

***** NOTICE OF GRANT AWARD *****
RESEARCH PROJECT COOPERATIVE AGREEMENT Issue Date: 02/07/2000

Department of Health and Human Services
National Institutes Of Health
NATIONAL CANCER INSTITUTE



Grant Number: 5 U01 CA33193-18 (Revised)
Principal Investigator: RICE, JERRY M PHD
Project Title: EVALUATION OF CARCINOGENIC RISKS

DIRECTOR, ADMIN & FINANCE
INTER AGENCY FOR RES ON CANCER
150 COURS ALBERT THOMAS
69372 LYON CEDEX 08
FRANCE

Budget Period: 03/01/1999 - 02/28/2001
Project Period: 09/01/1985 - 02/28/2001

Dear Business Official:

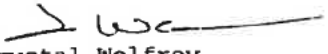
The National Institutes of Health hereby revises this award (see 'Award Calculation' in Section I and 'Terms and Conditions' in Section III) to WORLD HLTH ORG INTL AGCY RES ON CANCER in support of the above referenced project. This award is pursuant to the authority of 42 USC 241 31 USC 6305 & 6306 and is subject to attached terms and conditions.

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

Award recipients are responsible for reporting inventions derived or reduced to practice in the performance of work under this grant. Rights to inventions vest with the grantee organization provided certain requirements are met and there is acknowledgement of NIH support. In addition, recipients must ensure that patent and license activities are consistent with their responsibility to make unique research resources developed under this award available to the scientific community, in accordance with NIH policy. For additional information, please visit <http://www.iedison.gov>.

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

Sincerely yours,


Crystal Wolfrey
Grants Management Officer
NATIONAL CANCER INSTITUTE

Attachments

SECTION I - AWARD DATA - 5 U01 CA33193-18 (Revised)

AWARD CALCULATION (U.S. Dollars):

Salaries and Wages	\$292,663
Fringe Benefits	\$92,388
Personnel Costs	\$385,051
Consultant Services	\$49,994
Travel Costs	\$3,900
Other Costs	\$215,473
Direct Costs	\$654,418
F&A Costs	\$85,074
APPROVED BUDGET	\$739,492
Less Unobligated Balance	\$163,129
TOTAL	\$576,363

AMOUNT OF THIS ACTION (FEDERAL SHARE) +\$0

FINANCIAL INFORMATION:

CFL Number: 93.393

EIN: 1900210016A1

Document Number: U1CA33193D

IC/ CAN / FY1999

CA/8423126 / 576,363

NIH ADMINISTRATIVE DATA:

PCC: 38AI3126 / OC: 41.4P /Processed: WOLFREYC 000204 0208

SECTION II - PAYMENT/HOTLINE INFORMATION - 5 U01 CA33193-18 (Revised)

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

SECTION III - TERMS AND CONDITIONS - 5 U01 CA33193-18 (Revised)

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

- a. The grant program legislation and program regulation cited in this Notice of Grant Award.
- b. The restrictions on the expenditure of federal funds in appropriations acts, to the extent those restrictions are pertinent to the award.
- c. 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://www.nih.gov/grants/policy/awardconditions.htm> for certain references cited above.)

This grant is excluded from Expanded Authorities.

Treatment of Program Income:
Other Research (Add/Deduct Option)

INFORMATION This award is issued as a Cooperative Agreement, a financial assistance mechanism which requires cooperation between the awardee and the National Cancer Institute (NCI). The following Terms of Cooperation include (1) the Programmatic Responsibilities of

the Awardees, the Nature of Assistance by NCI Staff, Collaborative Responsibilities, and Arbitration Procedures (Attachment 1); and (2) the following administrative terms.

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.

INFORMATION This revised award extends the 18 year budget period and project period 12 months, as requested in the grantee's letter dated November 18, 1999. The new budget and project period expiration date will be 02/28/2001. Funds remaining in the 18 year may be used during the extension; however, no additional funds have been awarded.

THE FOLLOWING TERMS FROM THE PREVIOUS NOTICE OF GRANT AWARD ISSUED ON June 9, 1999 ALSO APPLY TO THIS AWARD:

INFORMATION The National Cancer Institute shall have access to all data generated under this grant award and may periodically review the data. The awardee will retain custody and primary rights to the data consistent with current HHS, PHS, and NIH policies.

INFORMATION For administrative and management concerns, contact the Grants Management Specialist, Crystal Wolfrey, at (301) 496-8634, or via e-mail at crystal.wolfrey@nih.gov. For programmatic and scientific concerns, contact the Program Director, Dr. David Longfellow, at (301) 496-5471.

INFORMATION In a continuing effort to provide exceptional customer service, the NCI Grants Administration Branch has set up a Feedback address on its web site (<http://www.nci.nih.gov/admin/gab/index.htm>). General concerns and issues related to NCI grants policies, procedures, and practices can be sent to the Customer Liaison using this feature. Specific questions or concerns related to this grant should be addressed to the Grants Management Specialist listed in the Terms of Award.

Crystal Wolfrey, Grants Specialist

SPREADSHEET

GRA NUMBER: 5 U01 CA33193-18 (Revised)

P.I.: RICE, JERRY M

INSTITUTION: WORLD HLTH ORG INTL AGCY RES ON CANCER

	YEAR 18
	=====
Salaries and Wages	292,663
Fringe Benefits	92,388
Personnel Costs	385,051
Consultant Services	49,994
Travel Costs	3,900
Other Costs	215,473
TOTAL DC	654,418
TOTAL F&A	85,074
TOTAL COST	739,492

YEAR 18

=====

F&A Cost Rate 1	13.00%
F&A Cost Base 1	654,418
F&A Costs 1	85,074

***** NOTICE OF GRANT AWARD *****
RESEARCH PROJECT COOPERATIVE AGREEMENT Issue Date: 09/29/2000

Department of Health and Human Services
National Institutes of Health
NATIONAL CANCER INSTITUTE

Grant Number: 5 U01 CA33193-18 (Revised)
Principal Investigator: RICE, JERRY M PHD
Project Title: EVALUATION OF CARCINOGENIC RISKS

DIRECTOR, ADMIN & FINANCE
INTER AGENCY FOR RES ON CANCER
150 COURS ALBERT THOMAS
69372 LYON CEDEX 08
FRANCE

Budget Period: 03/01/1999 - 09/29/2000
Project Period: 09/01/1985 - 09/29/2000

Business Official:

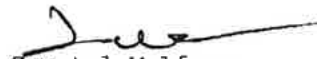
The National Institutes of Health hereby revises this award (see 'Award Calculation' in Section I and 'Terms and Conditions' in Section III) to WORLD HLTH ORG INTL AGCY RES ON CANCER in support of the above referenced project. This award is pursuant to the authority of 42 USC 241 31 USC 6305 & 6306 and is subject to terms and conditions referenced below.

