Director's Report

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World Health Organization



Table of Contents			
	 1. Biennial report 2020-2021: major scientific highlights Introduction Cancer Surveillance Nutrition and Metabolism Environment and Radiation Genetics Mechanisms of Carcinogenesis Infections Early Detection and Prevention Evidence Synthesis and Classification Education and Training Laboratory Services and Biobank Cancer Prevention Knowledge Translation and Transfer Working Group 	4-5 6-11 12-16 17-21 22-25 26-29 30-31 32-34 35-39 40-43 44-45 46	
	 2. Highlights from the meeting of the 63rd Session of the Governing Council 3. Update from the 57th Session from the Scientific Council 	47-54 55-62	
	Table of Contents - Director's Report 9-11 February 2022		2





The Directors' report consists of three parts: **1**) Scientific highlights from the Biennial Report 2020-2021 (SC/58/2); this Biennial Report covers the **period 2020–2021** and showcases a selection of the work conducted by IARC in collaboration with its global network of experts; **2**) Highlights from the meeting of the 63rd Session of the Governing Council; **3**) Director's update from the 57th Session from the Scientific Council.

Please visit the companion webpage for the Biennial Report which is live at: <u>https://www.iarc.who.int/biennial-report-2020-2021web/</u>

Because of the COVID-19 pandemic, the past two unprecedented years have brought IARC many challenges. From March to May 2020, we adapted to working remotely. IARC's operations continued thanks to the outstanding commitment of its personnel and significant investment in the digitalization of its activities. Subsequently, there was a gradual return to on-site operations, with most personnel (~70%) working remotely for the following months. Despite the challenges, IARC successfully conducted most of its research remotely and deployed innovative tools and technologies such as digital signatures and online conferencing solutions. For the first time in IARC's history, all meetings were successfully transformed into virtual meetings, including five *Monographs* meetings, two *Handbooks of Cancer Prevention* meetings, the IARC Scientific Council session in 2021 and the IARC Governing Council sessions in 2020 and 2021, in addition to various other scientific events. Unfortunately, the COVID-19 pandemic had a negative impact on IARC's fundraising activities and resulted in the suspension of certain activities and projects that could not be conducted remotely, such as fieldwork.

Despite the pandemic, IARC continued to fulfil its mission, and after more than a year of external consultation, reflection, and discussion, **the IARC Medium-Term Strategy 2021–2025 was finalized and adopted by the IARC Governing Council in May 2021.** This exciting new roadmap will guide IARC for the next 5 years. The Medium-Term Strategy is based on the IARC Statute and an objective that has guided IARC's work since 1965: *to promote international collaboration in cancer research*.

IARC continues to address its *fundamental priorities*: Data for Action (to describe the occurrence of cancer), Understanding the Causes (to identify cancer risk factors), From Understanding to Prevention (to effectively implement cancer research), and Knowledge Mobilization (to share knowledge about cancer). In addition to its fundamental priorities, IARC has identified three *emerging priorities* that are important and evolving global issues for cancer prevention research: Evolving Cancer Risk Factors and Populations in Transition, Implementation Research, and Economic and Societal Impacts of Cancer. IARC will gradually strengthen its engagement in these three emerging priorities, increasing its activity in *implementation research*.



Aiming for a more agile organization, IARC's organizational structure was reviewed and revised to enable greater flexibility in resource management and to promote collaboration across the Agency.

The four pillars reflect IARC's fundamental activities.

In 2021, the former Section and Group structure was replaced by a Branch structure (8 scientific Branches and the administrative "Services to Science and Research" Branch), as reported in the slide. This structure is complemented by the conceptual idea of four scientific Pillars representing IARC's four fundamental research priorities, as described above.



The former Section of Cancer Surveillance has been renamed the "Cancer Surveillance" (CSU) Branch (new organizational structure slide 5).

CSU continues to develop studies that signal how the global cancer agenda must be continually adapted to ongoing epidemiologic transitions linked to income and development. We have reported that cancer is likely to surpass cardiovascular disease (CVD) as the leading cause of premature death (affecting ages 30-70) in most countries over the course of this century. As seen on the left figure in this slide, in many high-income countries, cancer (as shaded in dark blue) now ranks above CVD given the relatively greater progress in reducing the risk of CVD death over the last few decades; the rankings are unlikely to change should the reported downward trends in both diseases continue.

In most middle-income countries at an earlier stage of this transition, CVD still ranks above cancer as the leading cause of premature death (shaded in light blue), but as the right figure depicts this is likely to reverse over the next

decades given the predominant temporal pattern over the last 20 years are major declines in CVD death, relative to cancer.

In lower-income countries, many of which are at an early stage of such an NCD transition, premature deaths from both CVD and cancer appear to be uniformly rising.



The **Global Cancer Observatory (GCO)** is hosted, maintained, and developed by IARC as an interactive web-based platform presenting global cancer statistics to inform cancer control action. Launched in May 2016, the platform focuses on the visualization of cancer indicators to illustrate the changing scale, epidemiological profile, and impact of the disease worldwide.

Cancer Over Time, a new subsite of the GCO was launched in November 2021.

Cancer Over Time enables interactive visualizations of the trends in cancerspecific incidence and mortality rates in **60 countries over the past 65 years**. The underlying data are the recorded national or subnational incidence data from cancer registries compiled in successive volumes of Cancer Incidence in Five Continents (CI5) underway, recorded national cancer-specific mortality data from the World Health Organization (WHO) Mortality Database. With a new call for registry incidence data for Volume 12 of CI5, the aim going forward is to enable registries to submit timely aggregated data on a routine basis to ensure the subsite always contains up-to-date recorded data on both incidence and mortality worldwide.

This graphic illustrates the increasing trends in early onset colorectal cancer incidence among young women (aged 25-49) in Australia, Sweden and the USA.

The analytical tools included in Cancer Over Time subsite age-period-cohort analysis, including visual inspection of the rates versus birth cohort and calendar period by age group, and a quantification of the direction and magnitude of time.



CSU has been actively involved in technical and regional consultation meetings on the **Cervical Cancer Elimination Initiative** (CCEI) since its launch and wrote Chapter 9 on "Surveillance, monitoring and evaluation" in the WHO 2020 publication, *Global strategy to accelerate the elimination of cervical cancer as a public health problem*, with input from the IARC/Early Detection, Prevention and Infections (EPR) Branch.

