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2005-0336-F

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2005-0336-F

# FOIA MARKER

**This is not a textual record. This is used as an  
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Library Staff.**

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**Record Group/Collection:** George H.W. Bush Presidential Records  
**Collection/Office of Origin:** Science and Technology Policy, Office of (OSTP)  
**Series:** Bromley, D. Allan, Files  
**Subseries:** General Science Files

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**OA/ID Number:** 62040  
**Folder ID Number:** 62040-001

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**Folder Title:**  
Life Sciences: Biotechnology [4 of 4] [1991]

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Stack:

Row:

Section:

Shelf:

Position:

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Science Advisor to the President

Oct 4, 1991

White House

Washington D.C

Dear Sir;

Enclosed in an important MS which we have submitted for publication, the Science here shows that

- 1) Decontamination of nuclear waste has been achieved
- 2) Clean cheap power generation which is safe has been achieved.

Sincerely yours

William A. Morley

540 Weldell Dr

Sunnyvale, CA

940 69



"Document Control for Division of Life Sciences"

TYPE: INFORMATION DOCUMENT NUMBER: 9125046  
ORIGINATOR: 02 STATUS C DIRECTORATE STATUS C  
\*\*\*\*\*

FROM: STEWART, William D.: CHIEF SCIENTIFIC ADVISER, CABINET OFFICE,  
LONDON

TO: DR. D.A. BROMLEY

DATE OF  
CORRESPONDENCE: 12/03/91

SUBJECT: A FAX INFORMING DR. BROMLEY OF A MEETING BETWEEN DAI  
REES AND BERNADINE HEALY. HE ALSO EXPRESSES HIS  
DESIRE TO DISCUSS NIH'S PLANS TO SEEK PATENTS ON  
GENE SEQUENCES.

\*\*\*\*\*  
DIRECTORATE STAFF  
ASSIGNED: ASSIGNED: D.A. Henderson

ACTION STAFF  
REQUIRED: ACTION: Comments to Bromley

\*\*\*\*\*  
SENDER'S DUE DATE:  
OSTP DUE DATE: STAFF DUE DATE  
DATE COMPLETED: DATE COMPLETED/DEPT: 12/11/91

\*\*\*\*\*  
COPIES TO: D. Allan Bromley  
D.A. Henderson

\*\*\*\*\*  
WHITE HOUSE TRACKING #: CONTACT PERSON:  
PHONE: EXT:  
REMARKS: Stewart's FAX was received 12/4 and appointment was arranged  
with Dai Rees, D.A., Raub, Levinson and Gary Smith on 12/6/91;  
Bromley was informed that request for action had been fulfilled  
unless we hear further from either Stewart or Rees.

OSTP RECEIVED: 12/03/91  
FILE: P-LIFE SCIENCES

DEPT RECEIVED: 12/11/91

CENTRAL FILES:

## CHRONOLOGY OF EVENTS

Wed., 12/3, at 5:58pm  
(London time)

William Stewart, Chief Scientific Adviser in the Cabinet Office at Whitehall, London sent a FAX to Dr. Bromley stating that Dai Rees was meeting with Bernadine Healy on Thursday, 12/4.

Wed., 12/4, at 6:00 pm

Damar handed me a copy of the FAX. I showed it to both Michelle Huguelet (International) and Bill Raub. I read it to both DAH in Baltimore and Rachel at home. Raub had suggested contacting the British Embassy Thursday morning; DAH and I decided to send a FAX back to Whitehall Wednesday night stating the willingness of DLS to meet with Rees. FAX was sent at 7:20 pm.

Thurs, 12/5, at 8:45 am

Telephone message from Dai Rees upon my arrival stating his interest in meeting with DLS, but no phone number; said he would call back. He mentioned later that he was scheduled to meet someone at JHU, Baltimore (McKusick?) Friday morning and flying back to England Friday evening. He managed to change his appointment in Baltimore to the afternoon and later (5:30 pm) confirmed that he would be here Friday morning.

Fri., 12/6, at 9:00 am

Dai Rees met with DAH, Bill Raub, Rachel Levinson and Gary Smith and seemed very pleased with the discussions when he departed EOB.

Dr. Henderson feels that OSTP has fulfilled request for action unless we hear further from Stewart/Rees.



"Document Control"

TYPE: INFORMATION

DOCUMENT NUMBER: 9125046

ORIGINATOR: 02

STATUS C

DIRECTORATE STATUS

\*\*\*\*\*

FROM: STEWART, William D.: CHIEF SCIENTIFIC ADVISER, CABINET OFFICE,  
LONDON

TO: DR. D.A. BROMLEY

DATE OF  
CORRESPONDENCE: 12/03/91

SUBJECT: A FAX INFORMING DR. BROMLEY OF A MEETING BETWEEN DAI  
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GENE SEQUENCES.

\*\*\*\*\*

DIRECTORATE  
ASSIGNED:

STAFF  
ASSIGNED:

ACTION  
REQUIRED:

STAFF  
ACTION:

\*\*\*\*\*

OSTP DUE DATE:  
DATE COMPLETED:

SENDER'S DUE DATE:

STAFF DUE DATE  
DATE COMPLETED/DEPT:

\*\*\*\*\*

COPIES TO: D. Allan Bromley  
D.A. Henderson

\*\*\*\*\*

WHITE HOUSE TRACKING #:

CONTACT PERSON:  
PHONE:

EXT:

REMARKS:

OSTP RECEIVED: 12/03/91  
FILE: P-LIFE SCIENCES

DEPT RECEIVED:

CENTRAL FILES:

5046

TO; DR ALLAN BROMLEY, CHIEF SCIENTIFIC ADVISER TO THE PRESIDENT,  
THE WHITE HOUSE, WASHINGTON FAX 202 395 3719.

FROM; PROFESSOR WILLIAM D P STEWART, CHIEF SCIENTIFIC ADVISER,  
CABINET OFFICE, WHITEHALL, LONDON FAX 071 270 0432

3 December 1991

RECEIVED  
OSTP  
MAIL ROOM

You are probably aware that Dai Rees, top official of the UK Medical Research Council, has arranged to meet Bernadine Healy of the NIH on Thursday this week to discuss the patenting of gene sequences. Following that meeting, I think it would be useful for the two of us to go over the issues to see if we can find a way of taking this difficult matter forward.

2. The UK, and Europe generally, would like to work constructively towards a policy which makes commercial and scientific sense. While we understand and respect the motives of the NIH in filing their patent applications, the implications for genome research and its commercialisation throughout the world could be far-reaching if everyone followed the US lead.

3. This is an area where both the commercial and scientific stakes are high. There might be considerable benefit for all the main players in genome research to agree a common approach to patenting of gene sequences rather than to leave the question of patentability to be decided in the courts. I look forward to being able to discuss with you how we might develop these ideas.

PROFESSOR WILLIAM D P STEWART



## TRANSMIT CONFIRMATION REPORT

NO. : 008  
RECEIVER : 071 270 0432  
TRANSMITTER : PIA&DLS/OSTP  
DATE : DEC 04 '91 19:37  
DURATION : 01'26  
MODE : FINE  
PAGES : 02  
RESULT : OK

To 48 Date 12/5 Time 8:14

**WHILE YOU WERE OUT**  
M Dr. Reese  
of Medical Research Council

Phone Area Code Number Extension

|                    |  |  |  |  |
|--------------------|--|--|--|--|
| TELEPHONED         |  |  |  |  |
| CALLED TO SEE YOU  |  |  |  |  |
| WANTS TO SEE YOU   |  |  |  |  |
| RETURNED YOUR CALL |  |  |  |  |
| PLEASE CALL        |  |  |  |  |
| WILL CALL AGAIN    |  |  |  |  |
| URGENT             |  |  |  |  |

Message Will call today or tomorrow  
Will call you later  
AM on 230

AMP  
FR

EXECUTIVE OFFICE OF THE PRESIDENT  
OFFICE OF SCIENCE AND TECHNOLOGY POLICY  
WASHINGTON, D.C. 20506

## FAX Transmittal Sheet

DATE: 12/04/91

TO: Prof. William Stewart  
ORGANIZATION: Cabinet Office, Whitehall, London  
TELEPHONE: 011/44/~~313~~71/270/0259  
FAX: 011/44/~~313~~71/270/0432

FROM: MARGARET C. QUINLAN  
TELEPHONE: 202/456-2892  
FAX: 202/395-3719

NUMBER OF PAGES, INCLUDING COVER PAGE: 2

SPECIAL INSTRUCTIONS:



EXECUTIVE OFFICE OF THE PRESIDENT  
OFFICE OF SCIENCE AND TECHNOLOGY POLICY  
WASHINGTON, D.C. 20506

December 4, 1991

Dear Professor Stewart:

Thank you for your telefax to Dr. Allan Bromley, Assistant to President Bush for Science and Technology, about the current visit to Washington, D.C., of Mr. Dai Rees of the U.K. Medical Research Council. I am responding for Dr. Bromley, who is out of the office the rest of this week.

As Associate Director for Life Sciences in the Office of Science and Technology Policy, I have led the ongoing discussions on the issues of gene sequencing and patenting the human genome for the Office. I and Ms. Rachel Levinson of my staff would be delighted to meet with Mr. Rees either Thursday or Friday, December 5 or 6, should his schedule allow. Is there someplace here in the Metropolitan Washington area my office could contact Mr. Rees, or is there someone at the British Embassy here in Washington that could help us arrange a meeting during Mr. Rees' stay?

I appreciate your contacting our Office and anticipate constructive discussions with Mr. Rees.

Sincerely yours,

A handwritten signature in dark ink, appearing to read 'D.A. Henderson', with a stylized, cursive script.

D.A. Henderson, M.D., M.P.H.  
Associate Director for Life Sciences

Professor William D. P. Stewart  
Chief Scientific Adviser  
Cabinet Office  
Whitehall  
London, England

# FACSIMILE TRANSMISSION

From:

SCIENCE AND TECHNOLOGY SECRETARIAT  
CABINET OFFICE  
70 WHITEHALL  
LONDON  
SW1A 2AS



Fax machine: 071 270 0432  
Fax enquiries: 071 270 0375

Name of sender:

STEWART

Telephone number:

071 270 0259

To:

Name:

Dr ALLAN BLOMLEY

Department:

WHITE HOUSE -

CSA OFFICE

Document  
title:

GENE SEQUENCES

Date sent:

3. 12. 91

NUMBER OF PAGES

(excluding this sheet)

ACKNOWLEDGEMENT REQUIRED

NO

☐

YES

☒

TO; DR ALLAN BROMLEY, CHIEF SCIENTIFIC ADVISER TO THE PRESIDENT,  
THE WHITE HOUSE, WASHINGTON FAX 202 395 3719.

FROM; PROFESSOR WILLIAM D P STEWART, CHIEF SCIENTIFIC ADVISER,  
CABINET OFFICE, WHITEHALL, LONDON FAX 071 270 0432

44/11

3 December 1991

You are probably aware that Dai Rees, top official of the UK Medical Research Council, has arranged to meet Bernadine Healy of the NIH on Thursday this week to discuss the patenting of gene sequences. Following that meeting, I think it would be useful for the two of us to go over the issues to see if we can find a way of taking this difficult matter forward.

2. The UK, and Europe generally, would like to work constructively towards a policy which makes commercial and scientific sense. While we understand and respect the motives of the NIH in filing their patent applications, the implications for genome research and its commercialisation throughout the world could be far-reaching if everyone followed the US lead.

3. This is an area where both the commercial and scientific stakes are high. There might be considerable benefit for all the main players in genome research to agree a common approach to patenting of gene sequences rather than to leave the question of patentability to be decided in the courts. I look forward to being able to discuss with you how we might develop these ideas.

PROFESSOR WILLIAM D P STEWART

12/4/91

DLS DISTRIBUTION:

HENDERSON

LEVINSON

RAUB

BOWDEN





RECEIVED

RECEIVED

## CABINET OFFICE

70 Whitehall London SW1A 2AS Telephone 071-276 0259 51

91 DEC 19 A10:21

From the Chief Scientific Adviser  
Professor William D. P. Stewart, FRS., FRSE.

W0126

OSTP  
MAIL ROOMOSTP  
MAIL ROOM

Dr Allan Bromley  
Chief Scientific Adviser to the President  
The White House  
Washington DC

FAXed this date.

3 December 1991

*Dear Allan,*

You are probably aware that Dai Rees, top official of the UK Medical Research Council, has arranged to meet Bernadine Healy of the NIH on Thursday this week to discuss the patenting of gene sequences. Following that meeting, I think it would be useful for the two of us to go over the issues to see if we can find a way of taking this difficult matter forward.

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3. This is an area where both the commercial and scientific stakes are high. There might be considerable benefit for all the main players in genome research to agree a common approach to patenting of gene sequences rather than to leave the question of patentability to be decided in the courts. I look forward to being able to discuss with you how we might develop these ideas.

*Yours sincerely,**W.D.P.*

PROFESSOR WILLIAM D P STEWART

*I hope that you and I can personally take this issue forward on an international basis*

*W.D.P.*

"CORRESPONDENCE TRACKING"

TYPE: INFORMATION

DOCUMENT NUMBER: 9122648

ORIGINATOR: 02

STATUS C

DIRECTORATE STATUS

\*\*\*\*\*

FROM: DAVIS, Jay C.: LAWRENCE LIVERMORE NATIONAL LABORATORY

TO: DR. D.A. BROMLEY

DATE OF  
CORRESPONDENCE: 07/17/91

SUBJECT: RE: AMS ACTIVITY AND MENTION OF THE POSSIBILITY OF  
GIVING OSTP A SUMMARY BRIEFING ON THE IRAQI PROBLEM  
WHEN HE RETURNS IN MID-AUGUST.

\*\*\*\*\*

DIRECTORATE  
ASSIGNED:

STAFF  
ASSIGNED:

ACTION  
REQUIRED:

STAFF  
ACTION:

\*\*\*\*\*

SENDER'S DUE DATE:

OSTP DUE DATE:  
DATE COMPLETED:

STAFF DUE DATE  
DATE COMPLETED/DEPT:

\*\*\*\*\*

COPIES TO: D. Allan Bromley  
LIFE SCIENCES  
Marian Nida

\*\*\*\*\*

WHITE HOUSE TRACKING #:

CONTACT PERSON:

REMARKS:

PHONE:

EXT:

**CLOSED**

OSTP RECEIVED: 07/23/91  
DEPT RECEIVED:

FILE: DAB-PERSONAL\*LIFE SCIENCES

P-





2648  
Lawrence Livermore National Laboratory

RECEIVED

July 17, 1991

91 JUL 23 P 2: 45

OFFICE OF THE  
DIRECTOR

Professor D. Allan Bromley  
Executive Office of the President  
Old Executive Office Building, R-360  
17th and Pennsylvania Avenue, NW  
Washington, DC 20506

Dear Allan:

I'm sorry to have missed connections with you yet again. It might be better use of Marian's time to just instruct her to hang up when she hears my voice. Rarely has an individual worked so diligently and been able to achieve so little for her efforts.

I'd wanted to drop by to fill you in on a couple of things. The AMS activity goes very well. Our UC Steering Committee has given the work a ringing endorsement, calling it the "most valuable example to date of laboratory-campus collaboration." Our internal research has gone well. The biomedical portion has been given a five-year NIH/NCI grant for carcinogen/mutagen work, we expect DOE funding for a collaborative research project with Caterpillar to investigate the origin of particulates in combustion in diesel engines, and we are developing and testing new technology for bulk sample preparation and tritium AMS for clinical work. Funding for geochemistry and paleoclimatology work seem to be the hardest to develop. However, David Galas at OHER is receptive to taking ownership of us as both biomedical and climate-related research programs fall within his purview. Hans Mark is making strong statements to Secretary Watkins about the quality of our work; we hope for a trickle-down effect eventually.

I've broadened our program with a major push in the microbeam area as well. With our Sandia collaborators, we are stressing intelligence and structural biology uses of this tool. Internally, we appear to have the best method for the precision characterization of ICF targets. Proton energy loss tomography sure beats radiography any time. If you toss in PIXIE and neutron time-of-flight to measure D and T distributions, their problems are pretty well wrapped up.



July 17, 1991

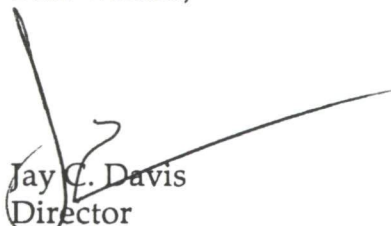
Page 2

I've also been leading the Laboratory's effort to respond to Hans Mark's tasking on new sample acquisition and analytical tools for a quick response nuclear forensics program. Present technology can return samples in 72 hours at best and take days to provide further answers such as isotopic signatures. Having stood on the ground at Tuwaitha taking samples that could have been acquired with RPV or even pod-mounted systems during the combat, I've got some typically strong opinions on how to proceed.

Off to Vienna Monday night to start another stint of nuclear archaeology in Iraq. There was fear and trembling at LLNL when they found out that I would address the Security Council. My old viewgraph offering Massachusetts as a Palestinian homeland still sticks in people's minds for some reason. Will be glad to give your office a summary briefing on the Iraqi program when I get back in mid-August. These people were doing a first rate job. I've made a strong request to be part of the debriefing team for the project leadership if they ever come out.

Keep holding the fort and doing good work. Seeing you stalk down the corridor like a lion last week told me that you were bearing up under what must be becoming an ever more difficult job.

Best wishes,



Jay C. Davis  
Director  
Center for Accelerator  
Mass Spectrometry

JCD:nms

THE WHITE HOUSE  
WASHINGTON

July 31, 1991

Dear Jay:

I too am very sorry that we missed making contact on your last trip through, but my schedule has been a very hectic one. I have not, however, given up and I hope that this also applied to you. It is in the nature of statistics that one of these days our paths will actually cross here in Washington.

I was delighted to learn that the AMS activity is going well and your leadership is clearly what has made the difference in this entire area. You were entirely correct in that this is a field that can enliven a number of the California campuses. I will have an opportunity to talk to David Galas in the near future because I have convinced him to chair the government-wide examination of where we are and where we are going in biotechnology and see him quite frequently.

The microbeam area seems to me a very important and widely applicable one as well and I have a feeling that its use is just beginning to be appreciated.

I am sorry that interaction last time was so brief, but I was on my way to the Oval Office and nothing, but nothing, stands in the way of those particular sorties.

With all best wishes,

Sincerely yours,



D. Allan Bromley  
The Assistant to the President  
for  
Science and Technology

Dr. Jay C. Davis  
Director  
Center for Accelerator Mass Spectrometry  
Lawrence Livermore National Laboratory  
Post Office Box 808  
Livermore, California 94550

"CORRESPONDENCE TRACKING"

TYPE: Action DOCUMENT NUMBER: 9121975  
ORIGINATOR: 02 STATUS *ATC* DIRECTORATE STATUS C  
\*\*\*\*\*

FROM: RAVEN, Peter H.: DIRECTOR, MISSOURI BOTANICAL GARDEN.

TO: DR. D.A. BROMLEY

DATE OF  
CORRESPONDENCE: 07/01/91

SUBJECT: HOPES THAT THE ISSUE OF BIODIVERSITY WILL EMERGE AS  
AN IMPORTANT INITIATIVE.

\*\*\*\*\*  
DIRECTORATE STAFF  
ASSIGNED: *Life Sciences* ASSIGNED: D.A. Henderson

ACTION STAFF  
REQUIRED: *Comments to DAB* ACTION: Comments to DAB

\*\*\*\*\*  
SENDER'S DUE DATE:  
OSTP DUE DATE: STAFF DUE DATE  
DATE COMPLETED: DATE COMPLETED/DEPT: 07/15/91

\*\*\*\*\*  
COPIES TO: D. Allan Bromley  
LIFE SCIENCES  
ENVIRONMENT

\*\*\*\*\*  
WHITE HOUSE TRACKING #: CONTACT PERSON:  
REMARKS: PHONE: EXT:

**CLOSED**

OSTP RECEIVED: 07/05/91 FILE: **P-LIFE SCIENCES**\*P-ENVIRONMENT  
DEPT RECEIVED: 07/11/91



Missouri  
Botanical  
Garden



RECEIVED

July 1, 1991  
91 JUL 3 A 9:50

OFFICE OF THE  
DIRECTOR

Dr. Allan D. Bromley  
Assistant to the President  
for Science and Technology  
Office of Science and Technology Policy  
Old Executive Office Building, Room 358  
Washington, D. C. 20500

Dear Allan:

Just working on the 1993 budget at the National Science Board makes me think of your mention, at the NAS annual garden party, that biodiversity might emerge as the initiative -- after biotechnology and material science.

I hope you are still considering that might be the case, and I would be delighted to do anything that I could to help. Having recently worked on the Advisory Committee for the Global Environment Facility, which looks likely to spend about \$450 million in the area of biodiversity in developing countries with a per capita income of less than \$4,000 annually over the next three years, having just persuaded the Council of the National Academy of Sciences to issue a "White Paper" on biodiversity and being quite involved with the NSF budget as mentioned, I can see a lot of reasons that biodiversity is an issue whose time has really come. I, therefore, simply want to encourage you to keep considering this area, as I know you are, and to offer to help in any way that I can as the matter develops.