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.

Award recipients are responsible for reporting inventions derived or reduced to practice in the performance of work under this grant. Rights to inventions vest with the grantee organization provided certain requirements are met and there is acknowledgement of NIH support. In addition, recipients must ensure that patent and license activities are consistent with their responsibility to make unique research resources developed under this award available to the scientific community, in accordance with NIH policy. For additional information, please visit <http://www.iedison.gov>.

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

Sincerely yours,


Crystal Wolfrey
Grants Management Officer
NATIONAL CANCER INSTITUTE

See additional information below

SECTION I - AWARD DATA - 5 U01 CA33193-18 (Revised)

AWARD CALCULATION (U.S. Dollars):

Salaries and Wages	\$292,663
Fringe Benefits	\$92,388
Personnel Costs	\$385,051
Consultant Services	\$49,994
Travel Costs	\$3,900
Other Costs	\$215,473
Direct Costs	\$654,418
F&A Costs	\$85,074
APPROVED BUDGET	\$739,492
Less Unobligated Balance	\$163,129
TOTAL	\$576,363

AMOUNT OF THIS ACTION (FEDERAL SHARE) +\$0

FISCAL INFORMATION:

CFDA Number: 93.393
F#: 1900210016A1
Document Number: U1CA33193D

IC/ CAN / FY1999
CA/8423126 / 576,363

NIH ADMINISTRATIVE DATA:

PCC: 38AI3126 / OC: 41.4P /Processed: WOLFREYC 000927 1107

SECTION II - PAYMENT/HOTLINE INFORMATION - 5 U01 CA33193-18 (Revised)

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 - 5 U01 CA33193-18 (Revised)

This award is based on the application submitted to, and as approved by, the NIH on the re-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 Grant Award.
- The restrictions on the expenditure of federal funds in appropriations acts, to the extent those restrictions are pertinent to the award.
- 45 CFR Part 74 or 45 CFR Part 92 as applicable.
- The NIH Grants Policy Statement, including addenda in effect as of the beginning date of the budget period.
- 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.)

This grant is excluded from Expanded Authorities.

Treatment of Program Income:
Other Research (Add/Deduct Option)

INFORMATION This award is issued as a Cooperative Agreement, a financial assistance mechanism which requires cooperation between the awardee and the National Cancer Institute (NCI). The following Terms of Cooperation include (1) the Programmatic Responsibilities of

the Awardees, the Nature of Assistance by NCI Staff, Collaborative Responsibilities, and Arbitration Procedures (Attachment 1); and (2) the following administrative terms.

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.

INFORMATION This revised award terminates the budget period effective 9/29/2000 to reflect NCI funding of 2 U01 CA 33193-19.

THE FOLLOWING TERMS FROM THE PREVIOUS NOTICE OF GRANT AWARD ISSUED ON 02/07/2000 ALSO APPLY TO THIS AWARD:

INFORMATION The National Cancer Institute shall have access to all data generated under this grant award and may periodically review the data. The awardee will retain custody and primary rights to the data consistent with current HHS, PHS, and NIH policies.

INFORMATION For administrative and management concerns, contact the Grants Management Specialist, Crystal Wolfrey, at (301) 496-8634, or via e-mail at crystal.wolfrey@nih.gov. For programmatic and scientific concerns, contact the Program Director, Dr. David Longfellow, at (301) 496-5471.

INFORMATION In a continuing effort to provide exceptional customer service, the NCI Grants Administration Branch has set up a Feedback address on its web site (<http://www.nci.nih.gov/admin/gab/index.htm>). General concerns and issues related to NCI grants policies, procedures, and practices can be sent to the Customer Liaison using this feature. Specific questions or concerns related to this grant should be addressed to the Grants Management Specialist listed in the Terms of Award.

DAVID G. LONGFELLOW, Program Official 301-496-5471 d158s@nih.gov
Crystal Wolfrey, Grants Specialist (301) 496-8634 cw104j@nih.gov

SPREADSHEET

GRANT NUMBER: 5 U01 CA33193-18 (Revised)
P I.: RICE, JERRY M
I NSTITUTION: WORLD HLTH ORG INTL AGCY RES ON CANCER

	YEAR 18
	=====
Salaries and Wages	292,663
Fringe Benefits	92,388
Personnel Costs	385,051
Consultant Services	49,994
Travel Costs	3,900
Other Costs	215,473
TOTAL DC	654,418
TOTAL F&A	85,074
TOTAL COST	739,492

YEAR 18

=====

F&A Cost Rate 1	13.00%
F&A Cost Base 1	654,418
F&A Costs 1	85,074

Department of Health and Human Services
Public Health Service

Review Group	Type	Activity	Grant Number
SRC (K2)	5	U01	CA33193-18
Total Project Period			
From: 09/01/1985		Through 02/28/2000	
Requested Budget Period			
From: 03/01/1999		Through: 02/29/2000	

Application **DEC 21 1998**
for Continuation Grant

To be verified by applicant. Check information in items 1 through 6. If incorrect, furnish correct information in item 13.

