

PN-ABL-298  
7/2/92

**Conclusions, Recommendations & Minutes  
of the  
Scientific Consultants Group Meeting**

April 6-7, 1992  
Arlington, Virginia

Approved: \_\_\_\_\_

*Robin D. Powell*  
Robin D. Powell, M.D.  
Chairman

Date: 5-14-92

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Conclusions and Recommendations of the Meeting of the  
A.I.D. Malaria Vaccine Development Program  
Scientific Consultants Group  
April 7, 1992

The charge to the Scientific Consultants Group (SCG) was to provide advice on three specific issues, as well as in any other areas relating to the A.I.D. Malaria Vaccine Development Program (MVDP) direction and strategy deemed appropriate. The three specific requests were for the SCG's advice regarding:

1. future activities in the MVDP supported Papua New Guinea and Kenya field sites in the context of the just completed evaluations of both sites;
2. the MVDP 1992 funding plan, including several new awards to institutions that responded to the Requests for Applications (RFA) published in 1991; and
3. the draft RFA's for publication in 1992 in the context of overall Program strategy, as presented by staff during the meeting.

The SCG's response is as follows:

1. Papua New Guinea (PNG) and Kenya Visits

- 1a. PNG: The SCG notes that significant progress has been made in achieving the goals stated in the original proposal. We are particularly encouraged by the development of the facilities, staffing, working relationships with the local populations, and apparent resolution of equipment procurement difficulties. The IMR should provide AID with full, clear, updated protocols. We recommend continued funding subject to submission of protocols and compliance with U.S. human subjects requirements.
- 1b. Kenya: The SCG appreciates the progress in some areas as noted in the evaluation team's report but is disappointed with overall progress relating to the original proposal. Noteworthy were the substantial departures from the original protocols and initial failure to take into account local conditions. The SCG urges pursuit of the important goals stated in the original proposal. We encourage A.I.D. to expand the potential for the Kenya activities to include the possibility for testing of malaria vaccine candidates as appropriate.
- 1c. The SCG concurs with the proposed "implementation letters" as discussed.

2. The SCG concurs with the 1992 A.I.D. MVDP funding plans and with current A.I.D. plans for new solicitations.
3. The SCG views as important the field activities and the continued encouragement and development of basic research-clinical research linkages.
4. The SCG concurs with the alternative methods to achieve goals of the vaccine production initiative as presented.
5. The A.I.D. MVDP program appears to have reasonable overall balance and direction.
6. The SCG is pleased by the multi-agency information presented at this meeting and the malaria vaccine research information coordination between those agencies. The SCG encourages further work to coordinate malaria vaccine research and development in the U.S. and internationally.

**Minutes**  
**Agency for International Development**  
**Malaria Vaccine Development Program**  
**Scientific Consulting Group Meeting**  
**April 6 & 7, 1992, 9 - 5 pm**  
**held at 1901 North Fort Meyer Drive, Suite 400**  
**Arlington, VA 22209**

**Present:**

**Scientific Consultant Group (Advisory Committee Members)**

Dr. Adetokunbo Lucas  
Dr. Ian McGregor  
Dr. Margaret Perkins  
Dr. Robin Powell  
Dr. Peter Reeve  
Dr. Frederick Robbins  
Dr. Kenneth Stuart  
Dr. William Weidanz

**A.I.D. Employees**

Dr. Ann Van Dusen, Director – Office of Health  
Mr. Robert Wrin, Chief – Communicable Diseases Division  
Dr. Kirk Miller, Project Officer – Malaria Vaccine Development Project  
Dr. Dennis Carroll, Project Officer – Vector Biology & Control Project  
Dr. Steve Landry, AAAS Fellow – Malaria Vaccine Development Project  
Dr. Hiram Larue, Research Coordinator – Office of Strategic Planning

**Invited Guests who Presented Statements**

Dr. Dan Gordon – Walter Reed Army Institute of Research  
Dr. Lee Hall – National Institute of Allergy & Infectious Diseases  
Dr. David Kaslow – National Institute of Allergy & Infectious Diseases  
Dr. Robert Lennox, Director – Vector Biology & Control Project  
Dr. Andy Arata, Deputy Director – Vector Biology & Control Project

**Other Attendees**

Dr. Carter Diggs, Consultant - Atlantic Resources Corporation  
Ms. Cathy Savino, Project Director – Atlantic Resources Corporation  
Ms. Lolita Jackmon, Project Assistant – Atlantic Resources Corporation  
Ms. Laura Hillier, Admin. Assistant – Atlantic Resources Corporation

**Scientific Consultants Group Members not Present**

Dr. Wenceslaus Kilama  
Dr. Kamini Mendis  
Dr. Harry Rozmiarek

- 1.0 **Welcome**  
Dr. Robin Powell opened the meeting and welcomed the Scientific Consultant Group (SCG) members. Dr. Ann Van Dusen, Director of the Office of Health, was introduced and brought an official welcome from A.I.D. Dr. Van Dusen noted the importance of the SCG and the high regard with which their recommendations were taken. Dr. Van Dusen also gave some background into A.I.D.'s work in the area of the Children's Vaccine Initiative (CVI), and suggested that the SCG evaluate the need for links between the CVI and the Malaria Vaccine Development Program (MVDP) and the CVI at a future meeting.
- 2.0 **Adoption of the Agenda**  
The agenda was adopted. (see Appendix A)
- 3.0 **SCG Minutes, Principle Investigators/SCG Meeting October 1991**  
It was moved, seconded and duly carried that the minutes from the October 7-9, 1991 meeting be adopted.
- 4.0 **Review of the Role of the SCG**
  - 4.1 **SCG Duties/Responsibilities (see Appendix B)**  
Robert Wrin, Chief of the Communicable Disease Division of the Office of Health, discussed the role of the SCG in terms of their scope of activities. He noted that the objective of the SCG was to provide broad scientific overview of malaria vaccine programs to the Assistant Administrator of A.I.D. and the advisory nature of their role.
  - 4.2 **SCG Operations/Meetings**
  - 4.3 **Evaluation of the SCG**  
An open critique of the SCG was suggested as an appropriate agenda item for future meetings.
- 5.0 **Outline of MVDP - Scope, Status & Strategy (see Appendix C)**  
Dr. Kirk Miller outlined the organizational framework of MVDP within A.I.D. He presented the project goal and discussed the three functional components of the portfolio.  
  
An inquiry was made as to the status of the Institute of Medicine report recommendation regarding the constituting of an executive committee. No action to date has been reported on forming this committee. It was noted that the IOM recommendations were not just for oversight but also stressed coordination to avoid duplication of effort.
- 6.0 **Kenya & PNG Field Projects**  
Dr. Carter Diggs led off with a slide show of the Papua New Guinea and Kenya evaluations. Drs. Reeve, Powell and McGregor gave their individual perspectives of the trip. Dr. Miller reported on the funding for each of these projects. The directives to be included in an implementation letter (see Appendix D) for each project was presented for discussion. The SCG members made specific wording recommendations for incorporation into the final letters. A major focus of the discussion was the need for protocols for each study and consultation with A.I.D. whenever deviations from protocols are contemplated. Comments were also made regarding the political sensitivity of A.I.D.'s bilateral agreement with Papua New Guinea.

Items 6.0 through 6.5 were addressed in closed session since they related to procurement activities.

6.0 Pending Program Actions

6.1 Update of Vaccine Production Initiative

The background of the VPI was presented. A representative from NIH discussed the current status of the initiative from their perspective.

6.2 1992 Funding Plan

6.3 Planning Process for New solicitations

6.4 Review of 1992 RFAs

6.5 The MVDP Project Paper (see Appendix E)

Bob Wrin presented general information about the Project Paper defining its purpose and content. The Malaria Vaccine Project Paper, which provides the framework under which the MVDP will operate, was currently being reviewed within A.I.D. and was to be available for distribution in the near future.

7.0 Review of Other Malaria Vaccine Development Efforts

7.1 NIH (extramural) (see Appendix F)

Dr. Lee Hall presented information on the organizational structure of NIAID. He presented their funding portfolio and distributed a handout of research grants and career programs. In particular, he discussed the Parasite and Tropical Diseases Branch within the Division of Microbiology and Infectious Diseases.

7.2 NIH (intramural) (see Appendix G)

Dr. David Kaslow presented a summary of NIH intramural placing it within the organizational structure of NIH. He went on to discuss their basic research and goals in vaccine development. In particular, he focused on the status of a transmission blocking vaccine within the Laboratory of Malaria Research.

7.3 WHO/TDR (see Appendix H)

Dr. Peter Reeve talked about the World Health Organization's TDR program. He discussed the activity within the Product Development Unit (PDU), discussed its funding, and presented a strategic workplan used within the PDU. He announced an important upcoming meeting on vaccines to be attended by pharmaceutical representatives in The Gambia in October.

7.4 U.S. Department of Defense (see Appendix I)

Dr. Dan Gordon of the Walter Reed Army Institute of Research presented information regarding their malaria vaccine program including the objectives of basic research, exploration and advanced development. Specifically, he discussed *P. falciparum* vaccine trials in humans from 1986-1995.

7.5 Pharmaceutical Industry (see Appendix J)

Dr. Peter Reeve highlighted the companies currently involved in vaccine development. It was noted that interest in commercial development was lacking. Some ascribed this reluctance to the lack of a promising vaccine candidate. Others, however, thought that the pharmaceutical companies were focusing their interest towards a very small population within the market, specifically the developed world traveller.

7.6 Other/Miscellaneous (see Appendix K)

Dr. Carter Diggs presented a brief synopsis of non-industrial malaria vaccine efforts being conducted outside the U.S.

- 8.0 Review of Other A.I.D. Malaria Control Activities
- 8.1 A.I.D. Malaria Control Efforts (see Appendix L)  
Dr. Dennis Carroll presented overall trends in malaria mortality. He delineated A.I.D.'s approach to the prevention and treatment of malaria including pesticides and bednets.
- 8.2 Vector Biology & Control Project (see Appendix M)  
Dr. Andy Arata of the VBC Project discussed the scope of their project highlighting their training program and interest in needs assessment, control, management and strategy.
- 9.0 Miscellaneous Program Items
- 9.1 Human Subjects Procedures (see Appendix N)  
Dr. Steve Landry discussed new federal guidelines for the protection of Human Subjects and presented procedural steps that need to be followed.
- 9.2 PI/Industry relationship (see Appendix O)  
Dr. Carter Diggs discussed the current status of A.I.D. regulations regarding patents. He noted the requirement for inclusion of a formula price clause in all cooperative agreements which protects A.I.D.'s interest in developing a vaccine.
- 9.3 Ethical Standards for A.I.D. Programs (see Appendix P)  
Bob Wrin presented the A.I.D. Code of Ethics for Government Service pointing out its applicability to SCG members and contractors.
- 10.0 Miscellaneous Items for Discussion and Comment
- 10.1 Finalization of Report of October 1992 meeting (see item 3.0)
- 10.2 Indices/Markers/Milestones for Evaluation MVDP  
This item was postponed until the next meeting
- 10.3 Appraisal of MVDP General Direction/Strategy  
A general consensus was reached supporting the MVDP general direction and strategy
- 10.4 Appraisal of MVDP Portfolio Balance  
A general consensus was reached supporting the MVDP portfolio balance
- 10.5 Special Needs, Recommendations  
No topics were taken up in this category.
- 10.6 Planning for Fall '1992 PI/SCG Meeting  
It was suggested that the Fall PI meeting was not a highly useful forum for the exchange of information. The opinion was expressed that PIs seemed protective of their research and mostly presented already published information and that little sense of mission was evident nor was it clear to the PIs what role the SCG members played.
- One member inquired as to the need for a PI/SCG meeting at all. If a meeting is required, he called for a reorganization of that meeting so that it would be more productive. One member recommended a workshop format for the meeting be investigated. The October 1991 SCG suggestions merit consideration.
- It was noted that time constraints are a consideration if the format is expanded. The last suggestion was to conduct a poll among PIs to get their opinion or to involve a small subgroup of PIs in planning the fall meeting.
- 11.0 Adjournment  
Dr. Robin Powell adjourned the meeting at 5:00 pm.



**MALARIA VACCINE DEVELOPMENT PROGRAM  
SCIENTIFIC CONSULTANTS GROUP**

1992

SPRING MEETING

—AGENDA—

VBC CONFERENCE ROOM—1901 North Fort Myer Drive—Suite 400—Arlington, VA 22209

Monday Morning — 9 to 12:00 o'clock

OPEN SESSION

- |  |  |
|--|--|
| I. WELCOME & ANNOUNCEMENTS   | <i>Dr. Ann Van Dusen<br/>Ms. Cathy Savino<br/>Dr. Kirk Miller</i>                                    |
| II. REVIEW OF THE ROLE OF THE SCG:<br>Discussion<br>—SCG Duties/ Responsibilities<br>—SCG Operations/ Meetings<br>—Evaluation of the SCG | <i>Mr. Robert Wrin<br/>Dr. Robin Powell<br/>&amp; SCG Members</i>                                    |
| III. KENYA AND PNG FIELD PROJECTS:<br>Report on Comprehensive Evaluation<br><br>Discussion<br>Tentative Implementation Plans             | <i>Dr. Robin Powell<br/>Dr. Peter Reeve<br/>Sir Ian McGregor<br/>SCG Members<br/>Dr. Kirk Miller</i> |
| IV. OUTLINE OF MVDP:<br>Scope, Status & Strategy   | <i>Dr. Kirk Miller</i>   |

Monday Afternoon — 1 to 4:30 o'clock

CLOSED SESSION

V. PENDING PROGRAM ACTIONS:

- |    |   |   |
|----|---|---|
| 1. | Update of Vaccine Production Initiative   | <i>Dr. Carter Diggs<br/>Dr. Lee Hall</i>      |
| 2. | 1992 Funding Plan<br>Discussion<br>—Implications Beyond 1992<br>—Relationship to Other Agencies | <i>Dr. Kirk Miller<br/>SCG Members</i>        |
| 3. | Planning Process for New Solicitations  | <i>Dr. Kirk Miller</i>                        |
| 4. | Review (Draft ) 1992 RFAs   | <i>Dr. Carter Diggs<br/>Dr. Steven Landry</i> |
| 5. | The MVDP Project Paper  | <i>Mr. Robert Wrin</i>                        |

Tuesday Morning — 9 to 12:00 o'clock

OPEN SESSION

VI. Review of Other Malaria Vaccine  
Development Efforts:

NIH (extramural)  
NIH (intramural)  
WHO/TDR  
U.S. Department of Defense  
Pharmaceutical Industry  
Other/ Miscellaneous

*Dr. Lee Hall*  
*Dr. David Kaslow*  
*Dr. Peter Reeve*  
*Dr. Dan Gordon*  
*Dr. Peter Reeve*  
*Dr. Carter Diggs*

