Duration:	12 months
Funds for IARC:	€188 183 (US\$ 224 830)
Funds for partners:	€102 902 (US\$ 122 942)
Total:	€291 085 (US\$ 347 772)

Partners:

Le Cancéropôle Lyon Auvergne Rhône-Alpes (CLARA), France, €0 (US\$ 0)

L'Université Lumière Lyon, France, €78 174 (US\$ 93 398)

L'Université Jean Monnet Saint Etienne, France, €24 728 (US\$ 29 544)

Section of Early Detection and Prevention (EDP)

Screening Group (SCR)

1.4 Project title: **Implementation of a pilot cervical cancer screening programme based on single visit approach and improving capacity for breast cancer early detection in Burkina Faso, Chad, Cote d'Ivoire, and Senegal (Care4Afrique)**

Breast cancer is the commonest and cervical cancer is the fourth most common cancer in the world. Both are responsible for large number of premature deaths in the sub-Saharan African countries and breast cancer mortality is on the rise.

LMICs have suboptimal health system capacity to implement the multiple-visit based western model cancer screening programmes and most African countries will require specific recommendations on how to organize or improve cancer screening services based on local evidence, which till date is very limited.

The third edition of the Disease Control Priorities Project of the World Bank recommends opportunistic cervical cancer screening with VIA or HPV testing and treatment of precancerous lesions ('screen and treat' using single-visit or two-visits approach) as part of an essential package of health interventions in low-income countries, due to the high cost of population screening. Very few countries in sub-Saharan Africa have taken steps to introduce such 'screen and treat' programmes. Sporadic VIA based screening activities are going on in some of the countries with no proper evaluation and quality assurance. The experiences gained from properly implemented pilot projects will inform pragmatic decision making by the policy makers to scale up the programmes.

The Disease Control Priorities project also identified early diagnosis of symptomatic women linked with access to good quality surgery and subsequent treatment as the most pragmatic essential strategy to tackle the growing burden of breast cancer in the countries with basic or limited resource environments. Providing the basic components of cancer early diagnosis in an equitable and timely manner through cancer health awareness, accurate clinical, radiological and pathologic diagnosis, and quality and affordable treatment can make significant improvement in breast cancer control in the LMICs.

In Burkina Faso, Chad, Cote d'Ivoire and Senegal breast and cervical cancer are the two most common causes of cancer deaths with cervical cancer mortality surpassing that caused by breast cancer.

The Screening Group of IARC with the Lalla Salma Foundation for Prevention and Treatment of Cancers (LSF) propose to implement and evaluate pilot projects on cervical cancer screening using the 'VIA – screen and treat' approach in collaboration with the respective ministries of health in Burkina Faso, Chad, Cote d'Ivoire and Senegal. We will also evaluate some of the novel approaches like use of thermo-coagulation for the treatment of the eligible VIA positive women. We will assess the feasibility, safety and acceptability of cervical cancer screening in the opportunistic settings in the four African countries by integrating the 'screen and treat' approach within the existing public health services to inform and guide the eventual scaling up of cervical cancer screening covering the entire country.

We will enhance the capacities of at least one tertiary care institution in each country to early diagnose breast cancers. This will also help these countries to introduce pilot breast cancer screening programmes in future (based on clinical breast examination) if their resources permit.

Donor: Lalla Salma Foundation - Cancer Prevention and Treatment, Morocco
Duration: 24 months
Funds for IARC: €346 294 (US\$ 416 219)
Funds for partners: -
Total: €346 294 (US\$ 416 219)

Partners: n/a

Section of Environment and Radiation (ENV)

1.5 Project title: International Expert Group on Long-term Strategies for Thyroid Monitoring after the Fukushima Daiichi Nuclear Power Plant Accident

Following the March 2011 Fukushima Daiichi Nuclear Power Plant accident, the Fukushima Prefectural Government initiated the Fukushima Health Management Survey (FHMS). One element of this survey is the thyroid ultrasound examination (TUE) programme, launched in October 2011 including children aged up to 18 years inclusively at the time of the accident. Up to now, periodical surveys involving in total over 300 000 children were conducted, revealing a high incidence of thyroid abnormalities including thyroid cancers in children and young adults in Fukushima. For the affected families, the detected thyroid disorders cause psychological stress along with the treatment of their children, and overall it raises anxiety in the population associated with the steep increase of a cancer following the nuclear accident.

To respond to concerns about dramatic increases over recent decades in the incidence of thyroid cancer and potential for overdiagnosis and/or overtreatment, IARC conducted a study to evaluate changes in thyroid cancer incidence worldwide and to assess the impact of large-scale thyroid gland surveillance in various countries. This raises the question of how a long-term TUE strategy following nuclear accidents can be developed taking into account all these factors. This was already discussed at a workshop in October 2013 of IARC and the Fukushima Medical University (FMU).