1. TITLE OF PROJECT

EVALUATION OF CARCINOGENIC RISKS

2. PRINCIPAL INVESTIGATOR OR PROGRAM DIRECTOR (Name and address, street, city, state, zip code)

RICE, JERRY M
INTERNATIONAL AGENCY/RES CA
150 COURTS ALBERT THOMAS
69372 LYON CEDEX 08
LYON, FRANCE

4. APPLICANT ORGANIZATION (Name and address, street, city, state, zip code)

INTL AGENCY FOR RES ON CANCER
150 COURS ALBERT THOMAS
69372 LYON CEDEX 08
FRANCE

2b. E-MAIL ADDRESS
rice@iarc.fr

5. ENTITY IDENTIFICATION NUMBER
1900210016A1

2c. DEPARTMENT, SERVICE, LABORATORY, OR EQUIVALENT
CARCINOGEN IDENTIFICATION

MAJOR SUBDIVISION
SCIENTIFIC ACTIVITIES

6. TITLE AND ADDRESS OF ADMINISTRATIVE OFFICIAL

DIRECTOR, ADMIN & FINANCE
INTERNATIONAL AGENCY
FOR RESEARCH ON CANCER
150 COURS ALBERT THOMAS
69372 LYON CEDEX 08, FRANCE

3. ORGANIZATIONAL CODE

60 OTHER RESEARCH ORGANIZATION

E-MAIL ADDRESS mjohnson@iarc.fr

Complete the following (see instructions).

7. HUMAN SUBJECTS

<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes	7a. If "Yes," Exemption no. or IRB approval date	<input type="checkbox"/> Full IRB or <input type="checkbox"/> Expedited Review	7b. Assurance of compliance no.

8. VERTEBRATE ANIMALS

<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes	8a. If "Yes," IACUC approval date	8b. Animal welfare assurance no.
--	-----------------------------------	----------------------------------

9. COSTS REQUESTED FOR NEXT BUDGET PERIOD

9a. DIRECT \$ 654 500 9b. TOTAL \$ 739 585

10. INVENTIONS AND PATENTS (See instructions)

<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes	If "Yes,"	<input type="checkbox"/> Previously reported <input type="checkbox"/> Not previously reported
--	-----------	--

11. PERFORMANCE SITE(S) (Organizations and addresses)

International Agency
for Research on Cancer
150 cours Albert Thomas
69372 Lyon Cédex 08
France

12a. PRINCIPAL INVESTIGATOR OR PROGRAM DIRECTOR (Item 2a)

J.M. Rice

AREA CODE	TELEPHONE NO. AND FAX NO.
33	472.73.84.76
33	472.73.85.75

12b. NAME OF ADMINISTRATIVE OFFICIAL (Item 6)

M.P. Johnson

33	472.73.84.67
33	472.73.85.75

12c. NAME AND TITLE OF OFFICIAL SIGNING FOR APPLICANT ORGANIZATION (Item 15)

P. Kleihues,
Director

33	472.73.84.85
33	472.73.85.75

E-MAIL ADDRESS rice@iarc.fr

13. USE THIS SPACE FOR CORRECTIONS TO ITEMS 1 THROUGH 6. INDICATE THE NUMBERS(S) WHERE ANSWERS APPLY.

14. PRINCIPAL INVESTIGATOR/PROGRAM DIRECTOR ASSURANCE: I certify that the statements herein are true, complete and accurate to the best of my knowledge. I am aware that any false, fictitious, or fraudulent statements or claims may subject me to criminal, civil, or administrative penalties. I agree to accept responsibility for the scientific conduct of the project and to provide the required progress reports if a grant is awarded as a result of this application.

SIGNATURE OF PIV/PD NAMED IN 2a
(In ink. "Per" signature not acceptable.)

Jerry M. Rice

DATE
17.12.98

15. APPLICANT ORGANIZATION CERTIFICATION AND ACCEPTANCE: I certify that the statements herein are true, complete and accurate to the best of my knowledge and accept the obligation to comply with Public Health Service terms and condition if a grant is awarded as a result of this application. I am aware that any false, fictitious, or fraudulent statements or claims may subject me to criminal, civil, or administrative penalties.

SIGNATURE OF OFFICIAL NAMED IN 12c
(In ink. "Per" signature not acceptable.)

P. Kleihues

DATE
17.12.98

DETAILED BUDGET FOR NEXT BUDGET PERIOD—DIRECT COSTS ONLY

FROM 03/01/99

THROUGH 02/28/00

GRANT NUMBER CA33193-18

PERSONNEL (Applicant organization only)		TYPE APPT. (months)	% EFFORT ON PROJ.	DOLLAR AMOUNT REQUESTED (omit cents)		
NAME	ROLE ON PROJECT			SALARY REQUESTED	FRINGE BENEFITS	TOTALS
Rice, J.M.	Principal Investigator	(b)(4), (b)(6)	(b)(4), (b)(6)	-	-	-
Vacant	Scientist (epidemiologist)	12	100 ✓	22 000	7 000	29 000
McGregor, D.	Scientist	(b)(4), (b)(6)	(b)(4), (b)(6)	86 600	27 400	114 000
Lézère, M	Secretary			49 800	15 700	65 500
Ruiz, S.	Clerk			27 100	8 500	35 600
Grosse, Y.	Scientist <i>new</i>			39 600	12 500	52 100
Baan, R.	Scientist <i>new</i>			67 600	21 300	89 900

Only principal investigator and staff for whom support is requested are listed here. For all other professional and non-professional staff, see pp. 3-4

SUBTOTALS →

292 700	92 400	385 100
---------	--------	---------

CONSULTANT COSTS
 Preparation of draft Monographs: 20 000
 Editing of Monographs: 30 000

332 259
50804
 50 000 ✓

EQUIPMENT (Itemize)

SUPPLIES (Itemize by category)

TRAVEL See details on page 5

3977 3 900 ✓

PATIENT CARE COSTS
 INPATIENT
 OUTPATIENT

ALTERATIONS AND RENOVATIONS (Itemize by category)

