

PURCHASE OF SCIENTIFIC EQUIPMENT

Introduction

1. The Agency takes an inter-disciplinary approach to its research, permitting knowledge and tools from studies on carcinogenic mechanisms to be innovatively applied to epidemiological investigations of the causes and prevention of cancer, as described in the IARC Medium-Term Strategy (2010–2015). The IARC Laboratory Steering Committee monitors the key items of scientific equipment for renewal and new investment and provides recommendations to the Director based on priorities across the Agency's research groups.

2. Using the regular budget to fund major equipment items would detract from financing the on-going research projects of the Agency, whilst obtaining funds for major equipment through competitive grant applications is difficult given the restricted sources of extra-budgetary channels open to Agency scientists. Therefore the Director would like to approach the Governing Council at its 56th session in May 2014, to request a contribution of €353 000 from the Governing Council Special Fund for essential scientific equipment. This approach is first submitted to the Scientific Council for its consideration.

3. Major items included in this request are to support the development of the recently established metabolomic activities and to build on the success following the recent investment in DNA sequencing. In the former case a new mass spectrometer is needed, with the two machines acquired in 2011 no longer being sufficient to analyse the increasing number of samples obtained from large cohorts. In the latter case, a bench-top next-generation sequencer of medium capacity is needed to permit a new range of studies not currently optimally covered by existing equipment. It is notable that the Scientific Council previously advised the Director and the Governing Council of the need to plan additional investment in sequencing equipment to maintain the ability of the organization to take advantage of its many research opportunities (see previous Scientific Council reports – documents SC/46/11 (2010) and SC/48/10 (2012)).

4. These new equipment items will provide shared resources for use in collaborative and interdisciplinary projects involving several research groups across the Agency. It is notable that the recent investment by the Governing Council in metabolomics and sequencing capacity has resulted in some major research awards. Specifically, for the Biomarkers Group (BMA) three large European Framework Programme 7 projects have been awarded to study associations between the exposome and cancer risk (EU-FP7 NutriTech, EU-FP7 EXPOSOMICS, EU-FP7 TRANSCAN CRC-Metabolome) in addition to grants from the World Cancer Research Fund and the French National Cancer Institute with a total value of €2 500 000. In the area of genetics and DNA sequencing the Genetic Cancer Susceptibility Group (GCS) attracted funding

from the US National Cancer Institute (three grants) and the French National Cancer Institute (INCa), for a total value of around US\$ 1 340 000. In the case of metabolomics the above grant awards have provided around 25% of the funding needed for the proposed new mass spectrometer.

5. The annual maintenance costs of the requested equipment will be covered by the regular budget as well as by collaborative programmes through grant applications.

6. The Scientific Council is requested to advise the Director and Governing Council on the proposed request to use funds from the Governing Council Special Fund to purchase the following equipment:

- a) Bench-top next-generation sequencer of medium capacity; and
 - b) Tandem mass spectrometer coupled to Ultra Performance Liquid Chromatography.
- a) Bench-top next-generation sequencer of medium capacity**

7. The successful identification and functional evaluation of genetic and epigenetic alterations in tumour cells depends on the development of specific and sensitive biomarkers of exposure and carcinogenesis in pre-neoplastic lesions and tumours for various cancer types under study. IARC researchers currently use small-throughput and high-throughput sequencers, allowing at a maximum 2 Gb data output for 200–400 nt single reads (Ion PGM), or 80–320 Gb output for short reads of 50–75 nt (SOLiD 5500w) respectively. However, the available equipment is currently not capable of producing long sequence reads in a paired-end arrangement (such as 2 x 300 bp) with intermediate output capacity (10–15 Gb) that would allow novel sequencing strategies to be implemented by various research groups at IARC. The proposed medium-capacity, long-read length sequencer will be notably used for:

- cancer driver gene mutation screening across full gene-length panels in highly multiplexed sample sets (Research Groups: MMB, EGE, GCS, MPA)¹;
- Bisulfite sequencing applications (e.g. targeted quantification of DNA methylation at the most informative loci across many samples) (EGE);
- Large structural alteration mapping, including analysis of fusion genes (GCS);
- Viral integrations and 16S metagenomics (ICB);
- ChIP-seq and targeted RNA-seq to determine gene regulation mechanisms and their outcomes (several IARC Groups);
- Discovery of non-invasive and specific biomarkers based on nucleic acids in body fluids (MMB, GCS, GEP, EGE);
- Mechanistic carcinogen evaluation using in vitro mutagenicity assays (MMB, IMO).

