



Grant Number: 3U01CA033193-32S1
FAIN: U01CA033193

Principal Investigator(s):
Kurt Straif

Project Title: Evaluation of Carcinogenic Risks to Humans

INTERNATIONAL AGENCY-RES CANCER
150 COURS ALBERT THOMAS
F-69372 LYON CEDEX 08, FRANCE,
FRANCE

Award e-mailed to: igo@iarc.fr

Budget Period: 09/01/2013 – 08/31/2014
Project Period: 09/01/1985 – 08/31/2015

Dear Business Official:

The National Institutes of Health hereby awards a grant in the amount of \$20,000 (see “Award Calculation” in Section I and “Terms and Conditions” in Section III) to INTERNATIONAL AGENCY FOR RES ON CANCER in support of the above referenced project. This award is pursuant to the authority of 42 USC 241 31 USC 6305 42 CFR 52 and is subject to the requirements of this statute and regulation and of other referenced, incorporated or attached terms and conditions.

Acceptance of this award including the “Terms and Conditions” is acknowledged by the grantee when funds are drawn down or otherwise obtained from the grant payment system.

Each publication, press release, or other document about research supported by an NIH award must include an acknowledgment of NIH award support and a disclaimer such as “Research reported in this publication was supported by the National Cancer Institute of the National Institutes of Health under Award Number U01CA033193. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.” Prior to issuing a press release concerning the outcome of this research, please notify the NIH awarding IC in advance to allow for coordination.

Award recipients must promote objectivity in research by establishing standards that provide a reasonable expectation that the design, conduct and reporting of research funded under NIH awards will be free from bias resulting from an Investigator’s Financial Conflict of Interest (FCOI), in accordance with the 2011 revised regulation at 42 CFR Part 50 Subpart F. The Institution shall submit all FCOI reports to the NIH through the eRA Commons FCOI Module. The regulation does not apply to Phase I Small Business Innovative Research (SBIR) and Small Business Technology Transfer (STTR) awards. Consult the NIH website <http://grants.nih.gov/grants/policy/coi/> for a link to the regulation and additional important information.

If you have any questions about this award, please contact the individual(s) referenced in Section IV.

Sincerely yours,

Joy Kearse

Grants Management Officer
NATIONAL CANCER INSTITUTE

Additional information follows

SECTION I – AWARD DATA – 3U01CA033193-32S1**Award Calculation (U.S. Dollars)**

Other Costs	\$20,000
Federal Direct Costs	\$20,000
Approved Budget	\$20,000
Federal Share	\$20,000
TOTAL FEDERAL AWARD AMOUNT	\$20,000
AMOUNT OF THIS ACTION (FEDERAL SHARE)	\$20,000

SUMMARY TOTAL FEDERAL AWARD AMOUNT YEAR (32)	
GRANT NUMBER	TOTAL FEDERAL AWARD AMOUNT
3U01CA033193-32S1	\$20,000
4U01CA033193-32	\$780,856
TOTAL	\$800,856

SUMMARY TOTALS FOR ALL YEARS		
YR	THIS AWARD	CUMULATIVE TOTALS
32	\$20,000	\$800,856
33	(b)(5)	

Recommended future year total cost support, subject to the availability of funds and satisfactory progress of the project

Fiscal Information:

CFDA Number: 93.393
EIN: 1900210016A1
Document Number: UCA033193H

PMS Account Type: B (Subaccount)
Fiscal Year: 2014

IC	CAN	2014
CA	8479565	\$20,000

Recommended future year total cost support, subject to the availability of funds and satisfactory progress of the project

NIH Administrative Data:

PCC: Y7DC / **OC:** 414N / **Released:** KEARSEJ 05/13/2014
Award Processed: 05/08/2014 01:52:21 PM

SECTION II – PAYMENT/HOTLINE INFORMATION – 3U01CA033193-32S1

For payment and HHS Office of Inspector General Hotline information, see the NIH Home Page at <http://grants.nih.gov/grants/policy/awardconditions.htm>

SECTION III – TERMS AND CONDITIONS – 3U01CA033193-32S1

This award is based on the application submitted to, and as approved by, NIH on the above-titled project and is subject to the terms and conditions incorporated either directly or by reference in the following:

- The grant program legislation and program regulation cited in this Notice of Award.
- Conditions on activities and expenditure of funds in other statutory requirements, such as those included in appropriations acts.
- 45 CFR Part 74 or 45 CFR Part 92 as applicable.