OTHER EXPENSES (Itemize by category)

See details on page 5

267897 215 500

SUBTOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD

654417 \$ 654 500

CONSORTIUM/CONTRACTUAL COSTS
 DIRECT COSTS
 INDIRECT COSTS

TOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD (Item 7a, Face Page) →

\$ 654 500

Budget justification

Grant number
CA33193-18

Name, title and Unit or Programme*	Time on programme	Cost to NCI	Function
J.M. Rice Chief, CIE	(b)(4), (b)(6)	none	Principal investigator. Overall planning and running of the monographs and survey programmes; selection of priorities for future consideration and selection of experts.
(vacant) Scientist (epidemiologist), CIE	100% (3 months)	100%	Assistance with planning, organization and implementation of meetings. Preparation and checking of monograph sections related to carcinogenicity studies in humans.
D. McGregor, Ph.D. Scientist, CIE	(b)(4), (b)(6)	100%	Assistance with planning, organization and implementation of meetings. Preparation and checking of monograph sections on other relevant data and genetic effects.
R. Baan, Ph.D. Scientist, CIE	(b)(4), (b)(6)	100%	Assistance with planning, organization and implementation of meetings. Preparation and checking of monograph sections on other relevant data and genetic effects.
C. Partensky, M.Sc. Technical Editor, CIE	(b)(4), (b)(6)	none	Collection of exposure data, checking of monographs for accuracy prior to publication.
Grosse, Y., Ph.D. Scientist, CIE	(b)(4), (b)(6)	100%	Assist in collection of exposure data and checking of monographs for accuracy prior to publication.
J. Wilbourn, B.Sc. Scientist, CIE	(b)(4), (b)(6)	none	Assistance with planning, organization and implementation of meetings. Preparation and checking of monograph sections on animal carcinogenicity. Supervision of Internet Website.
M. Lézère Secretary, CIE	(b)(4), (b)(6)	100%	Entry of draft monographs onto word processors; production of final monographs for printing.
D. Mietton Library Assistant, CIE	(b)(4), (b)(6)	none	Maintaining an index and files for papers for IARC Monographs; survey of literature and collection of data on substances already considered by a Working Group.
J. Mitchell Technical Assistant, CIE	(b)(4), (b)(6)	none	Entry of draft monographs onto word processors; formatting and revision of English; production of monographs during meetings.

Budget justification**Grant number
CA33193-18**

Name, title and Unit or Programme*	Time on programme	Cost to NCI	Function
S. Reynaud Secretary, CIE	(b)(4), (b)(6)	none	Administrative organization of Working Group meetings.
S. Ruiz Clerk, CIE	(b)(4), (b)(6)	100%	Reprint collection and filing; data entry to bibliographic computer files; assistance in entering draft monographs onto word processor and in maintaining Internet Website.
P. Boffetta, M.D. Scientist, ECE	(b)(4), (b)(6)	none	To advise on sections on epidemiology
M. Friesen, Ph.D. Scientist, GEI	(b)(4), (b)(6)	none	To advise on chemistry and analysis
C. Malaveille, Ph.D. Scientist, ECR	(b)(4), (b)(6)	none	To advise on short-term tests for genetic and related effects
Cardis, E., Ph.D. Chief, RCA	(b)(4), (b)(6)	none	To advise on studies of radiation (including electromagnetic fields) and cancer
Krutovskikh, V., M.D. Scientist, MSC	(b)(4), (b)(6)	none	To advise on studies of cancer in experimental animals

* CIE: Carcinogen Identification and Evaluation (Unit of)
ECE: Environmental Cancer Epidemiology (Unit of)
ECR: Endogenous Cancer Risk Factors (Unit of)
GEI: Gene Environment Interactions (Unit of)
MSC: Multistage Carcinogenesis (Unit of)
RCA: Radiation and Cancer (Unit of)

BUDGET JUSTIFICATION

GRANT NUMBER

CA33193-18

Provide a detailed budget justification for those line items and amounts which represent a significant change from that previously recommended.

Consultant expenses

- Preparation of draft monographs:
 \$400/expert x 25 experts x 2 working groups = 20 000

- Editing of monographs:
 \$15 000 per monograph x 2 = 30 000
 50 000

Travel

- one trip of the principal investigator to USA to visit the contracting officer in the NCI and to attend an international meeting in the field of cancer research

Fare:	2 100	
Per diem: (\$250 x 7)	1 750	
	<u>3 850</u>	i.e. 3 900

Other expenses

- Working Groups (\$54 000 x 2) =	108 000
- Printing costs of two monographs (\$15 000 x 2)	30 000
- Distribution costs of free monographs	40 000
- Reprint requests	16 000
- Books, journals and reproduction costs	15 500
- Information databases on CD-ROM (Toxline and Medline)	6 000
	<u>215 500</u>

CURRENT BUDGET PERIOD	FROM 03/01/98	THROUGH 02/28/99
-----------------------	------------------	---------------------

Explain any estimated unobligated balance (including prior year carryover) which is greater than 25% of the current year's total budget or more than \$250,000.

	Total estimated expenditure and obligations	Estimated unobligated balance
Total direct costs	615 300	12 200
Indirect costs	<u>79 989</u>	<u>1 586</u>
	695 289	13 786

Budget justification**Grant number
CA33193-18**

For the period 03/01/98 to 02/28/99 the following funds are requested

	<u>Recommended support</u>	<u>Requested support</u>	<u>Increase/(Decrease)</u>
Personnel	(b)(5)	385 100	(b)(5)
Consultant		50 000	
Duty travel		3 900	
Other		<u>215 500</u>	
Total direct costs		654 500	

Justification

The funds requested from the National Cancer Institute for the continuation of the project amount to \$654 500, indirect costs excluded, for Year 18 of the present contract, as compared with the recommended level of (b)(5). There is an increase of \$52 861 in PERSONNEL, partly offset by a decrease of \$(b)(5) in non-staff costs, which leaves a net increase of (b) of total direct costs.