International collaborations with bodies such as IARC, among others, should be encouraged and strengthened, for instance with an expert working group especially focusing on thyroid problems. As key partner of research on radiation and cancer related to the other major nuclear accidents in Chernobyl and in the Southern Urals, with recent research on global trends of thyroid cancer and the effects of screening, and as a partner of FMU since the early activities on health effects related to the nuclear accident, IARC is particularly well positioned to convene and lead such an expert working group.

The IARC experience on the subject matter mainly stems from the involvement and lead of several activities related to the Chernobyl nuclear accident. Since 1990, scientists from IARC have been conducting studies on the health consequences of the Chernobyl accident, in close collaboration with many institutions in Belarus, the Russian Federation, Ukraine, Baltic countries, as well as elsewhere in Europe, North America and Japan. IARC also has just completed a feasibility study on behalf of the European Commission with advisors from Europe, the USA and Japan on future studies investigating health risks related to nuclear tests at the Semipalatinsk nuclear test site in Kazakhstan, of whether a follow-up study of those screened for thyroid nodules in 1997 can be carried out.

The diversity of expertise at IARC on all the relevant topics, including health effects due to radiation exposure from nuclear accidents, thyroid screening in relation to nuclear accidents, and thyroid screening irrespective of nuclear accidents and its impact on thyroid cancer rates, allow the Agency to lead such required multidisciplinary expert group in evaluating a thyroid monitoring system after a nuclear accident in general based on the most updated knowledge and experience available.

Donor: Ministry of the Environment, Japan
Duration: 8 months
Funds for IARC: €281 700 (US\$ 332 586)
Funds for partners: -
Total: €281 700 (US\$ 332 586)

Partners: n/a

1.6 Project title: **Exposure of the French population to radio frequencies (RF) due to mobile phone use**

Mobile telephony exposes users to RF waves from near-body sources, mainly related to the use of mobile devices by the subjects themselves, and exposures from more distant sources (relay antennas and other mobiles). A recent Swiss study estimated that 70%–93% of total RF exposures were due to mobile phone use in the reference period 2012–2013.

The Devin system, developed thanks to previous support of the “Agence Nationale de Sécurité sanitaire de l’alimentation, de l’Environnement et du travail” (ANSES), measures the intensities and frequencies of RF (MHz) along the chain of transmissions from the mobile device to the base station. The body of the Devin is stuck to the mobile and three electronic badges, placed on the chest and in two pockets, monitor the position of the phone in relation to the body. Xmobisense, an application uploaded onto the mobile phone, records the communication protocols, the reception levels of the downstream channel (transmissions from the base station to the mobile), and the usage information (laterality, hands-free kits).

It is important to investigate the exposure of individuals in France, in order to verify the hypothesis that the switch to 3G and 4G networks reduces the exposure as compared with 2G and to study the influence of parameters such as density, antennas, protocols and frequencies on the exposures of individuals. In addition, little is known about the positions of phones in use and the actual exposure of different parts of the body of the user.

COSMOS is a cohort of mobile phone users that was set up to study the potential effects of mobile telephony and other new technologies on health. The project CORIOLIS will develop and refine the methods for exposure estimates in the COSMOS study.

Donor: Agence Nationale de Sécurité sanitaire de l’alimentation, de l’Environnement et du travail (ANSES), France
Duration: 40 months
Funds for IARC: €147 763 (US\$ 175 075)
Funds for partners: €251 111 (US\$ 297 525)
Total: €398 874 (US\$ 472 600)

Partners:

Institut Mines Telecom – Telecom ParisTech, France, €62 400 (US\$ 73 934)

University of Utrecht, the Netherlands, €25 006 (US\$ 29 628)

Le Commissariat à l’énergie atomique et aux énergies alternatives (CEA), France, €113 749 (US\$ 134 774)

Centre Scientifique et Technique du Bâtiment (CSTB), France, €12 428 (US\$ 14 725)

Université de Rennes 1, France, €12 368 (US\$ 14 654)

Ecole Pratique des Hautes Etudes, France €12 584 (US\$ 14 910)

Centre Hospitalier Universitaire Toulouse, France €12 576 (US\$ 14 900)

Agence nationale des fréquences, France €0 (US\$ 0)

Section of Genetics (GEN)

Genetic Cancer Susceptibility Group (GCS)

1.7 Project title: **Genomic analysis of inherited lung cancer (Geniluc)**

Lung cancer (LC) is a leading cause of death worldwide. Despite efforts to reduce the use of tobacco products, global consumption continues at very high levels and the legacy of former use will result in lung cancer remaining a major worldwide public health problem for the foreseeable future.