We have further developed a framework for scaling-up the CCEI in the context of surveillance in a publication in 2021 in Preventative Medicine, which argues that initiation and sustainable development of a population-based cancer registry must be a critical early step in the scale-up of activities so as to ensure progress in national cervical cancer control is successfully monitored and appraised.



This year, CSU published global, regional, and national estimates of **alcoholattributable cancer burden in 2020** to inform alcohol policy and cancer control across different settings globally.

Globally, an estimated **740 000 or 4.1% of all new cases of cancer in 2020** were attributable to alcohol consumption. Oesophageal, colorectal and liver cancers contributed the most cases, though this varies largely by world regions, e.g. in high income countries breast cancer is the most important alcohol related cancer. Males accounted for 570 000 of total alcohol-attributable cancer cases or ³⁄₄ of all alcohol related cancers. Population attributable fractions (PAFs) were lowest in northern Africa and western Asia and highest in eastern Asia and central and eastern Europe. The results are also presented by for each country globally, and by groups of alcohol consumption which are available online in the Global Cancer Observatory as noted here.



This year, CSU published global, regional, and national estimates of alcoholattributable cancer burden in 2020 to inform alcohol policy and cancer control across different settings globally.

Increasing alcohol taxation can effectively reduce the burden of alcoholrelated cancers. Almost **11 000 new cancer cases and nearly 5000 alcoholrelated cancer deaths could be avoided annually in the WHO European Region by doubling current excise duties on alcoholic beverages**. This represents **6% of new alcohol-attributable cancer cases and 6% of cancer deaths attributable to alcohol consumption in the region**.



In May 2020, IARC became a member of the **Covid-19 and Cancer Taskforce**, part of a globally representative group spanning multiple disciplines and including representatives of cancer centre networks and advocacy groups. To assess the impact of the pandemic on the delivery of preventative, screening and cancer treatment services and subsequent cancer outcomes, we partnered with CPAC, ICSN, UICC and the Daffodil Centre (a joint venture between Cancer Council NSW and the University of Sydney) to bring together the global modelling community to support decision-making in cancer control both during and after the crisis on a global concern.

The focus is on the longer-, as well as the shorter-term, recognising that recovery strategies would be critical as countries move beyond the acute phase of the crisis.

The figure shows the various ongoing activities of the CCGMC – we wish to curate a "COVID-19 and Cancer Global Observatory" that will provide dynamic evidence-based assessments of the current situation that will include a

systematic mapping of policy responses that impact cancer-related services and outcomes.

The principle behind the observatory is to ensure the evidence is continually updated and relevant to IARC Participating States through engagement with the consortium at large so as to enable recovery strategies as countries move beyond the acute phase of the pandemic.

From an IARC perspective, this is very much in line with our mission: supporting a coordinated approach among networks of cancer experts and institutions worldwide, in close cooperation with WHO.

The **IARC-C19 proposal – COVID-19 and cancer initiative**: building back better – will be fully discussed under a separate item (see Document SC/58/5) on Thursday 10 February 2022.



The former Section of Nutrition and Metabolism (NME) included three groups: the Biomarkers Group (BMA), the Nutritional Epidemiology Group (NEP), and the Nutritional Methodology and Biostatistics Group (NMB). In early 2021, the three Groups were merged into a single Branch, the "Nutrition and Metabolism" (NME) Branch (new organizational structure slide 5).

Worldwide industrialization importantly increased the consumption of ultraprocessed foods (**UPFs**) while reducing food biodiversity globally. Epidemiological evidence suggests this worldwide shift partly responsible for the global obesity epidemic and chronic disease burden. Our recent analyses examining associations between UPF consumption and cancer risk in the EPIC cohort also demonstrated positive associations between UPFs and several cancer types while an inverse association was observed for minimally processed foods in relation with most of the cancer outcomes.

Evidence suggests that UPFs may increase cancer risk via their obesogenic properties and their poor nutritional value as well as through exposure to

potentially carcinogenic compounds such as certain food additives and neoformed processing contaminants. Our ongoing research aims to disentangle these pathways further via mediation analyses using biological data available in nested case-control studies embedded in EPIC and other cohorts (e.g. Nutrinet-Sante). This increase in UPF consumption goes hand in hand with a steady decrease in food biodiversity due to industrialization. Our ongoing studies already demonstrate an increased risk of premature death and cancer risk with lower species diversity in our diets.

Through collaborations, we are currently investigating these hypotheses on food processing and biodiversity in relation with human and planetary health in various studies, including EPIC, UK Biobank, the Latin America case-control study on breast cancer (PRECAMA), the South-Africa breast cancer study (SABC) and Nutrinet-Santé.



Ultra-processed food intake has been linked to an increased risk of breast cancer in Western populations. No data is available in countries in epidemiological transitions, although the consumption of ultra-processed foods is increasing rapidly in these regions.

We evaluated the association of ultra-processed food (**UPFs**) intake to breast cancer risk in two population-based case-control studies: the first study set up in Latina America (**The PRECAMA study**, including 525 premenopausal cases, and 525 matched population-based controls from Chile, Colombia, Costa Rica, and Mexico), the second study set up in Johannesburg, South Africa (**The SABC study**, including 396 cases and 396 matched population-based controls from Black women in Soweto). Dietary intake was assessed by using a validated food frequency questionnaire, and the degree of processing of foods was classified according to the NOVA classification.

In PRECAMA, UPF intake was positively associated with the risk of breast cancer overall, and more strongly so with estrogen receptor positive cancers.

Major contributors of UPF intake in this population are detailed in the slide (left panel) and include ready-to-eat/heat foods, carbonated and industrial fruit juice beverage, breakfast cereals and reconstituted meat products.

In SABC, no significant association was observed between UPF intake and breast cancer risk, **but unprocessed/minimally processed food consumption showed a significant inverse association with breast cancer risk overall**, as well as in pre and post-menopausal women separately. Major contributors to unprocessed/minimally processed food in this population are shown in the slide (right panel) and include maize, white rice, apple beetroot, and eggs.

Our findings suggest that the consumption of ultra-processed foods may be associated with the risk of breast cancer in countries in epidemiological transition, and that the consumption of unprocessed/minimally processed foods should be promoted.



Obesity is a major risk factor for endometrial cancer, but the underlying pathways are still unclear. Using targeted metabolomics in samples from the European Prospective Investigation into Cancer and Nutrition (EPIC), we discovered alterations in concentrations of glycine and sphingomyelin C18:O associated with endometrial cancer risk.