The increase in PERSONNEL is mainly due to the recruitment of two additional scientists who are necessary to complete Monographs volumes within the six-months guideline period, partly offset by departure of one senior experienced scientist who leaves a vacancy, for which recruitment is expected to be complete by the end of the third quarter (i.e., by 30 November 1999).

BIOGRAPHICAL SKETCHGive the following information for all **new** key personnel.

Copy this page for each person.

NAME Baan, Robert A.	POSITION TITLE Scientist
-------------------------	-----------------------------

EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing. Include postdoctoral training.)

INSTITUTION AND LOCATION	DEGREE (if applicable)	YEAR(s)	FIELD OF STUDY
Faculty of Sciences, University of Leiden, The Netherlands	MSc.	1967-72	Chemistry/ Biochemistry
Laboratory of Biochemistry, University of Leiden	Ph.D.	1973-77	Biochemistry
Division of Biology and Medicine, Brown University Providence RI, USA	Post-doctoral training	1977-79	Biochemistry

RESEARCH AND PROFESSIONAL EXPERIENCE: Concluding with present position, list, in chronological order, previous employment, experience, and honors. Include present membership on any Federal Government public advisory committee. List, in chronological order, the titles, all authors, and complete references to all publications during the past three years and representative earlier publications pertinent to this application. If the list of publications in the last three years exceeds two pages, select the most pertinent publications. **DO NOT EXCEED TWO PAGES.**

- Sept. 1979-Dec. 1986 Research scientist,
Department of Genetic Toxicology, TNO Medical Biological Laboratory,
Rijswijk, The Netherlands
- Jan. 1987-May 1995 Head, Department of Genetic Toxicology, TNO Medical Biological Laboratory,
Rijswijk, The Netherlands
- June 1995-Sept. 1998 Senior scientist Genetic Toxicology, TNO Nutrition and Food Research Institute,
Zeist, The Netherlands
- Oct. 1998- present Scientist, Unit of Carcinogen Identification and Evaluation,
International Agency for Research on Cancer, Lyon, France

List of publications

- Fichtinger-Schepman AMJ, Welters MJP, Van Dijk-Knijenburg HCM, Van der Sterre MLT, Tilby MJ, Berends F, (1996) Detection of adducts formed upon treatment of DNA with cisplatin and carboplatin. In: Platinum and other metal coordination compounds in cancer chemotherapy 2, Pinedo HM, Schornagel JH, Eds, Plenum Press, New York and London, pp 107-119
- Van Delft JHM, Luiten-Schuite A, Souliotis V, Kyrtopoulos SA, Keizer HJ, Ouwerkerk J, Baan RA (1996) N7-methyl-guanine and O⁶-methylguanine levels in DNA of white blood cells from cancer patients treated with dacarbazine. *Biomarkers* 1, 94-98
- Farmer PB, Sepai O, Lawrence R, Autrup H, Sabro Nielsen P, Vestergård AB, Waters R, Leuratti C, Jones NJ, Stone J, Baan RA, Van Delft JHM, Kyrtopoulos SA, Souliotis VL, Theodorakopoulos N, Bacalis NC, Natarajan AT, Bates AD, Haugen A, Andreassen Å, Øvrebø S, Shuker DEG, Amaning KS, Schouft A, Ellul A, Garner RC, Dingley KH, Abbondandolo A, Merlo F, Cole J, Aldrich K, Beare D, Capulas E, Rowley G, Waugh APW, Povey AC, Kirsch-Volders M, Van Hummelen P, Castelain Ph (1996) Biomonitoring human exposure to environmental carcinogenic chemicals (Final Report of STEP-Biomonitoring Project EV5V-CT91-0013). *Mutagenesis* 11, 363-381
- Wolterbeek APM, Ciotti MALT, Schoevers EJ, Roggeband R, Baan RA, Feron VJ, Rutten AAJL (1996) Effect of Vitamin A on benzo(a)pyrene-induced cell proliferation in hamster tracheal epithelium cultured in different media. *Toxicology in vitro* 10, 359-369
- Roggeband R, Wolterbeek APM, Van den Berg PTM, Rutten AAJL, Feron VJ, Baan RA (1996) Cell proliferation and DNA adducts in hamster tracheal epithelium exposed to benzo(a)pyrene in organ culture. *Toxicology in vitro* 10, 371-375
- Mientjes EJ, Steenwinkel M-JST, Van Delft JHM, Lohman PHM, Baan RA (1996) Comparison of the X-gal- and P-gal-based systems for screening of mutant lacZ phages originating from the transgenic mouse strain 40.6. *Mutation Res* 360, 101-106