VII. Review of Other A.I.D.  
Malaria Control Activities:

A.I.D. Malaria Control Efforts  
Vector Biology & Control Project

*Dr. Dennis Carroll*  
*Dr. Andy Arata*

Tuesday Afternoon — 1 to 4:30 o'clock

OPEN SESSION

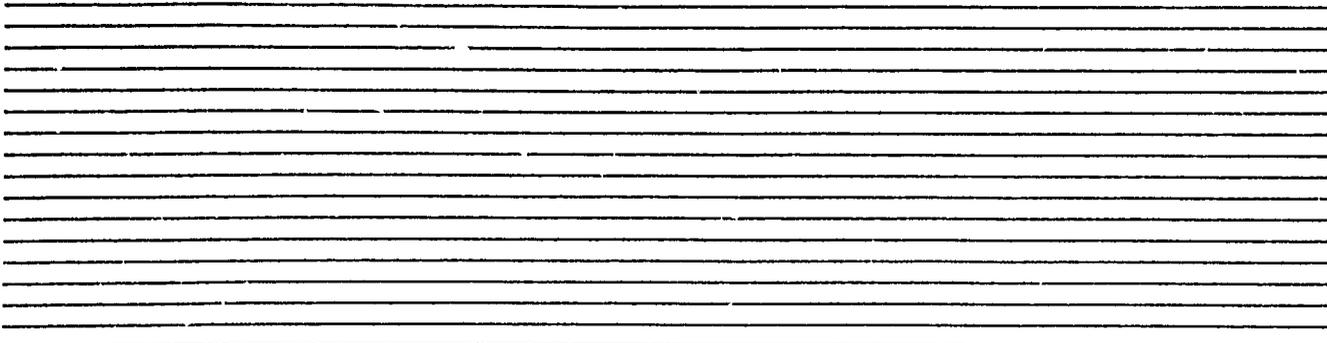
VIII. MISCELLANEOUS PROGRAM ITEMS:

- Human Subjects Procedures *Dr. Stephen Landry*
- PI/Industry Relationship *Dr. Carter Diggs*
- Ethical Standards for A.I.D. Programs *Mr. Robert Wrin*

IX. MISCELLANEOUS ITEMS FOR DISCUSSION & COMMENT *D. Robin Powell & SCG Members*

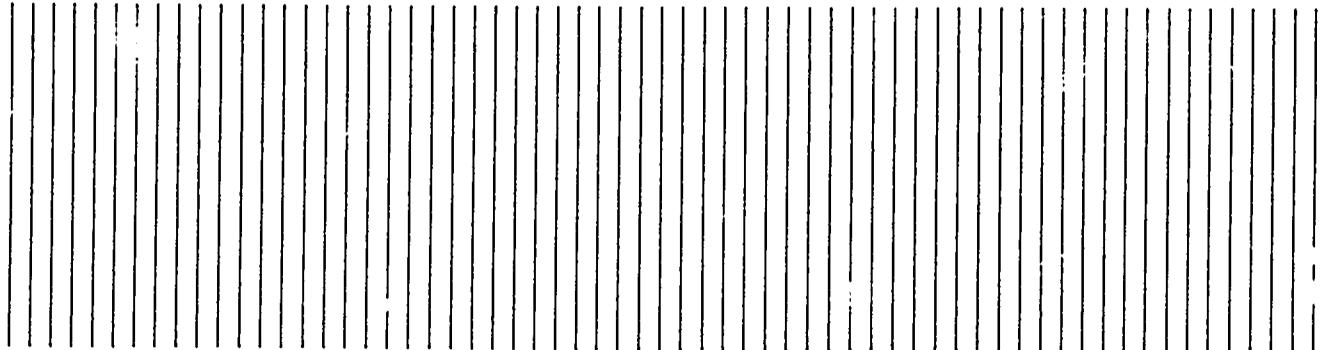
- Finalization of Report of October 1991 Meeting
- Indices/ Markers/ Milestones for Evaluating MVDP
- Appraisal of MVDP General Direction/ Strategy
- Appraisal of MVDP Portfolio Balance
- Special Needs, Recommendations
- Planning for Fall '92 PI/SCG Meeting

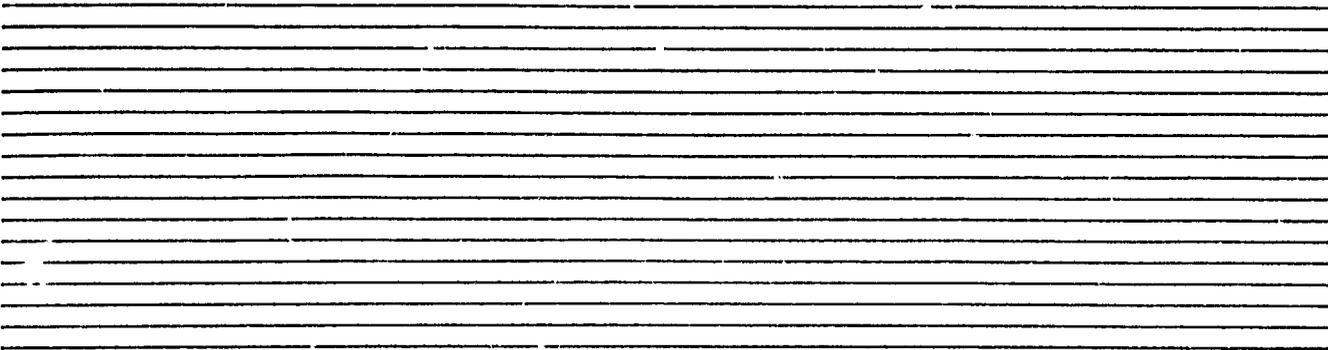
X. ADJOURNMENT



Scientific Consultants Group	Invited Guests	A.I.D. & ARC
Dr. Wenceslaus Kilama	Dr. Dan Gordon Walter Reed Army Institute of Research	Dr. Ann Van Dusen, Director Office of Health
Dr. Adelokunbo Lucas	Dr. Lee Hail National Institute of Allergy & Infectious Diseases	Mr. Robert Wrin, Chief Communicable Diseases Division
Dr. Ian McGregor	Dr. David Kaslow National Institute of Allergy & Infectious Diseases	Dr. Kirk Miller, Project Officer Malaria Vaccine Development Project
Dr. Kamini Mendis *	Dr. Andy Arata, Deputy Director Vector Biology & Control Project	Dr. Dennis Carroll, Project Officer Vector Biology & Control Project
Dr. Margaret Perkins		Dr. Steve Landry, AAAS Fellow Malaria Vaccine Development Project
Dr. Robin Powell		Dr. Carter Diggs, Consultant Atlantic Resources Corporation
Dr. Peter Reeve		Ms. Cathy Savino, Project Director Atlantic Resources Corporation
Dr. Frederick Robbins		Ms. Lolita Jackmon, Project Assistant Atlantic Resources Corporation
Dr. Harry Rozmiarek *		Ms. Laura Hillier, Admin. Assistant Atlantic Resources Corporation
Dr. Kenneth Stuart		
Dr. William Weidanz		

\* Denotes unable to attend this meeting.





## CHARGE TO THE SCIENTIFIC CONSULTANTS GROUP

- ★ Value of field activities.
- ★ 1992 Funding plan.
- ★ Plans for new solicitations.
- ★ Overall direction and strategy.

**ROLE**

**of the**

**SCG**

**CHARTER**  
**of the**  
**Agency for International**  
**Development**  
**Advisory Committee of**  
**the Malaria Vaccine**  
**Program**

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COMMITTEE OBJECTIVE

To provide *broad* senior scientific *overview* of  
Malaria Vaccine Programs

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DUTIES  
&  
SCOPE OF ACTIVITY

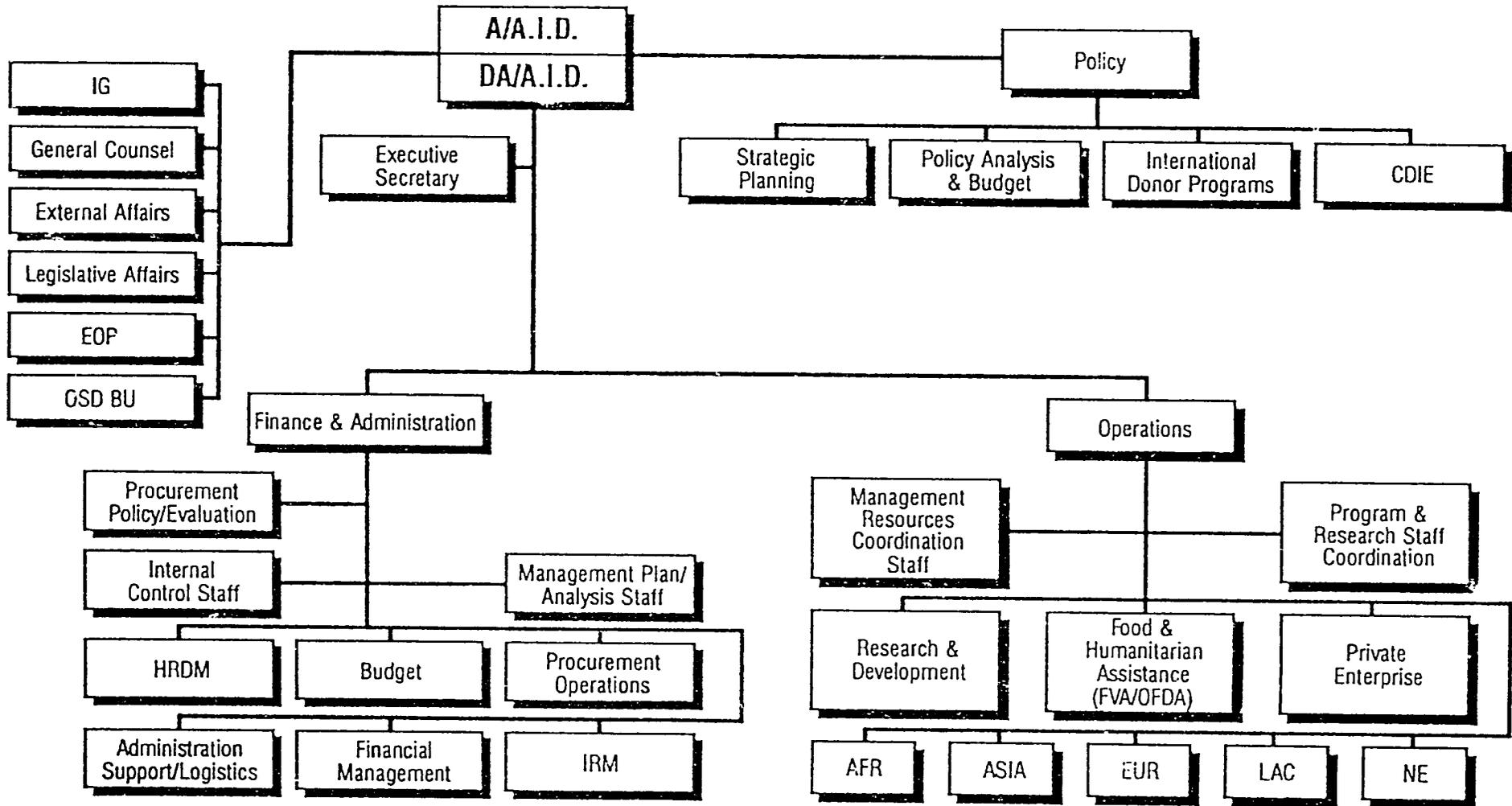
- To ensure Malaria Vaccine *Program focus and coherence*, and to ensure the application of the *highest standards of technical and scientific excellence*.
- To assist in the development of *overall Program strategy* and in the monitoring of *Program goals*.
- To *provide strategic advice and guidance*, based upon periodic review of ongoing and proposed Program activities.
- To *help identify new opportunities* for lines of research as well as to identify appropriate additional institutions and scientists to participate in the Program.

REPORTING

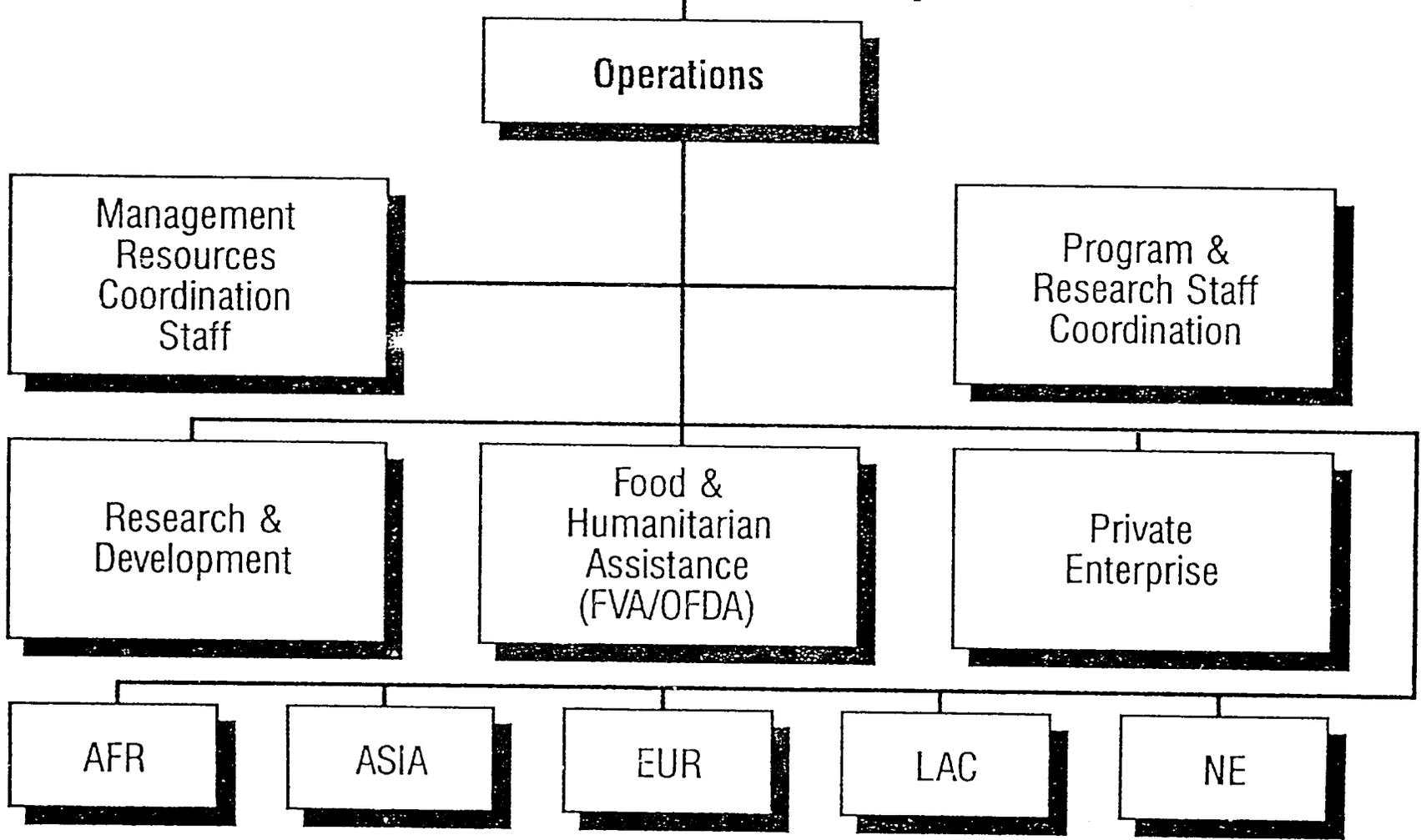
- The Advisory Committee of the Malaria Vaccine Program will *provide advice to the Assistant Administrator for Research and Development* of the Agency for International Development.

