GEORGIA INSTITUTE OF TECHNOLOGY

OFFICE OF CONTRACT ADMINISTRATION

PROJECT ADMINISTRATION DATA SHEET

[X] ORIGINAL   [ ] REVISION NO. ______

Project No. G-32-~~617~~ 620 (R5949-0A0)   GTRC/~~GIT~~XXXX   DATE 6 / 5 / 85

Project Director: D. B. Dusenberry   School/~~Lab~~XXX App. Biology

Sponsor: DHHS/PHS/NIH/CDC

Type Agreement: Grant No. 1 R03-OH02095-01

Award Period: From 6/1/85 To 5/31/87 ? (Performance) 8/31/87 (Reports)

Sponsor Amount:

	This Change	Total to Date
Estimated:	$	$ 16,941
Funded:	$	$ 16,941

Cost Sharing Amount: $ 1,834   Cost Sharing No: G-32-305

Title: Test for Neurotoxins Using Caenorhabditis Elegans

ADMINISTRATIVE DATA   OCA Contact John Schonk x4820

1) Sponsor Technical Contact:	2) Sponsor Admin/Contractual Matters:
Roy M. Fleming	Betty Feeley
Assoc. Director for Grants, NIOSH	Grants Management Branch, PGO
CDC	CDC
Bldg. 1, Room 3053	255 E. Paces Ferry Rd., Rm 321
Atlanta, GA 30333	Atlanta, GA 30305
404/329-3343	404/262-6575

Defense Priority Rating: N/A   Military Security Classification: N/A

(or) Company/Industrial Proprietary: N/A

RESTRICTIONS

See Attached NIH Supplemental Information Sheet for Additional Requirements.

Travel: Foreign travel must have prior approval — Contact OCA in each case. Domestic travel requires sponsor approval where total will exceed greater of $500 or 125% of approved proposal budget category.

Equipment: Title vests with GIT

COMMENTS:

No Funds may be expended after 5/31/87.

RECEIVED Research Reports Office JUN 1985

COPIES TO: SPONSOR'S I. D. NO. 02.108.001.84.027

Project Director	Procurement/EES Supply Services	GTRC
Research Administrative Network	Research Security Services	Library
Research Property Management	Reports Coordinator (OCA)	Project File
Accounting	Research Communications (2)	Other A. Jones

GEORGIA INSTITUTE OF TECHNOLOGY OFFICE OF CONTRACT ADMINISTRATION

SPONSORED PROJECT TERMINATION/CLOSEOUT SHEET

Date 9/12/86

Project No. G-32-620 School/~~Lab~~ BIO

Includes Subproject No.(s) N/A

Project Director(s) D. B. Dusenberry ~~GTRC~~/ GIT

Sponsor DHHS/PHS/NIH/CDC

Title Test for Neurotoxins Using Caenorhabditis Elegans

Effective Completion Date: 5/31/86 (Performance) 8/31/86 (Reports)

Grant/Contract Closeout Actions Remaining:

- [ ] None
- [x] Final Invoice or Final Fiscal Report
- [ ] Closing Documents
- [ ] Final Report of Inventions
- [ ] Govt. Property Inventory & Related Certificate
- [ ] Classified Material Certificate
- [ ] Other

Continues Project No. Continued by Project No. G-32-627

COPIES TO:

Project Director
Research Administrative Network
Research Property Management
Accounting
Procurement/GTRI Supply Services
Research Security Services
Reports Coordinator (OCA)
Legal Services

Library
GTRC
Research Communications (2)
Project File
Other I. Newton
A. Jones
R. Embry

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE

APPLICATION FOR CONTINUATION GRANT

REVIEW GROUP	TYPE	ACTIVITY	GRANT NUMBER (insert on all pages)
SOH (AHR)	5	R03	OH02095-02

TOTAL PROJECT PERIOD
From: 06/01/85 Through: 05/31/87

REQUESTED BUDGET PERIOD
From: 06/01/86 Through: 05/31/87

To Be Verified By Applicant. Check Information in Items 1 Through 6. If Incorrect, Furnish Correct Information In Item 13.