- Rompelberg CJM, Steenwinkel M-JST, Van Asten JG, Van Delft JHM, Baan RA, Verhagen H (1996) Effect of eugenol on the mutagenicity of benzo(a)pyrene and the formation of benzo(a)pyrene-DNA adducts in the *lacZ*-transgenic mouse. *Mutation Res* 369, 87-96
- Mientjes EJ, Hochleitner K, Luiten-Schuite A, Van Delft JHM, Thomale J, Berends F, Rajewsky MF, Lohman PHM, Baan RA (1996) Formation and persistence of O⁶-ethylguanine in genomic and transgene DNA of liver and brain of *lacZ* transgenic mice treated with N-ethyl-N-nitrosourea. *Carcinogenesis* 17, 2449-2454
- Frijhoff AFW, Bol SA, Groot PC, Van Zeeland AA, Demant P, Baan RA (1996) Production of a congenic mouse strain carrying the hairless mutation in a 129/Ola genetic background: a suitable strain to generate transgenic and knockout mice for studies on toxicity and carcinogenesis of skin. *Mouse Genome* 4, 866-867
- Van Delft JHM, Steenwinkel M-JST, De Groot AJL, Van Zeeland AA, Eberle-Adamkiewicz G, Rajewsky MF, Thomale J, Baan RA (1997) Determination of N7- and O⁶-methylguanine in rat liver DNA after oral exposure to hydrazine by use of immunochemical and electrochemical detection methods. *Fundam Appl Toxicol* 35, 131-137
- Van Delft JHM, Bergmans A, Baan RA (1997) Germ cell mutagenesis in *lacZ* transgenic mice treated with ethylating and methylating agents; comparison with specific-locus test. *Mutation Res* 388, 165-173
- Frijhoff AFW, Rebel H, Mientjes EJ, Kelders MCJM, Steenwinkel M-JST, Baan RA, Van Zeeland AA, Roza L (1997) UVB-induced mutagenesis in hairless *lacZ*-transgenic mice. *Environm and Molecular Mutagenesis* 29, 136-142
- Welters MJP, Fichtinger-Schepman AMJ, Baan RA, Hermsen MAJA, Van der Vijgh WJF, Cloos J, Braakhuis BJM (1997) Relationship between the parameters cellular differentiation, doubling time and platinum accumulation and cisplatin sensitivity in a panel of head and neck cancer cell lines. *Int J Cancer* 71, 410-415
- Baan RA, Steenwinkel M-JST, Van Asten JG, Roggeband R, Van Delft JHM (1997) The use of benzo(a)pyrene diol-epoxide-modified DNA standards for adduct quantification in ³²P-postlabelling to assess exposure to polycyclic aromatic hydrocarbons; application in a biomonitoring study. *Mutation Res* 378 (Special Issue ³²P-postlabeling, DH Phillips, Ed), 41-50
- Welters MJP, Maliepaard M, Jacobs-Bergmans AJ, Baan RA, Schellens JHM, Ma J, Van der Vijgh WJF, Braakhuis BJM, Fichtinger-Schepman AMJ (1997) Improved ³²P-postlabelling assay for the quantification of the major platinum-DNA adducts. *Carcinogenesis* 18, 1767-1774
- Mientjes EJ, Luiten-Schuite A, Van der Wolf E, Borsboom Y, Bergmans A, Berends F, Lohman PHM, Baan RA, Van Delft JHM (1998) DNA adducts, mutant frequencies and mutation spectra in various organs of *lacZ* mice exposed to ethylating agents. *Environm and Molecular Mutagenesis* 31, 18-31
- Frijhoff AFW, Krul CAM, Kelders MCJM, De Vries A, Weeda G, Van Steeg H, Baan RA (1998) Influence of nucleotide excision repair on N-hydroxy-2-acetylaminofluorene-induced mutagenesis studied in *lacZ*-transgenic mice. *Environm and Molecular Mutagenesis* 31, 41-47
- Blommaert FA, Floot BGJ, Van Dijk-Knijnenburg HCM, Berends F, Baan RA, Schornagel JH, Den Engelse L, Fichtinger-Schepman AMJ (1998) The formation and repair of cisplatin-DNA adducts in wild-type and cisplatin-resistant L1210 cells: comparison of immunocytochemical determination with detection in isolated DNA. *Chem-Biol Interactions* 108, 209-225
- Welters MJP, Fichtinger-Schepman AMJ, Baan RA, Flens MJ, Schepers RJ, Braakhuis BJM (1998) Role of glutathione, glutathione-S-transferases and multidrug resistance-related proteins in cisplatin sensitivity of head and neck cancer cell lines. *Brit J Cancer* 77, 556-561
- Van Delft JHM, Steenwinkel M-JST, Van Asten JG, Van Es J, Kraak A, Baan RA (1998) Monitoring of occupational exposure to polycyclic aromatic hydrocarbons in a carbon-electrode manufacturing plant. *Ann occup Hyg* 42, 105-114
- Randerath K, Sriram P, Moorthy B, Aston JP, Baan RA, Van den Berg PTM, Booth ED, Watson WP (1998) Comparison of immunoaffinity chromatography enrichment and nuclease P1 procedures for ³²P-postlabelling analysis of PAH-DNA adducts. *Chem-Biol Interactions* 110, 85-102
- Souliotis V, Van Delft JHM, Steenwinkel M-JST, Baan RA, Kyrtopoulos SA (1998) DNA adducts, mutant frequencies and mutation spectra in *lacZ*-transgenic mice treated with N-nitrosodimethylamine. *Carcinogenesis* 19, 731-739
- Van Delft JHM, Bergmans A, Van Dam FJ, Bates AD, Howard L, Winton DJ, Baan RA (1998) Gene-mutation assays in *lacZ* transgenic mice: comparison of *lacZ* with endogenous genes in splenocytes and small intestinal epithelium. *Mutation Res* 415, 85-96
- Van Delft JHM, Baan RA, Roza L (1998) Biological effect markers for exposure to carcinogenic compounds and their relevance for risk assessment. *Crit Rev Toxicol*, in press

ACTIVE OTHER SUPPORT

I. European Sources

Name: Chief, Unit of Carcinogen Identification and Evaluation

a. *Source and identifying No.:* European Commission, Directorate General V P.I.: J. M. Rice
Agreement SOC98 201160 05F05

Title: "Cooperation between the European Union and the International Agency for Research on Cancer in relation to the IARC Monographs on the Evaluation of Carcinogenic Risks to Humans"

b. *Your role in project:* Project manager

c. *Dates and costs of entire project:* 1 September 1998 -31 August 1999;
Total costs: ECU 30 000 (Direct cost, ECU 26 549; Indirect cost, ECU 3 451)

d. *Dates and costs of current year:* as above

e. *Specific aims of project:* Support for publications, ad-hoc advisory group meetings, and third annual IARC Monographs Working Group

f. No scientific and budgetary overlap.

II. US sources other than the National Institutes of Health

Name: International Agency for Research on Cancer (multiple projects)

a. *Source and identifying No.:* U. S. Environmental Protection Agency P.I.: J. M. Rice
Cooperative Agreement CR 824264-01-2

Title: "International research, evaluation and education in environmental carcinogenesis"

b. *Your role in Project:* Overall Programme Coordinator; Project Manager for IARC Monographs

c. *Dates and costs of entire project (IARC Monographs Programme Project only):*
1 December 1994 - 30 November 1999; total costs, \$ 122 450 through 30 November 1999.

d. *Dates and costs of current year:* 1 December 1998 - 30 November 1998; \$ 25 000

e. *Specific aims of project:* Support for publications, ad-hoc advisory group meetings, and the third annual IARC Monographs Working Group meeting

f. No scientific and budgetary overlap.