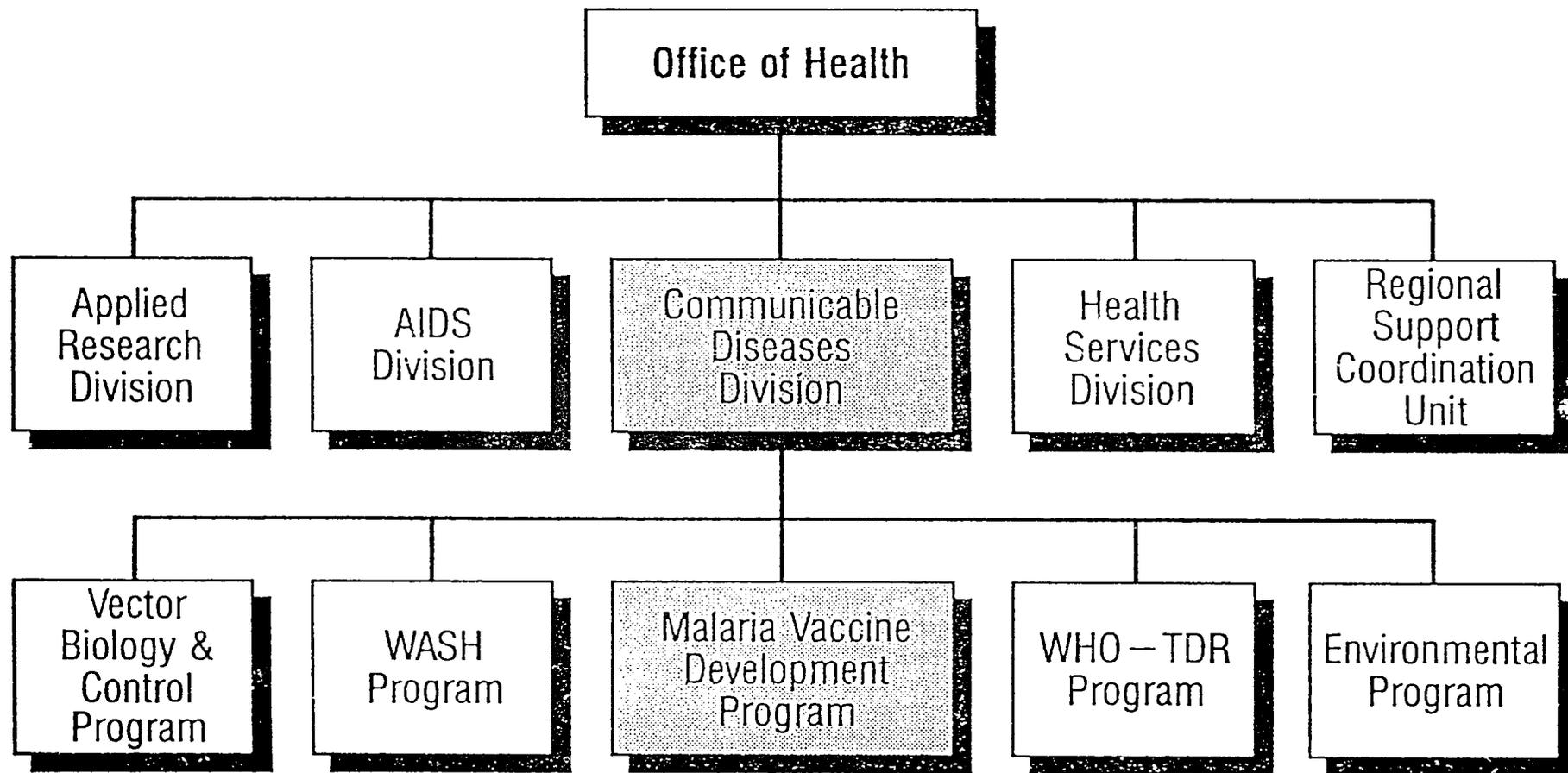
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## Agency Organization Chart



## Agency Organization Chart: Operations





## **Project Goal**

*(circa 1989)*

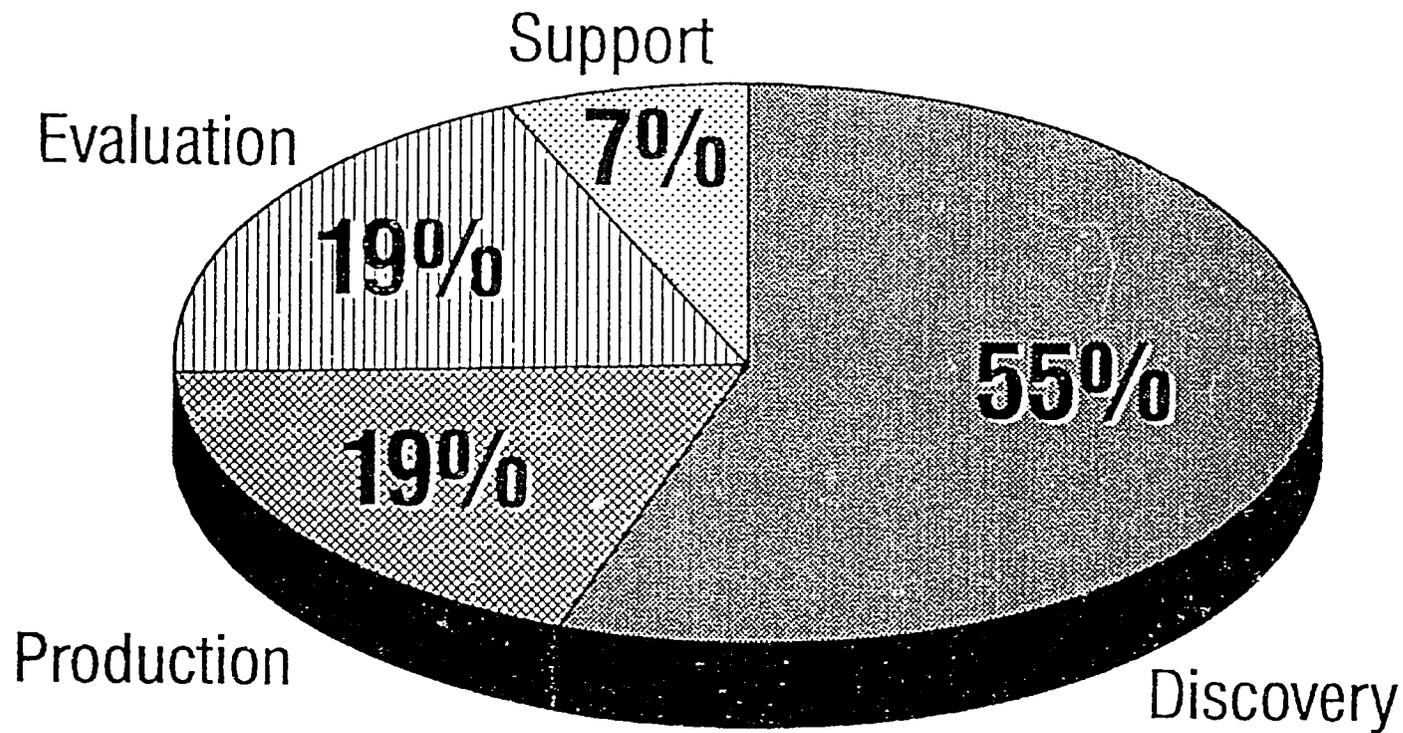
Develop vaccine(s) that will reduce malaria-associated mortality and morbidity in developing countries, especially in children.

## MVDP

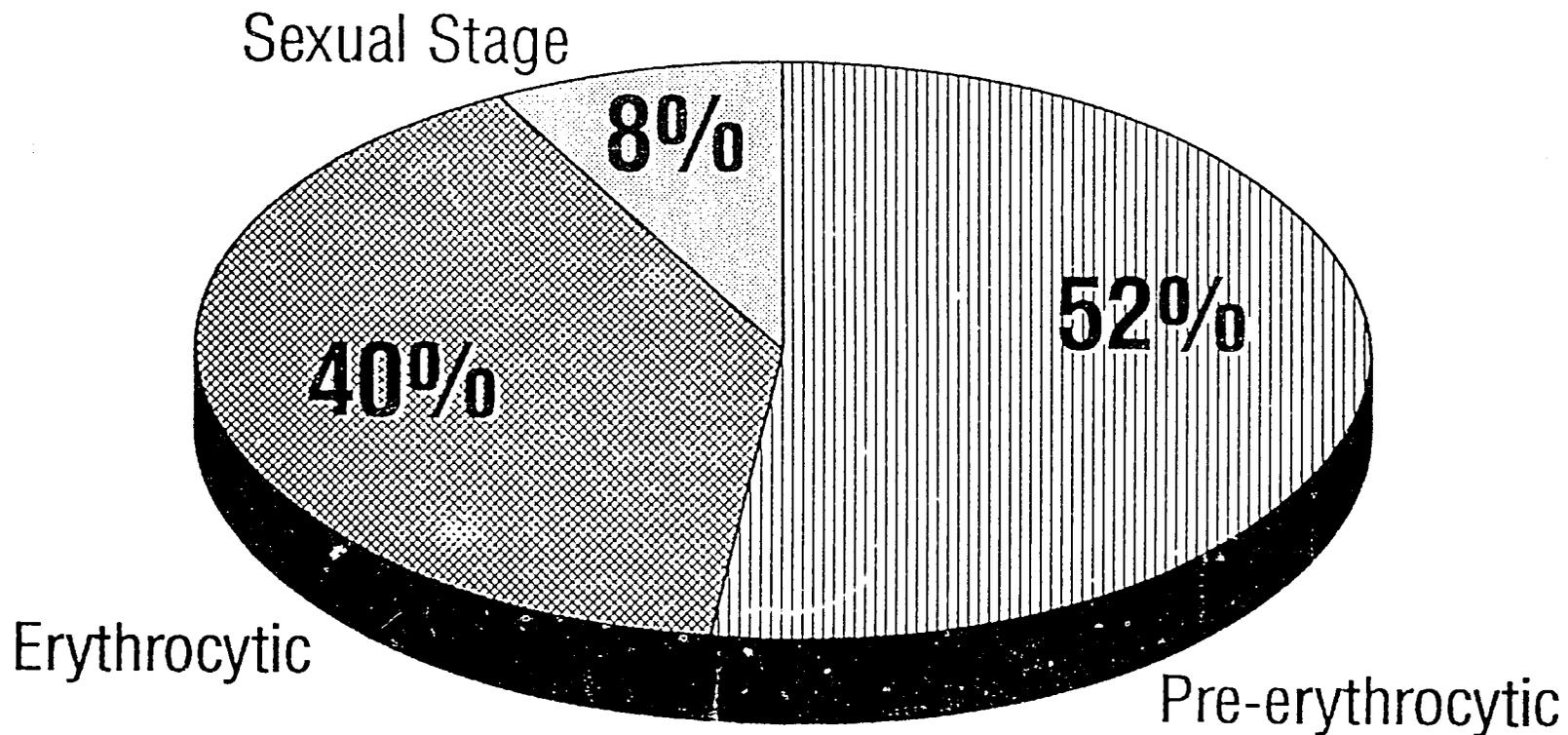
Three functional components within the portfolio:

1. Discovery
2. Production
3. Evaluation
- ★ Support

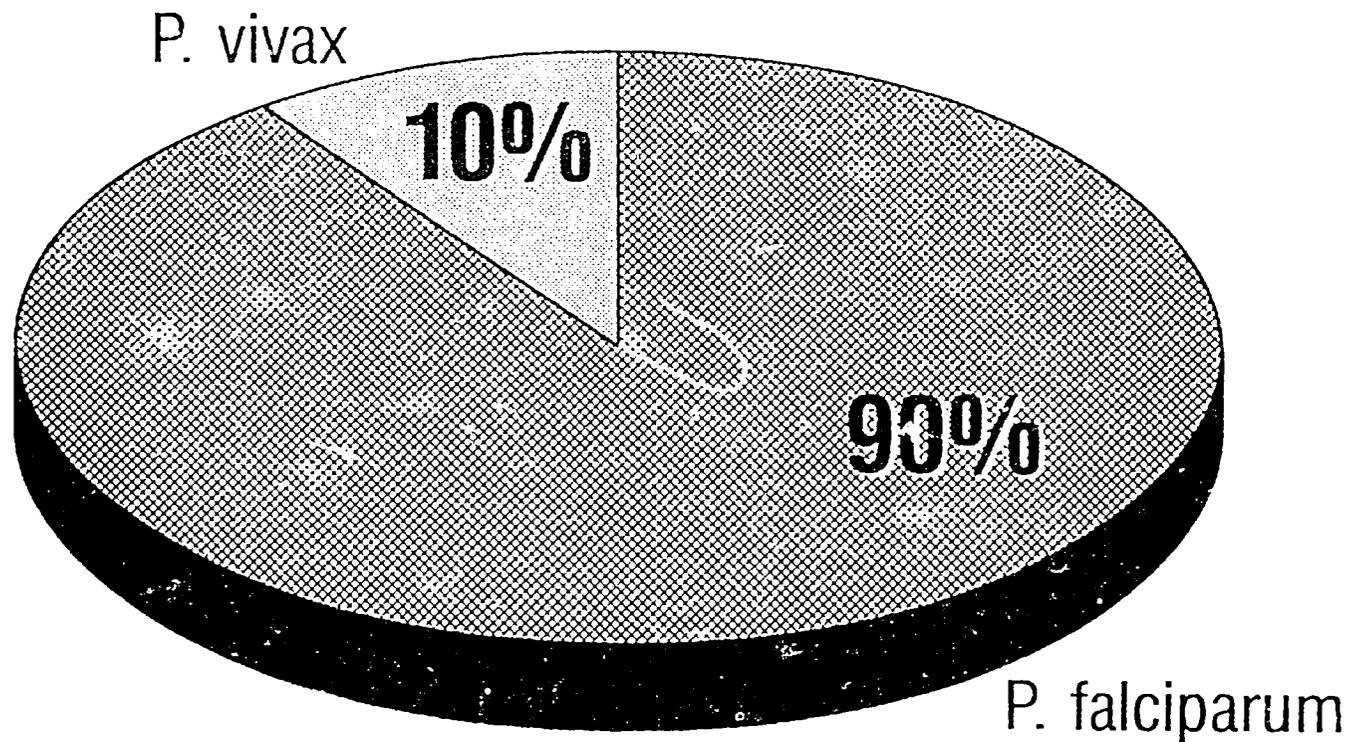
## Allocation of MVDP Funds 1992



## Discovery Component: Resource Allocation by Stage of Parasite



## Discovery Component: Resource Allocation by Species of Parasite



## Discovery Component

### Cooperative Agreements

- ❖ Limited to domestic, non-U.S. Government institutions;
- ❖ Proposals solicited annually by announcements in:
  - Science, Nature, Commerce & Business Daily,
  - Secondary excerpting process, and
  - Direct mailings to ASTM&H members.
- ❖ Results in a full and open competition;
- ❖ Review for responsiveness by MVDP; and
- ❖ Peer review for scientific merit by NIH.