The major goal of the Section of Genetics is to identify the genes involved in lung cancer susceptibility and to understand the mechanisms by which environmental factors exert their effects through interaction with these genes. Working with international consortia, the section is involved in some of the world's largest genetic studies of lung cancer, most recently identifying 12 novel lung cancer susceptibility loci through genome-wide association studies (GWAS) of 29 863 patients and 55 586 controls.

These large-scale studies have identified multiple genetic loci that are highly relevant for the susceptibility to lung cancer. The loci identified relate to nicotine dependency (CHRNA5/3/2, CYP2A6), DNA repair (CHEK2, BRCA2, CDNK2A), immune response (MHC/HLA), telomerase functions (TERT, RTEL, OBFC1) and have been observed near genes mutated somatically in lung cancer (TP63 and NRG1), as well as near genes where relevance to lung cancer remains unclear.

While these discoveries are statistically robust, it remains to be shown how these genetic factors predispose individuals to lung cancer. The goal of this project is to explore how the germ-line genetic variants, in conjunction with tobacco smoke, impact the lung epithelial tissue. The central hypothesis of the study is that the identified genetic variants modify the effect of tobacco smoking, thereby leading to higher observed rates of lung cancer in afflicted individuals.

Donor: Institut National du Cancer (INCa), France

Duration: 36 months

Funds for IARC: €533 005 (US\$ 606 376)

Funds for partners: €120 824 (US\$ 137 457)

Total: €653 829 (US\$ 743 833)

Partners:

Fondation Synergie Lyon Cancer, France, €120 824 (US\$ 137 457)

Section of Nutrition and Metabolism (NME)

Biomarkers Group (BMA)

1.8 Project title: Investigating the etiology of oesophageal and gastric cancers: the role of hormones

Oesophageal and gastric cancer patients have a poor survival rate and the etiology of these cancers is largely unclear and understudied. These tumours are hypothesized to have distinct etiologies within histologic subtypes and subsites; yet few studies have been of sufficient size to investigate these subtypes. Observational evidence suggests that these tumours may be linked to variation in endocrinologic pathways; for example, both oesophageal and gastric cancers are more common in men, while obesity, which is frequently accompanied by metabolic and hormonal abnormalities such as hyperinsulinemia, is positively associated with oesophageal adenocarcinoma (OA) and gastric cardia cancer (GCC). Most strikingly, preliminary data suggests that lower circulating levels of ghrelin, a gut hormone, increases the risk of OA, oesophageal squamous cell carcinoma (OSCC), GCC, and gastric non-cardia cancer (GNCC). Several hormone-related mechanisms could thus contribute to oesophageal and gastric cancer risk, including sex steroids, appetite/digestive hormones, and the insulin-insulin-like growth factor (IGF)-I signalling pathways. Previous studies have not comprehensively assessed anthropometric measures, reproductive factors, and hormonal pathways in relation to upper gastrointestinal malignancies.

The aim of this study is to investigate hormones and hormone-related factors in relation to oesophageal and gastric cancers by prospectively examining lifestyle, behavioural and biochemical data. Specifically, it is intended to: 1) Investigate anthropometric and reproductive factors in relation to OA, OSCC, GCC, and GNCC; and 2) Examine serum levels of sex hormones, appetite/digestive hormones, and insulin/IGF-axis components in relation to OA, OSCC, GCC, and GNCC.

Anthropometric and reproductive data and incident upper gastrointestinal cancers (356 OA, 287 OSCC, 366 GCC, 666 GNCC) will be investigated in around 1.1 million participants from four large cohorts. Body mass index, waist-to-hip ratio, height, weight, ages at menarche, menopause, and first child's birth, parity, breastfeeding, menopausal hormone therapy and oral contraceptive use will be assessed. For serologic analyses, sex hormones (estrogen, estradiol, testosterone, sex hormone-binding globulin), appetite/digestive hormones (ghrelin, leptin, adiponectin), and levels of insulin, glucose, IGF-1, IGF-binding protein (BP)1, and IGF-BP3 will be examined in a case-cohort study of cases with fasting baseline serum (137 OA, 161 OSCC, 215 GCC, 215 GNCC) and a representative subcohort (n=400).

This study has direct translational potential by using the data generated to identify specific risk factors that can be used to identify individuals who would most benefit from interventions and more targeted screening and surveillance programmes.

Donor:	Imperial College of Science, Technology and Medicine London (ICL), United Kingdom
Duration:	11 months
Funds for IARC:	€204 750 (US\$ 254 348)
Funds for partners:	-
Total:	€204 750 (US\$ 254 348)

1.9 Project title: **The epidemiology and etiology of high risk prostate cancer**

Prostate cancer is the most common cancer among men in the UK but its etiology is poorly understood and there are no modifiable risk factors. This project intends to bring together large epidemiological studies incorporating recent developments in high-throughput technologies to provide detailed information on biomarkers of exposure and metabolic phenotype, combined with tumour characteristics and survival data. This will enable an integrated analysis of the etiology of clinically significant "high risk" prostate cancer, with the aim of identifying modifiable factors to inform both population-based and stratified approaches to risk reduction.