We also identified a **metabolic signature of obesity** comprising changes in levels of **specific amino acids and lipids** among more than 4000 EPIC participants and that was more predictive of endometrial cancer risk than anthropometric measures. This metabolic signature seemed potentially reversible following weight loss.



Glycemic traits - such as hyperinsulinemia and hyperglycemia - have been associated with higher colorectal cancer risk in observational studies; however, it is unknown if these associations are causal.

We used Mendelian randomization (MR) to examine potential causal associations of glycemic with colorectal cancer using genetic data from 48 214 colorectal cancer cases and 64 159 controls.

In summary, we found that higher circulating fasting insulin levels increased colorectal cancer risk, while there was little evidence of effects of 2-hour glucose and fasting glucose on colorectal cancer risk.

These results provide strong support for a causal effect of fasting insulin, but not hyperglycemia, on increasing colorectal cancer risk.

The findings suggest that pharmacological or lifestyle interventions that lower circulating insulin levels may be beneficial in preventing colorectal tumorigenesis.



Epidemiological studies that assessed the association between dietary polyphenol intakes and colon cancer risk have reported largely null results, possibly due to measurement error associated with dietary assessment. NME investigated the association between prediagnostic concentrations of 35 polyphenol biomarkers and colon cancer risk.

NME conducted a nested case-control study within the Japan Public health Centre-based prospective study (JPHC study) using plasma samples collected at the time of a five-year follow-up survey between 1995 and 1999. Prediagnostic concentrations of 35 polyphenols from 375 incident colon cancer cases and 710 matched controls were measured by tandem mass spectrometry coupled with ultra-high pressure liquid chromatography.

In sexes combined continuous multivariate models, circulating levels of 3,4dihydroxyphenylpropionic acid, ferulic acid, and caffeic acid were inversely associated with colon cancer risk. These results suggest a possible role of coffee and coffee polyphenols in preventing colorectal cancer.



In early 2021, the former Section of Environment and Radiation was renamed the "Environment and Lifestyle Epidemiology" (ENV) Branch (new organizational structure slide 5).

ENV has been undertaking research into the peculiar high incidence of oesophageal cancer in East Africa. To date, we have established one of Africa's largest cancer studies, specifically focused on this poor prognosis cancer. Our findings to date point to several factors clearly contributing to the disease burden: poor oral health in general and alcohol and tobacco use in men.

We have also examined thermal exposures from the consumption of <u>very hot</u> <u>beverages</u>. We developed the first and easy-to-ascertain THERMAL EXPOSURE INDEX, based on 4 questions: average times you burn your mouth per month, drinking temperature, waiting time between pouring and drinking, and drinking speed. This index shows a very strong increased oesophageal cancer risk as shown in the figure. Most importantly, thermal injury from hot drinks/food might represent a modifiable risk factor in these high-altitude settings.

This work was conducted by two African postdoctoral fellows, generously supported by the UK Medical Research Council (thanks to Dr Mark Palmer) and demonstrates the way we work at IARC – cancer prevention research through capacity building.



This work, funded by the German Radiation Protection board, aims at investigating if mobile phone use is related to glioma risk. Indeed, some casecontrol studies have reported markedly increased Odds-Ratios for glioma in relation to any use of phones. If this relationship was true and causal, it would have led to recent sizable increases in the number of glioma cases.

In collaboration with colleagues from Denmark, Finland, Norway and Sweden, we have conducted a study of the incidence rates of glioma to investigate if the incidence of glioma cases had increased between 1979 and 2016.

Based on 48 645 cases, we observed no recent changes in the long-term time trends as illustrated on the right. We could not detect an impact of the massive use of mobile phones in the Nordic populations on the incidence of glioma.

Moreover, we have computed the number of cases that would have been expected if the Odds-Ratios reported by Hardell and colleagues were causal.

We observed that the expected numbers of cases were not compatible with the observed number of cases, pointing to the role of recall biases in the results of these case-control studies.



The SYNERGY study is a pooled analysis of 14 case-control studies conducted in Europe and Canada including 17 000 lung cancer cases and 21 000 controls with information on lifetime occupational and smoking histories. Exposure to benzo[a]pyrene (BaP) was used as a proxy of polycyclic aromatic hydrocarbons (PAH) and estimated from a quantitative general population job exposure matrix. The main results show that occupational PAH exposure was modestly associated with an increased risk of lung cancer in both men and women, after adjusting for potential confounders. In addition, joint effects of occupational PAH exposure and smoking were present for squamous cell lung cancer both in men and women, and also for small cell lung cancer and adenocarcinoma in women.



ABC-DO treatment data from 5 countries were analysed to inform the third pillar of the WHO Global Breast Cancer Initiative (GBCI), to promote comprehensive breast cancer (BC) management.

On the graph you see the cumulative proportion of women initiating multimodality treatment (at least surgery and systemic treatment) divided by those who completed treatment (dark red), those who abandoned treatment (light blue) and those whose completion remained unknown (dark blue).

The graph shows the huge inter-region disparities: 88% in Namibian non-black women (center top) initiated multimodality treatment against only 41% in Nigeria (top right). **One of the major drivers here was the lack of tumour removal.**

Also, not shown on the graph, only 50% of all women initiating chemotherapy completed at least five cycles, corresponding to 80% of the total dose and needed to experience any curative effect.

The sad conclusion of this findings is that the high TX abandonment in all settings minder the success of what is already achieved in some places and pose an additional barrier to the **low access to multimodality TX** in large parts of Sub-Saharan Africa.



- Taking the European Code against Cancer as a model, the World Code against Cancer serves as a framework to develop Regional Codes, suited to the different regional epidemiological, socio-economic and cultural conditions.
- The Latin America and the Caribbean Code against Cancer is currently under development.
- The outcomes that we will get with each Regional Code are:
- 1. A set of region-specific recommendations on cancer prevention, for the population but also to policy-makers, as new Codes will include recommendations on polices
- 2. Capacity building of primary care professionals on cancer prevention, as new Codes will also specifically target these frontline health professionals
- 3. And Knowledge on the main preventive measures disseminated and impact evaluated
- Therefore, the Latin America and the Caribbean Code against Cancer will offer an exceptional public health tool to guide and support governments in

the implementation of their cancer control strategies, as well as to educate the population on healthy behaviours and encourage participation in prevention programmes.