1. TITLE
TEST FOR NEUROTOXINS USING CAENORHABDITIS ELEGANS

2a. PRINCIPAL INVESTIGATOR OR PROGRAM DIRECTOR *(name and address, street, city, state, zip code)*
DUSENBERY, DAVID B
GEORGIA INST OF TECHNOLOGY
ATLANTA, GA 30332

4. APPLICANT ORGANIZATION *(name and address, street, city, state, zip code)*
GEORGIA INSTITUTE OF TECHNOLOGY
ATLANTA, GA 30332

5. ENTITY IDENTIFICATION NUMBER
1580603146A1

2b. DEPARTMENT, SERVICE, LABORATORY OR EQUIVALENT
SCHOOL OF BIOLOGY

2c. MAJOR SUBDIVISION
COLL OF SCIS & LIBERAL STUDIES

3. ORGANIZATIONAL COMPONENT TO RECEIVE CREDIT FOR BIOMEDICAL RESEARCH SUPPORT GRANT *(see instructions)*
20 OTHER

6. TITLE AND ADDRESS OF OFFICIAL IN BUSINESS OFFICE OF APPLICANT ORGANIZATION
CONTRACTING OFFICER
GEORGIA TECH RESEARCH INSTITUTE
GEORGIA INSTITUTE OF TECHNOLOGY
ATLANTA, GA 30332-0420

COMPLETE THE FOLLOWING *(See Instructions)*

7. HUMAN SUBJECTS
☒ NO ☐ YES { ☐ Exemption # ______ OR ☐ Form HHS 596 enclosed

8. RECOMBINANT DNA
☒ NO ☐ YES

11. INVENTIONS *(see instructions)*
☒ NO ☐ YES { ☐ Previously reported OR ☐ Not previously reported

9. PERFORMANCE SITES(S) *(organizations and addresses)*
School of Applied Biology
Georgia Institute of Technology
Atlanta, GA 30332

TELEPHONE INFORMATION

	AREA CODE	TELEPHONE NO. AND EXTENSION
12a. PRINCIPAL INVESTIGATOR OR PROGRAM DIRECTOR *(Item 2a)*	404	894-3700
12b. NAME OF BUSINESS OFFICIAL *(Item 6)*		
12c. NAME AND TITLE OF OFFICIAL SIGNING FOR APPLICANT ORGANIZATION *(Item 15)*		

10. DIRECT COSTS REQUESTED FOR BUDGET PERIOD
$9,020.

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

14. PRINCIPAL INVESTIGATOR/PROGRAM DIRECTOR ASSURANCE: 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. Willful provision of false information is a criminal offense *(U.S. Code, Title 18, Section 1001)*.

SIGNATURE OF PERSON NAMED IN 2a. *(In ink. "Per" signature not acceptable)*

DATE
19 March 86

15. CERTIFICATION AND ACCEPTANCE: I certify that the statements herein are true and complete to the best of my knowledge, and accept the obligation to comply with the Public Health Service terms and conditions if a grant is awarded as the result of this application. A willfully false certification is a criminal offense *(U.S. Code, Title 18, Section 1001.)*

SIGNATURE OF PERSON NAMED ~~IN 12c~~. *(In ink. "Per" signature not acceptable)*
Original Signed by E F Glass...

DATE
25 March 1986

RETURN COMPLETED APPLICATION TO PHS AS SOON AS POSSIBLE:

SECTION I *(continued)*

SUMMARY OF PROPOSED WORK

GRANT NUMBER

OH02095-02

KEY PROFESSIONAL PERSONNEL ENGAGED ON PROJECT

NAME	POSITION TITLE	DEPARTMENT AND ORGANIZATION
David B. Dusenbery	Associate Professor	School of Applied Biology Georgia Institute of Technology
Phillip L. Williams	Graduate Student	School of Applied Biology Georgia Institute of Technology

Give a brief summary of plans for the next year of support, including the objectives and specific aims as well as the methodology to be used to achieve these aims. **DO NOT EXCEED THE SPACE PROVIDED.**

The first year of the study has concentrated on establishing testing protocol and performing initial tests to define behavioral endpoints. Seven metals have been used: Hg, Cd, Cu, Zn, Pb, Ni, and Al. In order to determine sensitivity acute lethality levels (LC_{50}) are first determined and this has been completed for all the metals. Computer tracking using a video camera interfaced to a micro computer has been conducted with Hg and Cu. Preliminary data show C. elegans to have behavioral responses when exposed to low levels of Hg (a human neurotoxin) but not for exposure to Cu (a non-neurotoxin).