## Evaluation and Monitoring of Agreements

- ❖ Competitive Renewal — every 3 years
- ❖ Presentation at SCG Meeting — every year
- ❖ Progress Reports, Administrative — quarterly
- ❖ Progress Reports, Technical — 9, 18, 36 months
- ❖ Site Visits

## Production Component

- ❖ Potential linchpin of program: linkage between discovery and evaluation;
- ❖ Adds clinical product development component; and
- ❖ Allows the development of orphan vaccines.

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## Evaluation Component

The MVDP currently maintains the capability to:

- ❖ Conduct monkey trials at CDC;
- ❖ Conduct Phase I and II trials in the United States;
- ❖ Repeat Phase I and II trials in endemic areas; and
- ❖ Conduct Phase III trials in endemic areas.

## New Trends

- ❖ Increased collaboration with other U.S. Government Agencies (NIAID, WRAIR);
- ❖ Increased capability to expedite antigen evaluation to the point of clinical testing;
- ❖ Increased effort to communicate with program investigators; and
- ❖ Continued effort to focus the program.

# Implementation Letter - Kenya

—Studies will be supported at current level until present agreement expires (April 1993).

—Major emphasis should be placed on defining clinical malaria and attempting to correlate development of immunological markers with clinical immunity; minimal emphasis shall be placed on other types of studies unless there is clearcut relationship to immunologic studies (*i.e.*, bednet studies, anemia studies, and entomological studies).

—A protocol should be developed to make the best possible use of specimens collected during already completed cohort studies.

—All newly developed protocols shall be submitted to A.I.D. for internal review for program relatedness and external review for scientific merit. A format for protocols will be provided by A.I.D.

—Progress will again be evaluated prior to negotiation of a new Interagency Agreement with CDC for field studies in Kenya.

# Implementation Letter - PNG

—Studies will be supported at negotiated level until present until expiration of extended agreement (September 1994).

—As soon as possible, detailed scientific protocols should be constructed and submitted to A.I.D. for all ongoing studies. These will be reviewed by an external panel for scientific merit. A format for protocols will be provided by A.I.D.

—If suitable protocols are developed and submitted demographic studies and epidemiologic surveillance should be continued as planned for the next 2 years; genetic studies underway should be completed; and entomologic studies should be continued until the end of this year. Immunologic studies should continue on an ongoing basis and should correlate specific immune responses with naturally acquired immunity to malaria.

—Similarly, in the future, detailed scientific protocols should be constructed and submitted to A.I.D. for all planned studies well in advance of contemplated start date.

—Progress will again be evaluated prior to negotiation of a new Project Grant Agreement in 1994.

**The  
Project  
Paper**

## PROJECT PAPER

*Purpose:*

*Formalize Long-term Commitment*

● *A.I.D.*

*(Executive Branch)*

*Congress*

Usual Functions of Project Paper

Provides HQ commitment to field-mission's program

Process allows for concensus-building among various development specialities, as well as between A.I.D. and host country staff.

*Content:*

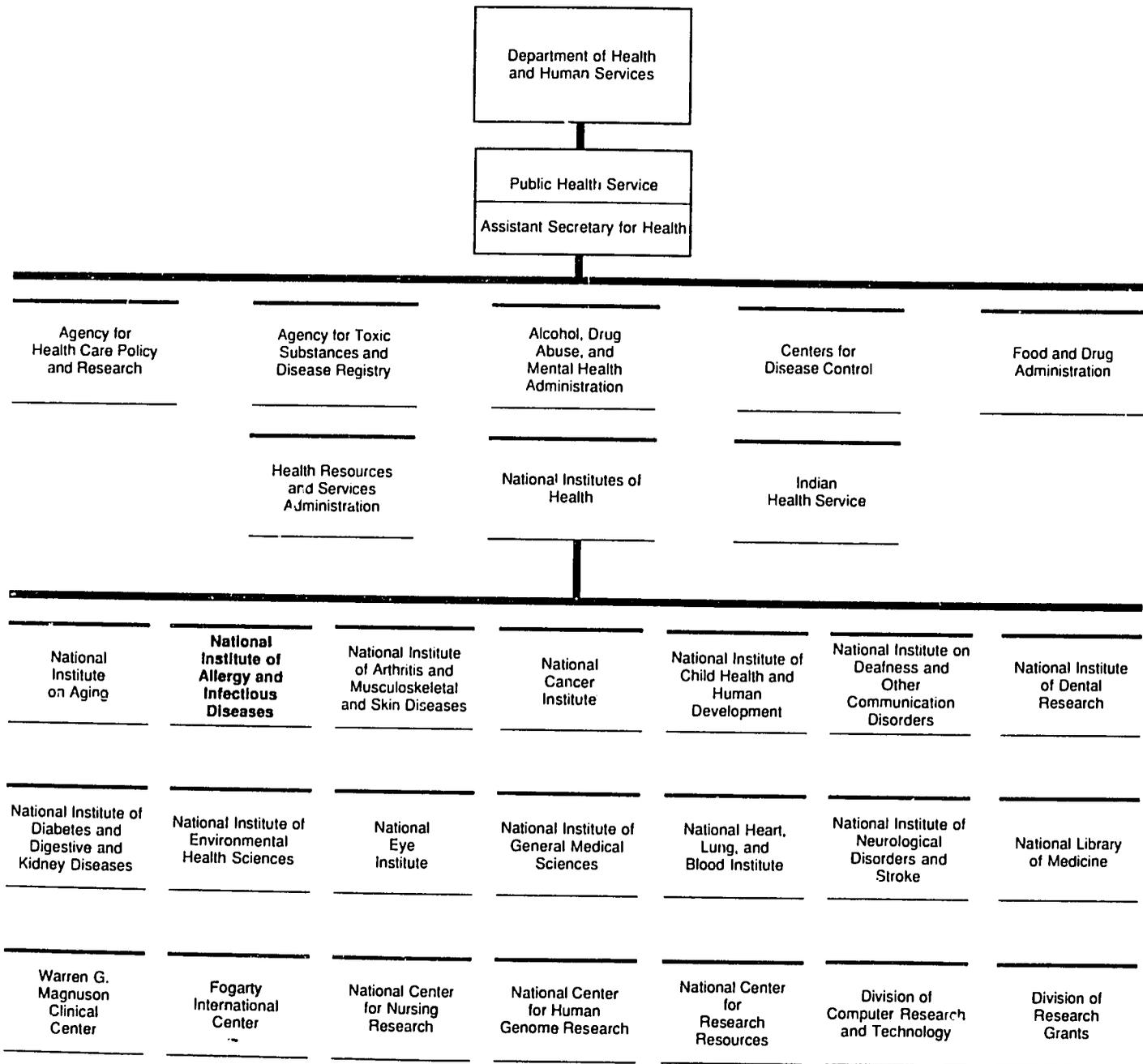
*Goal & Purpose of Project*

*Management Plan*

*Implementation*

*Evaluation*

# Location of NIAID in the Department of Health and Human Services

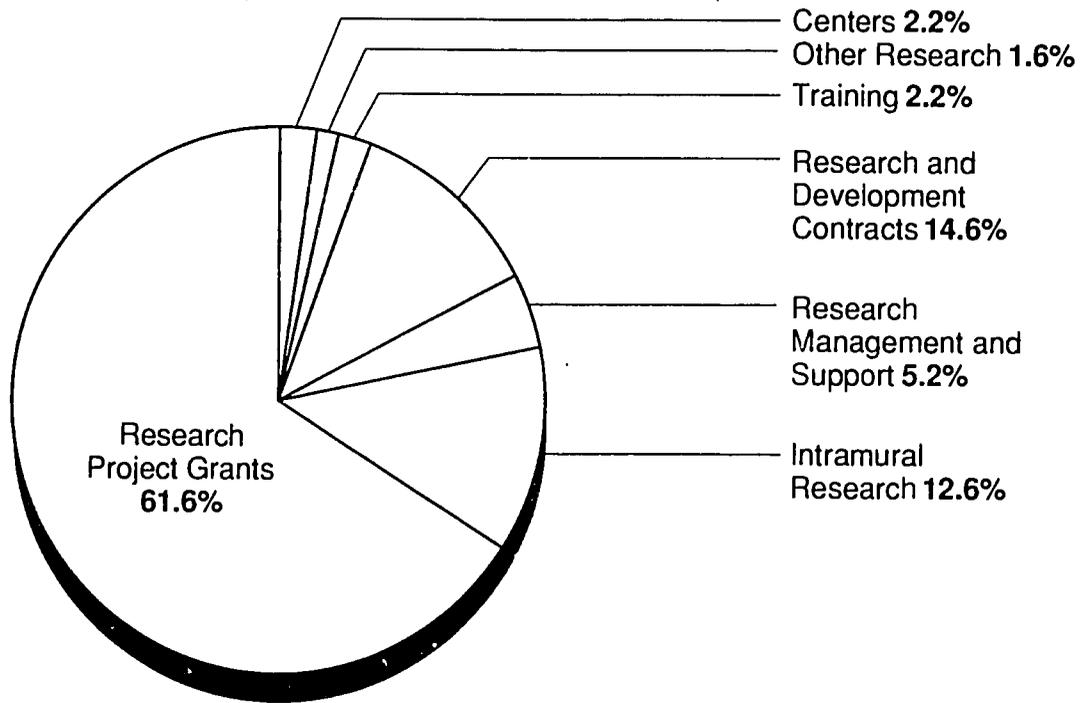


**". . . NIAID has maintained its strong commitment to basic research and to studies on other infectious and immunologic diseases within its mission by continuing to conduct and support work in the prevention and treatment of sexually transmitted diseases, asthma and allergies, and parasitic and fungal diseases; diagnostics for infectious diseases; evaluation of antiviral drugs; and transplantation immunology. NIAID also continues to provide support for research on international health issues and in tropical medicine."**

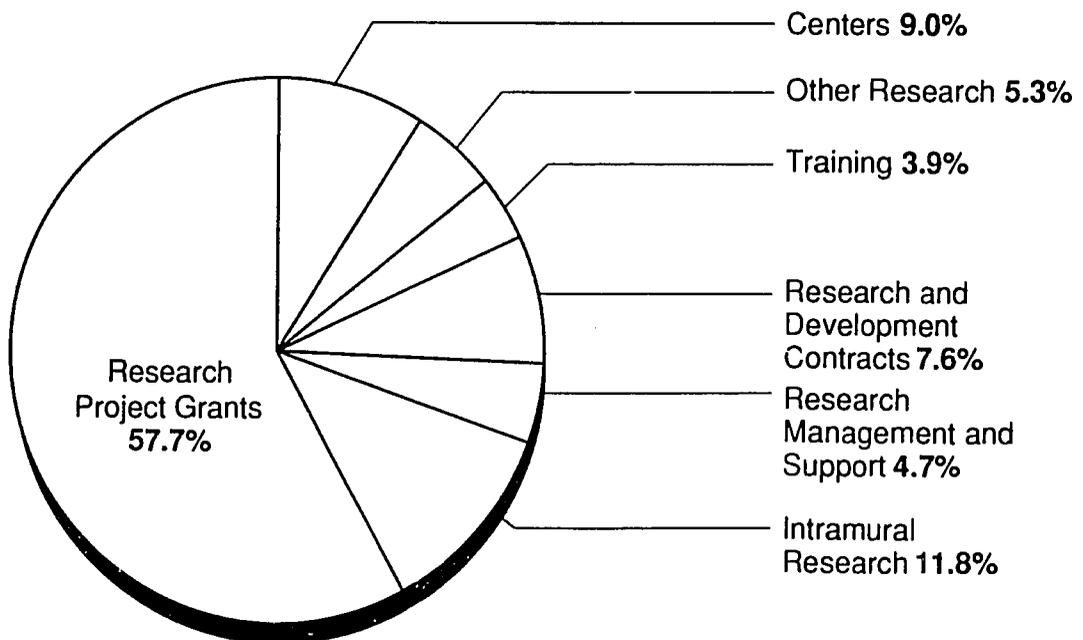
- Anthony S. Fauci, M.D.  
Director, NIAID  
Profile, Fiscal Year 1991

# NIAID and NIH Funding By Budget Mechanism: FY 1991

**NIAID**  
Total: \$906,003,000

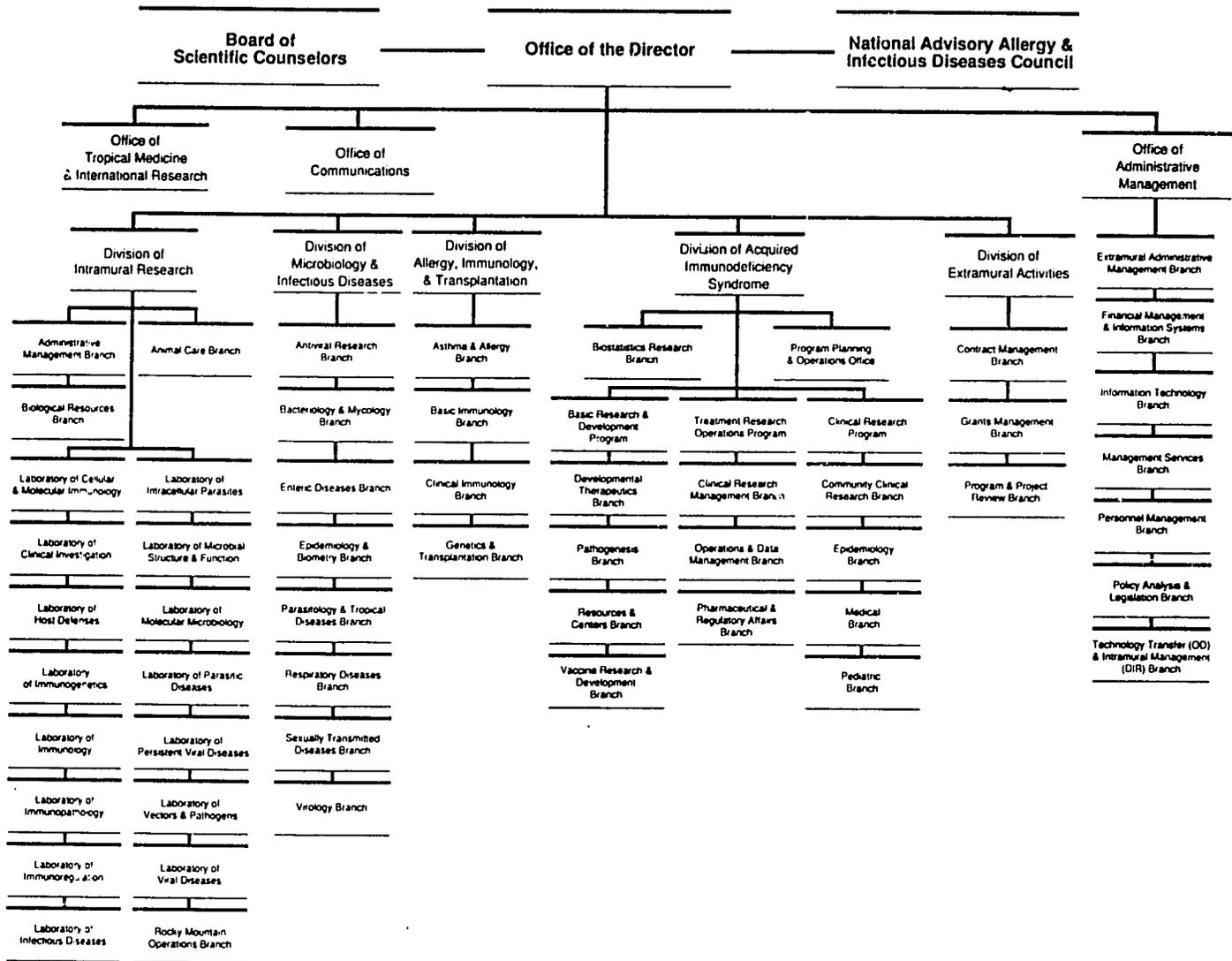


**NIH**  
Total: \$7,825,011,000<sup>a</sup>



<sup>a</sup> Excludes funds for cancer control; construction; National Library of Medicine; Office of the Director, National Institutes of Health; and buildings and facilities.