• The Governance is based in multi-stakeholder participation, where experts and key players from the region are involved from the planning to the dissemination, monitoring and evaluation phases of the project, to ensure ownership of all players to embrace and adopt the Code.



The former Section of Genetics included 2 Groups: the Genetic Epidemiology (GEP) Group and the Genetic Cancer Susceptibility (GCS) Group. In early 2021, the two Groups were merged into a single Branch, the "Genomic Epidemiology" (GEM) Branch (new organizational structure slide 5).

In the context of how germline variation influences cancer susceptibility, GCS has worked within the International Lung Cancer Consortium (ILCCO) to identify a lung cancer susceptibility variant in the DNA repair gene *ATM*. This variant is a missense variant in *ATM* and has an important genetic effect, with allele carriers having an up to 3–4-fold increase in the risk of lung cancer relative to non-carriers. It also appears to be most relevant to lung cancer in women and lung adenocarcinomas in never-smokers; although it is very rare in most parts of the world, it approaches frequencies of 3% in Ashkenazi Jewish populations (Ji et al., 2020).

The Review of the Section of Genetics (2021) will be discussed in a separate item of SC/58 on Wednesday 9 February 2022.



GEP combined the fields of mutational signature analysis with cancer epidemiology to study 552 ESCC genomes from 8 countries with varying incidence rates. The main findings were:

- Mutational profiles were similar across all countries studied
- No evidence of a mutational signature indicative of an exogenous exposure capable of explaining differences in ESCC incidence was found

New research strategies are needed to identify new causes of ESCC.



The effect of smoking cessation in lung cancer survival was evaluated using information collected as part of the 15-year collaborative study with the N.N. Blokhin National Medical Research Centre of Oncology of the Russian Academy of Medical Sciences. GEP showed that smoking cessation after lung cancer diagnosis substantially improved overall and progression-free survival among current smokers with early-stage lung cancer; similar effects were observed among mild to moderate smokers and heavy smokers, and among patients with earlier-stage and later-stage tumours.

This study provides robust evidence indicating that quitting smoking after diagnosis of lung cancer is associated with significant improvement in overall survival and disease-free survival among these patients.



Kidney cancer is a complex disease caused by a combination of genetic and modifiable risk factors, most notably various obesity-related risk factors. To improve our understanding of the metabolic pathways underlying kidney cancer development, with a combination of targeted and untargeted metabolomics, GEP assessed the association between circulating levels of 1415 metabolites and kidney cancer risk, using pre-diagnostic blood samples from up to 1305 kidney cancer case-control pairs from 5 independent European cohorts.

GEP identified **25 metabolites** robustly associated with kidney cancer risk in at least 2 cohorts (p-values below 10-⁴), including 14 glycerophospholipids inversely associated with risk, 5 amino acids positively associated with risk, and one inversely associated with risk, as well as risk association for a carotenoid, 2 peptides, a nucleotide, and an unidentified feature. GEP demonstrated that risk profile of some –but not all– of these risk metabolites were related to BMI. Other risk factors did not appear to have an important role in explaining the association.
GEP showed a potential role for multiple circulating metabolites in kidney cancer etiology that cannot be readily explained by known modifiable risk factors.



The former Section of "Mechanisms of Carcinogenesis" (MCA) included two groups: the Epigenetics Group (EGE), and the Molecular Mechanisms and Biomarkers Group (MMB). In early 2021, the two Groups were merged into a single Branch, the "Epigenomics and Mechanisms" (EGM) Branch (new organizational structure slide 5).

IARC scientists from the MCA Section and partners from Centre Léon Bérard investigated the mutational signatures in ovarian high-grade serous carcinomas (HGSCs) linked to occupational and household exposure to asbestos.

- They identified an enrichment of specific endogenous mutagenic processes in the exposed subgroup.
- And also specific decreased endogenous mutagenesis in the exposed patients, including less frequent mutations in the TP53 gene.
- Experimental exposure to chrysotile asbestos conducted in cells revealed high cytotoxicity.

• and a genome-wide induction of DNA damaging oxidative stress.

This study describes for the first time the specific molecular programs in ovarian HGSCs linked to asbestos exposure.



IARC scientists from the MCA Section, working with international partners, have identified new epigenetic changes that are specific to oesophageal squamous cell carcinoma in tumour samples from populations from different parts of the world. These changes could become the target of new methods to detect this cancer at an early stage in high incidence populations.

The scientists examined incidents of aberrant epigenome (DNA methylation) profiles, alterations of the DNA markings which can be caused by agents in the individual's environment interacting with DNA, in the largest genome-wide DNA methylation study of its kind, using oesophageal squamous cell carcinoma samples from nine countries with high incidence of this disease, including countries in Africa, Asia, and South America.

The scientists found that seven alterations affecting three genes could identify tumours with high sensitivity and specificity, with the potential to be used as oesophageal squamous cell carcinoma markers in low resource settings.



IARC scientists and partners investigated upper tract urothelial cancer patients from the region of endemic nephropathy linked to environmental exposure to the herbal carcinogen aristolochic acid.

- Using a multi-omic approach, they identified complex molecular networks & mutational signatures of these specific urothelial tumours
- A signature of tumour-specific, cell-free urine microRNAs has been identified as potential non-invasive biomarker of presence/recurrence of urinary tract tumours.



IARC scientists from the MCA Section and international partners (including those from Brazil) applied multi-OMICs analysis and state-of-the-art molecular mapping in cutaneous and acral melanomas uncovered novel cancer driver genes affecting patient prognosis and biological mechanisms and biomarkers underpinning intrinsic pathological characteristics and extrinsic responses to UV exposure. These findings impact melanoma classification and patient risk stratification and reveal driver genes for targeted therapy.

DNA methylome, genome and transcriptome analyses of cutaneous melanoma in two cohorts identified UV-related alterations in regulatory regions and immunological pathways and revealed novel cancer driver genes affecting patient survival. *TAPBP*, the top gene and a member of the immunoglobulin superfamily, encompassed several CpG methylation sites altered by UV and independently validated by bisulfite pyrosequencing, providing cost-effective opportunities for clinical application. The DNA methylome also highlighted non UV-related aberrations underlying pathological differences between cutaneous and acral melanomas.

Unsupervised epigenomic mapping demonstrated that non UV-mutant cutaneous melanoma more closely resembles acral rather than UV-exposed cutaneous melanoma, with the latter showing better patient prognosis than the other two forms. These gene-environment interactions reveal translationally impactful mechanisms in melanomagenesis.