Ultimately, biodiversity is the only source of stability for any biological system, and our wisdom in using it well and saving it will clearly determine the structure of the kind of world that people will be able to put together in the future.

With all good wishes to you, I am

Cordially,

Peter H. Raven  
Director

PHR/bsm

P.O. Box 299  
St. Louis, Missouri 63166-0299  
Telephone: (314) 577-5100  
Telex: 466224 MOBOT CI  
Cable: MOBOTSTL

Director's Office  
Fax: (314) 577-9595  
Bitnet: PRAVEN @ NAS

"CORRESPONDENCE TRACKING"

TYPE: INFORMATION

ORIGINATOR: 02

DOCUMENT NUMBER: 9121934

STATUS C

DIRECTORATE STATUS

FROM: HUBBELL, John H.: DEPARTMENT OF COMMERCE, NIST

TO: DR. D.A. BROMLEY

DATE OF  
CORRESPONDENCE: 06/26/91

SUBJECT: RE: INFORMATION ON ISRP-5 AND THE STATUS OF THE  
FLEDGING IRPS

\*\*\*\*\*  
DIRECTORATE  
ASSIGNED: STAFF  
ASSIGNED:

ACTION  
REQUIRED: STAFF  
ACTION:

\*\*\*\*\*  
SENDER'S DUE DATE:  
OSTP DUE DATE: STAFF DUE DATE  
DATE COMPLETED: DATE COMPLETED/DEPT:

\*\*\*\*\*  
COPIES TO: D. Allan Bromley  
LIFE SCIENCES

\*\*\*\*\*  
WHITE HOUSE TRACKING #: CONTACT PERSON:  
REMARKS: PHONE: EXT:

OSTP RECEIVED: 07/01/91  
DEPT RECEIVED:

FILE: P LIFE SCIENCES-RADIATION

**NIST****UNITED STATES DEPARTMENT OF COMMERCE  
National Institute of Standards and Technology**

Gaithersburg, Maryland 20899

RECEIVED

91 JUL 1 A 9:12

**Applied Radiation and Isotopes**(International Journal of Radiation  
Applications and Instrumentation Part A)

Pergamon Press

**JOHN H. HUBBELL (Editor)**Physicist/Consultant:  
National Institute of Standards  
& Technology  
Rm C-311, Radiation Physics Bldg  
Gaithersburg MD 20899, USATel: (301) 975 5550  
Fax: (301) 869 7682  
FTS: 879-5550  
Telex: 197674 NIST UT

June 26, 1991

Prof. Dr. D. Allan Bromley  
Assistant to the President for  
Science and Technology  
The White House  
1600 Pennsylvania Ave., NW  
Washington, DC 20500OFFICE OF THE  
DIRECTOR

Dear Dr. Bromley (Allan):

Rex and Ilmary Keddy (Johannesburg), with whom Jean and I shared a delightful evening at the Folkloric Entertainment in the gymnasium-hall near the Libertas Hotel, during the 5th International Symposium on Radiation Physics (ISRP-5) in Dubrovnik June 10-14, 1991, asked me to pass along to you their special regards, so here they are. They apparently feel "family-close" to you, from your past interactions and visits back and forth. I had had considerable correspondence and exchanges of reprints with Rex over the past years, but had never yet met him in person, one of the "profound joys" of such international conferences. The Keddys are a nice couple, and we may likely see them again at ISRP-6 (1994) in Rabat, Morocco (now firm). There were about 20 spouses (in some cases husbands) at ISRP-5, which added a new and social dimension to this Symposium.

Other information on ISRP-5, and on the status of the fledgling IRPS, now with over 300 members drawn from 51 countries, is in the enclosed report, for your interest, to appear as an item in IRPS-News. Dubrovnik is indeed an "absolute jewel" as you had mentioned to me in your January 4, 1991 letter, including the walk around the Old City atop the ancient walls.

With best regards and thanks again for your interest in the IRPS and other matters.

Sincerely,

John H. Hubbell  
Vice President for North America (1991-1994),  
International Radiation Physics Society (IRPS)Ionizing Radiation Division, "Emeritus"  
Physics Laboratory, NIST



*Allan .  
For your further interest .  
John*

**REPORT ON THE 5TH INTERNATIONAL SYMPOSIUM ON RADIATION PHYSICS (ISRP-5)**

**DUBROVNIK, CROATIA, YUGOSLAVIA, JUNE 10-14, 1991**

**J. H. Hubbell  
National Institute of Standards and Technology  
Gaithersburg, MD 20899, USA**

Despite the political turmoil in Yugoslavia in June 1991, 119 participants from 32 countries braved the uncertain situation to materialize at the Libertas Hotel in the historic and picturesque Adriatic seacoast city of Dubrovnik for the Fifth International Symposium on Radiation Physics (ISRP-5), June 10-14, 1991, to present 21 oral invited papers and 102 contributed poster papers on a stimulating and mind-stretching variety of radiation physics topics. This Symposium was a sequel to ISRP-1 (Calcutta, India 1974), ISRP-2 (Penang, Malaysia 1982), ISRP-3 (Ferrara, Italy 1985), and ISRP-4 (Sao Paulo, Brazil 1988). This Symposium, sponsored by the International Radiation Physics Society (IRPS), was organized with the support of the Ruder Boskovic Institute (RBI), Croatia, with financial support from the Ministry for Science, Technology and Informatics of Croatia and additional contributions from the European Research Office.

The ISRP-5 Local Organizing Committee consisted of Chairman A. Ljubicic (RBI, Zagreb), Scientific Secretary D. Miljanic, plus additional members I. Anicic, M. Krcmar, M. Kregar, I. Picek, D. Rendic, D. Srdoc, V. Valkovic, and N. Zovko, with the indispensable help of administrative secretary Mrs. Zdenka Kuzmic. The International Programme Committee was chaired by M.J. Cooper (UK) and otherwise consisted of M. Berrada (Morocco), D.C. Creagh (Australia), J. Csikai (Hungary), D.B. Isabelle (France), Y. Isozumi (Japan), A. Ljubicic (Yugoslavia), B.A. Logan (Canada), G. Paic (Yugoslavia), A.S. Paschoa (Brazil), R.H. Pratt (USA), and S.C. Roy (India), with D.A. Bradley (Malaysia) serving as Editorial Secretary.

The above working committees were assisted in a variety of ways, including general promotion of the Symposium, by an International Advisory Board (IAB) consisting of D. Berenyi (Hungary), I. Derado (Germany), R.F. Fleming (USA), A.M. Ghose (India), R. Haensel (France), M. Hart (UK), J.H. Hubbell (USA), M. Inokuti (USA), P.K. Iyengar (India), D.F. Jackson (UK), I.C. Nascimento (Brazil), W.R. Nelson (USA), K. Pisk (Yugoslavia), A.A. Pomansky (USSR), B. Povh (Germany), P. Povinec (Czechoslovakia), R.A. Ricci (Italy), G. Senjanovic (Yugoslavia), S. Shimizu (Japan), I.B. Whittingham (Australia), and M. Zifferero (IAEA). The sad news of the recent death of IAB member Daphne F. Jackson was announced at the Symposium.

The Symposium was opened with welcoming remarks by the Mayor of Dubrovnik and other local officials, also by R.H. Pratt (USA), IRPS Secretary, in the absence of IRPS Retiring President P.K. Iyengar (India), by M.J. Cooper (UK), Chairman of the International Programme Committee and also IRPS Vice President for Western Europe, and by A. Ljubicic (Yugoslavia), Chairman of the Local Organizing Committee and also IRPS Vice President for Eastern Europe and the USSR. The opening ceremony session continued with an enlightening and stimulating lecture by K. Pisk (Yugoslavia), Director General of the Ruder Boskovic Institute, on astronomer-mathematician Ruder Boskovic, born in 1711 in Dubrovnik and died in Italy in 1787, whose life-span overlapped that of Isaac Newton (1642-1727). Largely independent of Newton's novel concepts of



gravitational attraction and Newton's invention of the calculus, Boskovic envisioned a single law of force which he treated with mathematical tools based solely on geometry, without recourse to calculus. His published works, nearly 70, treating such diverse topics as optics, astronomy, gravitation, meteorology and trigonometry, marked him as one of the scientific giants of his age.

ISRP-5 focused on six topical areas of radiation physics:

- I. Fundamental Processes in Radiation Physics. Sessions chaired by J.H. Hubbell (USA) and R.H. Pratt (USA).
- II. Radiation Sources and Detectors. Sessions chaired by S. Shimizu (Japan) and M.J. Cooper (UK).
- III. Radiation in Fundamental Research. Sessions chaired by M.J. Cooper (UK) and A.M. Ghose (India).
- IV. Radiation in Medical, Environmental and Earth Sciences. Sessions chaired by M.J. Cooper (UK) and V. Valkovic (USSR).
- V. Radiation in Technology. Sessions chaired by J.B. Forsyth (UK) and M. Berrada (Morocco).
- VI. Radiation in Astrophysics and Cosmology. Sessions chaired by B.A. Logan (Canada) and V. Novikov (USSR).

Attendance cancellations, including six of the 22 invited speakers, due to the uncertain political situation in Yugoslavia, resulted in deviations from the original programme. The substitute speakers, drawn from contributed-paper attendees with topics considered by the attending Programme Committee members to be appropriate replacements, with advance notice ranging from two weeks down to a few hours, rose superbly to the occasion, and were acclaimed in all cases to be at least equal in interest to the originally scheduled offerings. The following account thus describes the papers actually presented at ISRP-5, both oral and poster.

Topic I invited papers on fundamental processes in radiation physics included "The 17 keV Neutrino" by B.A. Logan (Canada), "Polarization Radiation or 'Atomic' Bremsstrahlung" by M. Ya. Amusia (USSR), "X-Ray Standing-Wave Experiments: Application to the Study of Surfaces and Interfaces" by C. Malgrange (France), and "Compton Scattering from Bound Electrons" by T. Suric (Yugoslavia). In addition, 29 poster papers covered a wide range of other theoretical and experimental work including electromagnetic radiation in neutron-atom collisions, nuclear excitation in an electron transition, lyoluminescence, single quantum annihilation, double photon Compton scattering, incoherent scattering at low momentum transfers, the nature of electromagnetic radiation, electron-generation corrections to the continuous-slowing-down approximation, small angle elastic scattering of gamma rays, enhancement ratio of thick target K x-rays, equipartition in Planck's radiation law and quanta, level excitation in Cs-137 decay, multiple scattering effects in photon transport including tilt of propagation plane, polarization, spectrometry and attenuation coefficient measurements, nuclear excitation by gamma scattering at the giant dipole resonance, nuclear excitation by positron annihilation with K-shell electrons, heavy neutrino emission, L-shell fluorescence, K x-ray satellite spectra, electron subexcitation in H<sub>2</sub> and D<sub>2</sub> gases,



thermoluminescence and defect stability, atomic photoeffect measurements and critique of theory, scattering of radiation by electrons in the Coulomb field, S-matrix calculation of whole-atom Compton scattering, and an experimental study of the electron-antineutrino rest mass limit.

Topic II invited papers on radiation sources and detectors included "Low energy Antiproton Beams" by R. Klapisch (CERN), "Developments in Superconducting Tunnel Junction Detectors" by M. Kurakado (Japan) and "Ring Imaging Cherenkov Detectors" by D. Vranic (Yugoslavia). In addition, 26 poster papers presented developments on natural quartz thermoluminescence from heavy ion bombardment, nuclear track detector irradiation and temperature effects, optical fibre radiation dosimeter, neutron and gamma dosimetry in fast neutron fields, TLD gamma spectral response, silicon surface barrier dielectric effect, window size limitations on resolution of a gas proportional scintillation counter, a semiconductor  $^3\text{He}$  neutron spectrometer, research reactor core optimization, background reduction from a Compton suppression shield, neutron admixtures in linac bremsstrahlung,  $^{138}\text{La}$  activity with reference to  $^{40}\text{K}$  activity, radiation field mathematical model, XRF annular source Monte Carlo backscatter simulation, cylindrical source height optimization for gamma spectroscopy, Monte Carlo study of window entry electron loss for Xe x-ray detectors, low energy position-sensitive proportional counters, spectral unfolding method influence on fast neutron dose determination, digital evaluation of alpha tracks in Cr-39 detector, miniaturized tissue-equivalent dose-rate monitors using synthetic diamond crystals, thermoluminescence of some natural Egyptian materials, the Fano factor for Ar and  $\text{H}_2$  mixtures, studies of Au photocathode and microchannel plate devices using synchrotron radiation, and use of a silicon surface barrier detector for observations of the central-cell region of the GAMMA-10 tandem-mirror plasma fusion device.

ex  
Keddy's  
paper :

Topic III invited papers on radiation in fundamental research included "First Experiments at the Heavy-Ion Storage Ring ESR, Darmstadt" by F. Bosch (Germany), "Schwinger Scattering of Neutrons in the Study of Condensed Matter" by J.B. Forsyth (UK), and "Recent Progress in the Understanding of the Neutron-Nucleus Interaction" by D. Seeliger (Germany). In addition, 3 poster papers presented results on the depopulation of the 6 hr isomeric state of  $^{99}\text{Tc}$  by photon irradiation, on the slowing-down of polarized muons in an Al-C-Ag target, and on the effect of solvents on the diffusion of ions by a radioactive tracer method.

Topic IV invited papers on radiation in medical, environmental and earth sciences included "Angiography Using Synchrotron Radiation" by W.R. Dix (Germany), "Basics of the Detector for Direct Measurement of Radon and thoron Concentrations in Air" by V.M. Novikov (USSR), and "Radon in Soil, Air, and in Groundwater Related to Major Geophysical Events: Recent Advances" by M.M. Monnin (France). In addition, 25 poster papers presented studies of shielding for an 8 GeV synchrotron in Japan, radiological impact of power plants during convective storm, penetration through Fe and concrete of 20-35 MeV neutrons, neutron activation elemental analysis of breast tissue, radiation effects on laser crystals for space applications, tritium in the atmospheric air, R-function calculations of radiation transport in complex geometry, environmental neutrons seen by a Ge gamma-ray detector, the first atomic bomb - 45 years later, a formula for neutron/gamma transmission and dose in ordinary concrete, tissue characterization by Compton scattering profile, shielding for a heavy-ion accelerator, earthquake prediction from radon, radiation safety of the Japanese Hadron Project, radioactive nuclides in global studies of recent



environmental changes, monazite and radionuclide distributions in the Mangalore environment, TLD archeological dating using a pre-dose technique, 10-300 keV photon attenuation coefficients in soils, micro-tomography in soil physics, serum trace elements in malnourished children in Tanzania by XRF spectroscopy, the air kerma-rate constant of  $^{192}\text{Ir}$ , phototransfer-thermoluminescence of high temperature TL peaks in zircon, air-collision-kerma to dose-equivalent conversion coefficients for dosimeter calibration in gamma fields, aconitic acid transformation in a clay mineral by gamma irradiation, and an improved multiple scattering algorithm for charged particle transport modelling.

Topic V invited papers on radiation in technology included "Radiation Hardness Assurance of Space Electronics" by L. Adams (Netherlands), "Industrial Applications of Synchrotron Radiation" by P. Barnes (UK), "Small Angle Neutron Scattering Studies of Irradiated Metallic Materials" by G. Albertini (Italy), and "Positron Annihilation in the Study of Material Damage" by P. Sen (India). In addition, 16 poster papers presented developments in Compton profiles in Co-Ni and Fe-Ni-based amorphous alloys, polymer viscosity changes using a random resistance network model, distribution of Ca, K, and Cl in different parts of a spinach plant using XRF, comparison of PIXE and XRF for analysis of grown epitaxial layers with ingrown dopants, radiation effects in optoelectronic devices and possibilities for dosimetry, environmental impact of coal burning power stations, x-ray and gamma spectroscopy of coal and coal ash samples, corrections for density and volumetric H content in coal by neutron activation prompt gamma analysis, small-angle neutron scattering for microstructural examination of a steel for fusion technology, two-phase-flow void-fraction determination using photon-attenuation techniques, thermoluminescence study of semiconductor materials, computer simulation of coloring curves in alkali halide doped with divalent impurities, influence of radiation intensity and Pb concentration in F-center coloring in KCl, room temperature F-coloring kinetics in Pb and Sn doped NaCl, and the influence of inhomogeneous  $\text{N}_2$  laser irradiance on radiance from a laser produced plasma.

Topic VI invited papers on radiation in astrophysics and cosmology included "Sudbury Neutrino Observatory" by G.T. Ewan (Canada), "Study of Cosmic Radiation by Underground Detectors" by C. de Marzo (Italy), "Neutrino Radiation from Supernovae" by J.A. Grifols (Spain), and "Dark Matter in the Universe" by B.V. Pritychenko (USSR). In addition, 3 poster papers presented work on redshifts of atomic radiation in fields of differing temperatures, integral cosmic-ray intensity monitoring as a serendipitous benefit from background measurements in gamma-ray spectroscopy, and evaluation of radiation dose in the space environment.

### Epilogue

In this reporter's opinion, both the invited papers and contributed papers at ISRP-5 met or exceeded the high standards of quality, density of information, interest, and clarity of presentation set at the previous Symposia in this series. The question periods were lively, always a good sign, and sometimes grew quite heated when the topics touched responsive chords on the underlying nature of reality. Of almost equal, or perhaps greater value, were the hallway and social-event face-to-face conversations between long-term pen-pals and new acquaintances alike, the fertile idea-breeding grounds marking all international scientific conferences, forming and reinforcing stimulating contacts with far-flung representatives of the global human family.



On behalf of the IRPS and the general radiation physics community, this reporter thanks Professors Ante Ljubicic and D. Miljanic and their hard-working Organizing Committee for their organizational genius, their scientific expertise, their warm Croatian hospitality, and particularly for their improvisations for substitute speakers which restored to ISRP-5 a full, stimulating, and cutting-edge programme in the cross-disciplinary field of radiation physics. The welcoming reception Sunday evening prior to the conference and the boat excursion to Cavtat for a sumptuous seafood banquet, the conference scheduled events, were a fine exposure to Yugoslav hospitality and cuisine. The hike across the hill from the Libertas Hotel to the massive-walled Old Town was retraced many time by the ISRP-5 participants, who also took advantage of tours to Mostar and other nearby places of scenic and historic interest. Much credit also goes to Prof. Malcolm Cooper and his Programme Committee for their creativity, imagination, and evolving perception of "radiation physics" as an emerging identity, in their superb selection of invited topics and speakers (including the heroic short-notice substitutes).

#### IRPS General Meeting

The triennial International Radiation Physics Society General Meeting was held June 13, 1991, during ISRP-5, presided over by M.J. Cooper (UK, Vice President for Western Europe) in the absence of Retiring President P.K. Iyengar (India) and President-Elect D.J. Beninson (Argentina). The results of the mail-ballot triennial election of IRPS Officers, held just prior to ISRP-5, were announced. Based on 102 valid ballots received in time to be counted, the IRPS officers for 1991-1994 will be:

**President;** D.J. Beninson (Argentina)  
**Secretary:** R.H. Pratt (USA)  
**Treasurer:** A. Ljubicic (Yugoslavia)

#### **Vice Presidents:**

|                           |                          |
|---------------------------|--------------------------|
| North America:            | J.H. Hubbell (USA)       |
| South America:            | I.C. Nascimento (Brazil) |
| Africa and Middle East:   | M. Berrada (Morocco)     |
| Eastern Europe and USSR:  | D. Berenyi (Hungary)     |
| Western Europe:           | M.J. Cooper (UK)         |
| Rest of Asia and Oceania: | B. Sinha (India)         |

#### **Executive Councillors:**

D.A. Bradley (Malaysia)  
D.C. Creagh (Australia)  
A.M. Ghose (India)  
D.B. Isabelle (France)

#### **Continuing terms as Councillor:**

T. Nakamura (Japan)  
F. Rustichelli (Italy)

Prof. S.C. Roy (India), IRPS Membership Coordinator, announced that the IRPS now has 305 members, drawn from 51 countries. A new membership sign-up and renewal form is being drafted, to reflect a Council-enacted dues increase for developed-country members (to \$15.00/yr or \$40.00/3-yrs; developing-country dues unchanged) and to facilitate dues payment in some currencies other than US dollars or Swiss francs. This revised form will be included in a future issue of IRPS-News. Special votes of thanks were offered to D.A. Bradley (Malaysia)

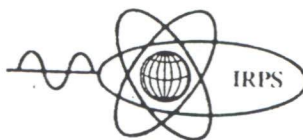
→ Allan:

by J. Hubbell. Latest version attached following.



for his valiant editing of IRPS-News despite almost-overwhelming obstacles, and to P.K. Iyengar (India) for his Presidency and support of the IRPS over the past six years. A.M. Ghose (India) will assume major editorial responsibility for IRPS-News, starting January 1992, from Calcutta. M.J. Cooper (UK) offered a eulogy, followed by a moment of silence with all standing, for Prof. Daphne Jackson (UK), who died two months prior to ISRP-5.