Now that the protocols have been established, the second year of the study will concentrate on evaluating a variety of known human neuro-toxins. Several of the metals (e.g., Pb) will be studied and new families of chemicals will be tested. These will center on organophosphate pesticides and organic solvents (those known to be CNS depressants).

Too date, all the chemicals have administered using water as a vehicle but, in the coming year, the vapor route of exposure will be tested.

As additional data is generated, statistical analyses of the data will be conducted to determine the repeatability and reliability of the test procedure. Finally, a general comparison will be made between the observed data and known human responses to the various chemicals. In this manner, the usefulness of the data as a screening test for neurotoxins can be determined.

VERTEBRATE ANIMALS INVOLVED ☒ NO ☐ YES If "YES," identify by common names and underline primates.

SECTION II

NEXT BUDGET PERIOD

Follow instructions carefully

FROM 6/01/86 | THR... 5/31/87 | DHC...

A. ITEMIZE DIRECT COSTS REQUESTED FOR NEXT BUDGET PERIOD | DOLLAR AMOUNT REQUESTED (O...

PERSONNEL *(Applicant organization only) (See instructions)*

NAME	TITLE OF POSITION	TIME/EFFORT %	Hours per Week	SALARY	FRINGE BENEFITS	TOTA
David B. Dusenbery	Principal Investigator	–	–	–		
Phillip L. Williams	Graduate Student	–	–	–		
Steve Donkin	Technician	20	8	3570	750	
SUBTOTALS ⟶				3570	750	432

CONSULTANT COSTS *(See instructions)*

NONE — 0

EQUIPMENT *(Itemize)*

NONE — 0

SUPPLIES *(Itemize by category)*

Chemicals - 2000.00
Glass and plasticware - 1000.00
Computer software - 500.00

35

TRAVEL	DOMESTIC To make presentation of the study at a conference (1).	1
	FOREIGN	
PATIENT CARE COSTS	INPATIENT	
	OUTPATIENT	

ALTERATIONS AND RENOVATIONS *(Itemize by category)*

CONSORTIUM/CONTRACTUAL COSTS *(See instructions)*

OTHER EXPENSES *(Itemize by category)*

Publication Costs

TOTAL DIRECT COST *(Enter on Page 1, Item 10)*

INDIRECT COST *(See instructions)*	% S&W*	*If this is a special rate *(e.g. off-site)* explain	Date of DHHS agreement	☐ Not requeste... ☐ Under negot...
	63.5% TDC*			

GRANT NUMBER
OH02095-02

B. Supplemental information regarding ITEMS in the proposed budget for the next period which require explanation or justification. *(See instructions)*

Other expenses:

Publication Costs:

Page charges and manuscript preparation costs are estimated to be $200.00

SECTION III CURRENT BUDGET PERIOD	FROM 6/01/85	THROUGH 5/31/86	GRANT NUMBER OH02095-02

The following pertains to your CURRENT PHS budget. Do not include cost sharing funds. This information in conjunction with that provided on Page 2 will be used in determining the amount of support for the NEXT budget period.