The former "Infections and Cancer Biology" (ICB) Group within the former Section of "Infections" is now embedded in the new "Epigenomics and Mechanisms" (EGM) Branch (new organizational structure slide 5).

Under physiological conditions, UV irradiation of the skin induces DNA mutations in keratinocytes and immunosuppression. The UV-induced damage results in either cell-cycle arrest and repair of DNA mutations, or apoptosis if the DNA damage is unrepairable. The β -HPV early proteins E6 and E7 can alter the cellular response to UV-induced stress and promote the survival of DNA-damaged cells that have a high risk of evolving into cancer cells. After accumulation of mutations in oncogenic driver genes (for example, cellular tumour suppressor genes or oncogenes), the expression of the viral genes becomes dispensable.



The former "Infections and Cancer Epidemiology" (ICE) Group within the former Section of Infections is now embedded in the new "Early Detection, Prevention and Infections" (EPR) Branch (new organizational structure slide 5).

Given the amenability of infections to prevention, estimates of infectionattributable cancer burden are key public health indicators, ICE updated estimates of infection-attributable cancer burden at the country, regional, and global levels with the most pertinent exposure assessment tools and the latest global cancer incidence data for 11 infectious carcinogens (viruses, bacteria, and parasites).

Follow-up analyses focused on the global burden of cervical cancer attributable to HIV infection, showing that 5% of the global burden of cervical cancer was due to HIV infection. Southern Africa accounted for 44% of cervical cancer cases attributable to HIV infection. 71% of global burden of Kaposi sarcoma was due to HIV infection, with up to 93% of cancer cases due to HIV infection in Sub-Saharan

Africa.

These findings are important to raise awareness for the control of oncogenic infections, particularly in an era where global cancer prevention is seen within the context of noncommunicable diseases.



The former Section of "Early Detection and Prevention" included two Groups: the Screening Group (SCR) and the Prevention and Implementation Group (PRI). In early 2021, the two Groups were merged with the former "Infections and Cancer Epidemiology" Group (ICE) into a single Branch, the "Early Detection, Prevention and Infections" (EPR) Branch (new organizational structure slide 5).

The SCR study under way in India recently reported that the vaccine efficacy of a single dose of quadrivalent HPV vaccine was as high as that of two doses and three doses at a median follow-up of 9.0 years. Vaccine efficacy against persistent HPV16/18 infection was 95.4% in recipients of a single dose, 93.1% in recipients of two doses, and 93.3% in recipients of three doses.

A recommendation of a single dose will significantly improve the affordability of vaccination programmes against HPV.



The objective of SCR project "Reduction of inequalities in cancer screening: a case study in the Community of Caribbean and Latin American States (CELAC)" is to examine policies in CELAC aimed at reducing inequalities in effective participation of the eligible population in cancer screening. The project, implemented in collaboration with the Centre for Global Health Inequalities Research (CHAIN) in Norway (supported by the Research Council of Norway) and the Pan American Health Organization (PAHO), also aims to enhance the capacity of the cancer screening programme managers in CELAC to implement quality-assured screening programmes. This has become an integral part of the IARC project Cancer Screening in Five Continents (CanScreen5) (<u>https://canscreen5.iarc.fr</u>).



This is a study from the former Prevention and Implementation Group (PRI) within the former Section of "Early Detection and Prevention" now embedded in the new "Early Detection, Prevention and Infections" Branch (new organizational structure slide 5).

The ESTAMPA study investigates **cervical cancer screening and triage techniques** in women (aged 30–64 years) in **nine countries in Latin America**. HPV-positive women receive colposcopy, biopsy, and treatment and a second screen after 18 months as needed. The main outcome is advanced cancer precursors. More than 42 000 women have been recruited, and a high adherence to the screening process has been reported; 95% of high-grade lesions detected have been treated. Results are supported by a study network promoting the sharing of experiences among more than 200 multidisciplinary professionals. In addition, the **Psycho-ESTAMPA tool** to assess the psychosocial impact of an HPV-positive screening result was developed and validated and will be used to measure the impact of various methods of communicating HPV test results.



The former Section of Evidence Synthesis and Classification (ESC) comprised three Groups: the IARC Monographs Group (IMO), the IARC Handbooks Group (IHB), and the WHO Classification of Tumours Group (WCT). In early 2021, the Section was renamed the "Evidence Synthesis and Classification" (ESC) Branch (new organizational structure slide 5).

The work of WCT encompasses the *WHO Classification of Tumours* series (also known as the WHO Blue Books), the IARC histopathology laboratory, and the International Collaboration for Cancer Classification and Research (IC³R).

During the 2020–2021 biennium, the following 4 volumes were published: Soft Tissue and Bone Tumours, fifth edition (2020) Female Genital Tumours, fifth edition (2020) Thoracic Tumours, fifth edition (2021). Central Nervous System Tumours, fifth edition (2021).



The International Collaboration for Cancer Classification and Research (IC³R; <u>https://ic3r.iarc.who.int/</u>) was established to bring cancer research institutions together to improve research quality and to meet the need for evaluation and synthesis of research findings. Currently, 22 institutions are involved in IC³R, and it is funded by membership dues.



This *Handbook* is a first-time evaluation of all approaches to oral cancer prevention, with a special emphasis on low- and middle-income countries and on oral cancer associated with the use of smokeless tobacco and products derived from the areca nut. This *Handbook* will cover primary prevention through the evaluation of whether reduction of exposure to the established (IARC Group 1) risk factors leads to reduced incidence or mortality, primary prevention through interventions aiming to reduce exposure to smokeless tobacco or products derived from the areca nut, and secondary prevention through screening.

A scoping meeting for Volume 19 took place in February 2021, and the meeting took place fully remotely between September and December, first in subgroups and then in plenary sessions. The evaluations reached at this *Handbooks* meeting will lead to the development of tools and recommendations for the implementation of prevention measures in those countries most in need.



IMO organized two virtual Working Group meetings in 2021. The agents evaluated at the two Working Group meetings included several that had been recommended as priorities for evaluation:

Volume 129: Gentian Violet, Leucogentian Violet, Malachite Green, Leucomalachite Green, and CI Direct Blue 218 (22 February–5 March 2021) Volume 130: 1,1,1-Trichloroethane, Hydrazobenzene, *N*-Methylolacrylamide, Diphenylamine, and Isophorone (7–22 October 2021).