Also announced at the IRPS General Meeting was the acceptance by the Council of the invitation from M. Berrada (Morocco) to organize and hold the Sixth International Symposium on Radiation Physics (ISRP-6) in Rabat, Morocco in 1994. Prof. Berrada offered some welcoming remarks. Thus the ISRP conference series continues its history of venues in geographically diverse countries, both developing and industrialized, to promote a well-balanced and useful global growth of the IRPS membership and resulting benefits in terms of both scientific/technical and human values.



## INTERNATIONAL RADIATION PHYSICS SOCIETY

The primary objective of the International Radiation Physics Society (IRPS) is to promote the global exchange and integration of scientific information pertaining to the interdisciplinary subject of radiation physics, including the promotion of (i) theoretical and experimental research in radiation physics, (ii) investigation of physical aspects of interactions of radiations with living systems, (iii) education in radiation physics, and (iv) utilization of radiations for peaceful purposes.

The Constitution of the IRPS defines Radiation Physics as "the branch of science which deals with the physical aspects of interactions of ionizing radiations (both electromagnetic and particulate) with matter." It thus differs in emphasis both from atomic and nuclear physics and from radiation biology and medicine, instead focusing on the radiations.

The International Radiation Physics Society (IRPS) was founded in 1985 in Ferrara, Italy at the 3rd International Symposium on Radiation Physics (ISRP-3, 1985), following Symposia in Calcutta, India (ISRP-1, 1974) and in Penang, Malaysia (ISRP-2, 1982). Further Symposia have been held in Sao Paulo, Brazil (ISRP-4, 1988) and Dubrovnik, Yugoslavia (ISRP-5, 1991). ISRP-6 (1994) will be in Rabat, Morocco. The IRPS also sponsors regional Radiation Physics Symposia.

A newsletter, IRPS-News, is published quarterly and sent to all IRPS members.

The IRPS Secretariat is (% Prof. R.H. Pratt, IRPS Sec.): Dept. of Physics and Astronomy, Univ. of Pittsburgh, Pittsburgh, PA 15260 USA, (412) 624-9052.

The IRPS welcomes your participation in this "global radiation physics family."

### Membership Registration Form:

1. Name: \_\_\_\_\_  
(First) (Initial) (Last)
2. Date and Place of Birth: \_\_\_\_\_
3. Business Address: \_\_\_\_\_  
\_\_\_\_\_  
\_\_\_\_\_  
\_\_\_\_\_  
(Postal Code) (Country)  
Telephone: \_\_\_\_\_ Telex: \_\_\_\_\_ FAX: \_\_\_\_\_
4. Current Title or Academic Rank: \_\_\_\_\_
5. Field(s) of interest in Radiation Physics (Please attach a list of your publications, if any, in the field): \_\_\_\_\_  
\_\_\_\_\_  
\_\_\_\_\_  
\_\_\_\_\_
6. Please list any national or international organization(s) involved in one or more branches of Radiation Physics, of which you are a member, also your status (e.g., student member, member, fellow, emeritus): \_\_\_\_\_  
\_\_\_\_\_  
\_\_\_\_\_



7. The IRPS has no entrance fee requirement, only annual membership dues (or 3-year dues payment option, with savings):

Membership Dues (Stated in US dollars; circle equivalent-amount sent):

| Full Voting Member: | <u>1 year</u> | <u>3 years</u> | Student Member:    | <u>1 year</u> | <u>3 years</u> |
|---------------------|---------------|----------------|--------------------|---------------|----------------|
| Developed country   | \$15.         | \$40.          | Developed country  | \$6.          | \$15.          |
| Developing country  | \$5.          | \$12.50        | Developing country | \$2.          | \$5.           |

Acceptable modes of IRPS membership dues payment, to start or to continue IRPS membership, are listed below. Please check payment-mode used, enter amount (in currency-type used), and follow instructions in item 8 below. All checks should be made **payable to the IRPS:**

- [ ] (in U.S. dollars, drawn on a U.S. bank): Send to Prof. Richard H. Pratt, IRPS Secretary, Dept. of Physics and Astronomy, University of Pittsburgh, Pittsburgh, PA 15260 USA.

Amount paid (in U.S. dollars): \_\_\_\_\_

Alternatively, IRPS dues may be paid by one of the following modes (consult newspaper financial page for conversion from U.S.\$ to currency used in payment, at time of payment), in check **payable to the IRPS:**

- [ ] (in Swiss francs): Send to IRPS Account No. C7-111.441.0, Swiss Bank Corporation N, CH-1211 Geneve 11, Switzerland. If you prefer, you may instead send a Eurocheck in Swiss francs to: Prof. Ante Ljubicic (IRPS Treasurer), Institute Rudjer Boskovic, P.O. Box 1016, 41000 Zagreb, Croatia, Yugoslavia.

Amount paid (in Swiss francs): \_\_\_\_\_

- [ ] (in U.K. pounds): Send to Prof. Malcolm J. Cooper, Physics Dept., University of Warwick, Coventry, CV4 7AL, U.K.. Bank transfer details: Account name: IRPS. Account number: 90512958. Bank and Branch code: Barclays, code 20-88-65. Eurochecks in U.K. pounds, sent to Prof. Cooper, also acceptable.

Amount paid (in U.K. pounds): \_\_\_\_\_

- [ ] (in Indian rupees): Send to Dr. D.V. Gopinath, Health and Safety Group, Bhabha Atomic Research Centre, Trombay, Bombay 400 085, India.

Amount paid (in Indian rupees): \_\_\_\_\_

- [ ] (in Hungarian forints): Send to Prof. Denes Berenyi, Dir., Institute of Nuclear Research of the Hungarian Academy of Sciences, Bem ter 18/C, PF. 51, H-4001 Debrecen, Hungary.

Amount paid (in Hungarian forints): \_\_\_\_\_

8. Send this Membership Registration Form and a copy of your bank transfer receipt (or copy of your check) to the membership coordinator:

Prof. S.C. Roy, Department of Physics, Bose Institute, 93/1 Acharya Prafulla Chandra Road, Calcutta 700 009, India, Telex: 021-2646 BI IN, FAX: 91-33-34-3886, Email: BOSEINSTISM@NCST.ERNET.IN.

10. \_\_\_\_\_  
(Signature)

\_\_\_\_\_  
(Date)

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*John H. Hubbell* June 18, 1991  
Signature Date

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Underlined information will not appear  
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HUBBELL, JOHN HOWARD, radiation  
physicist; b. Ann Arbor, Mich., Apr. 9, 1925;  
s. Howard Adams Hubbell and Mildred  
Jeanetta (Lipe) Hubbell Dyson; m. Jean Garber  
Norford, June 11, 1955; children: Anne  
Virginia Hubbell Cooper, Shelton Eric, Wendy  
Jean Hubbell Schlosser. BS in  
Engring. Physics, U. Mich., 1949, MS in  
Physics, 1950. Researcher x-ray  
crystal diffraction group Nat. Bur. Standards  
(name now Nat. Inst. Standards & Tech.),  
Washington, 1950-51, researcher  
thermodynamics sect., 1951, researcher  
radiation theory group, 1951-62; dir.  
x-ray and ionizing radiation data ctr. Nat.  
Bur. Standards (name now Nat. Inst. Standards  
& Tech.), Washington & Gaithersburg, Md.,  
1963-81; researcher Ctr. for Radiation  
Rsch. Nat. Bur. Standards (name now Nat.  
Inst. Standards & Tech.), Gaithersburg,  
1982-88, researcher, cons. Photon and  
Charged Particle Data Ctr., 1988—; mem.  
cross sect. evaluation working group  
Brookhaven (N.Y.) Nat. Lab., 1965—; cons.  
Lawrence Livermore (Calif.) Nat. Lab., 1966—,  
Lawrence Berkeley (Calif.) Lab., 1981—,  
Internat. Atomic Energy Agy., Vienna, 1987—,  
WHO, Geneva, 1989—; sec. task force on x-ray  
absorption coefficients Internat. Union  
Crystallography, 1979—; lectr. USSR Acad.

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→ Allan: Jean and I will be in the tip of Baja, Mexico, with my Meade 4" mirror lens (1000 mm), with and without a Kiron 2X (for 2000 mm, nearly filling the narrow dimension of the 35 mm slide). Our last eclipse was in Surabaya, Java, June 11, 1983, our 28<sup>th</sup> Wedding Anniversary. Will you also be observing, from Hawaii, Baja, or from somewhere?

17182651/N/260/950/ /1925/M/-----/A

Scis., 1979. People's Republic of China State Bur. Metrology, 1987. India under Indo-U.S. Spl. Fgn. Currency Program, 1972, 74, 90. Author: Photon Cross Sections, Attenuation Coefficients and Energy Absorption Coefficients, 1969 (citation classic award 1982); editor jour. Applied Radiation and Isotopes, 1988—; contr. articles to prof. jour. and ency., chpt. to book. Scoutmaster, Boy Scouts Am., Washington, 1953-60; ch. sch. tchr. Foundry United Methodist Ch., Washington, 1963-78. With U.S. Army, 1943-45, ETO. Decorated Bronze Star; recipient Faculty medal Tech. U. Prague, 1982. Fellow Am. Nuclear Soc. (Radiation Industry award 1985, Prof. Excellence award 1990), Health Physics Soc. (chmn. gen. radiation protection sect., standards com. 1984—); mem. Am. Phys. Soc., Radiation Resch. Soc., Soc. Nuclear Medicine (Paul C. Aebersold award 1985), Internat. Radiation Physics Soc. (exec. councillor 1985—), Philos. Soc. Washington, Hubbell Family Hist. Soc. Avocations: travel, photography, harmonica playing. Home: 11830 Rocking Horse Rd Rockville MD 20852 Office: Nat Inst Standards and Tech Radiation Physics Bldg Rm C-311 Gaithersburg MD 20899 (301) 975-5550

mathematical research on radiation fields from extended sources, including the (now called) "Hubbell rectangular source integral" and "Epstein-Hubbell generalized elliptic-type integrals;"

2 additional publications (1975, 1982) also named Citation Classics (1989, 1990);

-1990

-1991, Vice President for North America 1991-1994)

including eclipse chasing,

statement: In this later stage of my life I view my global science connections more and more as an opportunistic tool toward realizing, incrementally at least, Teilhard de Chardin's envisioned "noosphere" (humanity as a caring communicating "thinking skin" of the earth), declaring the pragmatic and compelling authenticity of the option of a friendly cosmos as not only a place to live, but also to bravely wear as a suit of clothes, in contrast to the hostile and judgemental cosmos envisioned, dwelt in, and worn by many. "Where there is no vision (or the wrong vision), the people perish."

→ Allan: The IRPS "in disguise" turn

THE WHITE HOUSE  
WASHINGTON

July 9, 1991

Dear John:

I was delighted to get your letter and the enclosed **Report on the 5th International Symposium on Radiation Physics** held in Dubrovnik. I was also delighted to find that you and Jean had enjoyed Dubrovnik and that you had an opportunity to meet Rex and Ilmary Keddy who are indeed old, old friends. Should you see them before I do, as is possible, please do give them my warmest regards. I have had Rex as a visiting scientist at my laboratory at Yale on two extended occasions and have had him as a shorter term visitor on a number of occasions. Ilmary and Rex's very attractive three daughters spent several weeks with us one summer to everyone's great pleasure.

It turns out that within this past week one of Rex's old colleagues who spent a year with me at Yale, Dr. Donald Mingay, came through Washington and we were able to have lunch and, by pure coincidence, the following day I had the director and deputy director of the new organization in South Africa that corresponds to our National Science Foundation here for an hour's discussion.

From the sound of things you had a very interesting time of it and the report covers some very interesting material about which I had been previously unaware. I noticed also that another of my very old friends, George Ewan, gave a talk on the Sudbury Neutrino Observatory, a project in which I myself have been involved for some time, and for which I think I may have played a substantial role in terms of obtaining funding.

I envy you your eclipse tracking activities and as the proud possessor of a Questar, I am sure you will have great fun with your Meade.



Unfortunately, I will not be eclipse tracking on this particular occasion, even though it is the last one to which I will even theoretically have access. I hope that you and Jean have an absolutely wonderful time.

Thanks for keeping me up to date, and with all best wishes,

Sincerely yours,

A handwritten signature in dark ink, appearing to read 'D. Allan Bromley', with a stylized, flowing script.

D. Allan Bromley  
The Assistant to the President  
for  
Science and Technology

Dr. John H. Hubbell  
National Institute of Standards and Technology  
Room C-311  
Radiation Physics Building  
Gaithersburg, Maryland 20899

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TO: DR. D.A. BROMLEY

DATE OF  
CORRESPONDENCE: 06/13/91

SUBJECT: A REPORT ON THE STATUS OF NEUTRON STRUCTURAL BIOLOGY  
IN THE U.S.

\*\*\*\*\*  
DIRECTORATE STAFF  
ASSIGNED: ASSIGNED:

ACTION STAFF  
REQUIRED: ACTION:

\*\*\*\*\*  
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OSTP DUE DATE: STAFF DUE DATE  
DATE COMPLETED: DATE COMPLETED/DEPT:

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# BIOPHYSICAL SOCIETY

Dr. Stephen H. White, Secretary  
Department of Physiology/Biophysics  
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DIRECTOR

13 June 1991

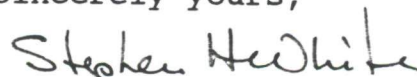
The Honorable D. Allan Bromley  
Assistant to the President for Science and Technology  
Old Executive Office Building  
17th & Pennsylvania NW  
Washington, D.C. 20506

Dear Dr. Bromley:

Enclosed for your information is a report on the status of neutron structural biology in the United States prepared by the Neutron Structural Biology Task Force of the Biophysical Society.

We are deeply concerned about the future of neutron structural biology in the United States. We believe that neutron-based approaches to important biological problems will not be viable by the turn of the century unless decisive and timely actions are taken. As a means of averting this calamity, we strongly recommend the development of a center for structural biology at Brookhaven National Laboratory. We believe that the opportunity exists for creating a facility of world-wide importance because of the presence at Brookhaven of the High Flux Beam Reactor and the National Synchrotron Light Source. We strongly urge that you support this objective as one means of maintaining the leadership of the United States in biomedical research and biotechnology.

Sincerely yours,



Stephen H. White, Ph.D.

adbrom01.31b

# BIOPHYSICAL SOCIETY

Dr. Stephen H. White, Secretary  
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13 June 1991

Dr. David Galas, Associate Director  
Office of Health and Environmental Research  
Route ER-70, Rm. F-208, GTN  
Department of Energy  
Washington, D.C. 20545

Dear Dr. Galas:

Enclosed for your consideration is a report and recommendations on neutron structural biology in the United States prepared by the The Neutron Structural Biology Task Force of the Biophysical Society. The report represents the view of the community of molecular biophysicists and structural biologists who have extensive experience in neutron structural methods.

The Biophysical Society undertook the task of preparing this report because we believe that neutron structural biology in the United States is in a serious state of decline. Unless vigorous and immediate action is taken, we believe that neutron-based approaches to important biological problems will not be viable by the turn of the century. Should this occur, the leadership of the United States in biomedical research and biotechnology will be adversely affected.

The report focuses primarily on Brookhaven National Laboratory (BNL) because we believe the fundamental resources there provide the best opportunity for a renewed commitment to neutron structural biology. The basic facilities at Brookhaven are unique in the world of structural biology because of the presence of the High Flux Beam Reactor, the National Synchrotron Light Source, the Protein Data Bank, and the Scanning Transmission Electron Microscope. We believe that an extraordinary opportunity exists at BNL to create the most important center for structural biology in the world in a very cost-effective manner. The United States long ago lost its lead in neutron scattering technology to Western Europe. A commitment to



page 2  
Dr. David Galas  
13 June 1991

the opportunity at Brookhaven could help reverse this unfortunate situation.

The Biophysical Society and the Task Force are prepared to help the Department of Energy accomplish the recommendations of the report in any way we can. We are firmly committed to the important task of assuring the future of neutron structural biology in the United States through the development of a world-class center for structural biology at BNL.

We are very impressed and encouraged by the DOE structural biology initiative and your leadership role in it. We fervently hope that neutron structural biology will benefit from your efforts.

Sincerely yours,

*Stephen H White*

Stephen H. White

galas01.31b

cc: Dr. D. Allan Bromley  
Dr. David Smith  
Dr. Nathaniel Barr  
Dr. Richard Setlow  
Dr. John Axe  
Dr. William Studier  
Dr. Benno Schoenborn

**NEUTRON STRUCTURAL BIOLOGY IN THE 1990'S:**

**A Renewed Commitment**

A report and recommendations prepared by  
The Neutron Structural Biology Task Force  
of

The Biophysical Society  
Bethesda, MD.

12 June 1991

Donald Caspar, Brandeis University  
Donald Engelman, Yale University  
Anthony Kossiakoff, Genentech  
Lee Makowski, Boston University  
Stephen White, Univ. of Calif. at Irvine (Chair)



### EXECUTIVE SUMMARY

1. Neutron diffraction methods have unique capabilities for biomolecular structure determinations and are important for biotechnology as well as basic biomedical research. The present United States capability in this area is weak and declining.
2. Brookhaven National Laboratory presents unique opportunities for the cost-effective creation of a world-class center for structural biology because of the presence there of the High Flux Beam Reactor (HFBR), the National Synchrotron Light Source (NSLS), the Scanning Transmission Electron Microscope (STEM), and the Protein Data Bank (PDB).
3. A number of problems exist at Brookhaven National Laboratory which prevent this important objective from being achieved. Unless these problems are directly and immediately addressed, the future of neutron structural biology in the United States is grim.
4. We present short-term and long-term recommendations for revitalizing neutron structural biology in the United States and for creating a major center for structural biology at Brookhaven National Laboratory.
5. In the short-term it is imperative that full-power operation of the HFBR be resumed as soon as possible and that all of the diffraction and scattering stations be brought to full operational status in the shortest time possible by using existing technology. A second protein crystallography station should be constructed as soon as possible using existing technology. A thorough and intense examination of various administrative/organizational models for creating a world-class center for structural biology should be undertaken.
6. In the long-term, the upgrading of the HFBR facility recommended in the Seitz-Eastman Committee report should be undertaken. Eight to ten positions for independent investigators of the highest caliber should be created and filled. One of the positions should be for a distinguished structural biologist who can provide the vision and leadership required to create a major structural biology facility. These independent-investigator positions should be augmented by a strong infrastructure of supporting scientists and professionals. The Protein Data Bank should be incorporated directly into the structural biology operation. Additional facilities in the areas of protein/lipid deuteration, protein purification/crystallization, and computational chemistry should be created and staffed.



## OPPORTUNITIES FOR NEUTRON STRUCTURAL BIOLOGY IN THE 1990'S

No one can doubt that the emergence of electron microscopy, protein crystallography, and magnetic resonance spectroscopy in the 1950's caused a revolution in biological and medical research. These technologies have made the study of structure-function relationships at the molecular, macromolecular, and supramolecular levels the central thrust of modern biological research. X-ray crystallographic methods have been particularly important and productive during the past two decades and are likely to become even more important as new synchrotron radiation sources become available. There is also considerable excitement about recent developments in protein engineering, in the application of molecular dynamics simulations and calculations to biological problems, and in the application of nuclear magnetic resonance to larger protein systems.

Despite the rapid progress that has been made, there are a large number of important biological problems which resist solution by these technologies. For many of these problems, neutron scattering methods provide the only realistic hope for solution. We list here a few examples of important directions that can be pursued effectively in the 1990's using the unique capabilities of neutron scattering measurements. The list is by no means exhaustive; it is probable that new directions and new opportunities will emerge as the field develops. However, biological neutron scattering in the United States can only be described in the direst of terms. In the most optimistic terms, it is in a state of decline. Without a renewed commitment to neutron structural biology, not only will the important obvious work not be pursued, but the new directions and opportunities will not arise because there will be neither adequate facilities nor a cadre of first-rate scientists trained in neutron scattering.

### *Protein Crystallography*

It has been recognized that neutron crystallography, by virtue of its ability to locate directly hydrogen and deuterium atoms and to differentiate between, has unique potential for structural studies at a level of detail unmatched by any other single technique. In the past neutrons have been especially powerful in elucidating protein mechanisms that required direct assignment of hydrogen atom locations at the active site. The technique will be an important adjunct to methods under development that show great promise for extending our current understanding of protein function at the atomic level. One of the most important and rapidly expanding approaches to the study of protein structure, function, and stability is the coupling of genetic engineering and crystallography. The power of the approach is derived from the fact that the overall energetics of



a folded protein are far too complex to allow the assessment of the role of individual groups without controlled and specific modifications of proteins. Such modifications are possible using site-directed mutagenesis. However, a surprising finding has been that x-ray analyses of mutant proteins often show only minor deviations from the native structures despite significant changes in one or more physicochemical properties. One problem is that time-averaged structure alone is not sufficient to identify cause and effect relationships. In many cases a protein's dynamic "breathing" behavior and its water structure may hold the real key to understanding protein folding forces. Neutron diffraction, through its enhanced ability to locate water molecules and its capability for assessing the dynamic characteristics of proteins by hydrogen exchange, may therefore play a pivotal role in sorting out these issues.