- d. The NIH Grants Policy Statement, including addenda in effect as of the beginning date of the budget period.
- e. This award notice, INCLUDING THE TERMS AND CONDITIONS CITED BELOW.

(See NIH Home Page at <http://grants.nih.gov/grants/policy/awardconditions.htm> for certain references cited above.)

Carry over of an unobligated balance into the next budget period requires Grants Management Officer prior approval.

This award is subject to the requirements of 2 CFR Part 25 for institutions to receive a Dun & Bradstreet Universal Numbering System (DUNS) number and maintain an active registration in the Central Contractor Registration. Should a consortium/subaward be issued under this award, a DUNS requirement must be included. See <http://grants.nih.gov/grants/policy/awardconditions.htm> for the full NIH award term implementing this requirement and other additional information.

This award has been assigned the Federal Award Identification Number (FAIN) U01CA033193. Recipients must document the assigned FAIN on each consortium/subaward issued under this award.

This award is not subject to the Transparency Act subaward and executive compensation reporting requirement of 2 CFR Part 170.

In accordance with P.L. 110-161, compliance with the NIH Public Access Policy is now mandatory. For more information, see NOT-OD-08-033 and the Public Access website: <http://publicaccess.nih.gov/>.

Treatment of Program Income:
Additional Costs

SECTION IV – CA Special Terms and Conditions – 3U01CA033193-32S1

REQUIREMENT: This award is issued as a cooperative agreement, a financial assistance mechanism in which substantial NIH scientific and/or programmatic involvement is anticipated in the performance of the activity. This award is subject to the Terms and Conditions of Award below, which are hereby incorporated by reference as special terms and conditions of this award.

These special Terms and Conditions of Award are in addition to and not in lieu of otherwise applicable OMB administrative guidelines, Federal Regulations, including HHS Grant Administration Regulations at 42 CFR Part 52, 45 CFR Parts 74 and 92, and other HHS, PHS, and NIH Grant Administration policy statements.

Collaborative Terms of Award

Nature of Collaboration with NCI Staff

NCI has certain responsibilities in terms of this cooperative agreement which involve assistance, information support, and scientific collaboration.

1. Scientific Resource

Since the monographs on each chemical which appear in the columns published by IARC are fundamentally an international information resource and data bank on carcinogenesis and evaluation of qualitative risk of chemicals to human, NCI, in an assistance and cooperative role, provides information and data which assist IARC staff in the preparation of certain sections of the final monograph (Sections 1.1 to 2.3). Sections 3.1 to 4.3 are developed by the Working Groups which consist of international scientists who review all these documents at the time of the meetings (3 per year) in Lyon, France. The National Cancer Institute, through arrangements with a contractor will provide such assistance.

2. Planning for Meetings of the Working Group

The IARC project is one of international support with NCI being the USA supporter for the monograph and the Information Bulletins on the Survey of Chemicals Being Tested for Carcinogenicity. This bulletin is a listing of chemicals being tested in laboratories throughout the world. Under the Cooperative Agreement, NCI:

- a. Makes suggestions to IARC on types of chemicals that should be evaluated at the three planned working group meetings per held in Lyon, France.
- b. Makes suggestions and gives assistance to IARC as to USA resource people who should attend and participate in Working Group meetings. Personnel from regulatory agencies and trade associations should attend as observers.

3. Program Involvement in Relation to Input from NCI

Under the section on scientific resources, reference was made to NCI input as to data on production, occurrence, analysis, and use of chemicals. NCI, also provides information relevant to carcinogenicity on chemicals tested in U.S. laboratories. These data are then incorporated in the Information Bulletin on the Survey of Chemicals Being Tested for Carcinogenicity.

In discussing certain phases of work that involve assistance and collaboration on the part of NCI with IARC, reference was made to the essentiality of effective liaison and support. Participation by the NCI Program Director in the working group meetings in Lyon, France could be either as an observer or as a representative of NCI or as a full member of the working group in his personal capacity as a scientist.

4. Reporting Requirements

NCI wishes to continue a semi-annual reporting requirement with scheduling or due dates for reports worked out by mutual agreement between NCI staff and the IARC principal investigators. The volumes of monographs, supplements and survey bulletins are actually exhibits of achievements and accomplishment. Consequently, the semi-annual reports should dwell on planning, participation, selection of chemicals, problems of interfacing and cooperation and logistical matters. In addition, an annual report to be included in the required continuation applications should reflect that the project continues to conform to the purposes, objectives and conditions of the award and has substantial programmatic involvement by NCI with the performer of the project.