The evaluations reached in these meetings included new or updated classifications for 10 agents:

- Group 2A: 1,1,1-Trichloroethane
- **Group 2B**: Gentian violet, leucomalachite green, CI Direct Blue 218, 1,2-diphenyl hydrazine, diphenylamine, *N*-methylol-acrylamide, isophorone
- **Group 3**: Leucogentian violet, malachite green

In 2021, the following *IARC Monographs* volumes were published: Volume 128: Acrolein, Crotonaldehyde, and Arecoline (2021) Volume 127: Some Aromatic Amines and Related Compounds (2021) Volume 126: Opium Consumption (2021)



In 2021, IMO provided an invited commentary on a new article about endocrine-disrupting chemicals and pollutants published in the journal *Environmental Health Perspectives*.

The scientists who prepared the article that is the subject of the commentary analysed more than 2000 chemicals. They provide evidence suggesting that several hundred common chemicals, including pesticides, ingredients in consumer products, food additives, and drinking-water contaminants, caused human cells in culture to produce more of the hormones estrogen or progesterone. Such excess hormone production is one known mechanism of breast cancer.

In their commentary, the authors from the *IARC Monographs* programme highlight important gaps in evidence on the causes of breast cancer and address how data from validated assays relevant to key characteristics of carcinogens, including in studies in exposed women, can help prioritize chemicals for further study and evaluation.

Prioritizing cancer hazard assessments: systematic evaluation of literature data on the cancer hazards of human exposures is an essential process underlying cancer prevention strategies. The scope and volume of evidence for suspected carcinogens can range from very few to thousands of publications, requiring a complex, systematically planned, and critical procedure to nominate, prioritize and evaluate carcinogenic agents. To aid in this process, database fusion, cheminformatics and text mining techniques can be combined into an integrated approach to inform agent prioritization, selection, and grouping.



In early 2021, the former "Education and Training" Group became the "Learning and Capacity Building" (LCB) Branch (new organizational structure slide 5).

ECVS data

The IARC Research Training and Fellowship Programme offers researchers at different levels of their career opportunities to get trained at IARC through their participation in collaborative research projects.

Those Early Career and Visiting Scientists (ECVS) are supported either by project funds from IARC Groups or by IARC Fellowships.

A total of 254 ECVSs from 58 different countries joined IARC during the biennium. This represents an overall 14% decrease as compared to the former biennium, which is related to the sanitary situation of the COVID-19 pandemic, with reduced mobility due to visa/entry and travel restrictions. Despite this overall decrease of ECVSs hosted at IARC during the biennium,

the number of postdoctoral scientists and doctoral students, priority target audience of the programme, has remained stable as compared to the previous biennium.

IARC Postdoctoral Fellowships

The Agency awarded seven IARC Postdoctoral Fellowships to LMIC **c**andidates for projects in line with IARC's emerging priorities or on the relation between cancer and COVID-19. In addition, and to identify complementary sources of funding for the programme, negotiations with Children with Cancer UK led to an ad hoc call for IARC Postdoctoral Fellowships targeting scientists wishing to carry our research on paediatric cancers or teenagers and young adults cancers. Two fellowships were awarded.

Three return grants were awarded, to help establishing the former IARC Postdoctoral Fellows' research activities in their home countries.

UICC-IARC Short-term fellowships

In collaboration with the Union for International Cancer Control, seven UICC-IARC Development Fellowship were awarded, to enable a selected number of LMIC participants of the IARC Summer School to come to IARC for a period of one month for further training and collaboration.

The Biennial Report on IARC education and training activities will be discussed in a separate items of Scientific Council (SC/58/6) on Thursday 10 February 2022.



An IARC Mentoring Programme was developed as part of the IARC Quality of Worklife Initiative.

In view of the limited available resources, a group of volunteers representing the variety of IARC personnel and led by LCB Head was set-up.

A needs assessment survey established and open to all IARC personnel in 2020 allowed the design and set-up of a programme adapted to the needs, resources and expectations of IARC personnel.

Based on those results, it appeared that, besides postdoctoral scientists and doctoral students, all IARC personnel would benefit from such a programme.

An IARC-wide call for volunteer mentors was therefore launched and over 40 colleagues expressed interest to support their colleagues in sharing knowledge, skills, network, information and perspectives to enhance personal and professional growth, as well as learn themselves through the process. A

list with short description of all mentors is available through the Career Prospects Portal, together with guidance and tools to set-up mentoring relationships.

The programme was launched in Summer 2021 as a one-year pilot and a first "IARC mentorship discussions" session was organized in October 2021. Surveys and discussions are planned to monitor the uptake of the programme and to allow refinements of its design and organization.



IARC Learning Portal

Launched in 2019, the IARC Learning portal is the entry door to thematic learning platforms (Biobanking, Cancer Prevention and Early Detection and World Cancer Report Updates). It also links to the IARC WebTV, including the Summer School video channel, as well as to the websites of other IARC-led projects with learning material on Cancer Surveillance and on the Exposome (Human Exposome Assessment Platform). IARC Learning attracts a growingly increasing audience. Since November 2019, 1554 persons (1423 in 2020-21) have created an account on the portal to freely access learning resources.

Learning resources

As a key complement to live events, IARC continued to produce self-learning resources. A new self-paced learning programme on cancer screening and early diagnosis, was launched in the framework of the CanScreen5 project. The resource was translated into Russian and will soon be available in Spanish (https://learning.iarc.fr/edp/resources/pgm-cancer-screening/).

As part of the Cancer Prevention Europe consortium, self-learning modules on the European Code Against Cancer, 4th edition, were produced and are translated into French, Spanish, Hungarian and Polish (<u>https://learning.iarc.fr/edp/cpe/</u>-Figure 3).



The IARC Summer School in Epidemiology aims to improve the methodological and practical skills of cancer researchers and health professionals. With the COVID-19 crisis, the 2021 course was entirely redesigned and conducted 100% online, with a priority to maintain what makes the course so unique: fostering international collaboration, offering multiple opportunities for interactions, as well as delivering high-quality multidisciplinary lectures and practical activities to facilitate the learning process of participants.

A blended learning approach was adopted for both modules: 4 weeks of selfpaced activities (recorded lectures and assignments punctuated by 2/3 live sessions and networking events), followed by 2 weeks of daily live sessions, and group work activities. Two modules were held "Introduction to Cancer Epidemiology" and "Implementing Cancer Prevention and Early Detection", with the participation of 73 cancer researchers and health professionals from over 45 countries, in vast majority from LMICs (Figure 5).