¹ EGE = Epigenetics Group
GCS = Genetic Cancer Susceptibility Group
GEP = Genetic Epidemiology Group
ICB = Infections and Cancer Biology Group
MMB = Molecular Mechanisms and Biomarkers Group
MPA = Section of Molecular Pathology

8. A highly versatile, cost-effective medium-capacity next generation sequencer is therefore needed to complement the currently available small-throughput and high-throughput sequencing platforms.

9. The proposed equipment would be operated as a shared resource overseen by a technician under the responsibility of MMB, providing access and support to other research groups at IARC. No difficulties are foreseen concerning dedicated Information Technology Services (ITS) support as the raw data will be of relatively low complexity and volume. Data storage and analysis will be well-accommodated within the current ITS infrastructure.

b) Tandem mass spectrometer coupled to Ultra Performance Liquid Chromatography (UPLC)

10. The Agency currently has two mass spectrometry instruments coupled to Ultra Performance Liquid Chromatography (UPLC) to perform metabolomic analyses for epidemiological studies: a high-resolution mass spectrometer (UPLC-QToF) to obtain metabolic fingerprints with semi-quantitative information on thousands of metabolites in biological specimens and a low-resolution triple quadrupole mass spectrometer (UPLC-MS/MS) dedicated to the quantitative analysis of tens to hundreds of small molecules (metabolites, nutrients, hormones).

11. The high-resolution instrument is used in fully agnostic approaches to identify novel biomarkers or sets of biomarkers characteristic of various exposures associated to disease risk (diet, environment, individual metabolic status). Measurements are usually made on a limited number (tens to hundreds) of samples collected from individuals with contrasting levels and types of exposures. The second low-resolution instrument is used for targeted quantitative analyses of the newly discovered biomarkers and other metabolites in blood or urine in exposome-wide association studies including dietary polyphenols, metabolites (acylcarnitines, amino acids, biogenic amines, hexoses, phospho- and sphingolipids) and steroid hormones. Associations with cancer outcomes are investigated in large case-control or cohort studies in which hundreds to thousands of samples are routinely analysed and this apparatus is already running full-time at its capacity (about 6 000 samples/year for routine activity).

12. In addition to the new grants that have resulted from the creation of the metabolomics platform (see above), a number of collaborative projects are now conducted or planned in collaboration with NEP, DEX², EGE and ICB Groups and external partners from Europe, North and South America to identify new risk factors for cancer in various cohorts [European Prospective Investigation into Cancer and Nutrition Study (EPIC), ESMAestras, South Africa Breast Cancer Study (SABC), Breast Cancer in Premenopausal Women Study (PRECAMA)].

13. A new triple quadrupole mass spectrometer coupled with UPLC is urgently needed to accompany the increase of BMA activity. Part of the cost (25%) will be covered by resources obtained through competitive grant awards. The new equipment will be a part of the mass spectrometry platform of BMA and will be run by trained BMA technicians.

² DEX = Dietary Exposure Assessment Group
NEP = Nutritional Epidemiology Group

Requested budget

	Quantity	Cost (€)	Annual maintenance cost (€)
Bench-top next-generation sequencer of medium capacity	1	110 000 ¹	16 000
Tandem mass spectrometer coupled to UPLC	1	243 000 ²	39 000
Total		353 000	

¹ This estimate includes installation costs.

² Seventy thousand euros of the full cost (313 000€) will be covered by the Biomarkers Group (BMA) resources.