5. Publication and Distribution

One of the significant features of the IARC project in development of this international authoritative reference source is the publication and distribution, on a world-wide basis, of these volumes, including the supplements to the volumes listing Chemicals and Industrial Processes Associated with Cancer in Humans, as well as the Survey Bulletins.

The National Cancer Institute will receive approximately 400 copies of each volume published. The NCI distributes these copies to NCI staff, representatives of other agencies interested in environmental and occupational carcinogenesis, selected university scientist engaged in carcinogenesis research, public health organizations and medical libraries. Therefore, many organizations and scientists in the USA and abroad benefit from this program, which is partially supported by the National Cancer Institute.

The following administrative terms also apply:

RESTRICTION: This supplemental award provides supplemental support in the amount of \$20,000 as requested in the awardee's letter dated July 31, 2013. These funds are restricted and may not be expended for any other purpose without the written prior approval of the National Cancer Institute. Funds awarded are available for carryover for awards given carryover authority as reflected in section III of this award notice. However, the funds remain restricted for the purpose for which the supplement is awarded.

REQUIREMENT: If a renewal application is submitted for this project, the requested budget is subject to the direct cost cap calculated in accordance with the National Cancer Institute's (NCI) policy, "Policy for Allowable Requested Budget Levels of Renewal (Type 2) R01, U01 and P01

Applications." This policy was announced in the NIH Guide for Grants and Contracts on August 15, 2008 and can be found at: <http://grants.nih.gov/grants/guide/notice-files/NOT-CA-08-026.html>

INFORMATION: The policies and procedures announced in Guide Notice NOT-OD-12-139, <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-12-139.html> apply to this award.

STAFF CONTACTS

The Grants Management Specialist is responsible for the negotiation, award and administration of this project and for interpretation of Grants Administration policies and provisions. The Program Official is responsible for the scientific, programmatic and technical aspects of this project. These individuals work together in overall project administration. Prior approval requests (signed by an Authorized Organizational Representative) should be submitted in writing to the Grants Management Specialist. Requests may be made via e-mail.

Grants Management Specialist: Joy Kearse
Email: kearsej@mail.nih.gov **Phone:** 301-631-3002 **Fax:** 301-451-5391

Program Official: Ronald L Johnson
Email: rjohnso2@mail.nih.gov **Phone:** 240-276-6190

SPREADSHEET SUMMARY

GRANT NUMBER: 3U01CA033193-32S1

INSTITUTION: INTERNATIONAL AGENCY FOR RES ON CANCER

Budget	Year 32	Year 33
Other Costs	\$20,000	(b)(5)
TOTAL FEDERAL DC	\$20,000	
TOTAL FEDERAL F&A		
TOTAL COST	\$20,000	

International Agency for Research on Cancer



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Ref.:

31 July 2013

Request for an administrative supplement to Grant No 5U01CA033193

Dear Dr Blair,

As previously discussed, we are pleased to attach our request for an administrative supplement to our grant for the IARC Monographs programme in order to develop a link on the IARC web-pages to access NCI grants relevant to a given agent.

We look forward to a continued fruitful collaboration between our institutes.

Yours sincerely,



Dr Kurt Straif
Head, IARC Monographs Section



Dr Christopher P. Wild
Director

ENCL: As mentioned

c.c.: Dr Betsy L. Read-Connole (bconnole@mail.nih.gov)
Dr Britt C. Reid (reidbr@mail.nih.gov)
Dr Sheri D. Schully (schullys@nih.gov)

Administrative Supplement Request to

Grant number: 5U01CA033193,

Program Director: STRAIF, Kurt

Organization: International Agency for Research on Cancer

Project Title: Evaluation of Carcinogenic Risks to Humans

For funds to support linking the IARC Monographs and the NCI grants databases

Summary

The aim of the IARC Monographs on the Evaluation of Carcinogenic Risks to Humans is to critically review and evaluate the published scientific evidence on carcinogenic hazards to which humans are exposed. These include chemicals, complex mixtures, physical agents, biological agents, occupational exposures, and lifestyle factors. International, interdisciplinary Working Groups (WG) of expert scientists develop the critical reviews and evaluations, which are published in the IARC Monographs series.

Wide dissemination of the information developed in the IARC Monographs is an important objective. The Monographs programme website (<http://monographs.iarc.fr/>) has become the primary means by which scientists and government officials access the Monographs, now that the full text of all Monographs developed to date is being made freely available. Lists of all evaluations and summaries of all Monographs are also available on IARC's website.