# NIAID Organizational Chart



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DMID: MAJOR AREAS OF INTEREST

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- **Emerging and Re-Emerging Infectious Diseases**
  - **Pathogenesis**
  - **Molecular Biology and Genetics of Infectious Agents**
  - **Structural Biology and Drug Development**
  - **Vaccine Research and Development**
  - **Control of Infectious Diseases**
-

DMID: SPECIFIC AREAS OF INTEREST - I

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- Antimicrobial Drug Resistance
  - Malaria and Other Tropical Diseases
  - STD's/Women's Health
  - Hepatitis, Cholera, and Other Enteric Diseases
  - Pertussis, GBS and Other Respiratory Diseases
  - Mycology
  - Tuberculosis
-

DMID: SUMMARY OF FY 1991 ACTIVITY

2/5

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(In Thousands of Dollars)

<u>Grants</u>	<u># Mechanisms</u>	<u>\$ Amount</u>
Research Projects	1140	215,012
Research Centers	3	1,181
Career	72	5,029
Other	29	1,503
Training, Individual	67	1,828
Training, Institute	53	7,029
<u>Contracts</u>		
Contracts	56	28,347
<u>Total</u>		259,930

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DMID: A SUMMARY OF CLINICAL ACTIVITY

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- 47 Active INDs
  - 123 Clinical Trials
    - 11 Drugs
    - 54 Vaccines
  - 26 Collaborating Companies
-

**RESEARCH OBJECTIVES**  
**Parasitology and Tropical Diseases Branch, DMID**

**Vaccine Development**

- ◆ To characterize the role of the immune system in protection and disease
- ◆ To identify suitable candidate vaccine antigens
- ◆ To facilitate clinical testing of candidate vaccines

**Diagnosis**

- ◆ To develop rapid, sensitive, cost-effective diagnostic assays
- ◆ To facilitate application of these assays in endemic areas

**Therapy**

- ◆ To identify new therapeutic agents and targets
- ◆ To improve the efficacy of currently available therapy
- ◆ To facilitate clinical testing of promising agents

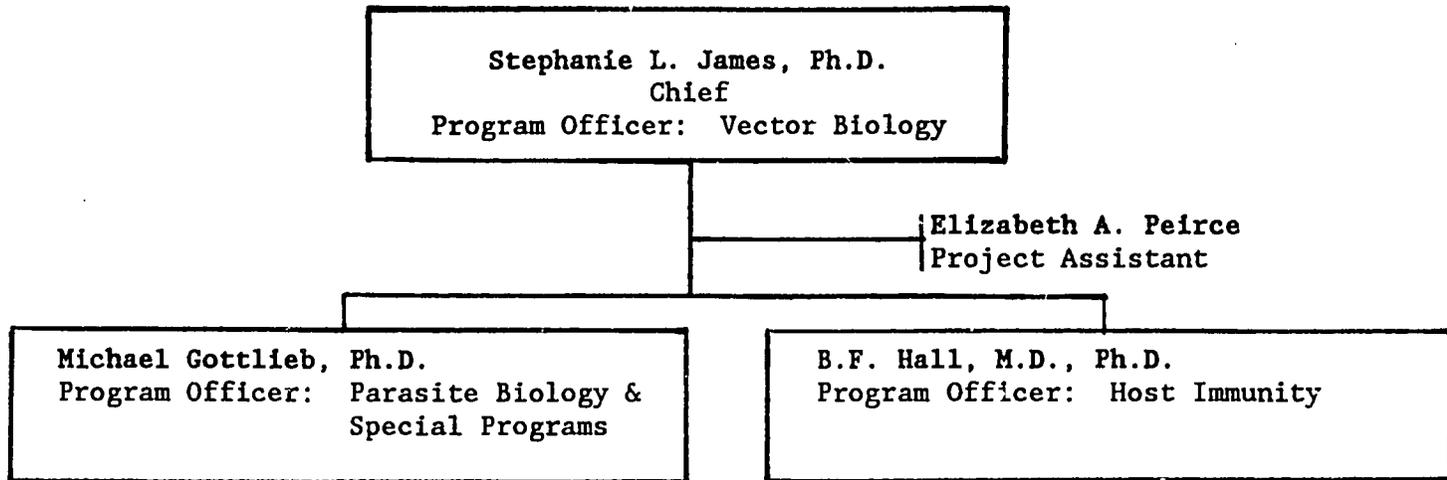
**Vector Biology**

- ◆ To develop methods to control vector populations and block pathogen transmission

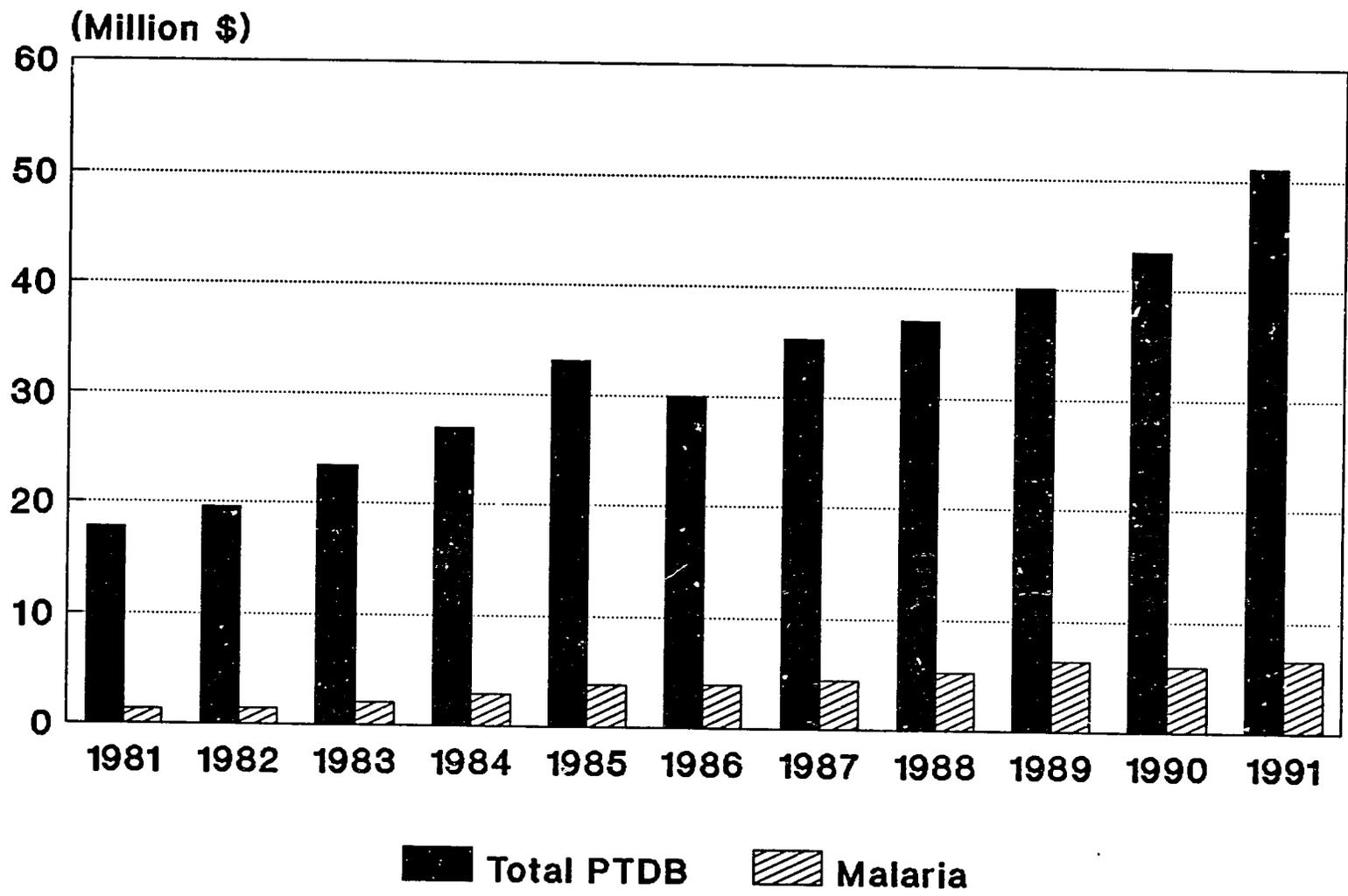
**Parasitology and Tropical Diseases Branch  
DMID, NIAID**

- ◆ Individual investigator-initiated research grants  
Approximately 300 grants in the areas of parasitology  
and vector biology
  
- ◆ Special Programs  
Tropical Disease Research Units - P01  
International Collaborations in Infectious Diseases  
Research - P01  
Tropical Medicine Research Centers - P50
  
- ◆ Contracts  
Supply of schistosome materials  
Supply of filarial materials  
Testing of candidate malaria vaccines in human  
volunteers (with USAID)

**Parasitology and Tropical Diseases Branch**



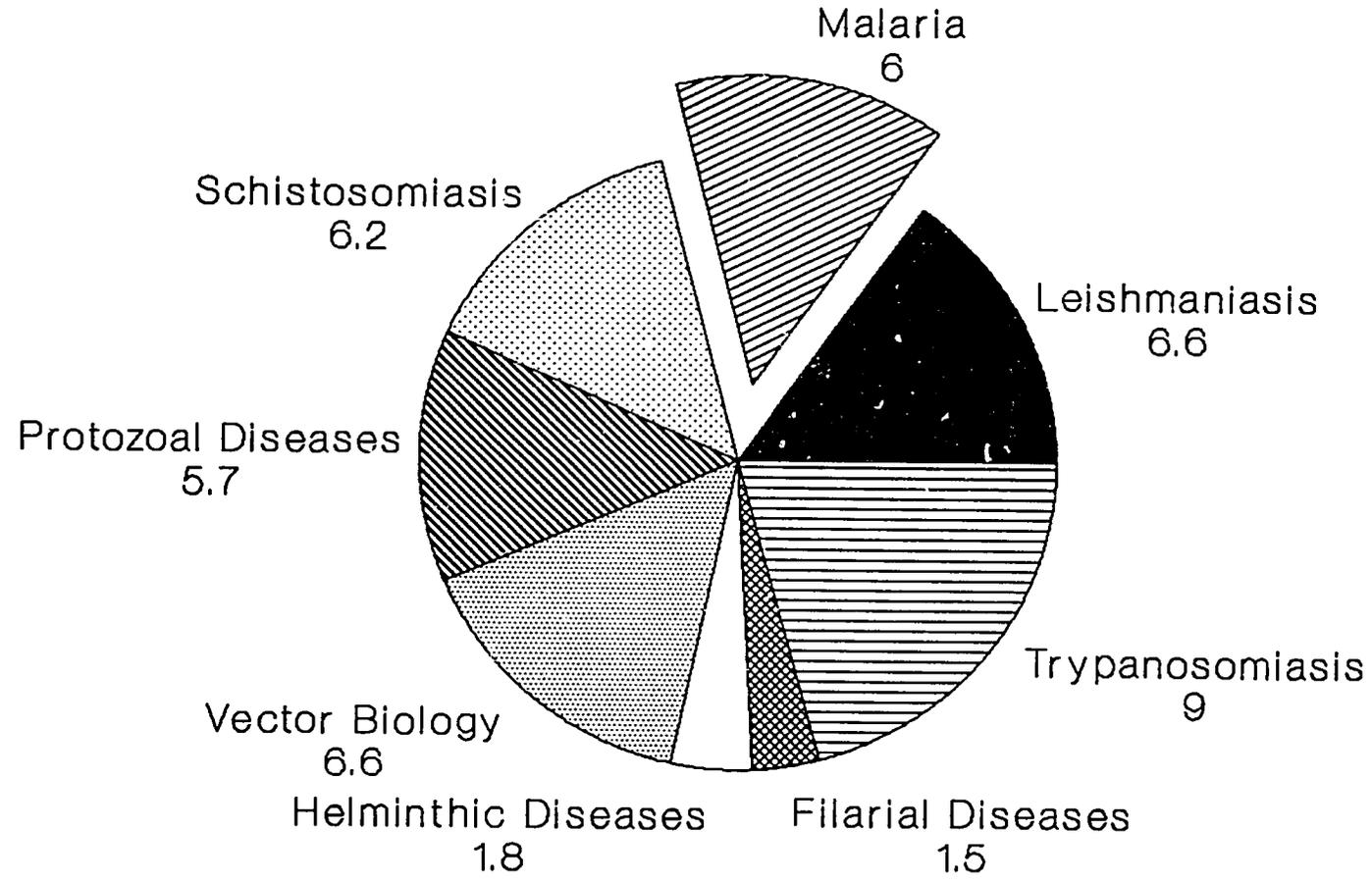
# PTDB Funding: 1981 - 1991



Source: NIAID Award Books, 1981-1990

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# Distribution of funds in PTDB: 1990 (million \$)