Novel biomarkers which may influence the development of prostate cancer through several pathways identified from previous studies will be systematically assessed. These biomarkers include metabolites which may upregulate the PI3K-Akt-mTOR pathway, nutritional biomarkers, inflammatory markers and markers of infections.

Risk factors and survival in 7000 incident prostate cancers with 20 years of follow-up will be investigated in the EPIC prospective cohort study. Potentially new biomarkers will be uncovered including metabolomic profile, β -microseminoprotein, kallikreins and a panel of sexually transmitted infections. Prostate cancer risk will be stratified by TNM stage, Gleason grade and survival.

This project will bring together an international consortium covering 30 prospective studies worldwide. This will allow the study team to investigate nutritional biomarkers and growth factors in relation to the risk for up to 15 000 incident cancers. Analyses will prioritize clinically significant prostate cancer, classified according to stage and grade and long-term survival.

Finally, the epidemiology of 3500 cases of prostate cancer will be examined in the UK Biobank. Using extensive electronic health records in the UK, potential medical precursors of prostate cancer including prostatic and systemic infections and benign prostatic hyperplasia can be studied. These analyses will be integrated into the detailed phenotyping and comprehensive panel of biomarkers and genotyping available in the UK Biobank.

Donor: Cancer Research (CRUK), United Kingdom
Duration: 14 months
Funds for IARC: €151 889 (US\$ 172 798)
Funds for partners: €549 489 (US\$ 625 129)
Total: €701 378 (US\$ 797 927)

Partners:

University of Oxford, United Kingdom, €549 489 (US\$ 625 129)

Section of Nutrition and Metabolism (NME)

Nutritional Epidemiology Group (NEP)

1.10 Project title: **Understanding the Role of Sex Hormones in Colorectal Cancer**

Experimental evidence supports an anti-tumorigenic role of estrogen in colorectal cancer (CRC), and observational studies have consistently reported that menopausal hormone use is associated with lower risk of CRC. Recently, IARC investigated the association of circulating sex hormones

with CRC in a case-control study nested within in the Women's Health Initiative and observed significant inverse relationships between endogenous estrogens and CRC risk. Further, sex hormone-binding globulin (SHBG) was positively associated with CRC incidence, even after control for estrogen and other CRC risk factors. These findings suggest sex hormones play a role in CRC etiology; however, they require validation in a large cohort study with prediagnostic blood specimens and detailed epidemiological data.

The goal of this project is to investigate the relation of the sex hormone axis with CRC development among postmenopausal women enrolled in the EPIC cohort. The analysis will be the largest to date with 700 incident CRC cases and 700 matched controls with existing data on related serologic factors already available. Measurements of estrogens, testosterone as well as SHBG will be performed on a liquid chromatography mass spectrometry platform. In addition, Mendelian randomization analyses will be conducted to investigate potential causality of the sex hormone axis-CRC relationship. Genetic risk scores will be created using single nucleotide polymorphisms (SNPs) which have previously been associated with circulating estradiol and SHBG levels. The scores will then be investigated in relation to CRC in 12 000 CRC cases and 12 000 matched controls from the Genetics and Epidemiology of Colorectal Cancer Consortium (GECCO), and the Colorectal Transdisciplinary (CORECT) Study.

The identification of significant relationships between circulating sex hormones and CRC raises the possibility of employing these biomarkers in risk stratification for CRC screening. Additionally, if the Mendelian Randomization analyses indicate causal relationships between sex hormones and CRC, these hormonal pathways could be exploited in novel chemo-preventative and therapeutic strategies.

Donor:	Institut National du Cancer (INCa), France
Duration:	36 months
Funds for IARC:	€321 297 (US\$ 378 888)
Funds for partners:	-
Total:	€321 297 (US\$ 378 888)

Partners: n/a

2. Prior approval for projects over €500 000 per annum

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.

There are no projects to be considered for prior approval this year.

3. Interest income from grants

In accordance with the standing authorization provided to the Director under Resolution GC/55/R23 and the conditions set forth in the signed agreements, interest income totalling €3813 was apportioned to two grants in 2017. Details are provided in the table below.

Grant	Project	Donor	Interest (€)
100401	Monitoring HPV vaccination and HPV screening programmes to promote sustained implementation in low- and middle-income countries	Bill and Melinda Gates Foundation	535
100639	Extended Follow-up of the Participants of IARC-INDIA HPV Vaccination Study to Evaluate the Effectiveness of one, two and three Doses of Quadrivalent HPV Vaccine in Preventing Cervical Neoplasia	Bill and Melinda Gates Foundation	3278
Total interest income apportioned to grants			3813