After a prolonged period of development, potential energy function algorithms have matured to the point where they can be applied with increasing confidence to protein structure and function. One of the least well understood parameters in these functions is, surprisingly, the electrostatic term. Here, neutron diffraction can provide unique information because water molecules can act as molecular electrostatic probes by orienting in the local environment. A high-resolution neutron analysis is capable of revealing these orientations to make exact hydrogen bonding geometries apparent. Recent analyses have focussed on comparing results of experiments with predictions from several commonly used potential functions. Because these theoretical methods influence so many facets of structural biology, it is essential to assess their validity and to improve them using experimental results. Neutron diffraction is arguably the only direct experimental method available for this purpose.

### *Solution Scattering*

The study of macromolecules and macromolecular complexes in solution has been greatly facilitated by the development of neutron scattering measurements. The combined use of selective deuteration of molecules for study, variation of solvent contrast, and exploitation of intrinsic variability of scattering by proteins, nucleic acids, and lipids has led to a range of important contributions. In the past, the structural mapping of large assemblies such as the ribosome and viruses have provided views not attainable by any other method. Further, studies of stoichiometry, as in the examination of complexes of tRNA with activating enzymes, have advanced perceptions and clarified murky areas of biochemistry. In the future, similar applications can be expected with particular advances possible in the study of molecular complexes and conformational distributions.



Growth and development of the solution scattering field has been strong wherever advances in computational methods and measuring techniques help to create new opportunities. The oversubscription levels of solution scattering facilities in Europe is an indication of the kind of activity that can result from support of the area. In contrast, the U. S. effort has been withering from lack of resources.

Protein folding is a field that is experiencing great growth because it has become increasingly clear that a proper understanding of the genetic messages in DNA requires that the conversion from the abstract one-dimensional code to three-dimensional functioning proteins is the essential step connecting genetics with function. An important aspect of folding that is not well understood concerns the nature of unfolded proteins in solution. Some evidence suggests that polypeptides under physiological conditions are disordered, yet compact, and that their arrangements predispose the pathways that will result in folded protein structures. Selective deuteration of polypeptides, coupled with neutron solution scattering measurements, may make it possible to dissect components of unfolded molecular conformations as has already been done in the polymer field. An array of suitable systems is now in place, including genetically altered staphylococcal nuclease molecules, which can be used as models for the study of unfolded states near physiological conditions.

The stoichiometry and geometry of molecular complexes is an increasing concern in molecular biology. Many assemblies have been identified, such as transcription complexes, signal recognition particles, and protein degradation complexes, that can in principle be studied using neutron methods that have been developed in the successful mapping of the ribosome and RNA polymerase. Of particular importance are changes seen in different functional states. The detailed study of quaternary structure is an area that has proved very difficult to approach by biochemical means or by crystallography. To take the next step from the properties of individual proteins to the organization of assemblies is an important challenge that can perhaps only be met by the use of neutron methods.

#### *Diffraction from membranes and other partially ordered systems*

The lateral and transverse organization of membrane components, the structure of membrane proteins, and the nature of molecular interactions within membranes are among the most pressing and important of biological problems. These systems are, however, extraordinarily difficult to study by diffraction methods without the use of neutrons. Fluid bilayers, within which membrane macromolecules reside, can form highly ordered one-dimensional lattices but thermal motion limits the number of



diffraction orders which can be obtained. Natural membranes tend to form highly disordered lattices which also limits the number of diffraction orders. In either case, the structural resolution is limited unless one can specifically label selected parts of the lipids or proteins within the bilayer. Neutron diffraction is an exceptionally important tool because of our ability to specifically deuterate lipid and protein components. Despite the great promise of this technology, only limited work has been done in this area because of a lack of suitable diffraction facilities on a regular basis.

The array of membrane-based problems which can and need to be examined is very large. There is a particular need to understand the fundamental nature of the fluid bilayer by a combination of neutron studies which can reveal the locations and thermal motions of the critical structural groups and molecular dynamics calculations to provide a theoretical framework for understanding the environmental constraints on proteins and peptides within membranes. Such studies should provide critical insights to the question of how proteins enter membranes and carry out their functions within that special environment. Because of the great difficulty of crystallizing membrane proteins, the development of structural methods for studying proteins within membranes and for understanding the organization of detergent/protein complexes are particularly important. Neutron diffraction studies of bacteriorhodopsin have already revealed the power of this approach. An area rich in possibilities is the study of the organization and oligomerization of membrane proteins. If multilayers of deuterated lipid can be formed with hydrogenated protein in them, an oriented experiment with the beam perpendicular to the planes of the multilayers should give a small angle scattering signal corresponding to a two-dimensional radius of gyration of the projected protein structures.

Another class of problems particularly amenable to neutron diffraction analysis involve partially-ordered structures which are made up of many copies of single subunit arranged into one- or two-dimensional arrays. Many biological fibers, for example, are made up of helical arrays of molecules which form one-dimensional crystals of a single repeating unit. Many membrane and cell wall systems are constructed from two-dimensionally ordered subunits. There are no well-established methods at present for determining the structures of these systems to high resolution and a combination of a number of methods is often required. Recently, for example, a combination of neutron diffraction and NMR spectroscopy has made it possible to understand the organization of the filamentous bacteriophage Pf1 coat protein and its membrane-associated assembly process.



### SPECIAL REQUIREMENTS OF NEUTRON METHODS

Neutrons for structural biology are a scarce and expensive commodity and must therefore be used carefully and efficiently. They are best used in conjunction with other technologies such as x-ray scattering and diffraction. For example, neutron protein crystallography is most efficient when the basic structure of the protein has already been determined. For studies of membrane systems, it is possible to combine neutron and x-ray measurements to double the amount of information available for structure determination because neutrons scatter from nuclei and x-rays from electrons. Therefore, the presence of both x-ray and neutron capabilities at a single physical location is highly desirable.

To exploit fully the capabilities of neutron methods, it is important to deuterate molecules entirely or at specific locations. Further, relatively large amounts of material are required. An important adjunct for neutron work is therefore special facilities, not generally available in universities for deuteration. For crystallography, the crystals used must be of a much larger size than generally used in x-ray work. Few proteins inherently produce large crystals and it is therefore essential that special efforts be devoted to improving methodologies for growing large crystals. Protein purification is likely to be especially important in this respect and must also receive special attention. Because it is unlikely that Federal agencies will provide adequate support for these activities at multiple locations, the need for a central well-funded national facility for these activities is apparent.

Most neutron work is computationally intense for both data collection and analysis. A major problem with neutron diffraction work in the United States is the lag time between gathering the data and analyzing it. A capability must be developed for doing at least a partial analysis during the data collection phase. Without this, experimental problems that might arise and be correctable during data collection go undetected until long after the experiment is completed. This means that first-rate computation and graphics capabilities must exist at the same locations as the neutron sources. This will become increasingly important as molecular dynamics methods mature. It seems clear that significant computational resources, physical and intellectual, must exist at the same sites as the neutron sources.

The methods of neutron diffraction have improved dramatically during the past twenty-five years but much remains to be done. Rapid progress in methodology is made only in highly competitive environments in which first-rate investigators constantly push technology to the limits and are motivated to



develop better approaches to problems. While external users of neutron facilities have this motivation, they do not have the advantage of the deep familiarity that comes with carrying out their research on a daily basis at the facilities. Therefore, it is imperative that there be a cadre of world-class scientists working "on-site" to stimulate the development of new methods and to assure their availability to outside users. These front-line individuals must be backed up by other scientists who are well-trained in structural biology and by professionals who are experts in the special technologies associated with neutron and synchrotron radiation.

New methodological approaches and the solution of "cutting-edge" problems occur best in an environment rich in intellectual resources. This means two things. First, the size of the cadre of "on-site" scientists must be at the critical mass necessary to generate scientific foment. Second, there needs to be a steady intercourse with "off-site" scientists. If the first objective is accomplished and if the experimental facilities are excellent, then the second objective follows automatically.

#### THE UNIQUE OPPORTUNITY AT BROOKHAVEN NATIONAL LABORATORY

Brookhaven National Laboratory (BNL) is unique in the world. It is the home of the High Flux Beam Reactor (HFBR), the National Synchrotron Light Source (NSLS), the Protein Data Bank (PDB), the scanning transmission electron microscope (STEM), and excellent resources in modern molecular biology. With the addition of a strong effort in computational structural biophysics and the development of special facilities for deuteration, protein purification, and crystallization, BNL has the potential to be the most important center for structural biology in the world. Compared to the current expenditures for creating advanced synchrotron sources, the cost of achieving this objective is certain to be rather modest. This objective can be achieved if the DOE has the vision to see the possibilities and the will to accomplish them. We believe that this can be done without seriously detracting from the other efforts. Indeed, we believe that the other efforts would be greatly enhanced as a result.

#### THE PROBLEMS WITH STRUCTURAL BIOLOGY AT BROOKHAVEN NATIONAL LABORATORY

Brookhaven National laboratory has not fulfilled its extraordinary promise as a major world-wide focal point for structural biology because the unique resources available there have not been pulled together in a coherent fashion. It is our opinion that this is the most underdeveloped of the major



scientific resources in the United States. Because it has languished, an extensive user community has not developed and new students have not been trained. If the present situation prevails much longer, we face the very real prospect of the death of neutron structural biology in the United States by the turn of the century.

The fundamental problems at BNL can be attributed broadly to (1) the lack of a steady supply of neutrons, (2) too few personnel and capital resources, and (3) and an atmosphere which has not been conducive to the recruitment and development of leaders in neutron structural biology at BNL. The last problem is direct result of the second one; it has been virtually impossible for the small number of scientific staff to simultaneously maintain instruments, serve the user community, and conduct their own research programs. Assuming that the availability of neutrons can be assured on a regular basis, we believe the principal problems which must be solved if BNL is to fulfill its promise are the following:

1. The overall quality of the scientific effort by the BNL structural biology staff must be greatly strengthened. This is not to say that there are not qualified investigators in structural biology but the truth is that the investigators using neutron and x-ray methods, with only a few exceptions, do not have research programs that are prominent or influential within the structural biology community. One of the reasons for this is that there has not been a sufficient commitment of resources to the recruitment of sufficient numbers first-rate scientists or to their nurturing. A strong supporting infrastructure has not been created which makes it possible for a scientist there to pursue an independent scientific career while providing vital support functions to the outside user community.

2. The leadership in structural biology is deteriorating. While Dr. Schoenborn has the highest respect of the structural biology community as a structural biologist and the undying gratitude of the community for having created the neutron structural facilities, his potential as an effective leader of structural biology has not been realized and is weakening. The reasons for this are unclear but seem to be related in part to the problem of attempting to run a dual-purpose program that supports, with insufficient resources, both in-house basic research and outside users. In many respects, the possible collaborations with molecular biologists and protein chemists in the Biology Department make for a potentially synergistic environment; however, a fully mature structural biology program will require special resources that need to be independent from the Biology Department's resource allocations.



3. While the basic diffraction instruments are of excellent quality, they are not convenient to use and in many respects are hopelessly frustrating because of a poor supporting infrastructure. It seems to take forever to bring a new station on-line or to upgrade an existing one. Computational resources are weak both in terms of equipment and software. It is reasonable to assume that these problems have arisen from an inadequate number of personnel, a shortage of funds, and the difficulties of setting priorities under such circumstances.

4. There are presently important safety and security concerns regarding the operation of the HFBR. These concerns are important but they have led to an atmosphere at the HFBR which is at odds with that required for the accomplishment of difficult and complex scientific experiments. More effort must be devoted to creating a productive scientific environment at the same time that the safety and security concerns are being addressed.

#### PROPOSALS FOR SHORT-TERM IMPROVEMENTS

1. Bring the reactor back to full-power operation as soon as possible.

2. Bring all of the diffraction and scattering stations into full operation using currently available technology. This should take priority, at the present time, over the development of new hardware and techniques. It is imperative that there be reliable and fully useable facilities even if they are not "state of the art".

3. Increase the number of scientific and professional personnel involved directly in the provision of scattering and diffraction resources to both the on-site and off-site users. Emphasis should be placed in those areas that will make it as easy as possible to obtain and analyze data in the shortest possible time with the least amount of frustration. This will increase the efficiency of the present facilities and encourage new users.

4. Begin construction immediately of a second protein crystallography station using current technology to assure the rapid deployment. With thoughtful planning it should be possible to create an effective facility which can be upgraded later to take advantage of new technical developments.

5. Establish a plan for involving both the on-site and off-site users in the planning for the operations of the diffraction and scattering resources. It is important that management establish a clear understanding of the users needs and problems and for the users understand the operating constraints. An

effort must be made to create common objectives shared by both users and management.

6. Establish a stronger peer-review system for the allocation of diffraction and scattering resources. There continues to be a perceived "old boy" network. It is not clear that the best science gets the highest priority for resources. It is also not clear that the progress of the users of the facilities are adequately accounted for in the allocation of resources.

7. Review and seek solutions to the problems of managing a potentially world-class structural biology facility within the confines of the present organizational scheme. Should there be a separate structural biology department? If there is not to be a separate department, what changes can be made to make the present organization more effective?

#### LONGER-TERM CHANGES:

##### THE CREATION OF A UNIQUE STRUCTURAL BIOLOGY FACILITY

1. The key to the creation of a world-class facility is a group of vigorous first-rate scientists who are doing research on-site which is not only at the frontiers of their fields but which also pushes scattering technology at the Brookhaven facilities to the limits. If the facilities and environment are satisfactory for these individuals, then they are likely to be satisfactory for visiting scientists. Because these individuals will form the connecting links to the outside users, they must be broadly informed and interactive and must be advocates for the facilities. We believe that the core staff of these independent investigators should number eight to ten people. The areas covered should include macromolecular crystallography, membrane diffraction, solution scattering, protein crystallization, and computational molecular biophysics. These latter areas are not presently represented at BNL and are of particular importance.

2. The core staff must be supported by an infrastructure of supporting scientists and specialists who can maintain and improve the facilities to meet the changing needs of the scientific effort. Further, they should provide operational support for both the core staff and the visiting scientists.

3. Strong scientific and administrative leadership is required to recruit the core staff, assure their development, unify the operation of the diverse facilities, and generally assure a high level of morale. Under the present circumstances, it would seem wise to recruit a senior structural biologist to fulfill this role. This person must be a distinguished scientist



with a clear vision of what needs to be accomplished to create a world-class facility.

4. The Rush and Seitz-Eastman reports strongly recommended upgrading the HFBR. These upgrades are important and we strongly urge that they be undertaken.

5. The primary biomolecular structure resources at Brookhaven are the HFBR, the NSLS, and the PDB. We strongly urge that the PDB be made an integral part of the structural biology operation. The interaction would cause the PDB to serve the structural biology community better. We believe that innovation is needed and that this will only come by integrating the PDB into the structural biology effort.

6. Additional facilities should be created in the areas of protein and lipid deuteration, protein purification and crystallization, and computational chemistry and molecular graphics. Such facilities are ideally located at national laboratories to provide resources for a broad scientific community. The intention should be to support innovative scientists on-site whose interests lie in these areas rather than just providing facilities to be used by visitors.

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FROM: LEE, Burton: THE WHITE HOUSE

TO: DR. D.A. BROMLEY

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SUBJECT: RE: THE BREAKDOWN FROM THE FDA ON THE RUSSIAN DRUG  
SENT TO LEE.

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REMARKS: Enclosures to DAB.

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9/21719 Wed.

THE WHITE HOUSE  
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OFFICE OF THE  
DIRECTOR

Here is the break-  
down from the FDA on  
the Russian drug you  
sent me. Note that  
its experimental use is to  
induce arrhythmias!

Regards

✓ ant

JUN 10 1991

NOTE TO: Burton Lee, M.D.

FROM: Bruce Burlington, M.D. *Bruce Burlington*  
Deputy Director for Scientific and Medical Affairs,  
Center for Drug Evaluation and Research,  
Food and Drug Administration

As you requested in our phone conversation on Thursday, June 6, enclosed please find six abstract printouts with references from literature searches on allapinine and three pages from the Merck Index highlighting the chemical names aconine, aconite, aconitine and lappaconitine. These provide chemical information on this compound and related compounds. Also enclosed is a copy of an electronic mail interoffice memorandum from Ms. Morgenstern regarding Ray Lipicky, M.D.'s comments on his familiarity with aconitine. Dr. Lipicky is Director of the FDA's Division of Cardio-Renal Drug Products and our primary expert on anti-arrhythmics. I'm sure he would be glad to follow up with more specific information, if you wish. His telephone number is 301-443-4730.

As mentioned in our telephone conversation, we are unaware of any domestic clinical research on this compound.

Enclosures

cc: Dr. Ray Lipicky  
Dr. Carl Peck, Director, Center for Drug  
Evaluation and Research



# THE MERCK INDEX

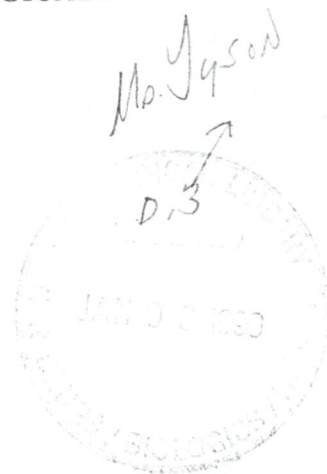
AN ENCYCLOPEDIA OF  
CHEMICALS, DRUGS, AND BIOLOGICALS

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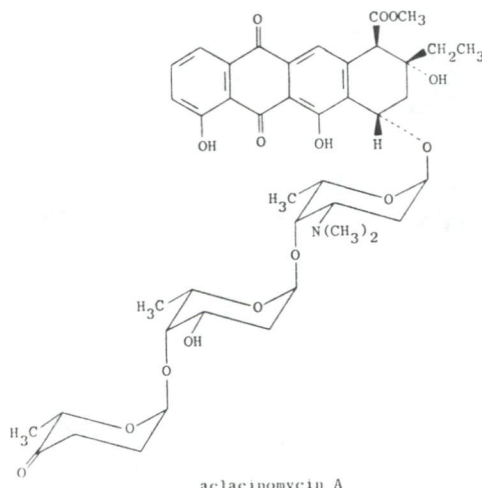
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1989





*eidem*, *ibid.* 32, 791, 801 (1979). The aglycone portion of aclacinomycin A is known as *aklavinone*. Isoln of aklavinone: J. J. Gordon *et al.*, *Tetrahedron Letters* 8, 28 (1960). Synthesis of racemic aklavinone: B. A. Pearlman *et al.*, *J. Am. Chem. Soc.* 103, 4248 (1981); P. A. Confalone, G. Pizzolotto, *ibid.* 4251; R. K. Boeckman, F. W. Sum, *ibid.* 104, 4604 (1982). Synthesis of optically active aklavinone: A. S. Kende, J. P. Rizzi, *ibid.* 103, 4247 (1981); J. M. McNamara, Y. Kishi, *ibid.* 104, 7371 (1982). *In vitro* metabolism of aclacinomycins: T. Komiya *et al.*, *Gann* 70, 395 (1979), *C.A.* 92, 15143x (1980). HPLC determ of aclacinomycin A and its metabolites: T. Ogasawara *et al.*, *J. Antibiot.* 34, 47, 52 (1981). Pharmacokinetics: M. J. Egorin *et al.*, *Cancer Chemother. Pharmacol.* 8, 41 (1982). Series of articles on absorption, excretion, distribution and general pharmacology: *Japan. J. Antibiot.* 33, 169-213 (1980), *C.A.* 93, 19316, 125326, 125649, 142986 (1980). Immunological study: M. Ishizuka *et al.*, *J. Antibiot.* 34, 331 (1981). Clinical studies: R. Maral, *Drugs Exp. Clin. Res.* 9, 375 (1983); R. P. Warrell, Jr., S. J. Kempin, *Am. J. Clin. Oncol.* 6, 81 (1983); A. Y. Bedikian *et al.*, *ibid.* 187 (1983). Review of pharmacology of aclacinomycin A: T. Oki, *Anthracyclines [Proc. Workshop]*, S. T. Crooke, S. D. Reich, Eds. (Academic Press, New York, 1980) pp 323-342, *C.A.* 93, 160778h (1980).