To further improve dissemination IARC is developing a web-based fully searchable database allowing all kinds of users to access all evaluations of the Monographs series in a user-friendly and intuitive way. It will be possible to search this database by carcinogenic agent, by cancer site and by classification, and search options using Boolean operators will enable the user to perform complex searches.

With this Administrative Supplement Request we propose to develop a link between this web-based and searchable database of the IARC Monographs and the NCI grants database. This link will allow IARC to better anticipate when to call for Monographs meetings on specific topics and in reverse will allow investigators to better assess current evidence and research gaps and how to tailor any projects they are planning. This project may also serve as a small pilot for linkage with other NCI databases.

Background

The IARC Monographs on the Evaluation of Carcinogenic Risks to Humans represent an international expert-consensus approach to carcinogen hazard identification. The long-term objective is to critically review and evaluate the published scientific evidence on carcinogenic hazards to which humans are exposed. These include chemicals, complex mixtures, physical agents, biological agents, occupational exposures, and lifestyle factors. National and international health agencies use the IARC Monographs as a source of scientific information and as the scientific basis for their actions to prevent exposure to known, probable, and possible carcinogens. Each IARC Monograph contains a critical review of the published scientific literature and an evaluation of the weight of the evidence that an agent can increase the risk of cancer. Agents are selected for evaluation based on evidence of

human exposure and some evidence of carcinogenicity. Agents can be re-evaluated if significant new data become available.

Wide dissemination of the information developed in the IARC Monographs is an important objective. The Monographs programme website (<http://monographs.iarc.fr/>) has become the primary means by which scientists and government officials access the Monographs, now that the full text of all Monographs developed to date is being made freely available. Immediately after each Monograph meeting, IARC scientists write a summary of the results for publication in the next issue of The Lancet Oncology. These, too, are freely available on IARC's website and on The Lancet Oncology's website.

The full text of all Monographs is available free of charge on <http://monographs.iarc.fr/>. All volumes published since Vol. 43 (1989) and Supplements 1, 4 and 7 are now available, as well as the summary sections of Vol. 1– 42. References in recent online versions of Monographs are hyperlinked, i.e., in-text citations are hyperlinked to the bibliography and from there it is possible to directly access each reference in PubMed via PMID.

With the update of the critical review for each Group 1 carcinogen in the framework of the Volume 100 series tumour sites with "sufficient evidence", "limited evidence" or "evidence suggesting lack of carcinogenicity" in humans and plausible mechanisms have been evaluated systematically. For all other agents that have been classified as "probably carcinogenic" or "possibly carcinogenic to humans", associated cancer sites have been summarized by Coglianò et al. (2011). Taken together, for each agent ever evaluated by the IARC Monographs classifications can now also be looked up by classifications by cancer-site specific level of evidence ("sufficient" or "limited"), in addition to the look-up by alphabetical order, by CAS[®] Registry Number, and by Group <http://monographs.iarc.fr/ENG/Classification/index.php>.

As a next step this listing of evaluations is currently developed into a fully searchable indexed database, including the possibility of Boolean searches, such as "agents with sufficient evidence for liver cancer in humans" (screenshot 1)

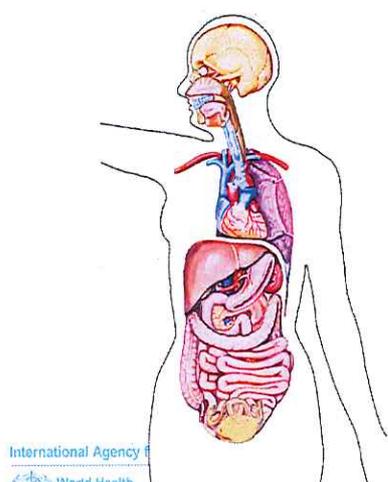
The screenshot shows the IARC Monographs website interface. At the top, there is a search bar and a 'LOGIN' link. The main heading is 'IARC Monographs on the Evaluation of Carcinogenic Risks to Humans'. On the left, there is a navigation menu with categories: AGENTS, ORGAN SITES/CANCER, CATEGORIES, and MONOGRAPHS. The main content area displays search results for 'Liver'. The WHO Classification of tumours is listed as C22.0. Below this, there is a table titled 'Evidence for carcinogenicity at humans' with columns for Agent, Evidence, and Remarks. The table lists several agents with 'sufficient' evidence.