The material of the Summer School 2021 has been shared widely via the IARC

Learning portal (<u>https://learning.iarc.fr</u>).

Participants were invited to record their impressions and experience as participants in the 2021 edition. Those <u>testimonials</u> illustrate well the spirit of the IARC Summer School: experience sharing, learning and international networking for cancer prevention across nations. The feedback from participants and the assessment from the course directors and main players of this edition will provide a good ground for the design of future editions of the IARC Summer School and other similar events, to make sure that, when permitted, potential onsite components of courses will be even more focused on practical and networking aspects.



The former "Laboratory Services and Biobank" Group (LSB) has been renamed the "Laboratory Support, Biobanking and Services" (LSB) (new organizational structure slide 5).

To address the underrepresentation of biological resources in low- and middle-income countries (LMICs) in research, the LMICs Biobank and Cohort Building Network (**BCNet**; <u>https://bcnet.iarc.fr/</u>) was established by IARC in 2013. Currently, **36 institutions in 24 countries are members of BCNet**. During the biennium, BCNet delivered four presentations to external collaborators (in Nigeria, Kenya, the Philippines, and Macao Special Administrative Region, China) and published several seminal articles.



During the biennium, LSB investigated the impact of the COVID-19 pandemic on Biopreservation and Biobanking, and published a special issue in "Biopreservation and Biobanking", vol 18, issue 6, 2020.



- The IARC cross-cutting Working Group **Knowledge Translation and Transfer** (**KTT**) was created in 2020 as a dynamic interdisciplinary group of scientists and experts in strategy and communication.
- It aims to build bridges between scientific findings and decision-making, and to fill the gap in communication of the knowledge that IARC and collaborators produce, to stakeholders' benefit and use.
- The objective is to call attention to research findings that can make a difference in cancer prevention and stimulate action.
- The target audience are Ministries of Health, policymakers, national public health institutes, civil society organizations, cancer leagues, health professionals' societies, IARC Participating States, etc.
- In the first year, the WG has launched the first output: the IARC Evidence Summary Brief Series which has gained positive media attention.
- The first brief was on "Breast cancer outcomes in Sub-saharan Africa", and the second one on "The Nutri-score: a science-based front-of-pack nutrition label".

- Each Evidence Summary Brief has a "Call to action" section, which calls upon stakeholders to take actions (such as advocacy, policy making, research, or the implementation of cancer prevention interventions and policies), as a result of the research outcomes presented.
- The WG has also done a pilot survey and interviews to key stakeholders, to assess the potential usability and impact of the briefs and get advice on how to improve them.





Here is a brief update of the 63rd session of the Governing Council, held virtually on 17 and 18 May 2021.

This was, for the second time, a virtual Governing Council meeting. Thanks to ITS and all other IARC personnel who helped making this happen so smoothly!



IARC is pleased to welcome China as a new Participating State. IARC now has a total of 27 Participating States.

This new membership will further strengthen collaboration in key cancer research areas and allow China to join a network of leading countries shaping global research priorities in cancer control and cancer prevention.



The Governing Council adopted the IARC Medium-Term Strategy for 2021–2025 during the 63rd Session of the Governing Council, in May 2021. This Medium-Term Strategy seeks to position IARC as the leading global cancer authority, promoting scientific excellence and improved knowledge of cancer prevention.

The Medium-Term Strategy sets out IARC's priorities for the period 2021–2025, with a view to ensuring that the Agency's activities have a significant and sustainable impact on the global burden of cancer and, ultimately, on the life and health of the world's citizens.

The Governing Council requested the Director to make a proposal for an evaluation approach of the MTS 2021-2025 at the next session of the Governing Council in 2022.

The Governing Council expressed its satisfaction with the Director's Report and commended the Director for her constructive responses to the
recommendations of the 57th session of the Scientific Council.

The "Evaluation Framework of the IARC Medium-Term Strategy 2021-2025 and its key performance indicators" will be discussed in a separate item of Scientific Council (see Document SC/58/4) on Thursday 10 February 2022.



With regard to the proposed Programme and Budget 2022-2023.

The initial proposed budget was not supported during the financial dialogue, and IARC was asked to prepare and submit an alternative proposal to the Governing Council.

This meant a ≤ 3.3 million cut from the initial budget proposal. Consequently, the initial proposed programme and activities would have to be scaled down.

While the revised budget that was approved by the Governing Council still has an increase of €1.22 million compared to the current biennium, this increase was not sufficient to cover the statutory cost increase.

In order to achieve a €3.3 million cut and be able to absorb the statutory cost increase, a total of 11 staff positions had to be removed from the initial proposed Programme and Budget. Those included new positions requested by some Branches and existing positions that are currently funded from extrabudgetary funds.

To fulfil the ambitious goals set in the approved Medium-Term Strategy, the Agency will need to mobilize extrabudgetary resources to strengthen its capacity.

		Programme and budget 2022-2023	•	
The Governing C	Council:			
• Approved t	he bud	get for the biennium 2022-2023 at the level of:		
		€45 371 329		
	-	at the presentation and priorities of the proposed bu Medium-Term Strategy 2021-2025, and	dget for 202	2-2023 are
Approved th Tree for the b		ation of budget to the six main level 2 objectives of 2022-2023:	of the new I	ARC Project
-	Section	IARC Project Tree – Level 2 Objectives	Amount (€)	
	1.	Describing the occurrence of cancer	3 947 686	
	2.	Understanding the causes of cancer	10 505 426	
	3.	Evaluating cancer prevention interventions	5 310 608	
	4.	Synthesizing and mobilizing knowledge and strengthening global capacities in cancer science	6 388 053	
	5.	Strengthening the Agency's leadership, governance, strategic engagement, and advocacy	5 184 683	
	6.	Strengthening the efficiency and effectiveness of the Agency's research and collaboration	14 034 873	
		Total	45 371 329	
Update 63 rd Sessio	on of the Gove	erning Council 9-11 February 2022		52

The Governing Council:

- Approved the budget for the biennium 2022-2023 at the level of: €45 371 329
- Acknowledged that the presentation and priorities of the proposed budget for 2022-2023 are aligned with the new Medium-Term Strategy 2021-2025
- Approved the allocation of this budget to the six main level 2 objectives of the new IARC Project Tree for the biennium 2022-2023, as reported in the Table.