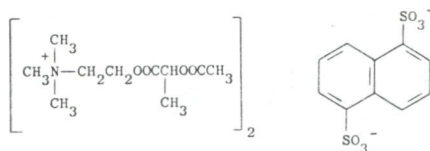
**Aclacinomycin A**,  $C_{42}H_{53}NO_{15}$ , 2-ethyl-1,2,3,4,6,11-hexahydro-2,5,7-trihydroxy-6,11-dioxo-4-[[[2,3,6-trideoxy-4-O-[2,6-dideoxy-4-O-[(2*R*-trans)-tetrahydro-6-methyl-5-oxo-2*H*-pyran-2-yl]- $\alpha$ -L-lyxo-hexopyranosyl]-3-(dimethylamino)- $\alpha$ -L-lyxo-hexopyranosyl]oxy]-1-naphthalenecarboxylic acid methyl ester, antibiotic MA 144A1, NSC-208734, *aclarubicin*, *Jaclacin*. Yellow microcryst powder from chloroform/hexane, mp 151-153° (dec).  $[\alpha]_D^{25} -11.5^\circ$  ( $c = 1$  in methylene chloride). uv max (methanol): 229.5, 259, 289.5, 431 nm ( $E_{1\%}^{1\text{cm}}$  550, 326, 135, 161); (0.1*N* HCl) 229.5, 258.5, 290, 431 nm ( $E_{1\%}^{1\text{cm}}$  571, 338, 130, 161); (0.1*N* NaOH) 239, 287, 523 nm ( $E_{1\%}^{1\text{cm}}$  450, 113, 127). Sol in  $CHCl_3$ , ethyl acetate, insol in ethyl ether, *n*-hexane, petr ether. Addn of alkali to aq solns gives an intense reddish-purple color; in conc HCl the soln is yellow. LD<sub>50</sub> in mice (mg/kg): 22.6 i.p., 33.7 i.v. (Oki).

Aclacinomycin A hydrochloride,  $C_{42}H_{54}ClNO_{15}$ , *aclarubicin hydrochloride*, *Aclacinon*, *Aclaplastin*.

**Aclacinomycin B**,  $C_{42}H_{51}NO_{15}$ , 4-[[[2'',3''-anhydro]-O-3,6-dideoxy- $\alpha$ -L-erythro-hexopyranos-4-ulos-1-yl-(1-4)-O-2,6-dideoxy- $\alpha$ -L-lyxo-hexopyranosyl-(1-4)-2,3,6-trideoxy-3-(dimethylamino)- $\alpha$ -L-lyxo-hexopyranosyl]oxy]-2-ethyl-1,2,3,4,6,11-hexahydro-2,5,7-trihydroxy-6,11-dioxo-1-naphthalenecarboxylic acid methyl ester, antibiotic MA 144B1. Yellow microcryst powder from chloroform/hexane, mp 163-167° (dec).  $[\alpha]_D^{25} +3^\circ$  ( $c = 1$  in methylene chloride). Other physical properties similar to aclacinomycin A. LD<sub>50</sub> in mice (mg/kg): 13.7 i.p., 16.4 i.v. (Oki).

THERAP CAT: Antineoplastic.

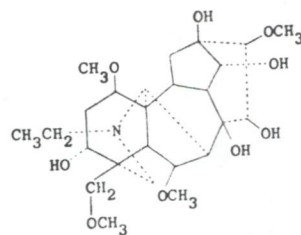
**109. Aclatonium Napadisilate**, 2-[2-(Acetyloxy)-1-oxopropoxy]-*N,N,N*-trimethylethanaminium 1,5-naphthalenedisulfonate (2:1); 1,5-naphthalenedisulfonic acid bis [2-(2-(acetyloxy)-1-oxopropoxy)-*N,N,N*-trimethylethanaminium]-ion (2-); acetylcholine 1,5-naphthalenedisulfonate; choline 1,5-naphthalenedisulfonate (2:1), dilactate, diacetate; TM 723; Abovis.  $C_{30}H_{46}N_3O_{14}S_2$ ; mol wt 722.83. C 49.85%, H 6.42%, N 3.87%, O 30.99%, S 8.87%. Spasmolytic agent related structurally to acetylcholine chloride, q.v. Prepn: K. Miura *et al.*, *Ger. pat.* 2,425,983 corresp to U.S. pat. 3,903,137 (1973, 1975 both to Toyama). Synthesis and smooth muscle activity: *eidem*, *Yakugaku Zasshi* 99, 1245 (1979), *C.A.* 92, 146197r (1980). Series of articles on metabolism, pharmacology, toxicity studies: *Oyo Yakuri* 18, 695-942 (1979), *C.A.* 92, 191015r, 191281z, 191282a, 208995k-7n (1980).



Crystals, mp 189-191°. LD<sub>50</sub> in mice: 15 g/kg orally, 826 mg/kg s.c., K. Miura *et al.*, *loc. cit.*; in dogs: >10 g/kg orally, A. Takai *et al.*, *Oyo Yakuri* 19, 93 (1980), *C.A.* 93, 613367 (1980).

THERAP CAT: Cholinergic.

**110. Aconine**, (1 $\alpha$ ,3 $\alpha$ ,6 $\alpha$ ,14 $\alpha$ ,15 $\alpha$ ,16 $\beta$ )-20-Ethyl-1,6,16-trimethoxy-4-(methoxymethyl)aconitane-3,8,13,14,15-pentol; Aconitinsat.  $C_{25}H_{41}NO_9$ ; mol wt 499.59. C 60.10%, H 8.27%, N 2.80%, O 28.82%. Obtained by hydrolysis of aconitine: Schulze, *Arch. Pharm.* 244, 165 (1906); Schneider, *Ber.* 89, 768 (1956). Structure: Schneider, Tausend, *Ann.* 628, 114 (1959); McCaldin, Marion, *Can. J. Chem.* 37, 1071 (1959).



Amorphous powder, mp 132°. Bitter taste.  $[\alpha]_D^{25} +23^\circ$ , pK 9.52. Absorption spectrum: Nath, *J. Indian Chem. Soc.* 32, 75 (1955). Very sol in water, alcohol; moderately sol in chloroform; slightly sol in benzene. Practically insol in ether, petr ether.

Hydrochloride dihydrate,  $C_{25}H_{42}ClNO_9 \cdot 2H_2O$ , crystals, mp 175-176°.  $[\alpha]_D^{25} -8^\circ$ .

Hydrobromide sesquihydrate,  $C_{25}H_{42}BrNO_9 \cdot 1\frac{1}{2}H_2O$ , crystals from water, mp 225°.

THERAP CAT: Antipyretic.

**111. Aconite**. Monkshood; wolf's-bane; friar's cowl; mouse-bane. Dried tuberous root of *Aconitum napellus* L., *Ranunculaceae*. *Habit*. Mountainous regions of Europe, Asia, and North America. *Constit.* 0.4-0.8% aconitine; aconine; napelline (isoaconitine, pseudoaconitine); picroaconitine; aconitic acid; itaconic acid; succinic acid; malonic acid; fat; levulose. *Quite toxic*. Ref: Freudenberg, *Ber.* 69, 1962 (1936); Rogers, Freudenberg, *ibid.* 70, 349 (1937); Lascombes, *Ann. Pharm. Franc.* 16, 429 (1958). See also "Aconite," A. Ph. A. Monograph No. 1 (Am. Pharm. Assoc., Washington, D.C., 1938).

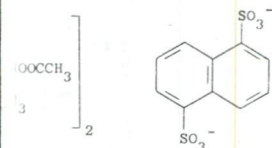
THERAP CAT: Antipyretic.

THERAP CAT (VET): Formerly used as an antihypertensive.

**112. Aconitic Acid**, 1-Propene-1,2,3-tricarboxylic acid; equisetac acid; citridic acid; achilleic acid.  $C_6H_6O_6$ ; mol wt 174.11. C 41.39%, H 3.47%, O 55.14%. Found in leaves and

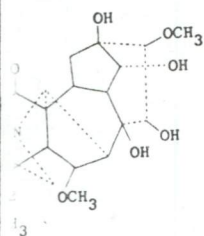


adisilate. 2-[2-(Acetyloxy)-1-oxo-  
ethanaminium 1,5-naphthalenedi-  
thalesulfonic acid bis [2-[2-  
-N,N,N-trimethylethanaminium]-  
oline 1,5-naphthalenedisulfonate;  
sulfonate (2:1), dilactate, diacetate;  
C<sub>25</sub>H<sub>24</sub>N<sub>4</sub>O<sub>10</sub>S<sub>2</sub>; mol wt 722.83. C 49.85%,  
H 3.99%, N 8.87%. Spasmolytic agent  
tylcholine chloride, q.v. Prepn: K.  
25,983 corresp to U.S. pat. 3,903,  
Toyama). Synthesis and smooth  
Yakugaku Zasshi 99, 1245 (1979).  
Series of articles on metabolism,  
studies: Oyo Yakuri 18, 695-942  
r, 191281z, 191282a, 208995k-7n



LD<sub>50</sub> in mice: 15 g/kg orally, 826  
al., loc. cit.; in dogs: >10 g/kg  
Oyo Yakuri 19, 93 (1980), C.A. 93,

3α,6α,14α,15α,16β)-20-Ethyl-1,6-  
xymethyl)aconitane-3,8,13,14,15-  
[41NO<sub>9</sub>; mol wt 499.59. C 60.10%,  
H 8.82%. Obtained by hydrolysis of  
Pharm. 244, 165 (1906); Schneider,  
structure: Schneider, Tausend, Ann.  
in, Marion, Can. J. Chem. 37, 1071



mp 132°. Bitter taste. [α]<sub>D</sub> +23°. IR  
spectrum: Nath, J. Indian Chem. Soc.  
in water, alcohol; moderately sol in  
in benzene. Practically insol in

ate, C<sub>25</sub>H<sub>42</sub>ClNO<sub>9</sub>·2H<sub>2</sub>O, crystals,

hydrate, C<sub>25</sub>H<sub>42</sub>BrNO<sub>9</sub>·1½H<sub>2</sub>O,  
225°.

akshood; wolf's-bane; friar's cowl;  
erous root of *Aconitum napellus* L.,

Mountainous regions of Europe,  
ica. *Constit.* 0.4-0.8% aconitine;  
onitine, pseudoaconitine; piraconi-  
ic acid; succinic acid; malonic acid;

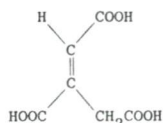
Ref: Freudenberg, Ber. 69, 1962  
berg, *ibid.* 70, 349 (1937); Las-  
anc. 16, 429 (1958). See also "Aco-  
graph No. 1 (Am. Pharm. Assoc.,

ic.

merly used as an antihypertensive.

1-Propene-1,2,3-iricarboxylic acid;  
id; achilleic acid. C<sub>6</sub>H<sub>6</sub>O<sub>6</sub>; mol wt  
17%, O 55.14%. Found in leaves and

tubers of *Aconitum napellus* L., *Ranunculaceae*, in various  
species of *Achillea* (Compositae) and *Equisetum* (*Equiseta-  
ceae*), in beet root, and in sugar cane. Can be prep com-  
mercially from calcium magnesium aconitate recovered from  
sugar cane juice: McCalip, Seibert, *Ind. Eng. Chem.* 33, 637  
(1941); from molasses: Regna, Bruins, *ibid.* 48, 1268 (1956).  
Most of the commercial aconitic acid is, however, manufac-  
tured by sulfuric acid dehydration of citric acid: Bruce, *Org.  
Syn. coll. vol. II*, p 12 (1943); by using methanesulfonic acid  
instead of sulfuric: Cranston, U.S. pat. 2,727,066 (1955 to  
Daniel F. Kelly). Aconitic acid prep by any of the above  
methods has the *trans*-configuration which is the form de-  
scribed here.

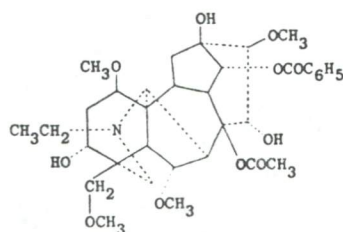


Leaflets, plates from water. Decompn 198-199° (capillary  
inserted in oil bath at 190°); decompn 204-205° (capillary in  
oil bath at 195°); decompn 209° (electrically heated bar). K<sub>1</sub>  
at 25° = 1.58 × 10<sup>-3</sup>; K<sub>2</sub> = 3.5 × 10<sup>-5</sup>. One gram dis-  
solves in 5.5 ml water at 13°, in 2 ml water at 25°. Soluble in  
2 parts of 88% alcohol at 12°. Slightly sol in ether.

Triethyl ester, bp<sub>5</sub> 155°.  
Tributyl ester, bp<sub>3</sub> 190°.

USE: Manuf itaconic acid. As plasticizer for buna rubber  
and plastics. Used in form of triethyl or tributyl ester.

**113. Aconitine.** (1α,3α,6α,14α,15α,16β)-20-Ethyl-1,6-  
16-trimethoxy-4-(methoxymethyl)aconitane-3,8,13,14,15-  
pentol 8-acetate 14-benzoate. C<sub>34</sub>H<sub>47</sub>NO<sub>11</sub>; mol wt 645.72. C  
63.24%, H 7.34%, N 2.17%, O 27.26%. Several isomers from  
*Aconitum napellus* L., *Ranunculaceae* and other aconites.  
Majima et al., Ber. 57, 1456 (1924); Proc. Imp. Acad. Tokyo  
5, 415 (1929); Freudenberg, Ber. 69, 1964 (1936); Swanson et  
al., Aconite, A. Ph. A. Monograph no. 1 (1938); *Methods of  
Analysis*, A.O.A.C., 8th ed., 598, 651 (1955). Structure:  
Wiesner et al., Coll. Czech. Chem. Commun. 28, 2462 (1963);  
Wiesner et al., Can. J. Chem. 47, 2734 (1969). Stereochemis-  
try: Bachelor et al., *Tetrahedron Letters* 1960, no. 10, 1;  
Gilman, Marion, *ibid.* 1961, 923; Tsuda, Marion, Can. J.  
Chem. 41, 1634 (1963); Birnbaum et al., *Tetrahedron Letters*  
1971, 867. Toxicity: Dybing et al., *Acta Pharmacol. Toxicol.*  
7, 337 (1951).



Hexagonal plates, mp 204°. [α]<sub>D</sub> +17.3° (chloroform).  
Aq soln is alkaline to litmus. pK 5.88. K 1.3 × 10<sup>-6</sup>. One  
gram dissolves in 2 ml chloroform, 7 ml benzene, 28 ml abs  
alcohol, 50 ml ether, 3300 ml water. Slightly sol in petr  
ether. *Poisonous!* LD<sub>50</sub> in mice (mg/kg): 0.166 i.v.; 0.328  
i.p.; approx 1 orally (Dybing).

Hydrobromide hemipentahydrate, C<sub>34</sub>H<sub>48</sub>BrNO<sub>11</sub>·2½H<sub>2</sub>O,  
hexagonal tablets from water, mp 200-207° (sinters at 160°).  
Amorphous form mp 115-120°. Also crystallizes from etha-  
nol + ether with ½H<sub>2</sub>O, mp 206-207°; [α]<sub>D</sub> -30.8°. *Violent  
poison!* Ref: Paech, Tracey, *Modern Methods of Plant  
Analysis vol. IV* (Springer-Verlag, Berlin, 1955) p 375.

Hydrochloride hemipentahydrate, C<sub>34</sub>H<sub>48</sub>ClNO<sub>11</sub>·2½H<sub>2</sub>O,  
crystals, mp 149-153°. mp 194-5° (dry). [α]<sub>D</sub> -30.9°. *Viol-  
ent poison!* Ref: Paech, Tracey, loc. cit.

Nitrate, C<sub>34</sub>H<sub>48</sub>N<sub>2</sub>O<sub>14</sub>, crystals, mp about 200° (dec). [α]<sub>D</sub><sup>20</sup>  
-35° (c = 2 in water). *Violent poison!* One gram dissolves  
in 10 ml boiling water. Less sol in cold water. Sol in alco-  
hol.

USE: Used in producing heart arrhythmia in experimental  
animals: Boyadzhiev, C.A. 73, 86256e (1970).  
THERAP CAT: Antipyretic.

**114. Aconitine, Amorphous.** Mild aconitine. Mixture  
of amorphous alkaloids from *Aconitum napellus* L., *Ranuncu-  
latae*. Contains aconitine, mesaconitine, hypaconitine,  
neopelline, l-ephedrine, sparteine, neoline and napelline.  
Ref: Rogers, Freudenberg, Ber. 70, 349 (1937); *eidem*, J.  
Am. Chem. Soc. 59, 2572 (1937).

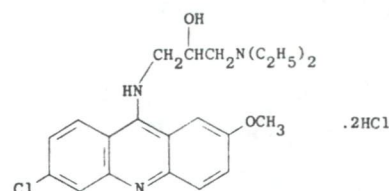
Yellowish-white, amorphous powder. *Violent poison!*  
Insol in water; sol in alcohol, chloroform, ether, dil acids.  
MLD s.c. in rats: 0.175 mg/kg, *Handbook of Toxicology  
Vol. 1*, W. S. Spector, Ed. (Saunders, Philadelphia, 1956)  
pp 12-13.

Caution: A highly toxic alkaloid. Can be absorbed  
through skin.

**115. Aconitum Ferox.** Indian aconite; bish; visha; bish-  
ma; bikhroot. Tuber of *Aconitum ferox* Wall., *Ranuncula-  
ceae*. *Habit.* Nepal, Himalaya Mountains, India. *Constit.*  
Pseudoaconitine, q.v. Most powerful of all the aconites.  
Used by natives as arrow poison in big game hunting; in  
neuralgia and rheumatism. Ref: Aconite, A. Ph. A. Mono-  
graph no. 1, p 78 and *passim* (Am. Pharm. Assoc., Washing-  
ton, D.C., 1938); N. B. Dutt, *Indian J. Pharm.* 1, 81-84  
(1939); C.A. 34, 6768 (1940).

Caution: Extremely toxic. A very small dose can cause  
fatal cardiac depression.

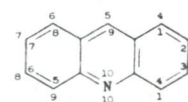
**116. Acranil.** 1-[(6-Chloro-2-methoxy-9-acridinyl)-  
amino]-3-(diethylamino)-2-propanol dihydrochloride; 5-[(γ-  
diethylamino-β-hydroxypropyl)amino]-3-methoxy-8-chlo-  
roacridine dihydrochloride; SKF 16214-A2; SN 186. C<sub>21</sub>-  
H<sub>28</sub>Cl<sub>2</sub>N<sub>3</sub>O<sub>2</sub>; mol wt 460.82. C 54.74%, H 6.12%, Cl 23.08%,  
N 9.12%, O 6.94%. Prepn: Mietzsch, Mauss, Ger. pat.  
553,072, *Frld.* 19, 1167; *Brit. pat.* 363,392; U.S. pat. 2,113,-  
357 (1930, 1930, 1938 all to I. G. Farben.); Maghidson,  
Grigorovski, Ber. 69, 396 (1936); J. Gen. Chem. (USSR) 6,  
806 (1936). Antiviral activity: T. E. Glaz et al., *Antimicrob.  
Ag. Chemother.* 3, 537 (1973). Interferon induction and  
radioprotective activity: T. E. Glaz, M. Talas, *Arch. Virol.*  
48, 375 (1975); M. Talas, E. Szolgay, *ibid.* 56, 309 (1978).



Bitter, yellow crystals, mp 237-239° (dec). Sol in water.  
Free base, C<sub>21</sub>H<sub>26</sub>ClN<sub>3</sub>O<sub>2</sub>, yellow crystals, mp 105-107°.  
Sparingly sol in ether.

THERAP CAT: Antiprotozoal (Giardia).

**117. Acridine.** Dibenzo[b,e]pyridine; 10-azaanthra-  
cene. C<sub>13</sub>H<sub>9</sub>N; mol wt 179.21. C 87.12%, H 5.06%, N  
7.82%. Occurs in coal tar. Isoln: Graebe, Caro, *Ann.* 158,  
265 (1871); from high boiling tar oils: Wirth, Ger. pat.  
440,771 (1926). Prepn from N-phenylanthranilic acid: Per-  
kin, Clemo, *Brit. pat.* 214,756 (1923); from Ca-anthranilate:  
Koller, Krakauer, *Monatsh.* 50, 51 (1928); by passing benz-  
ylaniline vapor over red-hot platinum wire: Meyer, Hof-  
mann, *ibid.* 37, 698 (1916); cf. Ullmann, Ber. 40, 2521  
(1907). Absorption spectrum: Pinnow, J. Prakt. Chem. [2]  
66, 276 (1902). Toxicity: S. D. Rubbo, *Brit. J. Exp. Pathol.*  
28, 1 (1947). Reviews: A. Albert, *The Acridines* (St. Mar-  
tin's Press, New York, 2nd ed., 1966); R. M. Acheson,  
*Acridines* (Interscience, New York, 2nd ed., 1973).



Orthorhombic plates, needles from diluted alcohol. There



450° producing a mixture of oxide and nitride; forms the hydride on heating in hydrogen. Forms alloys with several metals.

Oxide,  $\text{La}_2\text{O}_3$ , *lanthana*, *lanthanum sesquioxide*, *lanthanum trioxide*, almost white, amorphous powder. d 6.51. mp above 2000°. Insol in water; sol in dil mineral acids with formation of salts. Absorbs  $\text{CO}_2$  from the air.