PROGRESS REPORT SUMMARY		GRANT NUMBER CA33193-18	
PRINCIPAL INVESTIGATOR OR PROGRAM DIRECTOR Rice, J.M.		PERIOD COVERED BY THIS REPORT	
APPLICANT ORGANIZATION International Agency for Research on Cancer		FROM 03/01/1998	THROUGH 02/28/1999
TITLE OF PROJECT (Repeat title shown in Item 1 on first page) Evaluation of Carcinogenic Risks			
a. Human Subjects (Complete Item 7 on the Face Page) Use of Human Subjects <input type="checkbox"/> Change <input checked="" type="checkbox"/> No Change Since Previous Submission			
b. Vertebrate Animals (Complete Item 8 on the Face Page) Use of Vertebrate Animals <input type="checkbox"/> Change <input checked="" type="checkbox"/> No Change Since Previous Submission			

(SEE INSTRUCTIONS)

(a) Specific Aims

The objective of the *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans* is to identify, on the basis of all published epidemiological and experimental data relevant to carcinogenicity, agents (chemicals, groups of chemicals, complex mixtures, occupational exposures, cultural habits, physical and biological agents) that may pose a carcinogenic hazard to humans. Published data on selected agents are critically summarized and evaluated by international working groups of experts in carcinogenesis and related disciplines, and their deliberations assessments are published as volumes in the IARC Monographs series. Scientific meetings on subjects relevant to Monographs evaluations are also organized as the need arises, and ad-hoc meetings of experts to advise the Programme on specific issues, including selection of agents for evaluation, are convened as required. The US National Cancer Institute has provided valuable contributions to the programme via a contract to Dr. Steven Olin, ILSI, for the preparation of sections on exposure, and through the participation of NCI scientists in Working Groups. The programme also surveys the worldwide testing of chemicals for carcinogenicity in experimental animals and disseminates this information via Internet through a **Directory of Agents Being Tested for Carcinogenicity**.

(b) Current budget period

IARC Monographs. During the current budget period 03/01/98 – 02/28/99 three international working groups were convened in Lyon, in June 1998 to re-evaluate hormonal means of contraception and postmenopausal hormone therapy; in October 1998 to re-evaluate agents that target specific organ sites in rodents by mechanisms not necessarily applicable to humans; and in February 1999 to evaluate metallic and non-metallic surgical implants, prosthetic devices, and foreign bodies. The proceedings will be published as Volumes 72 – 74 of the IARC Monographs. A summary report of the June 1998 meeting together with a list of participants is attached as Appendix 1. A list of chemicals evaluated in October 1998, the table of resulting evaluations, and the list of participants are attached as Appendices 2-4. The outline of the February 1999 meeting and the list of invited participants are attached as Appendices 5-6. In addition, two international advisory meetings were convened, to advise on the evaluation of physical agents by the IARC Monographs and on the prioritization of exposures to be evaluated (other than physical and biological agents) during 2000 – 2005. The proceedings were published as IARC Internal Reports 98/002 (Appendix 7) and 98/004 (Appendix 8).

The Directory of Agents Being Tested for Carcinogenicity, previously published biannually in hard copy and now available by Internet at <http://www.iarc.fr>, is now available as an electronic publication only. Currently some 160 agents are being tested in 18 institutes in nine countries. This shows a severe downsizing of the number of

GENDER AND MINORITY INCLUSION Provide the number of subjects enrolled in the study to date (cumulatively since the most recent competitive award) according to the following categories. (See Page 8 for definitions.) If there is more than one study, provide a separate table for each study. In addition, report on the subpopulations which are included in the study.					Study Title		
	American Indian or Alaskan Native	Asian or Pacific Islander	Black, not of Hispanic Origin	Hispanic	White, not of Hispanic Origin	Other or Unknown	TOTAL
Female							
Male							
Unknown							
TOTAL							

chemicals being tested for carcinogenicity outside commercial testing facilities. A number of agents are also being studied in short-term tests using transgenic mice. Completed studies which have been published within the last few years in the peer-review of scientific literature are included in the published studies index of the Web Site.

(c) Significance

IARC Monographs are comprehensive, critical evaluations of the published scientific literature on carcinogenic hazards. They are of research interest to investigators and public health officials, and the evaluations based on them assist national and international authorities to formulate carcinogenic risk assessments and to make risk management decisions. The Directory of Agents Being Tested for Carcinogenicity facilitates allocation of resources for testing by helping avoid wasteful duplication of effort, increases communication among researchers, and contributes to planning future IARC Monographs Working Group meetings.

(d) Plans for next budget period

The next Monographs. During the next budget period, 03/01/1999 to 02/29/2000, three international working groups will be convened to produce volumes 75-77 of the IARC Monographs. Subjects include Ionizing Radiation, I: X-Rays, γ Rays and Neutrons (May 1999); Antiviral and Some Antineoplastic Drugs (October 1999); and Industrial Chemicals (February 2000), these last being compounds assigned high priority for evaluation by the September 1998 International Advisory Group on Priorities (see Attachment B).

The next Scientific Advisory Meeting will be convened in December 1999 to review and prepare a consensus statement on the use of rodent tumours of forestomach and gastric neuroendocrine cell origin in carcinogenic hazard identification. The proceeding will be published as an IARC Scientific Publication.

The Directory of Agents being Tested for Carcinogenic Activity which is now an electronic publication available on the IARC Internet website at <http://www.iarc.fr/> will continue to be updated frequently, as contributions are received from participating laboratories.