A. BUDGET	CURRENT BUDGET *(as approved by awarding unit)* (1)	ACTUAL EXPENDITURES THRU *(insert date):* 1/31/86 (2)	ESTIMATED ADDITIONAL EXPENDITURES AND OBLIGATIONS FOR REMAINDER OF CURRENT BUDGET PERIOD (3)	TOTAL ESTIMATED EXPENDITURES AND OBLIGATIONS *(Col. 2 plus Col. 3)* (4)	ESTIMATED UNOBLIGATED BALANCE *(Subtract Col. 4 from Col. 1)* (5)
TOTAL DIRECT COSTS	13,378	10,053	3,325	13,378	0
INDIRECT COSTS (as provided)	3,563	1,737	2,111	3,848	(285)
TOTALS ⟶	16,941	11,790	5,436	17,226	(285)

B. THROUGH F.
See instructions and provide the information required in items B. through F. Use this page and continuation pages as necessary.

Item B. Professional Personnel.

Name	Title	Category	Less than 25%
David B. Dusenbery	Assoc. Prof.	1	X

Item C. Equipment.

Microcomputer (IBM AT) $2,796
Video Interface (Imaging Technology PC Vision) $3,502

Item D. Travel.

No travel to date. Travel to a conference is planned for the coming year. (See page 3).

Item E. Explanation of Column 5.

University-wide overhead charges increase effective July 1, 1985.

Item F. Other Support.

Agrigenetics Research Corp.; "Search for Chemical Stimuli that Act on Plant-Parasite Nematodes;"

Calendar year 1985: $115,356
Calendar year 1986: 95,423

SECTION IV **PROGRESS REPORT SUMMARY**	GRANT NUMBER OH02095-02	
PRINCIPAL INVESTIGATOR OR PROGRAM DIRECTOR David B. Dusenbery	PERIOD COVERED BY THIS REPORT	
NAME OF ORGANIZATION School of Applied Biology, Georgia Institute of Technology	FROM 6/1/85	THROUGH 2/28/86

TITLE *(Repeat title shown in item 1 on first page)*

Test for Neurotoxins Using Caenorhabditis elegans.

(SEE INSTRUCTIONS)

1. No change from the original goals.

2. A strain of E. coli is grown on experimental plates until a lawn is well formed and then 0.4 ml of an aqueous solution of the test chemical is added to the plates. The plates are desicated for 24-hours at 50% relative humidity to allow for the excess water to evaporate. A number of three to four day-old C. elegans are placed on each plate. After 24-hours two types of evaluations are made: lethality and computer tracking to determine behavioral changes. Control cultures are tested concurrently with the neurotoxins.

With lethality tests, death is determined by the total lack of movement and/or response to probing with a needle. For behavioral studies, the worms are removed from the plates, washed, and placed on 1% agar. The worms are positioned under a video camera that is interfaced to a microcomputer computer. This arrangement allows for the simultaneous tracking of several hundred menatodes. The movements of the animals are analyzed to determine both the rate of movement and the number of changes in directions (reversals). In the future, responses to sensory stimulation will also be measured.

Lethality studies have been completed for seven metals: Hg, Cu, Pb, Cd, Zn, Al, and Ni. For each metal a dose-response has been determined and LC_{50} has been calculated using both probits and logits.

Computer tracking experiments have been conducted on Hg and Cu. The nematodes exposed to Hg show a biphasic response - at very low Hg concentrations there is hyperactivity that appears to peak at exposure concentrations of about .6 ppm Hg and as the concentration increases the activity falls to well below the controls. This peak activity Hg concentration is approximately 10% the nematode LC_{50} of 60 ppm Hg. The computer tracking for Cu has only shown decreased activity as the Cu concentration increases; however, very low concentrations of Cu show no change as compared to controls.

The lethality data has been compared to the LD_{50} data from mammalian studies and, except for one metal (Cd), there is a good correlation between the results. Although much more data is needed, it is believed that this test species shows much promise as a basic model for range-finding studies and initial lethality screening tests.

The computer tracking studies showing hyperactivity with Hg supports our hypothesis that computer tracking of C. elegans can provide a rapid, inexpensive means of screening chemicals for neurotoxicity.

3. Specific objectives for coming year:

- Complete evaluation of metals.
- Using the developed protocols evaluate organophosphates and organic solvents.
- Determine the repeatability and reliability of the test procedure using statistical analyses.
- Compare the observed data with known human responses and determine the usefulness of the data as a screening test for the particular neurotoxin.

4. Non-applicable.