Hydroxide,  $\text{La}(\text{OH})_3$ , white, amorphous precip, prepd by adding excess of caustic alkali to a lanthanum salt soln. Strongly basic, displaces ammonia from ammonium salts, absorbs  $\text{CO}_2$  from air. On dehydration yields  $\text{La}_2\text{O}_3 \cdot \text{H}_2\text{O}$ .

Chloride,  $\text{LaCl}_3$ , heptahydrate, triclinic crystals, sol in water or alc. On heating in HCl the anhydr salt (mp 852°) is formed.  $\text{LD}_{50}$  in rats: 4.2 g/kg orally; 350 mg/kg i.p., Cochran *et al.*, *Arch. Ind. Hyg. Occup. Med.* **1**, 637 (1950).

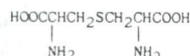
Carbonate octahydrate,  $\text{C}_3\text{La}_2\text{O}_9$ , *artificial lanthanite*. White, cryst powder, insol in water, freely sol in dil mineral acids.

Sulfate,  $\text{La}_2(\text{SO}_4)_3$ , nonahydrate, hexagonal prisms. Prep by treating a lanthanum salt with a slight excess of sulfuric acid. Dec at white heat. Is the least sol of the rare earth sulfates; soly in water decreases with increase in temp. Insol in alc. Forms double salts with alkali or ammonium hydroxide. Anhydr salt prep by heating hydrate.  $\text{LD}_{50}$  in rats: > 5000 g/kg orally; 275 mg/kg i.p. (Cochran).

Nitrate,  $\text{La}(\text{NO}_3)_3$ , hexahydrate, white deliquescent crystals, mp about 40°, at higher temp forms a basic salt. bp 126°. Very sol in water, alc. Forms double salts with bivalent ion nitrates and ammonium nitrates. *Keep well closed.*  $\text{LD}_{50}$  in rats: 4.5 g/kg orally; 450 mg/kg i.p. (Cochran).

USE: Oxide in glass to improve optical properties.  $\text{La}^{3+}$  used in experimental biology as a specific antagonist of Ca: Weiss, *Ann. Rev. Pharmacol.* **14**, 343 (1974).

**5234. Lanthionine.** *S*-(2-Amino-2-carboxyethyl)cysteine; 3,3'-thiodialanine; bis(2-amino-2-carboxyethyl)sulfide.  $\text{C}_6\text{H}_{12}\text{N}_2\text{O}_4\text{S}$ ; mol wt 208.24. C 34.60%, H 5.81%, N 13.45%, O 30.73%, S 15.40%. An amino acid found in proteins. First isolated as an artifact from wool hydrolysates: Horn *et al.*, *J. Biol. Chem.* **138**, 141 (1941). Isolated of naturally occurring L- and meso-lanthionine: N. H. Sloane, K. G. Utich, *Biochemistry* **5**, 2658 (1966). Synthesis: du Vigneaud, Brown, *ibid.* **151**; J. T. Snow *et al.*, *Int. J. Peptide Protein Res.* **8**, 57 (1976). Synthesis of L-lanthionine from cystine: D. N. Harpp, J. G. Gleason, *J. Org. Chem.* **36**, 73 (1971). Stereoisomerism: *eidem*, *J. Biol. Chem.* **140**, 767 (1941). Structure studies: I. W. Stapleton, O. A. Weber, *Int. J. Peptide Protein Res.* **3**, 243 (1971).



*meso*-Form, the form obtained from wool by the procedure of Horn *et al.*: Six-sided plates having a triangular appearance from dil  $\text{NH}_3$ . Softens at 207°, dec 304°. Stable to alkalis. Sol in dil acids and alkalis. Sparingly sol in water. Insol in alcohol, ether, chloroform, acetone.

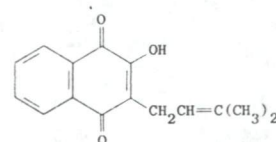
DL-Form, elongated hexagonal plates. Chars at 240°, dec 286-292°.

L-Form, elongated hexagonal plates. mp 295-296° (dec).  $[\alpha]_D^{25} +9.4^\circ$  (c = 1.4 in 2.4N NaOH);  $[\alpha]_D^{25} +8.6^\circ$  (c = 5 in 2.4N NaOH);  $[\alpha]_D^{25} +6.0^\circ$  (c = 1 in 1N NaOH).

D-Form, elongated hexagonal plates. Darkens at 245°, dec 293-295°.  $[\alpha]_D^{25} -8.0^\circ$  (c = 5 in 2.4N NaOH).

**5235. Lapachol.** 2-Hydroxy-3-(3-methyl-2-butenyl)-1,4-naphthalenedione; lapachic acid; taiguic acid; tecomin; greenhartin; NSC-11905.  $\text{C}_{15}\text{H}_{14}\text{O}_5$ ; mol wt 242.26. C 74.36%, H 5.83%, O 19.81%. Yellow crystalline material derived from the heartwood of Asian and South American bignonaceous plants, esp Surinam greenheart, Taigu wood, Lapacho heartwood and Bethabarra wood: Arnoudon, *Compt. Rend.* **41**, 1152 (1857); Stein, *J. Prakt. Chem.* **99**, 1 (1866); Paterno, *Gazz. Chim. Ital.* **9**, 506 (1879); Greene, Hooker, *Am. Chem. J.* **11**, 267 (1889). Structure: Paterno, *Gazz. Chim. Ital.* **12**, 337 (1882); Hooker *J. Chem. Soc.* **61**, 611 (1892); **69**, 1355 (1896); *J. Am. Chem. Soc.* **58**, 1168 (1936). Synthesis: Fieser, *ibid.* **49**, 857 (1927); Hooker, *ibid.* **58**, 1181 (1936); G. R. Pettit, L. E. Houghton, *J. Chem. Soc. (C)* **1971**, 509. Although it is related structurally to vitamin

K, q.v., it does not possess antihemorrhagic activity: H. J. Almquist, A. A. Klose, *J. Am. Chem. Soc.* **61**, 1923 (1939); L. F. Fieser *et al.*, *J. Biol. Chem.* **137**, 659 (1941). It is reported to be an inhibitor of respiratory processes: E. G. Ball *et al.*, *ibid.* **168**, 257 (1947). Lapachol has also exhibited antitumor activity vs Walker 256 carcinoma: K. V. Rao *et al.*, *Proc. Am. Assoc. Cancer Res.* **8**, 55 (1967). Mass spectrometry: T. A. Elwood *et al.*, *Org. Mass Spectrom.* **3**, 841 (1970). Chromatographic detection: M. H. Simatupang *et al.*, *J. Chromatog.* **52**, 180 (1970). Pharmacology: S. M. Sieber *et al.*, *Cancer Treat. Rep.* **60**, 1127 (1976). Review of antitumor activity: K. V. Rao, *Cancer Chemother. Rep. (pt. 2)* **4**(4), 11-17 (1974). Toxicity study: R. K. Morrison *et al.*, *Toxicol. Appl. Pharmacol.* **17**, 1 (1970).

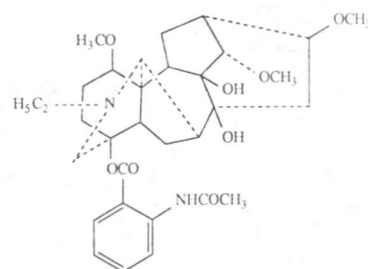


Yellow prisms from alcohol or ether, mp 140°. uv max: 251.5, 278, 331 nm (log  $\epsilon$  4.38, 4.28, 3.43). Soluble in alcohol, chloroform, benzene, acetic acid, slightly sol in ether, hot water. Sol in aq NaOH solns forming a bright red sodium salt.  $\text{LD}_{50}$  in BALB/c mice (g/kg): 0.487 (males); 0.792 (females); 0.621 (combined). R. K. Morrison *et al.*, *loc. cit.*

**5236. Lappa.** Burdock; clotbur; bardana. Dried first-year root of *Arctium lappa* L., or of *Arctium minus* Bernh., *Compositae*. *Habit.* Europe, Northern Asia; naturalized in N. America. *Constit.* Volatile oil, bitter principle, inulin, tannin.

Therap Cat: Dermatologic.

**5237. Lappaconitine.** (1 $\alpha$ ,14 $\alpha$ ,16 $\beta$ )-20-Ethyl-1,14,16-trimethoxyaconitane-4,8,9-triol 4-[2-(acetylaminobenzoate)].  $\text{C}_{32}\text{H}_{44}\text{N}_2\text{O}_8$ ; mol wt 584.69. C 65.73%, H 7.59%, N 4.79%, O 21.89%. From tubers and herb of *Aconitum septentrionale* Kölle, *A. orientale* Mill., *A. excelsum* Reichb., *A. ranunculifolium*, *Ranunculaceae*: Schulze, Ulfert, *Arch. Pharm.* **260**, 230 (1922); Kuzovkov, Massagetov; Platonova *et al.*, *Zh. Obshch. Khim.* **25**, 178 (1955); **28**, 258 (1958). *C.A.* **50**, 1852e (1956), *C.A.* **52**, 12883i (1958), resp.; Mollov *et al.*, *Compt. Rend. Acad. Bulgare Sci.* **17**, 251 (1964), *C.A.* **61**, 12324g (1964). Structure: Khaimova *et al.*, *Tetrahedron Letters* **1964**, 2711. Revised structure: V. A. Tel'nov *et al.*, *Khim. Prir. Soedin.* **6**, 583 (1970), *C.A.* **74**, 42527k (1971). Analgesic activity studies in mice and rats: N. Ono, J. Satoh, *Arzneimittel-Forsch.* **38**, 892 (1988). Toxicology: F. Dybing *et al.*, *Acta Pharmacol. Toxicol.* **7**, 337 (1951).



Bitter crystals, mp 217-218°.  $[\alpha]_D^{18} +27^\circ$  (chloroform). Sol in benzene; slightly sol in alcohol, ether. Practically insol in water.  $\text{LD}_{50}$  in mice (mg/kg): 6.9 i.v.; 9.1 i.p.; approx 20 orally (Dybing).

**5238. Lapyrium Chloride.** 1-[2-Oxo-2-[[2-[(1-oxododecyl)oxy]ethyl]amino]ethyl]pyridinium chloride; 1-[[[2-hydroxyethyl]carbamoyl]methyl]pyridinium chloride laurate (ester); N-(laurylcolaminoformylmethyl)pyridinium chloride; N-(acetylcolaminoformylmethyl)pyridinium chloride; emulsept (obsolete); E 607; Emcol E-607.  $\text{C}_{21}\text{H}_{35}\text{ClN}_2\text{O}_5$ ; mol wt 398.97. C 63.22%, H 8.84%, Cl 8.89%, N 7.02%, O 12.03%. Cationic surfactant. Prepn: A. K. Epstein, B. R.



## I N T E R O F F I C E   M E M O R A N D U M

Date: 04-Jun-1991 05:25pm DST  
From: VMSMail User PECK  
PECK@DONALD@MRGATE  
Dept:  
Tel No:

TO: TYSON@DONALD@MRGATE

Subject: DOESN'T RAY HAVE A COMPUTER?

From: DONALD::MORGENSTERN 4-JUN-1991 17:11:20.10  
To: PECK  
CC:  
Subj: RE: ACONITINE

## I N T E R O F F I C E   M E M O R A N D U M

Date: 04-Jun-1991 02:45pm DST  
From: Natalia Morgenstern  
MORGENSTERN  
Dept: HFD-110  
Tel No: 443-4730

TO: Mary Doug Tyson ( TYSON )  
CC: Raymond Lipicky ( LIPICKY )  
CC: ROBERT TEMPLE ( TEMPLE )  
CC: Carl Peck ( PECK )

Subject: RE: ACONITINE

MARY DOUG,

I AM RESPONDING FOR DR. LIPICKY ON YOUR QUESTION WHETHER ACONITINE IS "BEING DEVELOPED IN THIS COUNTRY." AS YOU HAVE ALREADY FOUND OUT, THERE IS NO IND FOR THIS DRUG.

DR. LIPICKY, HOWEVER, KNOWS A LOT ABOUT ACONITINE SINCE HE HAS PERSONALLY STUDIED IT IN SEVERAL ANIMAL SPECIES, INCLUDING, OF COURSE, IN THE SQUID AXON. HE HAS USED IT TO INDUCED ARRHYTHMIA IN DOGS.

NEEDLESS TO SAY HE WOULD BE MORE THAN GLAD TO ANSWER ANY QUESTIONS DR. PECK MAY HAVE CONCERNING THIS DRUG.

HE JUST GAVE ME THE FOLLOWING TO SEND TO YOU:

ACONITINE IS AN ALKALOID THAT INDUCES REPETITIVE ELECTRICAL ACTIVITY IN CELLS THAT HAVE ELECTRICALLY EXCITABLE MEMBRANES. IT IS USED EXTENSIVELY IN BIOPHYSICS RESEARCH AS A SODIUM CHANNEL OPENER AND IN HEART FOR PURPOSES OF INDUCING CARDIAC ARRHYTHMIAS.

IN INDIA, IT IS AVAILABLE (OTC, I THINK) AS A "SPRING TONIC." WHEN TAKEN SYSTEMICALLY IT CAUSES PERIPHERAL NERVE ENDINGS TO

FIRE REPETITIVELY AND THIS CAUSES THE TONGUE AND SKIN TO HAVE  
"GOOD" FEELINGS.



# Chemical Abstracts Registry File

U1 ANSWER 1 OF 1

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RN 97792-45-5

CN Aconitane-4,8,9-triol, 20-ethyl-1,14,16-trimethoxy-,  
4-[2-(acetylamino)benzoate], monohydrobromide,  
(1.alpha.,14.alpha.,16.beta.)- (9CI) (CA INDEX NAME)

CN Lappaconitine hydrobromide

CN 2H-12,3,6a-Ethanylylidene-7,9-methanonaphth[2,3-b]azocine,  
aconitane-4,8,9-triol deriv. (9CI)

CN Allapinine

DR 97673-48-8

MF C32 H44 N2 O8 . Br H

SR CA

LC ANABSTR, BIOSIS, CA, CIN, MEDLINE

STE 4:1A,14A,16B.ACONITANE



RINGDOC FILES, 1976-, ALLAPIN

-1-

AN - 91-01521 T S  
PN - (E) 35 57 64 66  
AU - Abdalla A; Mazur N  
LO - Moscow, USSR  
JN - EHJODF; Eur.Heart J. (11, Abstr. Suppl., 57, 1990)  
TI - Pharmacodynamic Interaction of Antiarrhythmic Drugs of Class IC.  
AB - The antiarrhythmic efficacy and safety of combinations of 2 drugs at reduced doses of the following class IC drugs: aetmozinum (EM, moracizine), ethacizine (EC), allapinin (A, lappaconitine), and propafenone (P), were evaluated in 47 patients with ventricular or supraventricular extrasystole. Drugs were administered p.o. in a blinded fashion. It was found that the combination of 2 drugs from class IC was characterized by a pharmacodynamic interaction that allowed a reduction in dosage and markedly decreased the frequency of side-effects (SE). (congress abstract)



MEDLINE, 1989-, ALLAPININE

1

UI - 91111246

AU - Smetnev AS ; Kadyrova MM ; Sobol' IuS ; Sokolov SF ; Kassirski:i  
SG

TI - [The effect of allapinine on external respiratory function in  
patients with diseases of the cardiovascular system]

AB - The cardiorespiratory system was studied comprehensively in 27  
patients with permanent atrial fibrillation (PAF) without the  
clinically marked signs of circulatory failure. After allapinine  
treatment 15 patients with bronchial obstruction manifestations  
demonstrated, in the presence of lasting PAF, a significant  
increase of the forced expiration capacity per s and of the  
maximum volumetric expiration rates. The data obtained may attest  
to the fact that the drug has beta-stimulating properties,  
confirming the reported evidence.

LA - Rus

MH - Aconitine/\*ANALOGS & DERIVATIVES/PHARMACOLOGY/THERAPEUTIC USE ;  
Adult ; Aged ; Anti-Arrhythmia Agents/\*PHARMACOLOGY/THERAPEUTIC  
USE ; Atrial Fibrillation/DRUG THERAPY/PHYSIOPATHOLOGY ;  
Bronchodilator Agents/\*PHARMACOLOGY/THERAPEUTIC USE ;  
Cardiovascular Diseases/\*DRUG THERAPY/PHYSIOPATHOLOGY ; Chronic  
Disease ; Comparative Study ; English Abstract ; Human ; Male ;  
Middle Age ; Respiration/\*DRUG EFFECTS ; Respiratory Function  
Tests

SO - Ter Arkh 1990;62(8):133-5

MEDLINE, 1983-85, ALLAPININE

1

- UI - 84227298
- AU - Tang XC ; Zhu MY ; Feng J ; Wang YE
- TI - [Pharmacologic actions of lappaconitine hydrobromide]
- LA - Chi
- MH - Aconite/\*ANALOGS & DERIVATIVES ; Aconitine/\*ANALOGS & DERIVATIVES/  
PHARMACOLOGY ; Analgesics/\*PHARMACOLOGY ; Anesthetics, Local/  
PHARMACOLOGY ; Animal ; Anthropeidea ; Anti-Inflammatory Agents,  
Non-Steroidal/PHARMACOLOGY ; English Abstract ; Female ; Human ;  
Male ; Mice ; Rats ; Substance Dependence
- SO - Yao Hsueh Hsueh Pao 1983 Aug;18(8):579-84

SS 2 /C?





DIALOG ONESEARCH (72,5,74,267,16), 1970-, ALLAPININE

2/7/2 (Item 2 from file: 72)

7921206 EMBASE No: 90355492

Bicycle ergometry-induced change in systemic and intracardiac hemodynamics in patients with cardiac fibrillation treated with allapinine before and after sinus rhythm recovery

Smetnev A.S.; Kadyrova M.M.; Sobol Yu.S.; Sokolov S.F.; Ageev F.T.; Rogoza A.N.; Gorshkov A.Sh.

Otdel Novykh Sredstv i Metodov Lechenija Instituta Klinicheskoy Kardiologii Vsesojuznogo Kardiologicheskogo Nauchnogo Tsentra AMN SSSR, Moskva USSR

KARDIOLOGIYA (USSR) , 1990, 30/9 (32-34) CODEN: KARD ISSN: 0022-9040

LANGUAGES: Russian SUMMARY LANGUAGES: English

DIALOG ONESEARCH (72,5,74,267,16), 1970-, ALLAPININE

2/7/52 (Item 1 from file: 74)

1600312 27-05839

Measurement for allapinine in tablets by ultraviolet and fluorescence  
spectroscopy

Zaitseva, T. M.; Rulin, V. A.

Farmatsiya (Moscow) 37:61-63 (6) 1988

Coden: FRMTAL

Languages: Russian

?



"CORRESPONDENCE TRACKING"

TYPE: INFORMATION DOCUMENT NUMBER: 9121712  
ORIGINATOR: 02 STATUS C DIRECTORATE STATUS  
\*\*\*\*\*

FROM: DEVAUL, Richard A.: TEXAS A&M UNIVERSITY, COLLEGE OF MEDICINE

TO: DR. D.A. BROMLEY

DATE OF  
CORRESPONDENCE:

SUBJECT: ANNOUNCEMENT OF THE APPOINTMENT OF JULIUS A. GORTON  
TO THE POSITION OF PROFESSOR AND HEAD OF THE  
DEPARTMENT OF MEDICAL PATHOLOGY AT THE TEXAS A&M  
UNIVERSITY COLLEGE OF MEDICINE.

\*\*\*\*\*  
DIRECTORATE STAFF  
ASSIGNED: ASSIGNED:

ACTION STAFF  
REQUIRED: ACTION:

\*\*\*\*\*  
SENDER'S DUE DATE:  
OSTP DUE DATE: STAFF DUE DATE  
DATE COMPLETED: DATE COMPLETED/DEPT:

\*\*\*\*\*  
COPIES TO: D. Allan Bromley  
LIFE SCIENCES

\*\*\*\*\*  
WHITE HOUSE TRACKING #: CONTACT PERSON:  
PHONE: EXT:  
REMARKS:

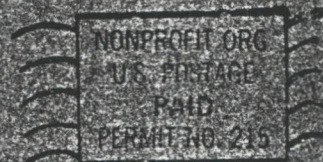
OSTP RECEIVED: 06/11/91  
DEPT RECEIVED:

FILE: P- LIFE SCIENCES





TEXAS A.M. UNIVERSITY  
COLLEGE OF MEDICINE



Mr. D. Allan Bromley  
Assistant to the President  
for Science and Technology  
The White House  
Washington, DC 20506





It is my sincere pleasure to announce the appointment of Julius A. Gordon, M.D., to the position of Professor and Head of the Department of Medical Pathology at the Texas A&M University College of Medicine.

The administration and faculty at the College of Medicine welcome Dr. Gordon and the distinguished expertise that he brings to the research, teaching and service missions of the College of Medicine and the Department of Medical Pathology.