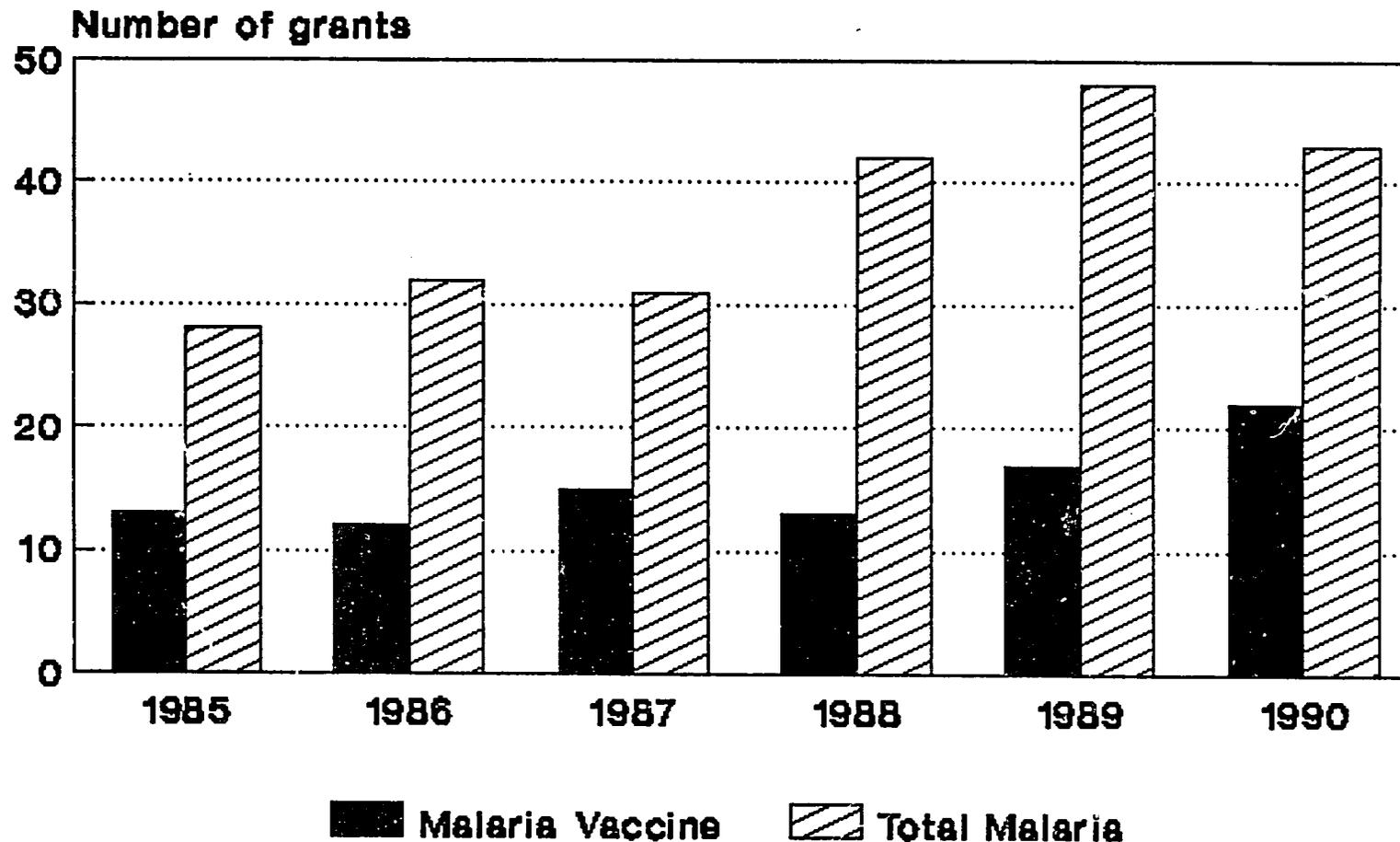


**Total \$ grants: \$43.5**

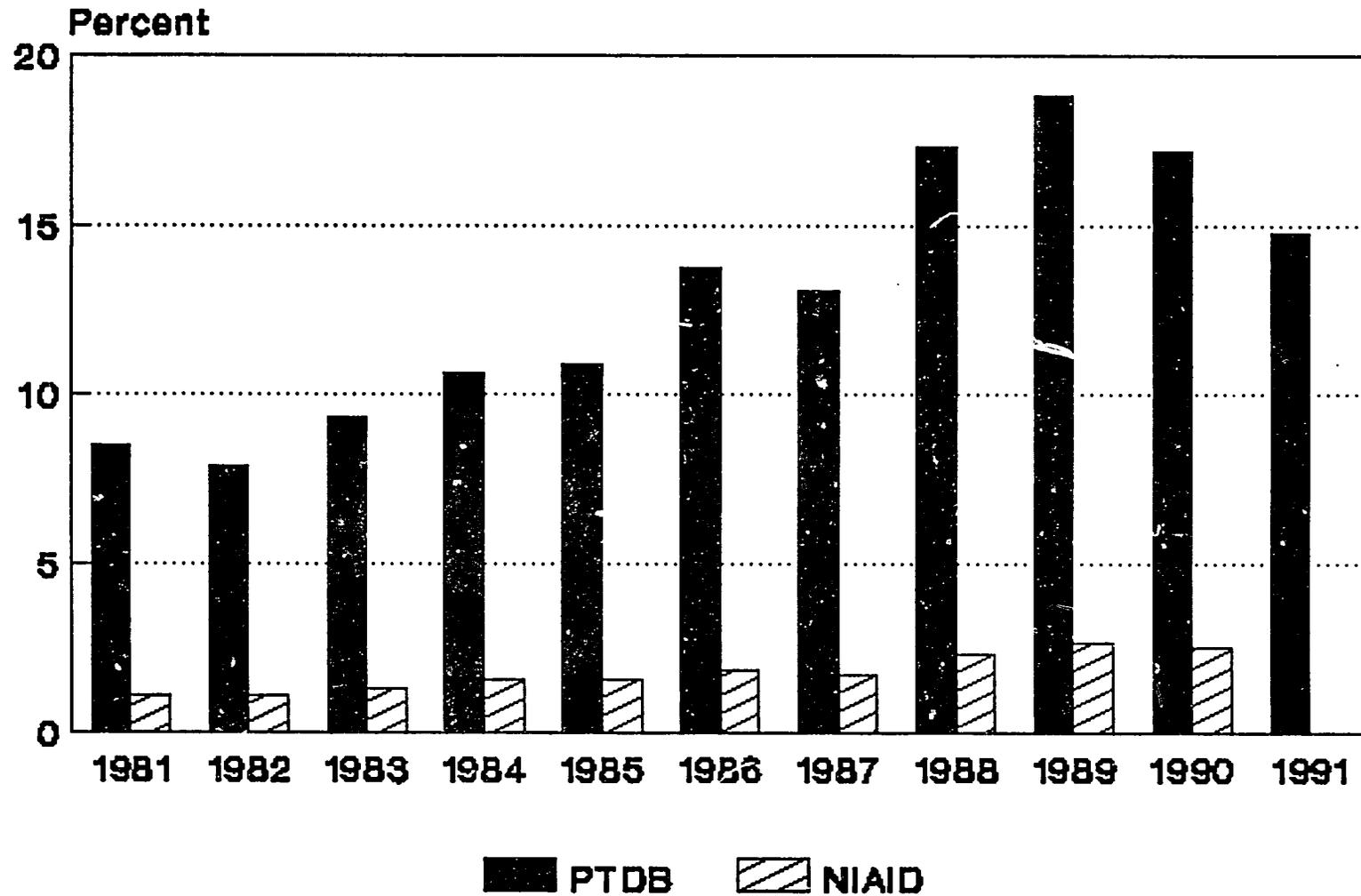
**Source: NIAID 1990 Awards Book**

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# Malaria Research Development 1985-90 Sponsored Vaccine Related Work



# Malaria as % of grants funded



Source: NIAID Award Books, 1981-1990

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RESEARCH GRANTS AND CAREER PROGRAMS  
ANIMAL PARASITES & PARASITIC DISEASES

INVESTIGATOR	GRANT NUMBER	AMOUNT	INSTITUTION/TITLE	BL
COCCIDIA & SARCOCYSTIS				
AINSWORTH, AVERY J	R15 AI 26264-01	0*	MISSISSIPPI STATE UNIVERSITY POTENTIAL USE OF ANTI-IDIOTYPE ANTIBODIES AS VACCINES	40
	1	----- 0		
PLASMODIA				
AIKAWA, MASAMICHI	R22 AI 10645-19	114,296	CASE WESTERN RESERVE UNIVERSITY ELECTRON MICROSCOPY OF PLASMODIUM HOST INTERACTIONS	40
BARNWELL, JOHN W	R22 AI 24710-04	137,827	NEW YORK UNIVERSITY MOLECULAR ANALYSIS OF PLASMODIUM VIVAX SURFACE ANTIGENS	40
BEIER, JOHN C	R22 AI 29000-01	190,143	JOHNS HOPKINS UNIVERSITY, BALTIMORE ANOPHELES VECTOR POTENTIAL FOR MALARIA TRANSMISSION	40
BREY, ROBERT N, III	R01 AI 25232-03	250,000	PRAXIS BIOLOGICS, INC. ORAL MALARIA VACCINE DEVELOPMENT IN A P. BERGHEI MODEL	40
BZIK, DAVID J	R29 AI 26651-03	105,350	DARTMOUTH COLLEGE GENE EXPRESSION AND REGULATION IN P. FALCIPARUM	40
CHANG, SANDRA P	R29 AI 27130-02	93,184	HAWAII, UNIV OF, MANOA B CELL & T CELL RECOGNITION SITES OF P FALCIPARUM GP195	40
DE LA CRUZ, VIDAL F	R43 AI 29761-01A1	46,766	MOLECULAR VACCINES, INC. USE OF RECOMBINANT MYCOBACTERIAL VACCINES FOR MALARIA	33
FEAGIN, JEAN E	R29 AI 25513-03	115,772	SEATTLE BIOMEDICAL RESEARCH INSTITUTE MITOCHONDRIAL GENES OF PLASMODIUM FALCIPARUM	40

(\* )=ACTIVE; NO FY 1990 FUNDS

RESEARCH GRANTS AND CAREER PROGRAMS  
ANIMAL PARASITES & PARASITIC DISEASES

INVESTIGATOR	GRANT NUMBER	AMOUNT	INSTITUTION/TITLE	BR.
PLASMODIA				
JODSON, G NIGEL	R22 AI 21494-07	173,243	NEW YORK UNIVERSITY MOLECULAR BIOLOGY OF THE MALARIA ORGANISM PLASMODIUM	40
HALDAR, KASTURI	R22 AI 26670-03	224,649	STANFORD UNIVERSITY RECEPTOR MEDIATED PINOCYTOSIS IN PLASMODIUM	40
HOWARD, RANDALL F	R29 AI 24520-03	115,135	SEATTLE BIOMEDICAL RESEARCH INSTITUTE RHOPTRY ANTIGENS OF PLASMODIUM FALCIPARUM MEROZOITES	40
INSELBURG, JOSEPH W	R22 AI 20437-08	194,186	DARTMOUTH COLLEGE ISOLATION AND STUDY OF MUTANTS OF PLASMODIUM FALCIPARUM	40
INSELBURG, JOSEPH W	R22 AI 22038-06	156,800	DARTMOUTH COLLEGE PLASMODIUM FALCIPARUM ANTIGENS FOR VACCINE PRODUCTION	40
JENSEN, JAMES B	P01 AI 16312-12	286,200	BRIGHAM YOUNG UNIVERSITY COLLABORATIVE RESEARCH ON PARASITIC DISEASES IN SUDAN	90
KILEJIAN, ARAXIE	R22 AI 19845-08	280,265	PUBLIC HLTH RES INST OF THE CITY OF NY HOST-PARASITE INTERACTIONS IN MALARIA	40
KUMAR, NIRBHAY	R29 AI 24704-04	108,737	JOHNS HOPKINS UNIVERSITY, BALTIMORE MEMBRANE ANTIGENS OF P. FALCIPARUM ANTI-GAMETE IMMUNITY	40
LANNERS, H NORBERT	R22 AI 26189-03	88,857	TULANE UNIVERSITY OF LOUISIANA IN VITRO CULTIVATION/MALARIA PARASITE PLASMODIUM VIVAX	40
LONG, CAROLE A	R01 AI 21089-05	159,640	HAHNEMANN UNIVERSITY IDIOTYPY AND IMMUNITY TO MALARIA	40
MESHNICK, STEVEN R	R22 AI 26848-01A2	174,129	CITY COLLEGE OF NEW YORK OXIDANT EFFECTS IN MALARIA-INFECTED ERYTHROCYTES	40

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RESEARCH GRANTS AND CAREER PROGRAMS  
ANIMAL PARASITES & PARASITIC DISEASES

INVESTIGATOR	GRANT NUMBER	AMOUNT	INSTITUTION/TITLE	BR.
PLASMODIA				
MIKKELSEN, ROSS B	R22 AI 24307-03	0*	VIRGINIA COMMONWEALTH UNIVERSITY VACUOLAR & MEMBRANES OF ISOLATED PLASMODIUM	40
HARDIN, ELIZABETH H	R29 AI 25085-04	116,160	NEW YORK UNIVERSITY T CELL EPITOPES OF THE MALARIA CS PROTEINS	40
NUSSENZWEIG, RUTH S	P01 AI 21642-05	0*	NEW YORK UNIVERSITY FUNCTION AND VARIABILITY OF PLASMODIAL ANTIGENS	40
PERKINS, MARGARET E	R22 AI 19585-08	228,828	ROCKEFELLER UNIVERSITY BIOCHEMICAL STUDIES ON ERYTHROCYTE INVASION BY PLASMODIA	40
RATHOD, PRADIPSINH K	R29 AI 26912-02	89,080	CATHOLIC UNIVERSITY OF AMERICA ANTIMALARIAL ACTIVITY OF OROTIC ACID ANALOGS	40
ROSSIGNOL, PHILIPPE A	R22 AI 27649-03	140,674	OREGON STATE UNIVERSITY MOSQUITO PROBING BEHAVIOR AND MALARIA EPIDEMIOLOGY	40
SHEAR, HANNAH L	R01 AI 15235-12A2	185,660	NEW YORK UNIVERSITY MACROPHAGE ACTIVATION IN EXPERIMENTAL MALARIA	40
SHERMAN, IRWIN W	R22 AI 21251-03	81,481	CALIFORNIA, UNIVERSITY OF, RIVERSIDE ERYTHROCYTE-ENDOTHELIAL INTERACTIONS IN MALARIA	40
STEWART, MICHAEL J	R29 AI 24615-03	109,501	NEW YORK UNIVERSITY MOTILITY AND INVASIVENESS OF PLASMODIUM SPOROZOITES	40
TARASCHI, THEODORE F	R22 AI 27247-02	167,480	THOMAS JEFFERSON UNIVERSITY MEMBRANE TRAFFICKING IN MALARIA INFECTED ERYTHROCYTES	40
TAYLOR, DIANE WALLACE	R22 AI 26153-02	129,844	GEORGETOWN UNIVERSITY RODENT MALARIAL ANTIGEN--PY117	40

(\*)=ACTIVE; NO FY 1990 FUNDS

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RESEARCH GRANTS AND CAREER PROGRAMS  
ANIMAL PARASITES & PARASITIC DISEASES

INVESTIGATOR	GRANT NUMBER	AMOUNT	INSTITUTION/TITLE	BR.
PLASMODIA				
TAYLOR, TERRIE E	R01 AI 25568-03	13,520	MICHIGAN STATE UNIVERSITY IMMUNOTHERAPY IN PEDIATRIC CEREBRAL MALARIA	40
VAIDYA, AKHIL B	R22 AI 28398-02	176,685	HAHNEMANN UNIVERSITY ORGANELLE GENOMES OF MALARIAL PARASITES	40
VANDER JAGT, DAVID L	R22 AI 21214-07	104,150	NEW MEXICO, UNIVERSITY OF, ALBUQUERQUE PROTEIN DEGRADATION IN P FALCIPARUM	40
VANDERBERG, JEROME P	R22 AI 24528-02	173,325	NEW YORK UNIVERSITY PLASMODIUM SPOOROZOITE--HOST CELL INTERACTIONS	40
VEZZA, ANNE C	R22 AI 20597-06	185,386	ALABAMA, UNIVERSITY OF, BIRMINGHAM TRANSCRIPTIONAL ANALYSES OF THE P. FALCIPARUM RRNA GENES	40
WASSOM, DONALD L	R22 AI 26904-02	142,911	WISCONSIN, UNIVERSITY OF, MADISON IMMUNOREGULATION IN MURINE MALARIA	40
WEIDANZ, WILLIAM P	R01 AI 12710-15	228,407	WISCONSIN, UNIVERSITY OF, MADISON MECHANISMS OF NONSTERILIZING IMMUNITY IN MALARIA	40
WELSH, KATHERINE M	R44 AI 25996-03	253,012	AGOURON PHARMACEUTICALS, INC. SITE-DIRECTED DRUG DESIGN AGAINST PLASMODIUM FALCIPARUM	40
WIRTH, DYANN F	R22 AI 27872-01A1	154,308	HARVARD UNIVERSITY GENETIC BASIS OF DRUG RESISTANCE IN P FALCIPARUM	40
WRIGHT, D CRAIG	R43 AI 29775-01	49,170	UNIVAX CORPORATION SYNTHETIC CONJUGATE VACCINES AGAINST FALCIPARUM	40
ZAVALA, FIDEL	R29 AI 27458-02	107,953	NEW YORK UNIVERSITY ROLE OF T CELLS IN OF ANTISPOOROZOITE IMMUNITY	40
	41	5,852,714		