Agent	Evidence	Remarks
Aflatoxins	sufficient	
Alcohol consumption	sufficient	
Hepatitis B virus	sufficient	
Hepatitis C virus	sufficient	
Plutonium-239	sufficient	
Thorium-232	sufficient	
Tobacco smoking	sufficient	
Vinyl Chloride	sufficient	

Screenshot 1 Text-based Boolean search option and results

Search results will link to full-text Monographs. In addition to this text-based search interface alternatively a graphical user interface will be provided for searches by cancer site (screenshot 2)

Touch-type Interface



Liver & biliary tract
Alcoholic beverages
Tobacco smoking
Aflatoxins
Vinyl chloride
Estrogen-progestogen
contraceptives
Hepatitis B virus
Hepatitis C virus
Clonorchis sinensis
Opisthorchis viverrini
Plutonium
Thorium-232

Screenshot 2 Graphical user interface with results

This fully searchable database of the IARC Monographs will be linked with other major IARC databases, such as

- Globocan, which provides access to the most recent estimates of the cancer incidence, mortality and prevalence for 27 cancers worldwide <http://globocan.iarc.fr/> and the
- IARC/WHO Classification of Tumours (WHO Blue Books) <http://whobluebooks.iarc.fr/>.

Links with these databases will be via cancer sites as indicated in screenshot 1. Altogether, this will provide users with a one-portal entry to WHO/IARC expert consensus on tumor pathology, descriptive cancer statistics and risk factors for cancer.

The searchable database will be continuously updated with new volumes of IARC Monographs, new editions of Blue Books and new data on cancer incidence, mortality and prevalence (Globocan). Ways to link with other authoritative internet-accessible and searchable databases are already being sought. This includes:

- The WHO International Classification of Diseases (ICD-11) – first meetings with the responsible WHO officer have been held;
- Chemical Safety Information from Intergovernmental Organizations (INCHEM of IPCS/WHO), particularly the Concise International Chemical Assessment Documents (CICADs) and the International Chemical Safety Cards (ICSCs) – the Head of the IARC Monographs programme is the cancer expert on the ICSC committee;
- NIH ChemID which already lists IARC Monographs evaluations in its “Superlist Classification Code”, however these are often not up-to-date.

Proposal

With this Administrative Supplement Request we propose to develop a link between the web-based and searchable database of the IARC Monographs and the NCI grants database <http://fundedresearch.cancer.gov/nciportfolio/search/SearchForm?formType=advanced>. This link will allow IARC to better anticipate when to call for Monographs meetings on specific topics and in

reverse will allow investigators to better assess current evidence and research gaps and how to tailor any projects they are planning.

Specifically, we propose to link with the website of the NCI Funded Research Portfolio on the level of 'Standard' or 'Advanced' search options by:

- Cancer Type (Standard search);
- Research Type, exogenous factors in the origin and cause of cancer (Advanced search);
- Research Emphasis, Cancer Etiology and "Chem and Phys Carcinogenesis" (Advanced search).

We propose a first virtual meeting (using IARC's GoToMeeting license) to develop with NCI's Knowledge Integration Team the detailed scope of the project and to define terminologies used in both databases and IT technologies to be employed for the linkage of the databases (e.g. ICD-10 for cancer sites, keywords for carcinogenic agents).

We propose to keep the responsibility of updating each database with the respective owners of the databases, and link the databases from their respective servers using linkage tools, such as webservices. This approach will guarantee sustainability of the interlinked databases without any or only minor additional costs beyond the regular updating of the individual databases (which remains the responsibility of the respective database owners).

We request financial support of \$20,000 for 12 months for IT support to develop the interlinked databases.

Outlook

This project for future linkage may also serve as a small pilot for linkage with other NCI/NIH databases. Other databases might include

- NCI's websites on Cancer Causes and Risk Factors
<http://www.cancer.gov/cancertopics/causes>;
- NTP Technical Reports Index <http://ntp-server.niehs.nih.gov/index.cfm?objectid=070E4402-959F-C0C5-9BB56CDB50750337>;
- the CCRIS database on Toxnet <http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?CCRIS>;
- the NLM A.D.A.M. Medical Encyclopedia on Cancer
http://www.ncbi.nlm.nih.gov/pubmedhealth/PMH0002267/#adam_001289.disease.causes.

Reference

Cogliano VJ, Baan R, Straif K, Grosse Y, Secretan B, El Ghissassi F, Bouvard V, Benbrahim-Tallaa L, Guha N, Freeman C, Galichet L, Wild CP. Preventable exposures associated with human cancers. *J Natl Cancer Inst.* 2011; 103: 1827-1839 PMID:22158127, PMCID: PMC3243677