---

Richard A. DeVaul, M.D.  
*Vice President for Health Affairs  
Executive Director of the  
Health Science Center  
and Dean, College of Medicine*



Julius A. Gordon, M.D., has been appointed Professor and Head of the Department of Medical Pathology at the Texas A&M University Health Science Center College of Medicine in College Station.

Dr. Gordon was formerly at the University of Colorado Health Sciences Center, where his research focused on cancer cell formation. His work in cell biology examines why and how cancer cells grow the way they do in order to discover how to repair the affected cells. Dr. Gordon's research in this field has been internationally recognized and widely published, and he has had continuous NIH funding for over 25 years.

After receiving his bachelor's and medical degrees from Washington University in St. Louis, Dr. Gordon completed pathology internship and residency at Duke University in 1956. From 1957 to 1959 he served as a Captain in the U.S. Army Medical Corps where he was Chief of Pathology at Ford Clinic Hospital. Dr. Gordon later trained with W.P. Jencks, the renowned biochemist, at Brandeis University Graduate School of Chemistry.

Among his many honors, Dr. Gordon was named a Scholar of the American Cancer Society Department of Biophysics at the Weizmann Institute in Rehovot, Israel; he was an invited participant at the Edmond De Rothschild School of Biophysics Glycoproteins, also in Rehovot; he received a Fogarty International Senior Fellowship while on sabbatical in 1978-79; served as session chairman for the International Meeting on Cell Fusion and Microinjection held in Jerusalem in 1979; he participated on the NIH Cancer Center Review Committee from 1980-86; and he was a charter member of the NIH Biomedical Fellowship Study Section.

Dr. Gordon's extensive experience in the medical academic setting includes a year as president of the medical school faculty, chair of the Promotions Committee and the Dean's Distinguished Seminar Series, and membership in the Faculty Senate for five years.

We are pleased to have Dr. Gordon join us in our pursuit of excellence.

---



Info 2B  
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w/ file

Document Originally  
Attached to  
Following Page

"CORRESPONDENCE TRACKING"

TYPE: INFORMATION

DOCUMENT NUMBER: 9121724

ORIGINATOR: 02

STATUS C

DIRECTORATE STATUS

\*\*\*\*\*

FROM: BLAIR, Mrs. William McCormick

TO: DR. D.A. BROMLEY

DATE OF  
CORRESPONDENCE: 06/08/91

SUBJECT: A COPY OF SIR JOHN WILSON'S KEYNOTE SPEECH AT THE  
PRESIDENT'S WEEKEND AT THE HARVARD SCHOOL OF PUBLIC  
HEALTH ON THE ISSUES OF GLOBAL PUBLIC HEALTH.

\*\*\*\*\*  
DIRECTORATE STAFF  
ASSIGNED: ASSIGNED:

ACTION STAFF  
REQUIRED: ACTION:

\*\*\*\*\*  
SENDER'S DUE DATE:  
OSTP DUE DATE: STAFF DUE DATE  
DATE COMPLETED: DATE COMPLETED/DEPT:

\*\*\*\*\*  
COPIES TO: D. Allan Bromley  
LIFE SCIENCES

\*\*\*\*\*  
WHITE HOUSE TRACKING #: CONTACT PERSON:  
PHONE: EXT:  
REMARKS:

OSTP RECEIVED: 06/12/91  
DEPT RECEIVED:

FILE: P- LIFE SCIENCES



2510 FOXHALL ROAD  
WASHINGTON, D. C. 20007

9121724  
RECEIVED

91 JUN 12 PM 12:41

June 8, 1991

OFFICE OF THE  
DIRECTOR

Dr. D. Allan Bromley  
Assistant to the President  
for Science and Technology  
Old Executive Office Building  
17th and Pennsylvania Avenue  
Washington, D.C. 20500

Dear Allan,

In early May we had The President's Weekend at The Harvard School of Public Health and we were able to get Sir John Wilson to be the keynote speaker. Without exception he is the most dazzling and brilliant speaker on issues of global public health. Sir John is blind and has dedicated his life to combating (very effectively) blindness in Africa and India as well as other devastating problems in developing countries. I thought you might enjoy seeing a copy of what was a breath taking talk.

I am sorry you won't be with us for the dinner to honor Bernadine on June 26th. Unfortunately this was the best date available, but we will try again. I hope your trip to the Soviet Union was wonderful.

All the best,

Deeda

Mrs. William McCormick Blair, Jr.





## Population and Public Health

Keynote speech by Sir John Wilson at a symposium  
at the Harvard School of Public Health, Boston, May 10, 1991

One of the things that I most admire in the United States is the optimism of your scientific community, the conviction that the movement of history is still forward, that there is no intellectual barrier which may not be crossed by the spirit of enquiry. More than your power or your money, it is that optimism which justifies your claim to leadership of the science of the modern world.

Nowhere is that optimism more evident or more justified than in your great centres of excellence like Harvard where, in a multidisciplinary framework, research at the limit of scientific imagination walks alongside a vigorous discipline of practical delivery.

I have had the privilege of meeting your students in many countries. They work at the centre of health and development programmes and, even more impressively, at the essential point of delivery in slums, villages, deserts and the wildernesses of the world. That vigour, that optimism, has never been more necessary than today in relation particularly to the theme of this symposium, "Population Control and the Role of Public Health."

We all know the statistics. Just about now the five billionth inhabitant of the world approaches a fourth birthday. By the time of the fortieth birthday, he, or more likely she, will share the world and its resources with 8 billion inhabitants. In the developing countries, population has doubled over the past thirty years and the urban population has quadrupled.

At a United Nations meeting recently, we were told that sometime during the next century there would be more people on the earth than in all previous generations put together. When that happens, apart from its other complexities, you might say that history will have become a minority subject.

Already, a billion people live in absolute poverty, 800 million go hungry every day, 100 million are permanently homeless and 450 million are disabled.



All this is compounded with violence. The developing countries have eight times more soldiers than physicians. In the background is the exploitation of unrennewable resources, desertification, global warming, which one of your writers has so graphically called "the dead heat."

Listening to the news in the past few weeks, we might be excused for wondering whether those riders of the apocalypse are putting on their spurs. There are "wars and rumours of wars" in the Middle East, famine in Africa, that unimaginable disaster in Bangladesh, cholera in the Americas.

The world has never been short of doomsayers from Job to the Reverend Al Sharpton (your most recent export to Britain). We must listen to these doomsayers but perhaps it is not being facetious or irreverent if sometimes we ask whether their more exuberant prophecy may be classified as science, art or sport.

If 200 years ago, Malthus had been right in his projection of increase of horse-drawn traffic, it is arguable that by now Boston streets would be knee-high in horse manure.

I confessed to a perverse delight the other day reading the report by one of those climatologists boring holes in the Arctic ice cap to recover bubbles of prehistoric air. One sample, recovered from 50,000 years ago, showed that our Neanderthal ancestors breathed air only marginally less polluted than ours. There was a bizarre comment in one of our newspapers that this unexpected pollution might be due to the flatulation of innumerable dinosaurs.

Of course the trends are intimidating. We should look at them with anxiety and humility but not I think with humiliation. For the first time in history, we are able through computerised technology to see cosmic changes in terms of real measurements, not just speculations of morbid saints or manic depressive economists. We face global perils alright, but we are also developing technology and systems of delivery and communication which, if they can be mobilised and aligned to a benevolent purpose, could, with political will, make possible for the first time a real effort at planetary management.

This is surely the link between the contrasting theme of this symposium. On the one hand, there is the evident menace of population growth. On the other hand, there is the potential of public health to change the ground rules of the human predicament.

No MIT engineer would have designed so powerful a reproductive machine as a



human being without an "on" and "off" switch. I am looking forward to hearing tomorrow from the faculty whether and where that technology for population limitation is likely to be found.

Meanwhile, there is impressive evidence for an altogether improbable hypothesis, that birth rate declines as child mortality declines. At an international meeting recently, that correlation was brilliantly presented by Dr. Foege. He explained that when parents know their children will survive they have fewer children. Sitting next to me was a social worker from Uganda and she said, "I'm most impressed, but in my country these decisions are not made in committees but in bed."

Infant mortality rates are declining in some countries and with them, but not so spectacularly, the birth rate. Even more convincing is the correlation between birth rate and female education. In Sri Lanka, where the per capita income is only \$400, they have achieved an adult literacy rate of 87% with consequent reduction in the birth rate.

The Bangkok conference last year called for universal primary education. It also emphasised that the education of women is not welfare or charity but essentially a factor in population limitation and child survival.

In North America, the demographic imperative is not birth rate but aging rate and the fact that disabilities cluster in the upper age groups. Your National Eye Institute estimates that if present trends continue, the number of blind people in the United States could double over the next 50 years. Dr. Morton Cramer has said that we may be faced with a pandemic of age-related disabilities. It's a race between the science which extends the span of life and the science which can influence the quality of life. It is a race which we can, and must, win.

If you turn from these foreboding statistics to what is actually happening in international public health, you get a much more optimistic scenario.

"With every breath you take, somewhere in the world a child dies or is disabled by six vaccine-preventable diseases." That was said by Dr. Ralph Henderson seven years ago, but that situation has now radically changed. International vaccination coverage has increased from about 20% to 80%.

In a temple in Southern India, there is a grotesque statue. Mothers lay votive offerings at its feet. She is the goddess of pestilence. Soon, with the global eradication of poliomyelitis, she should be moved to the museum of antiquities, along with the malign forces which preside over five other diseases which together kill 7



million children a year.

Oral rehydration therapy annually saves the life of two and a half million children. Among other targets affirmed for the year 2000, is the halving of pregnancy hazards which kill half a million mothers each year. Control of diet deficiency could prevent massive causes of blindness and mental retardation. Radical improvement is predicted in the provision of safe drinking water with consequent control of some major water-borne diseases.

It is not easy to see faces behind these mesmerizing statistics. May I tell you a personal story.

Shortly after we married, my wife and I stayed for a while in a mud hut in one of those river blindness villages in Northern Ghana. Our neighbours were the blind farmers who planted their grain along a straight piece of bamboo. A hemp rope led the blind women to the well. That blinding scourge, onchocerciasis, is now under control over most of the endemic area of West Africa. A new generation of children is growing up with sight as their normal expectation.

A year ago, Jean and I spent a day with a Bedouin community in the desert of Saudi Arabia. Ten years ago, at least one person in every family was blind from trachoma. Last year, not a single new case was recorded.

In the Indian subcontinent last year, more than a million blind people had sight restored by cataract operations. We now have the technology which, within a predictable period, could halve the incidence of avoidable disability in developing countries.

These developments are supported by a massive research effort, much of it focussed in the universities here in North America. Molecular biologists, exploiting the exquisite interaction of the human immune system, are dissecting the infinitesimal structures of viruses to reassemble them in new vaccines which could change the landmarks of public health. Neurological research workers are exploring the very life force which creates growth, with the prospect eventually of nerve regeneration giving a new dimension to remedial medicine.

In these directions, and so many others, we stand at the edge of unprecedented opportunity. Those things which in the United Nations Declaration forty years ago were affirmed as aspirations in public rights, are now being restated in terms of scientific and administrative possibility.

But as T.S. Eliot said, "Between the idea and the reality, there falls the shadow." There is AIDS, possible new mutant viruses, that hole in the ozone layer, pollution and the explosion of populations. The very technology which could oppose these things could as readily produce global destruction instead of global healing. We are developing Olympian powers to be wielded by far from Olympian humans through political mechanisms which were never designed to make moral judgement of such magnitude.

Yet, as you lift the curtain of immemorial ignorance, you reveal but the drama and majesty of human life itself and, so often, at the centre of the stage is a single, unrehearsed individual. A few days ago, on our television screen, was a 12 year-old Bangladeshi girl wading breast high through a flooded village carrying in her outstretched arms her 8 day-old baby brother. I hope it was not just a public relations invention which said that, in her Bengali language, the name that girl had given to that baby meant "Life."

We can only do the best we can. Here in a School such as this, leaders will be trained who in many countries will be at the centre of such development. It is essential that they should be exposed not just to technology and specialised scientific disciplines but also to the vision of the humanities, the reach of philosophy. They must have the capacity to think globally and act locally.

They must be given a sufficient shot of confidence to fight for their priorities in a competitive, political market. That can be a rough business. As Ibsen said, "When you go out to fight for truth and justice, you had better not wear your best pair of trousers."

President Bush has spoken of a new international order of social justice. That concept may have been trampled by events in the past months, but the values and the questions remain, in this extraordinary world of space ships and bullock carts, riches and poverty, cynicism and wonderful innocence.

For the time being, you in the United States have the challenge of leadership. Your academic institutions like Harvard must take their share in that leadership, adding academic rigour to idealism, science to technology and, hopefully, as computers compile new Himalayan ranges of data, identifying the wisdom locked in our knowledge.

So let us venture upon optimism and look for the light on the way ahead. It could be the glare of the nuclear Armageddon, the glow of the revolting Big Brother Utopia with its psychedelic dungeons in the air, but - and this is surely what this



symposium and this university is about - it could be the beacon light of a better world.

That is quite a task to challenge the renaissance men of the twenty-first century. But let us remember that the last renaissance was not made just by scientists and artists and philosophers. It was powered mainly by its patrons - governments, royal houses and, outstandingly, by the great mercantile adventurers who financed the new knowledge and sent their ships to find new worlds.

Here we are at the final decade of our tumultuous, wonderful, lethal century. Let me end by a quotation from Edmund Burke, the Scottish philosopher. Two hundred years ago at the beginning of his new decade, he said, "Let us do today those things which a man of intelligence and goodwill might wish, ten years from now, had been done."

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0433



RECEIVED

91 MAY 8 P 4: 36

Dear Allan

Even so many thank yous  
you were so nice to organize  
(such a delightful luncheon

I so much enjoyed meeting  
Bernadine. It was a joy  
to talk to her. She is  
going to be so wonderful for  
NIH. Better to wait those

long months and end up  
with a great star. One has  
an instant impression of  
intelligence - judgement -  
breadth - sensitivity - perception  
And to combine so many  
skills with enthusiasm  
and grace is going to be  
unbeatable

It occurred to me when  
we touched on the subject



of Dr Henderson that you might  
wish to write a letter in  
support of his nomination.  
Coming from you it could be  
meaningful -

I am  
enclosing a copy of what I  
think is a brilliant  
nomination from Sir John  
Wilson which you might find  
helpful to see. However  
this is confidential material  
not meant for circulation

- Don't give me away - and  
should often you read it -

If this is a nuisance on a  
burden - forget it - I

don't want you to think that  
woman is always asking  
me to do something!

But in case you do  
wish to write the letter  
it should go to



Dr Jordan Gutterman, Director  
Albert Lasker Medical Research Awards  
Dept of Immunology and Biological Therapy  
M. D Anderson Cancer Center  
1515 Holcombe Blvd  
Houston, Texas 77030

Again best wishes on the Academy  
- that was super great  
- Have a wonderful trip to the  
Soviet Union

- When Florence Mahoney's  
back from Arizona - and  
you're back from Russia  
let's try to get Bernadine  
and come for dinner

Again many thanks  
Deeda



# Withdrawal/Redaction Sheet

## (George Bush Library)

| Document No.<br>and Type | Subject/Title of Document                                                 | Date   | Restriction | Class. |
|--------------------------|---------------------------------------------------------------------------|--------|-------------|--------|
| 01. Letter               | To: Deeda McCormick Blair From: Allan Bromely<br>Re: Trip to USSR (3 pp.) | 7/9/91 | (b)(1)      |        |

**Collection:**

**Record Group:** Bush Presidential Records  
**Office:** Science and Technology Policy, Office of (OSTP)  
**Series:** Bromley, D. Allan, Files  
**Subseries:** General Science Files  
**WHORM Cat.:**  
**File Location:** Life Sciences: Biotechnology [4 of 4] [1991]

|                               |             |                             |           |
|-------------------------------|-------------|-----------------------------|-----------|
| <b>Date Closed:</b>           | 3/16/2010   | <b>OA/ID Number:</b>        | 62040-001 |
| <b>FOIA/SYS Case #:</b>       | 2005-0336-F | <b>Appeal Case #:</b>       |           |
| <b>Re-review Case #:</b>      |             | <b>Appeal Disposition:</b>  |           |
| <b>P-2/P-5 Review Case #:</b> |             | <b>Disposition Date:</b>    |           |
| <b>AR Case #:</b>             |             | <b>MR Case #:</b>           |           |
| <b>AR Disposition:</b>        |             | <b>MR Disposition:</b>      |           |
| <b>AR Disposition Date:</b>   |             | <b>MR Disposition Date:</b> |           |

### RESTRICTION CODES

**Presidential Records Act - [44 U.S.C. 2204(a)]**

P-1 National Security Classified Information [(a)(1) of the PRA]  
P-2 Relating to the appointment to Federal office [(a)(2) of the PRA]  
P-3 Release would violate a Federal statute [(a)(3) of the PRA]  
P-4 Release would disclose trade secrets or confidential commercial or financial information [(a)(4) of the PRA]  
P-5 Release would disclose confidential advice between the President and his advisors, or between such advisors [(a)(5) of the PRA]  
P-6 Release would constitute a clearly unwarranted invasion of personal privacy [(a)(6) of the PRA]

C. Closed in accordance with restrictions contained in donor's deed of gift.

PRM. Removed as a personal record misfile.

**Freedom of Information Act - [5 U.S.C. 552(b)]**

(b)(1) National security classified information [(b)(1) of the FOIA]  
(b)(2) Release would disclose internal personnel rules and practices of an agency [(b)(2) of the FOIA]  
(b)(3) Release would violate a Federal statute [(b)(3) of the FOIA]  
(b)(4) Release would disclose trade secrets or confidential or financial information [(b)(4) of the FOIA]  
(b)(6) Release would constitute a clearly unwarranted invasion of personal privacy [(b)(6) of the FOIA]  
(b)(7) Release would disclose information compiled for law enforcement purposes [(b)(7) of the FOIA]  
(b)(8) Release would disclose information concerning the regulation of financial institutions [(b)(8) of the FOIA]  
(b)(9) Release would disclose geological or geophysical information

"CORRESPONDENCE TRACKING"

TYPE: INFORMATION DOCUMENT NUMBER: 9121737  
ORIGINATOR: 02 STATUS C DIRECTORATE STATUS  
\*\*\*\*\*

FROM: WEISMILLER, Frances Power

TO: DR. D.A. BROMLEY

DATE OF  
CORRESPONDENCE: 06/06/91

SUBJECT: LETTER TO PRESIDENT BUSH REQUESTING THAT HE MODIFY  
WHITE HOUSE FAMILY PLANNING POLICIES SO THAT MUCH  
MORE CONTRACEPTION REACHES THE POOR OF  
LESS-DEVELOPED NATIONS.

\*\*\*\*\*  
DIRECTORATE STAFF  
ASSIGNED: ASSIGNED:

ACTION STAFF  
REQUIRED: ACTION:

\*\*\*\*\*  
SENDER'S DUE DATE:  
OSTP DUE DATE: STAFF DUE DATE  
DATE COMPLETED: DATE COMPLETED/DEPT:

\*\*\*\*\*  
COPIES TO: D. Allan Bromley  
LIFE SCIENCES

\*\*\*\*\*  
WHITE HOUSE TRACKING #: CONTACT PERSON:  
PHONE: EXT:  
REMARKS:

OSTP RECEIVED: 06/14/91  
DEPT RECEIVED:

FILE: *P* PRESIDENTIAL\*LIFE SCIENCES



*Copy to Dr. D. Allan Bromley*

RECEIVED

815 ROMERO CANYON ROAD  
SANTA BARBARA, CALIFORNIA 93108  
(805) 969-3612

91 JUN 14 A10:25

OFFICE OF THE  
DIRECTOR

President George Bush  
The White House  
Washington, D.C. 20500

June 6, 1991

Dear Mr. President:

This is a request. What I'm asking -- begging -- you to do would swing many environmentalist votes to you and the Republicans which would otherwise go elsewhere in the 1992 elections. It would offend very few anti-abortionists; that is, only those who believe that all sexuality is offensive to God, who views it as a distasteful necessary step toward the creation of souls for Heaven. The vast majority of anti-abortionists approve of contraception and many use it themselves. They know it reduces abortions.

The request: Please find a way to modify White House Family Planning policies so that much, much more contraception reaches the poor of the less-developed nations -- as much as the agencies that know how to distribute it can take, now and from now on.

Regardless of theories to the contrary, in real life famines, epidemics, rebellions and probably also warfare are now increasing at least in proportion to population growth and perhaps exponentially. The loss of fisheries, fertile lands and forests is clearly exponential. It also seems irreversible, for a good free-enterprise reason: the scarcer a valuable food or product gets, the higher its price goes and the stronger the incentive to exhaust its source becomes.

In your lifetime -- really since 1950 -- the human race has become the cancer of the planet. There is nothing in sight that might prevent its becoming terminal except saturation birth control.