(e) Publications

- Cardis, E. & Rice, J.M. (1997) Criteria for health risk assessment within the international EMF project. In: *Biological Effects of Static and ELF Electric and Magnetic Fields* (Matthes, R., Bernhardt, J.H. & Repacholi, M.H., eds), Munich, International Commission on Non-Ionizing Radiation Protection, 31-40
- Sasco, A.J. & Rice, J.M. (1998) Editorial: IARC evaluation of the carcinogenicity of antioestrogens. Basic facts and rationale for appropriate use in medicine. *Presentations in Focus*, Medical Education Network (Europe), Ltd., Issue 2, 3-6
- IARC (1998) *Report of an ad-hoc IARC Monographs Advisory Group on Physical Agents*, Internal Report No. 98/002, Lyon
- IARC (1998) *Report of an ad-hoc IARC Monographs Advisory Group on Priorities for Future Evaluations*, Internal Report No. 98/004, Lyon
- IARC (1999) *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans*, Vol. 71, *Re-evaluation of Some Organic Compounds*, Lyon (in press)
- IARC (1999) *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans*, Vol. 72, *Hormonal Contraception and Postmenopausal Hormone Therapies*, Lyon (in preparation)
- IARC (1999) *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans*, Vol. 73, *Some Agents that target Specific Organs in Rodent Bioassays*, Lyon (in preparation)
- McGregor, D.B., Rice, J.M. & Venitt, S., eds (1999) *The Use of Short- and Medium-term Tests for Carcinogens and Data on Genetic Effects in Carcinogenic Hazard Evaluation* (IARC Scientific Publications No. 146, Lyon, IARC (in press)
- Capen, C.C., Dybing, E., Rice, J.M. & Wilbourn, J.D., eds (1999) *Species Differences in Thyroid, Kidney, and Urinary Bladder Carcinogenesis* (IARC Scientific Publications No. 147), Lyon, IARC (in preparation)

PERSONNEL REPORT

GRANT NUMBER
CA33193-18

All Personnel for the Current Budget Period

Name	Degree(s)	SSN	Role on Project <i>e. g., PI, Res. Assoc.</i>	Date of Birth <i>(MM/DD/YY)</i>	Annual % Effort
J. Rice	Ph.D.	-	Unit Chief	(b)(6)	(b)(4), (b)(6)
M. Blettner	Ph.D.	-	Scientist	(b)(6)	(b)(4), (b)(6)
J. Wilbourn	B.Sc.	-	Scientist	(b)(6)	(b)(4), (b)(6)
D. McGregor	Ph.D.	-	Scientist	(b)(6)	(b)(4), (b)(6)
R. Baan	Ph.D.	-	Scientist	(b)(6)	(b)(4), (b)(6)
C. Partensky	M.Sc.	-	Tech. Editor	(b)(6)	(b)(4), (b)(6)
Y. Grosse	Ph.D.	-	Scientist	(b)(6)	(b)(4), (b)(6)
C. Genevois	Ph.D.	-	Scientist	(b)(6)	(b)(4), (b)(6)
D. Mietton	-	-	Lib. Assistant	(b)(6)	(b)(4), (b)(6)
J. Mitchell	-	-	Tech. Assistant	(b)(6)	(b)(4), (b)(6)
S. Reynaud	-	-	Secretary	(b)(6)	(b)(4), (b)(6)
M. Lézère	-	-	Secretary	(b)(6)	(b)(4), (b)(6)
S. Ruiz	-	-	Clerk	(b)(6)	(b)(4), (b)(6)
P. Boffetta	M.D.	-	Scientist	(b)(6)	(b)(4), (b)(6)
M. Friesen	Ph.D.	-	Scientist	(b)(6)	(b)(4), (b)(6)
C. Malaveille	Ph.D.	-	Scientist	(b)(6)	(b)(4), (b)(6)
R. Montesano	M.D.	-	Scientist	(b)(6)	(b)(4), (b)(6)

CHECKLIST

GRANT NUMBER
CA33193-18

1. ASSURANCES/CERTIFICATIONS (See Instructions, Page 9)

The following assurances/certifications are made and verified by the signature of the OFFICIAL SIGNING FOR APPLICANT ORGANIZATION on the FACE PAGE of the application. If unable to certify compliance where applicable, provide an explanation and place it after this page.

- Human Subjects; • Vertebrate Animals; • Debarment and Suspension;
- Lobbying; • Delinquent Federal Debt; • Research Misconduct; • Civil Rights (Form HHS 441 or HHS 690); • Handicapped Individuals (Form HHS 641 or HHS 690); • Sex Discrimination (Form HHS 639-A or HHS 690); • Age Discrimination (Form HHS 680 or 690); • Financial Conflict of Interest.

2. PROGRAM INCOME (See Instructions, Page 10)

All applications must indicate whether program income is anticipated during the period(s) for which grant support is requested. If program income is anticipated, use the format below to reflect the amount and source(s).

Budget Period	Anticipated Amount	Source(s)

3. INDIRECT COSTS

Indicate the applicant organization's most recent indirect cost rate established with the appropriate DHHS Regional Office, or, in the case of forprofit organizations, the rate established with the appropriate PHS Agency Cost Office. Indirect costs will not be paid on foreign grants, construction

grants, grants to Federal organizations, grants to individuals, and conference grants. Follow any additional instructions provided for Research Career Awards, Institutional National Research Service Awards, and specialized grant applications.

DHHS Agreement dated: _____

No Indirect Costs Requested.

No DHHS Agreement, but rate established with J. Wayne Barry, Accountant Date 18 October 1983
Accountant, DHHS

CALCULATION*

Entire proposed budget period:

Amount of base \$ 654 500 x Rate applied 13 % = Indirect costs \$ 85 085

Add to total direct costs from form page 2 and enter new total on FACE PAGE, Item 9b.

*Check appropriate box(es):

Salary and wages base Modified total direct costs base Other base (Explain below)

Off-site, other special rate, or more than one rate involved (Explain below) on total direct costs

Explanation (Attach separate sheet, if necessary.):