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RESEARCH GRANTS AND CAREER PROGRAMS  
ANIMAL PARASITES & PARASITIC DISEASES

INVESTIGATOR	GRANT NUMBER	AMOUNT	INSTITUTION/TITLE	BR.
MOSQUITOES				
CHRISTENSEN, BRUCE M	R37 AI 19769-08	188,249	WISCONSIN, UNIVERSITY OF, MADISON IMMUNE RESPONSE OF MOSQUITOES TO FILARIAL WORMS	40
CRAIG, GEORGE B, JR	R37 AI 02753-31	297,822	NOTRE DAME, UNIVERSITY OF VECTOR COMPETENCE FOR LA CROSSE VIRUS IN AEDES	40
EDGERLY-ROOKS, JANICE S	R15 AI 28039-01A1	89,003**	SANTA CLARA, UNIVERSITY OF EFFECT OF LARVAL BEHAVIOR ON MOSQUITO POPULATION ECOLOGY	40
FALLON, ANN M	R01 AI 20225-08	153,546	MINNESOTA, UNIVERSITY OF, MNPLS-ST PAUL SYNTHESIS AND DEGRADATION OF RIBOSOMES IN THE MOSQUITO	40
FOSTER, HOODBRIDGE A	R01 AI 24573-03	0*	OHIO STATE UNIVERSITY ETHOLOGY OF BLOOD/SUGAR ANTAGONISM IN MOSQUITOES	40
JAMES, ANTHONY A	R01 AI 29746-02	127,739	CALIFORNIA, UNIVERSITY OF, IRVINE EXPRESSION OF EXOGENOUS GENES IN VECTOR MOSQUITOES	40
JULIANO, STEVEN A	R15 AI 29629-01	101,198**	ILLINOIS STATE UNIVERSITY GEOGRAPHIC VARIATION IN AEDES TRISERIATUS	40
KLOWDEN, MARC J	R01 AI 24453-03	47,870	IDAHO, UNIVERSITY OF PHYSIOLOGY OF PRE-OVIPOSITION BEHAVIOR	40
LEA, ARDEN O	R01 AI 17297-11	207,283	GEORGIA, UNIVERSITY OF ENDOCRINOLOGY OF MOSQUITO REPRODUCTION	40
LIVDAHL, TODD P	R15 AI 27940-01	0*	CLARK UNIVERSITY (WORCESTER, MA) PREDICTING OUTCOMES OF THE AEDES ALBOPICTUS INVASION	40
HERRITT, RICHARD W	R01 AI 21884-06	127,664	MICHIGAN STATE UNIVERSITY FEEDING ECOLOGY OF LARVAL MOSQUITOES IN NATURAL HABITATS	40

(\*)=ACTIVE, NO FY 1990 FUNDS  
(\*\*)=REIMBURSABLE FUNDS

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RESEARCH GRANTS AND CAREER PROGRAMS  
ANIMAL PARASITES & PARASITIC DISEASES

INVESTIGATOR	GRANT NUMBER	AMOUNT	INSTITUTION/TITLE	DR.
MOSQUITOES				
APPAS, CAROL D	R15 AI 28044-01	0*	PERU STATE COLLEGE CHEMOSYSTEMATIC GEOGRAPHIC VARIATION IN AEDES ALBOPICTUS	40
RAI, KARAMJIT S	R01 AI 21443-07	129,198	NOTRE DAME, UNIVERSITY OF GENETIC DIFFERENTIATION IN AEDES ALBOPICIUS SUBGROUP	40
SUGUMARAN, MANICKAM	R01 AI 14753-12	263,368	MASSACHUSETTS, UNIVERSITY OF, BOSTON SCLEROTIN PRECURSORS IN DIPTERANS	40
	14	1,542,739		
PHLEBOTOMUS				
TITUS, RICHARD G	R01 AI 27511-02	131,963	HARVARD UNIVERSITY ROLE OF SANDFLY SALIVA IN LEISHMANIASIS	40
	1	131,963		
INSECTS, OTHER (DROSOPHILA)				
BRADFIELD, JAMES Y	R01 AI 28368-02	159,202	TEXAS A&I AND MECH UNIV COLLEGE STATION INSECT ADIPOKINETIC HORMONE GENE EXPRESSION	40
HILDEBRAND, JOHN G	R37 AI 23253-06	142,266	ARIZONA, UNIVERSITY OF CENTRAL MECHANISMS OF ANTENNAL SENSES IN INSECTS	40
HAPPI, ANTHONY J	R01 AI 24199-02	98,982	LOYOLA UNIVERSITY OF CHICAGO BIOCHEMICAL MECHANISMS IN INSECT IMMUNITY	40
NATHANSON, JAMES A	R01 AI 29533-01	194,349	MASSACHUSETTS GENERAL HOSPITAL STRUCTURE OF INSECT NEUROTRANSMITTER RECEPTORS	40

(\*)=ACTIVE; NO FY 1990 FUNDS

**NIAID INTRAMURAL PROGRAM**  
**Laboratory of Malaria Research**

**TRANSMISSION BLOCKING VACCINE**

**BASIC RESEARCH**

*Molecular Vaccine Section*

Kim Williamson

Pat Duffy

Michal Fried

Mohammed Shahabuddin

David Keister

**VACCINE DEVELOPMENT**

**Yeast**

*Chiron Corporation*

Ian Bathurst

Phil Barr

**Vaccinia/Live virus vectors**

*LVD, NIAID*

Stuart Isacacs

Bernie Moss

*US Army*

Joel Dalrymple

*Virogenetics*

Enzo Paoletti

**Bacterial/Mammalian**

*Smith, Kline, Beecham*

Mitch Gross

**NIAID INTRAMURAL PROGRAM**  
**Laboratory of Malaria Research**

***Plasmodium vivax* DUFFY RECEPTOR**  
**RED BLOOD CELL INVASION**

**BASIC RESEARCH**

*Cell Biology and Immunology Section*

Chatan Chitinis

Diana Hudson

Louis H. Miller

**VACCINE DEVELOPMENT**

**Yeast/Mammalian Cell**

*Chiron Corporation*

Ian Bathurst

Phil Barr

**NIAID INTRAMURAL PROGRAM  
Laboratory of Malaria Research**

***Plasmodium vivax* DUFFY RECEPTOR  
RED BLOOD CELL INVASION**

**Immediate goals:**

**Mammalian cell expression  
Immunogenicity  
Identify domains involved in erythrocyte binding  
Invasion blocking activity  
Polymorphism**

**NIAID INTRAMURAL PROGRAM  
Laboratory of Malaria Research**

**-TRANSMISSION BLOCKING VACCINE**

**-*Plasmodium vivax* DUFFY RECEPTOR (RED BLOOD CELL INVASION)**

**-ASEXUAL VACCINE**

NIAID INTRAMURAL PROGRAM  
Laboratory of Malaria Research

TRANSMISSION BLOCKING VACCINE

Immediate Goals:

- Pfs230-** Complete cloning and DNA sequencing  
Bacterial/mammalian cell expression  
B and T cell epitope mapping
- Pfs40-** Yeast/mammalian cell expression  
Transmission blocking activity  
B and T cell epitope mapping
- Pfs28-** Clone and sequence gene  
Yeast/vaccinia/mammalian cell expression  
Transmission blocking activity  
P. vivax equivalent
- Pfs25-** Preclinical/Phase I human trials  
Aotus vociferans monkey trial  
-in vivo efficacy  
-boosting following natural infection  
P. vivax equivalent
- Chitinase-** Clone and sequence gene  
Recombinant expression  
Transmission blocking activity

**STAC 1992**  
**PDU Budget forecast**

**1992 to 1991**

<b>Malaria</b>	
• Artemesenin	800.0
• BC-7	350.0
• Pfs 25	600.0
• Drug assay	150.0
<b>Schistosomiasis</b>	
• Multidisease	200.0
<b>Leishmaniasis</b>	
• LAMBS	300.0
• DAT.VL	250.0
<b>African Tryps.</b>	000.0
<b>Filariasis</b>	
• UMF 078	350.0
<b>Total allocated</b>	<b>3000.0</b>

**budsum**

**Malaria vaccine development  
TDR PDU**

<u>Objective</u>	<u>Activity</u>	<u>Status</u>
Treatment for cerebral malaria	Pilot study CB-6	Completed
	Pilot study BC-7	Completed
	Phase III trial BC-7 & artemether	Planned Fall 1992
Transmission blocking vaccine	Phase I & II Pfs 25Kd	Planned Fall 1992

aid3

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# Malaria Vaccine Development Efforts WHO

<u>Program</u>	<u>Objectives</u>	<u>Budget 1992</u>
TDR	R&D, 6 diseases	23,281.0
TDR-IMMAL	Malaria immunology	2,338.0
TDR-PDU	Product development	2,515.0
WHO-PVD	Vaccine research	-
WHO-CVI	Childrens vaccines	-

aid1

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# Malaria vaccine development efforts

## IMMAL Workplan, 1992-1993

<u>Objectives</u>	<u>Plans</u>	<u>Activities</u>
Vaccine development	Basic research	T&B antigens T cell immunity Role of cytokines in vitro assays
Combat severe malaria	Understand pathology  Identify therapies	CM, man & rodents Role of cytokines  TNF antagonists Chemotherapy
Diagnostics	Examine antigens antibodies	

<u>OBJECTIVES:</u>	<u>PLANS:</u>	<u>ACTIVITIES:</u>	<u>PRIORITY:</u>
To develop effective malaria vaccines	To promote research on the basic understanding of the mechanism(s) of protective immunity in malaria.	Identification of relevant T and B cell antigens/epitopes for the pre-erythrocytic, asexual and sexual forms of malaria parasites.	A
		Characterization of T cell immunity in immune individuals.	A
		Analysis of the role of cytokines in protective immunity.	A
		Development of improved <u>in vitro</u> assays for assessment of protective immunity in humans.	A
		Testing the cellular immune responses against malaria present in HIV <sup>+</sup> malaria patients and HIV <sup>+</sup> controls.	B
To identify and develop promising vaccine candidates.	To identify and develop promising vaccine candidates.	Identification and preclinical development of promising candidate vaccines to protect against disease and/or malaria infection.	A
		Elaboration of guidelines for malaria vaccine trials. Evaluation of vaccine candidates for safety/immunogenicity. Evaluation of selected candidates for vaccine efficacy.	B
			A
To promote the conduct of human vaccine trials (with TDR/PDU).	To promote the conduct of human vaccine trials (with TDR/PDU).	Evaluation of selected candidates for vaccine efficacy.	A
			A
To understand and prevent the (immuno)pathology seen in severe malaria	To investigate the pathogenic mechanisms involved in severe malaria.	Deliniation of the pathology of cerebral malaria in rodent models and in man.	B
		Define the role of TNF & other cytokines in cerebral malaria.	A
		Investigation of host and parasite phenotypes as possible risk factors for severe malaria (with FIELDMAL).	B
To identify and develop novel therapeutic regimens for treatment of cerebral malaria.	To identify and develop novel therapeutic regimens for treatment of cerebral malaria.	Clinical trials of TNF antagonists (with TDR/PDU).	A
		Evaluation of combined therapy with drug agonists/antagonists (with CHEMAL).	B
To develop and evaluate new tools for diagnosis and monitoring of malaria and its transmission	To promote research on the detection of malaria parasites, antigens and antibodies in humans and relevant vectors (with FIELDMAL and CTD/MAL).	Analysis of immune responses to malaria in field studies of naturally-exposed populations, and impact of chemotherapy.	B
		Evaluation of the role of test kits for sporozoite, blood stage antigen and blood meal detection.	C
		Evaluation of PCR-based tests for malaria, including epidemiology and identification of naturally occurring and vaccine-induced strain variants in infected individuals.	B

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PRODUCT DEVELOPMENT UNIT - WORKPLAN 1992-1993

MAJOR DIRECTIONS	COLLABORATING STEERING COMMITTEE	SPECIFIC ACTIVITIES	STATUS	PRIORITY
<b>1. MALARIA</b>				
1.1 Develop novel treatments for severe and cerebral malaria	Immunology of Malaria	(a) Phase II trial anti-tumour necrosis factor MAB B-C7	Completed January 1992	
		(b) Multicentre Phase III trials anti-tumour necrosis factor MAB B-C7 - Clinical plans - Clinical studies	March 1992- March 1993 June 1992 Oct. 1992/June 1993	A
		(c) Advise and assist with Centochor proposed trials	Ongoing	B
		(d) Identify low molecular weight TNF antagonists	Ongoing 1992-1993	B
		(e) Assist in French registration of artemether - Complete regulatory dossier file for registration	December 1992	A
1.2 Development of malaria vaccines	Immunology of Malaria	(a) Malaria transmission blocking vaccine Pfs 25: - Complete preclinical development - File IND - Phase I trials Washington - Phase I(b) Kenya - Phase II Kenya	Planned to begin: March 1992 March 1992 April-June 1992 June-Sept. 1992 September 1992	A A A
		(b) Other vaccines: - Bring at least one blood stage antigen and one exoerythrocytic antigen to development	December 1993	B
		- With IMMAL review vaccine clinical studies	October 1993	B
		- With IMMAL review TBV guidelines	April 1992	C
1.3 Malaria diagnostics	Applied Field Research in Malaria	(a) Test to determine drug levels in body fluids: - Complete field testing of kit - Seek commercial manufacturer	Trials planned to begin: December 1992 December 1993	A

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## Malaria vaccine development Pharmaceutical industry

<u>Company</u>	<u>Projects</u>	<u>Status</u>
SmithKline Beecham	Multiple sporozoite vaccines. RecDNA vaccines E.coli/yeast expr.	Phase III studies improved responses; efficacy critical to continuation;
Hoffmann-LaRoche	Sporozoite vaccine synthetic vaccine; rec DNA vaccines	Poor responses; Phase III
HLR-Suramane	merozoite vaccines	Preclinical
Behringwerke	Merozoite vaccines E.coli expression	Preclinical Primate protection

## DOD Malaria Vaccine Program

WRAIR - Dept of Immunology  
Dept of Bacterial Diseases  
Dept of Bacterial Immunology