Respectfully,

*Frances Power Weismiller*

Frances Power Weismiller

"LIFE SCIENCES (CORRESPONDENCE TRACKING)"

TYPE: ACTION DOCUMENT NUMBER: 9121700  
ORIGINATOR: 02 STATUS C DIRECTORATE STATUS C  
\*\*\*\*\*

FROM: HARRIS, Louis S.: THE COMMITTEE ON PROBLEMS OF DRUG DEPENDENCE

TO: DR. D.A. BROMLEY

DATE OF  
CORRESPONDENCE: 06/05/91

SUBJECT: REQUEST FOR CONSIDERATION OF CPDD'S VIEWS REGARDING  
ORGANIZATIONAL CHANGES, THAT THE OFFICE OF THE  
SECRETARY OF HEALTH & HUMAN SERVICES AND THE SENATE  
& HOUSE COMMITTEES INVOLVED IN THE REAUTHORIZATION  
OF THE ALCOHOL, DRUG ABUSE & MENTAL HEALTH

\*\*\*\*\*  
DIRECTORATE STAFF  
ASSIGNED: LIFE SCIENCES ASSIGNED: D.A. Henderson

ACTION STAFF  
REQUIRED: AS NECESSARY ACTION: DAB Signature

\*\*\*\*\*  
SENDER'S DUE DATE:  
OSTP DUE DATE: STAFF DUE DATE  
DATE COMPLETED: DATE COMPLETED/DEPT: 07/10/91

\*\*\*\*\*  
COPIES TO: D. Allan Bromley Rachel E. Levinson  
Jack C. Chow

\*\*\*\*\*  
WHITE HOUSE TRACKING #: CONTACT PERSON:  
PHONE: EXT:  
REMARKS: Sent 06/12/91 to DLS for Necessary Action; Bromley's request for  
a draft for his signature reached us 06/18/91.

OSTP RECEIVED: 06/10/91  
DEPT RECEIVED: 06/12/91

FILE: P-LIFE SCIENCES





"CORRESPONDENCE TRACKING"

TYPE: ACTION DOCUMENT NUMBER: 9121700  
ORIGINATOR: 02 STATUS I DIRECTORATE STATUS  
\*\*\*\*\*

FROM: HARRIS, Louis S.: THE COMMITTEE ON PROBLEMS OF DRUG DEPENDENCE

TO: DR. D.A. BROMLEY

DATE OF  
CORRESPONDENCE: 06/05/91

SUBJECT: REQUEST FOR CONSIDERATION OF CPDD'S VIEWS REGARDING  
ORGANIZATIONAL CHANGES, THAT THE OFFICE OF THE  
SECRETARY OF HEALTH & HUMAN SERVICES AND THE SENATE  
& HOUSE COMMITTEES INVOLVED IN THE REAUTHORIZATION  
OF THE ALCOHOL, DRUG ABUSE & MENTAL HEALTH

\*\*\*\*\*  
DIRECTORATE STAFF  
ASSIGNED: LIFE SCIENCES ASSIGNED:

ACTION  
REQUIRED: AS NECESSARY STAFF  
ACTION:

*Please draft a  
response in my  
signature*

\*\*\*\*\*  
SENDER'S DUE DATE:  
OSTP DUE DATE: STAFF DUE DATE  
DATE COMPLETED: DATE COMPLETED/DEPT:

\*\*\*\*\*  
COPIES TO: D. Allan Bromley

\*\*\*\*\*  
WHITE HOUSE TRACKING #: CONTACT PERSON:  
REMARKS: PHONE: EXT:

OSTP RECEIVED: 06/10/91 FILE: LIFE SCIENCES  
DEPT RECEIVED:

EXECUTIVE OFFICE OF THE PRESIDENT  
OFFICE OF SCIENCE AND TECHNOLOGY POLICY  
WASHINGTON, D.C. 20506

July 8, 1991

Dear Dr. Harris:

Thank you for your recent letter expressing your concern over the proposed reorganization of the Alcohol, Drug Abuse and Mental Health Administration and the return of its research components back to the National Institutes of Health.

As you know by now, Secretary Sullivan of HHS has proposed to transfer to NIH the three research components of ADAMHA: NIMH, NIAAA, and NIDA. The purpose of the transfer is to enhance the basic research capabilities of these three institutes by including them in the NIH. The NIH record over the years in managing and sustaining progress in the basic medical sciences has been quite remarkable. Recognizing that much of what is needed in reducing drug addiction is fundamental research in the pathophysiology of chemical dependency, the reorganization intent is to strengthen NIDA's accessibility to NIH's considerable resources in biomedical research and support.

Certainly, as you pointed out, there is a continuous need to address the social dimensions of substance abuse. I understand that efforts are being made by HHS to ensure effective collaboration between the research and service components after a reorganization takes place.

I trust Congress will move forward with Secretary Sullivan's proposal and ensure enhancement of both research and service. I appreciate learning of your concerns and I thank you for making the considerable talent of your organization available for consultation as this important plan moves forward.

Sincerely,



D. Allan Bromley  
Assistant to the President  
for  
Science and Technology Policy

Louis S. Harris, Ph.D.  
Chairman, The Committee on Problems  
of Drug Dependence  
Department of Pharmacology  
Medical College of Virginia  
MCV Station - Box 613  
Richmond, VA 23298



EXECUTIVE OFFICE OF THE PRESIDENT  
OFFICE OF SCIENCE AND TECHNOLOGY POLICY  
WASHINGTON, D.C. 20506

June 26, 1991

Dear Dr. Harris:

Thank you for your recent letter expressing your concern over the proposed reorganization of the Alcohol, Drug Abuse and Mental Health Administration and the return of its research components back to the National Institutes of Health.

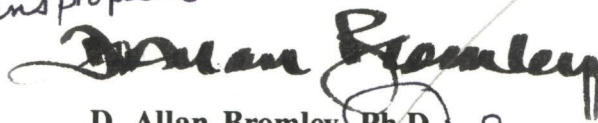
As you know by now, Secretary Sullivan of HHS has proposed to transfer to NIH the three research components of ADAMHA: NIMH, NIAAA, and NIDA. The purpose of the transfer is to enhance the basic research capabilities of these three institutes by including them in the NIH. The NIH record over the years in managing and sustaining progress in the basic medical sciences has been quite remarkable. Recognizing that much of what is needed in reducing drug addiction is fundamental research in the pathophysiology of chemical dependency, the reorganization intent is to strengthen NIDA's accessibility to NIH's considerable resources in biomedical research and support.

Certainly, as you pointed out, there is a continuous need to address the social dimensions of substance abuse. I understand that efforts are being made by HHS to ensure effective collaboration between the research and service components after a reorganization takes place.

As this proposal is considered by Congress, I will be interested in seeing a workable solution come to fruition that will enhance both research and service capabilities in substance abuse. I appreciate learning of your concerns and I thank you for making the considerable talent of your organization available for consultation as this important plan moves forward.

REPLACE WITH:

I trust Congress will move forward Sincerely,  
with Secretary Sullivan's proposal and ensure enhancement of both research and service.



D. Allan Bromley, Ph.D.  
Assistant to the President  
for  
Science and Technology Policy

Louis S. Harris, Ph.D.  
Chairman, The Committee on Problems of Drug Dependence  
Department of Pharmacology  
Medical College of Virginia  
MCV Station - Box 613  
Richmond, VA 23298





# THE COMMITTEE ON PROBLEMS OF DRUG DEPENDENCE

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91 JUN 10 P 2: 46

OFFICE OF THE  
DIRECTOR

June 5, 1991

**Chairman:**

Louis S. Harris, Ph.D.  
Department of Pharmacology  
Medical College of Virginia  
MCV Station - Box 613  
Richmond, VA 23298  
(804) 786-8434

**Executive Secretary:**

Martin W. Adler, PhD

**Board of Directors:**

Keith F. Killam, PhD, Chairman-Elect  
Thomas F. Burks, PhD, Past-Chairman  
Joseph V. Brady, PhD, Sec/Treas  
Robert L. Baister, PhD  
George E. Bigelow, PhD  
Thomas J. Crowley, MD  
Arthur Falek, PhD  
Loretta P. Finnegan, MD  
Jack Henningfield, PhD  
Donald R. Jasinski, MD  
Chris-Ellyn Johanson, PhD  
Reese T. Jones, MD  
Mary Jeanne Kreek, MD  
James M. Kulikowski, JD, MPH  
Donald E. McMillan, PhD  
Nancy K. Mello, PhD  
Jack H. Mendelson, MD  
David F. Musto, PhD  
Kenner C. Rice, PhD  
Edward Sellers, MD, PhD  
Eric J. Simon, PhD  
E. Leong Way, PhD  
James H. Woods, PhD  
George Woody, MD

The Honorable D. Allan Bromley  
Assistant to the President  
for Science and Technology  
The White House  
Washington, DC 20500

Dear Dr. Bromley:

It has come to our attention that the Office of the Secretary of Health and Human Services and the Senate and House Committees involved in the reauthorization of the Alcohol, Drug Abuse and Mental Health Administration (ADAMHA) are considering drastic organizational changes. These include, removal of all service functions, consolidation of the ADAMHA Institutes into a single entity and moving all research functions to the National Institutes of Health (NIH). It strongly concerns us that these precipitous changes are moving forward rapidly without sufficient study and consultation with the concerned constituencies.

For over fifty years the Committee on Problems of Drug Dependence (CPDD) has carried out the extremely important function of serving as an interface among agencies of the federal government, the pharmaceutical industry, the World Health Organization and academia in the areas of abuse potential and dependence liability of drugs and the development of therapeutic and prevention strategies for the chemical dependencies. We urge that the Administration, at least, for the present, support the status quo as far as the separation of the service functions from ADAMHA is concerned. We strongly oppose the consolidation of Drug Abuse and Alcohol Abuse and Alcoholism with Mental Health. This move would, in particular, downgrade the National Institute on Drug Abuse and blur its unique identity. It seems to us that this is the wrong way to fight the "War on Drugs". We also oppose the move to NIH until all ramifications have been carefully considered. The great research progress that has been made over the past two decades in our understanding of alcoholism, drug abuse and mental health, we believe, is a direct result of having a separate agency to address the special needs of the patient populations involved as well as the legal and social problems associated with the ADAMHA constellation of disease states.

We would welcome the opportunity to have greater input into organizational changes proposed for ADAMHA. The Board of Directors of CPDD is composed of distinguished scientists, treatment providers, sociologists and legal experts. Their expertise is at your service as the Administration considers policy changes in how to address the Nation's very serious public health and social problems of drug abuse, alcoholism and mental health.

Thank you for your consideration of our views concerning this matter.

Sincerely

Louis S. Harris, Ph.D.  
Chairman



INDCP

Goodwin - Mason →

Benadine OK

OK -

plan to  
had separate  
agency

Hatch / Kennedy  
Pryll

Sullivan - OK

↳ proposed O job

- 1) Guaranteed - intact transfers
- 2) full spectrum of research  
data capacity

Document Originally  
Attached to  
Following Page



THE SECRETARY OF HEALTH AND HUMAN SERVICES  
WASHINGTON, D.C. 20201

The Honorable Thomas S. Foley  
Speaker of the House  
of Representatives  
Washington, DC 20515

**DRAFT**

Dear Mr. Speaker:

Enclosed for consideration by the Congress is a draft bill "To reorganize the Alcohol, Drug Abuse, and Mental Health Administration".

This draft bill would reorganize the Alcohol, Drug Abuse, and Mental Health Administration (ADAMHA) as a \$1.9 billion service agency with increased emphasis on mental health and substance abuse activities and support. The new ADAMHA would include the Office of Substance Abuse Prevention, the Office of Treatment Improvement, and a new Office of Mental Health. ADAMHA's three research institutes -- the National Institute on Alcohol Abuse and Alcoholism, the National Institute on Drug Abuse, and the National Institute of Mental Health -- would become a part of the National Institutes of Health, where they would benefit from the exchange of science that goes on at the world's preeminent medical research center.

Our reason for proposing the reorganization is simple. ADAMHA's responsibilities in combating alcohol abuse, drug abuse and mental health problems have grown exponentially. We are now at the point where we must fully develop our ability to target effective drug abuse, alcohol, and mental health services to the people who need them, and to translate more rapidly basic research in these areas into the general health care system. We also believe that mental, behavioral, and addiction research will be enhanced, and that preventive and treatment services to people in need will be reinforced. Coordination will be maintained through the Public Health Service and through the Department as a whole.

We urge the Congress to give the draft bill its prompt and favorable consideration.

We are advised by the Office of Management and Budget that enactment of this draft bill would be in accord with the program of the President.

Sincerely,

Louis W. Sullivan, M.D.



## A B I L L

To reorganize the Alcohol, Drug Abuse, and Mental Health Administration.

Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled.

### SECTION 1. SHORT TITLE AND REFERENCES IN ACT.

(a) Short Title.--This Act may be cited as the "ADAMHA Reorganization Amendments of 1991".

(b) References in Act.--The amendments in this Act apply to the Public Health Service Act.

### SEC. 2. PREVENTION AND TREATMENT ACTIVITIES.

(a) ADAMHA as Locus of Prevention and Treatment Activities.--Section 501 is amended--

(1) by striking subsections (b), (d), (e), (j), (l), and (m),

(2) by redesignating subsections (c), (f), (g), (h), (i), and (k) as subsections (b), (d), (e), (f), (g), and (h), respectively, and

(3) by inserting after subsection (b) (as redesignated by paragraph (2)) the following:

"(c) The Secretary, acting through the Administrator, shall carry out the authorities under this Act relating to prevention and treatment for alcohol abuse, alcoholism, drug abuse, and mental illness.".

## 2

## (b) Conforming Amendments.--

(1) The heading to part A of title V is amended by striking "AND INSTITUTES".

(2) Sections 502, 504, 505, 507, 509B, and 509C are repealed.

(3) Section 503 is amended--

(A) by changing the heading to read "DRUG ABUSE INFORMATION",

(B) by striking subsections (a) through (c), and

(C) by striking the subsection designation "(d)".

(4) Section 512 is--

(A) amended in the matter in subsection (a) preceding paragraph (1) by striking "Director" and inserting "Administrator",

(B) amended in subsection (c)(1)--

(i) in the first sentence, by striking "Director of the Institute" and inserting "Administrator", and

(ii) by striking the second sentence,

(C) renumbered as section 502, and

(D) inserted after section 501.

(5) Section 516 is--

(A) amended in the matter in subsection (a) preceding paragraph (1) by striking "National Institute on Drug Abuse" and inserting "Administrator",

(B) renumbered as section 504, and

(C) inserted after section 503.



(6) Section 520 is--

(A) amended in the matter in subsection (a)(1) preceding subclause (A) by striking "the Director of the National Institute of Mental Health" and inserting "Administrator",

(B) amended in subsection (b)(1) by striking "Director" and inserting "Administrator",

(C) renumbered as section 505, and

(D) inserted after section 504 (as renumbered and transferred by paragraph (5)).

(7) The first sentence of section 521 is amended by striking "Director of the National Institute of Mental Health" and inserting "Administrator".

(8) The matter in section 528(a) preceding clause (1) is amended by striking ", the National Institute of Mental Health, the National Institute on Alcohol Abuse and Alcoholism, and the National Institute on Drug Abuse" and inserting "and the Administrator".

(9) Section 530 is amended by striking "National Institute of Mental Health" through "Drug Abuse" and inserting "Administrator".

(10) The matter in section 541(a) preceding paragraph (1) is amended by striking "National Institute on Alcohol Abuse and Alcoholism" and inserting "Administrator".

(11) Section 542(a) is amended by striking "Institute" each place it occurs and inserting "Administrator".

## 4

(12) The matter in section 545(a) preceding paragraph (1) is amended by striking "Director of the National Institute on Drug Abuse" and inserting "Administrator".

(13) Subsections (b) and (c) of section 545 are each amended by striking "Director" each place it occurs and inserting "Administrator".

(14) (A) Paragraphs (1) and (2) (A) of Section 546(a) are each amended by striking "National Institute on Drug Abuse" and inserting "Administrator".

(B) Section 546(a) (2) (B) is amended by striking "Institute" and inserting "Administrator".

(15) (A) Section 561(a) is amended--

(i) in the heading, by striking "National Institute on Drug Abuse" and inserting "Alcohol, Drug Abuse, and Mental Health Administration", and

(ii) in the matter preceding paragraph (1), by striking "Director of the National Institute on Drug Abuse" and inserting "Administrator".

(B) The heading to section 561 is amended by striking "NATIONAL INSTITUTE ON DRUG ABUSE" and inserting "ALCOHOL, DRUG ABUSE, AND MENTAL HEALTH ADMINISTRATION".

### SEC. 3. TRANSFER OF NIAAA, NIDA, AND NIMH TO NIH.

(a) Establishment of NIAAA as a Component of NIH.--

(1) Section 401(b) (1) is amended by adding at the end the following:

"(N) The National Institute on Alcohol Abuse and Alcoholism."



## 5

(2) Subpart 1 of part B of title V is amended by inserting after the subpart heading the following:

"PURPOSE OF THE INSTITUTE

"Sec. 464G. The general purpose of the National Institute on Alcohol Abuse and Alcoholism (hereafter in this subpart referred to as the 'Institute') is the conduct and support of research, investigations, experiments, and studies, into--

- "(1) the social, behavioral, and biomedical etiology,
- "(2) prevention,
- "(3) treatment,
- "(4) mental and physical health consequences,
- "(5) social and economic consequences, and
- "(6) the impact on families,

of alcohol abuse and alcoholism."

(3) Section 510 is amended--

(A) by striking subsection (a),

(B) in the matter in subsection (b) preceding paragraph (1), by striking "program described in subsection (a) of this section" and inserting "activities described in section 464G",

(C) in the matter in subsection (b)(3) preceding subclause (A), by striking out "such research projects" through "Alcoholism" and inserting "research projects",

(D) in subsection (b)(10), by striking out "the National" through "Alcoholism" and inserting "its advisory council", and

(E) by striking the subsection designation "(b)".

## 6

(4) Section 513 is repealed.

(5) Sections 510 and 511 are renumbered as sections 464H and 464I, respectively.

(6) The heading to subpart 1 of part B of title V is amended by inserting "National Institute on" before "Alcohol".

(7) Subpart 1 of part B of title V (as amended by the preceding paragraphs of this subsection and by section 2(b)(4)(D) of this Act) is renumbered as subpart 14 and is inserted after section 464F.

(b) Establishment of NIDA as a Component of NIH.--

(1) Section 401(b)(1) (as amended by subsection (a)(1) of this Act) is further amended by adding at the end the following:

"(O) The National Institute on Drug Abuse.".

(2) Subpart 2 of part B of title V is amended by inserting after the subpart heading the following:

"PURPOSE OF THE INSTITUTE

"Sec. 464J. The general purpose of the National Institute on Drug Abuse (hereafter in this subpart referred to as the 'Institute') is the conduct and support of research, investigations, experiments, and studies, into--

"(1) the social, behavioral, and biomedical etiology,

"(2) prevention,

"(3) treatment,

"(4) mental and physical health consequences,

"(5) social and economic consequences, and



7

"(6) the impact on families,  
of drug abuse."

(3) The matter in section 515(a) preceding paragraph (1) is amended by striking "National Institute on Drug Abuse" and inserting "Institute".

(4) Section 515 is renumbered as section 464K.

(5) Section 517 is repealed.

(6) The heading to subpart 2 of part B of title V is amended by striking "Drug Abuse Research" and adding "National Institute on Drug Abuse".

(7) Subpart 2 of part B of title V (as amended by the preceding paragraphs of this subsection and by section 2(b)(5)(C) of this Act) is renumbered as subpart 15 and is inserted after section 464I (as redesignated and transferred by subsection (a) of this section).

(c) Establishment of NIMH as a Component of NIH.--

(1) Section 401(b)(1) (as amended by subsection (b)(1) of this Act) is further amended by adding at the end the following:

"(P) The National Institute of Mental Health."

(2) Section 518 is amended by striking "The Secretary" through "coordination of," and inserting "The general purpose of the National Institute of Mental Health is the conduct and support of".

(3) The heading to section 518 is amended to read as follows:

"PURPOSE OF THE INSTITUTE".

(4) The matter in section 519 preceding paragraph (1) is amended by striking "Administrator" and inserting "Institute".

(5) Sections 518 and 519 are renumbered as sections 464L and 464M, respectively.

(6) The heading to subpart 3 of part B of title V is amended by striking "Mental Health Research" and adding "National Institute of Mental Health".

(7) Subpart 3 of part B of title V (as amended by the preceding paragraphs of this subsection and by section 2(b)(6)(D) of this Act) is renumbered as subpart 16 and is inserted after section 464K (as redesignated and transferred by subsection (b) of this section).

(d) Conforming Amendment.--Title V is amended by striking out the heading "PART B--RESEARCH" following section 509G.

#### SEC. 4. EFFECT OF ACT ON APPROPRIATIONS.

Amounts appropriated for periods before fiscal year 1993 for activities that are transferred by the amendments made by this Act from the Alcohol, Drug Abuse, and Mental Health Administration to the National Institutes of Health shall also be transferred, as determined by the Secretary of Health and Human Services.