The Governing Council authorized the Director to use up to a maximum of €420 000 from the GCSF for the acquisition of:

- Equipment for the histopathology platform
- Core IT infrastructures and services



With regards to the Nouveau Centre, the Governing Council:

- Acknowledged the remaining funding gap of €7.6 million for a fully operational, modern, smart and open building with €2.6 million to be mobilized prior to September 2021 to ensure that "Priority 1" operational equipment is purchased prior to the move to the Nouveau Centre.
- Authorized a loan up to €1 million from the GCSF to fund "Priority 1" items, to be reimbursed over a five-year period.

The "update on the Nouveau Centre and on resource mobilization" will be discussed in a separate item of Scientific Council (see Document SC/58/7) on Thursday 10 February 2022.





The 57th session of the IARC Scientific Council was held remotely for the first time on 10-12 February 2021 and it went very well.

The length of the meeting was reduced to approximately four hours per day. To accommodate the virtual meeting and the reduced length, all presentations normally given at the meeting were prepared by the IARC leadership and staff before the meeting.



Highlights from the Director's Report

The SC members were very pleased with the Director's Report on the activities and research accomplished during the past year. The main topics that were discussed were as follows:

- Professional development for personnel and scientists it is clear that the leadership has invested considerable thought and energy in developing a new Learning and Development Plan for 2021 that will cover not only core and job-specific competencies but also management and leadership skills. These courses are being offered online and will be addressing equity, diversity and inclusion topics as well.
- COVID-19 Impact there was a lengthy discussion regarding the impact of COVID-19:

First on the operations of IARC and then on the research that has been initiated as a result of the pandemic.

IARC is actively involved in the COVID-19 Cancer Taskforce (Dr Freddie Bray is the focal point at IARC) that is examining the impact of the pandemic on cancer surveillances, cancer screening and services and cancer policies in the

short- and long-term. The impact of COVID-19 on mortality from cancer was also highlighted as an important area to consider. There are key learnings from the pandemic that will be used to "build back better" after the pandemic.



The SC were very enthusiastic about both the content and layout of the MTS 2021-2025 and fully endorsed this plan.

They also recognized the extraordinary efforts made by the Director and her staff to respond to the GC's request for external evaluation of IARC's activities and the last MTS, as well as the approach that was taken in developing the new MTS.

The SC congratulated the Director for creating this outstanding strategic plan that provides clear goals and objectives for the next five years.

The SC was supportive of the emphasis on implementation science as an emerging area of focus.

The SC was also supportive of strengthened collaboration with the WHO on some major cancer initiatives for cervical, breast and childhood cancers.

The SC was supportive of the Open Science approach that is being emphasized in the MTS and discussed opportunities for more collaborations with scientists in Participating States.

	General Data Protection Regulation Rationale and Background of the Project
•	IARC is part of a complex data protection framework , with many collaborators being subject to national or EU law, while IARC as a UN institution operates outside of such framework
•	EU (and also some non-EU based) collaborators have increasing difficulties in transferring personal data to IARC. These collaborators are concerned about both the processing at IARC, but also about the onward transfer of samples and data to third parties
•	In 2021, IARC assessed current practices, identified the gaps, initiated a substantive evolution of the regulatory framework with the IARC Data Protection Policy (embedded into a WHO process) and transformed the technical infrastructure of IARC
•	The ultimate aim is to establish IARC as the most data privacy friendly cancer research institution, thus attracting data and researchers
•	The project followed the rationale of a policy making wheel, starting with an in-depth assessment, followed by a policy development phase (ongoing), that leads to an assurance step (as a next step)
•	We also transformed the organization by setting up a Data Protection Officer function, and by rolling out a Data Steward concept in the organization

Update $\rm 57^{th}\,Session$ from the Scientific Council

9-11 February 2022

57

	ssing activities within IARC (scientific and non-scientific);	
 Necessary to live up to worldwide data prot 		
 IARC's organization wide ROPA has been de almost finalized. 	eveloped and a 6 monthly audit process was created; The first audit process	s is
Goal of ROPA		
 Show all processing of data is intentional, w 	vell-thought-out and documented	
- Where does the data come from?		
- What is it used for?		
- With whom do we share it?		
- Where is it stored and for how long?		
- Are IT assets being used for the proces	ssing of the data?	
- Based on which contracts/policies/legal	basis is the data processed?	
 Point out gaps in day-to-day handling of data 	ta and trigger recommendations	
 Not well-thought-out/unintentional proc 	cessing of data;	
- Gaps in, or missing policies/work instru	ictions etc.;	
- Need for (adjustments in) contracts.		
Collaborators feel comfortable sharing data	with and receiving data from IARC and using IARC's platforms and biobank	
Ultimate goal		
IARC the agency of choice for storing and shari	ng global cancer research data	



- The SC congratulated the Director and her staff for preparing such a detailed plan and for sharing it with them which provided an unprecendented level of clarity and accountability.
- Given the Financing Dialogue meetings of the GC, regarding the biennum budget for 2022-2023, that resulted in an overall decrease in funds available for that time period, an additional revised budget was presented to the SC.
- The SC endorsed the areas for scaling down should budget be cut and discussed the implications for the implementation of the MTS 2021-2025 of this reduced budget
- There is a variety of strategies to deal with this impasse, with the chosen approach being a generalised cut across the board. It was indicated that several positions vacated over the past two years, due to natural attrition (i.e. retirement or resignation) have been unfortunately frozen. Mitigation measures include attraction of additional external grant income and support from current Participating States, along with attraction of new Participating States.

- The SC recognized the importance of all the research areas to the MTS and were concerned about the risks to the Agency to remain competitive internationally without additional resources.
- The SC explored various options of increasing capacity within the Agency including utilizing volunteers and supporting secondments of scientists from external universities, institutes and agencies.



The SC appreciated the updates on the Nouveau Centre and the efforts that are being made to identify and secure additional funding for the equipment, furniture and outfitting of the building.

Several types of fundraising for the Nouveau Centre were discussed and the need to identify more sources of philanthrophy was emphasized.

The SC recognized that the lack of suitable premises for IARC research could incur significant risk to the continuation and implementation of their strategic research plans.

During the meeting, the SC members learned that Norway has made a voluntary contribution of €150 000 towards the Nouveau Centre that was just received.

Other countries are urged to consider similar voluntary contributions towards the €9 million still needed to complete the infrastructure for the Nouveau Centre.