NMRI - Malaria Program

Special Foreign Activities

AFRIMS  
USAMRU-K  
NAMRU - Jakarta

## DOD Malaria Vaccine Development Program



# Objectives

## Basic Research

- Develop molecular/immunological basis for malaria vaccines
- Identify, clone, and sequence candidate parasite antigens
- Assess functional regions of target antigens
- Develop methods of measuring protective responses
- Characterize vaccine candidates using in vitro and in vivo models

# Objectives

## Exploratory Development

- Expression of recombinantly expressed malaria antigens
- Production of synthetic peptide malaria vaccines
- Establishment of fermentation and protein purification capabilities
- Development of live attenuated vaccines expressing malaria genes
- Development of novel antigen delivery and presentation systems
- Identification of cellular immune mechanisms involved in protection

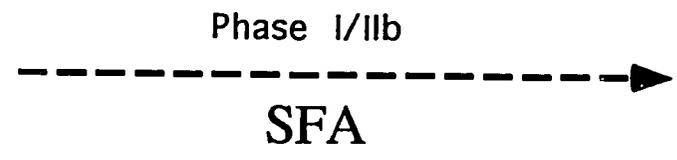
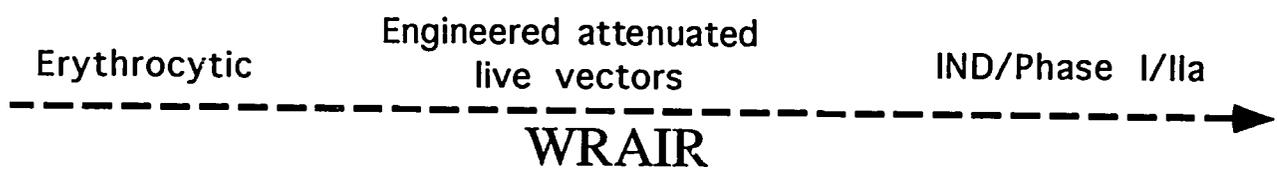
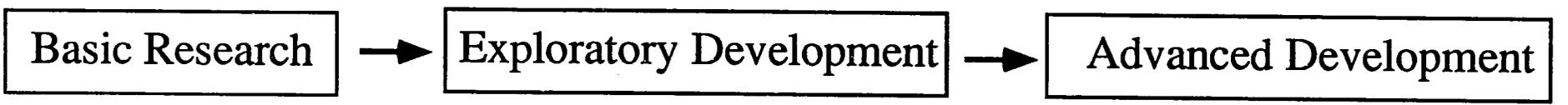
17

## Objectives

### Advanced Development

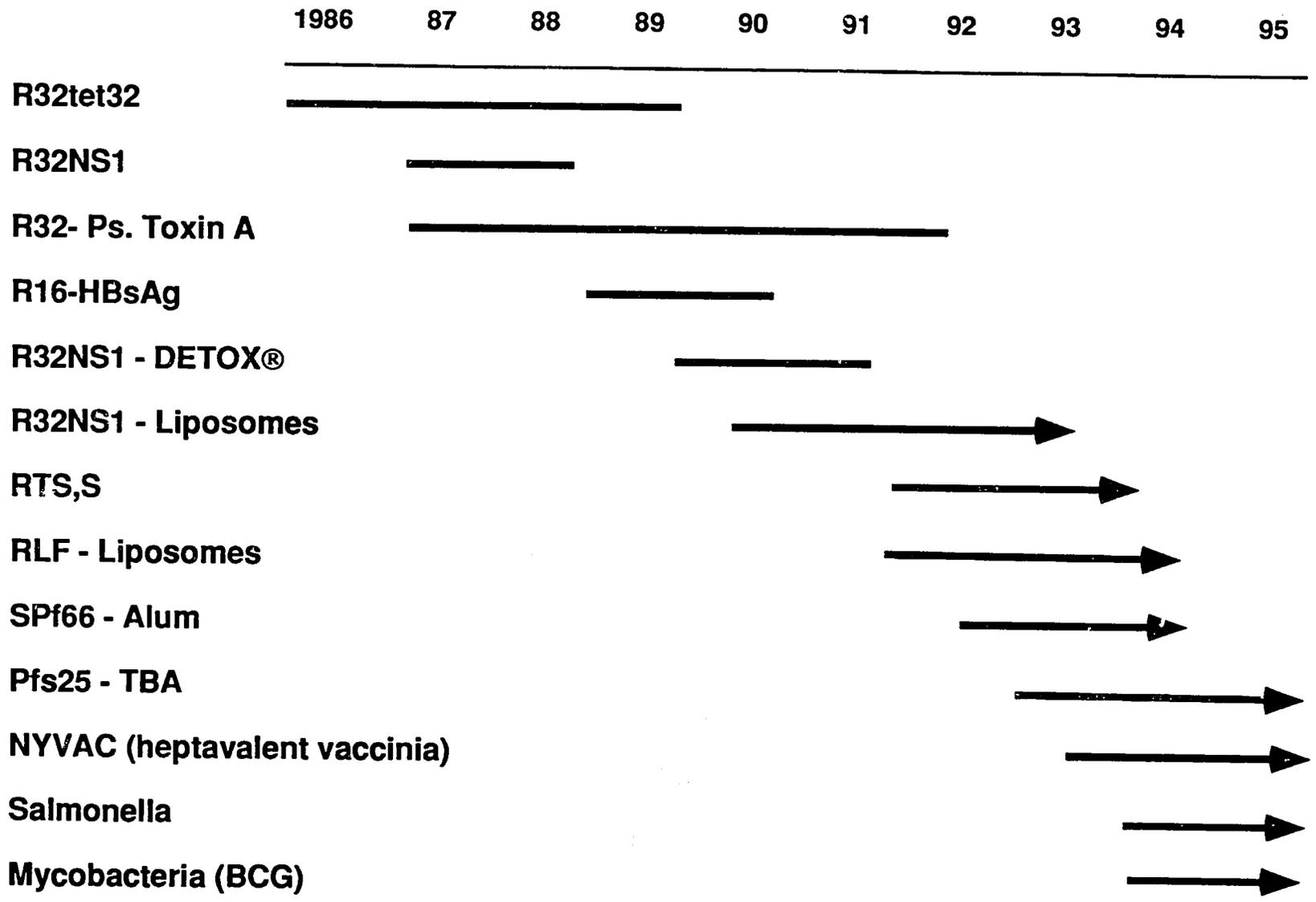
- Formulation, preclinical studies, IND preparation
- Experimental vaccine studies in primate models
- Phase I studies for safety and immunogenicity in human volunteers
- Phase IIa studies for safety, immunogenicity & experimental challenge
- Phase IIb studies for safety, immunogenicity & natural challenge
- Serological and cellular immunology support for vaccine studies

# DOD Malaria Vaccine Development Program



# *P. falciparum* malaria vaccine trials in humans

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# Malaria vaccine development

## Pharmaceutical industry

<u>Company</u>	<u>Projects</u>	<u>Status</u>
SmithKline Beecham	Multiple sporozoite vaccines. RecDNA vaccines E.coli/yeast expr.	Phase III studies improved responses; efficacy critical to continuation;
Hoffmann-LaRoche	Sporozoite vaccine synthetic vaccine; rec DNA vaccines	Poor responses; Phase III
HLR-Suramane	merozoite vaccines	Preclinical
Behringwerke	Merozoite vaccines E.coli expression	Preclinical Primate protection

## Review of Malaria Vaccine Efforts Outside A.I.D.

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### **NON—INDUSTRIAL EFFORTS OUTSIDE U.S.A.**

#### United Kingdom

- ❖ London School—transmission blocking immunity (Targett).
- ❖ Imperial College, London—pre-erythrocytic immunity (Sinden)
- ❖ National Institute for Medical Research, Mill Hil—gp195 (Holder), immunol (Brown).
- ❖ Middlesex School of Medicine, London—nonspecific immunity (Playfair).
- ❖ University of Edinburg—parasite genetics (Walliker, Carter).
- ❖ Wellcome Malaria Research Unit, Kalifi, Kenya—clinical immunology (Marsh).
- ❖ MRC Laboratories, The Gambia—clinical immunology (Greenwood).

## Review of Malaria Vaccine Efforts Outside A.I.D.

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### NON—INDUSTRIAL EFFORTS OUTSIDE U.S.A. (CONTINUED)

#### The Netherlands

- ❖ University of Nijmegen—transmission blocking immunity (Meuwissen).
- ❖ TNO—Chimpanzee model, liver stage antigens (Mons), Pf83 (Thomas).

#### France

- ❖ Institute Pasteur—blood stage, liver stage antigens (da Silva, Druile).
- ❖ Groupe Pitié-Salpêtrière, Paris—Immunology (Mazier).

## Review of Malaria Vaccine Efforts Outside A.I.D.

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### NON—INDUSTRIAL EFFORTS OUTSIDE U.S.A. (CONTINUED)

#### Australia

- ❖ Walter & Eliza Hall Institute, Melbourne—blood stage antigens (Anders).
- ❖ Queensland Institute, Brisbane—bloodstage antigens, immunology (Saul, Good).
- ❖ Australian National University, Canberra—nonspecific immunity (Clark).

#### Sweden

- ❖ Stockholm University—RESA, immune mechanisms.

#### Canada

- ❖ Montreal General Hospital Research Institute—role of cytokines (Stevenson)

## Review of Malaria Vaccine Efforts Outside A.I.D.

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### NON—INDUSTRIAL EFFORTS OUTSIDE U.S.A. (CONTINUED)

#### Sri Lanka

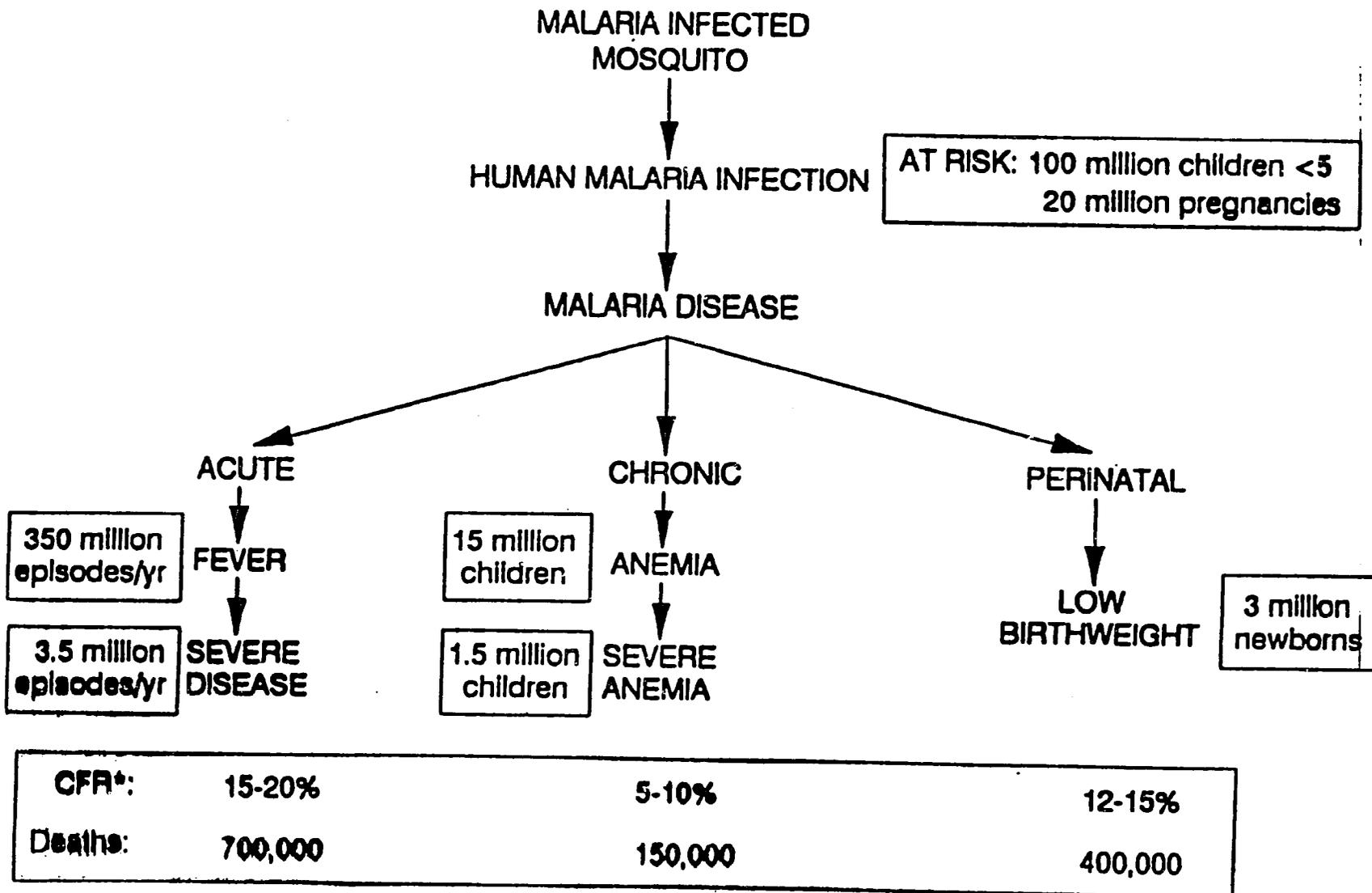
- ❖ University of Colombo—transmission blocking, nonspecific immunity (Mendis)

#### Colombia

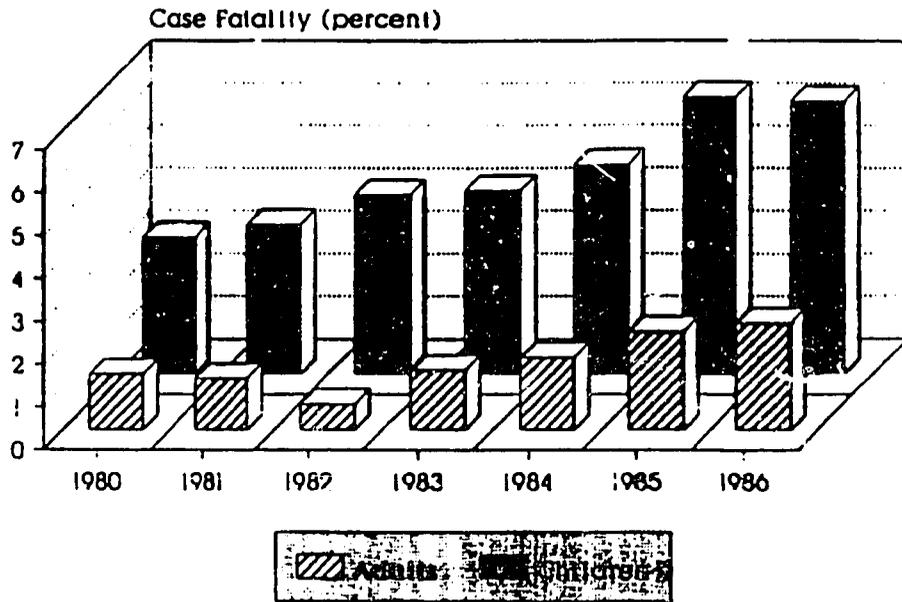
- ❖ Universidad de Valle, Cal—nonhuman primate trials, clinical immunology (Herrera)
- ❖ Universidad Nacional de Colombia, Bogotá—experimental vaccines (Patarroyo)

# MALARIA AND CHILD SURVIVAL - AFRICA

18

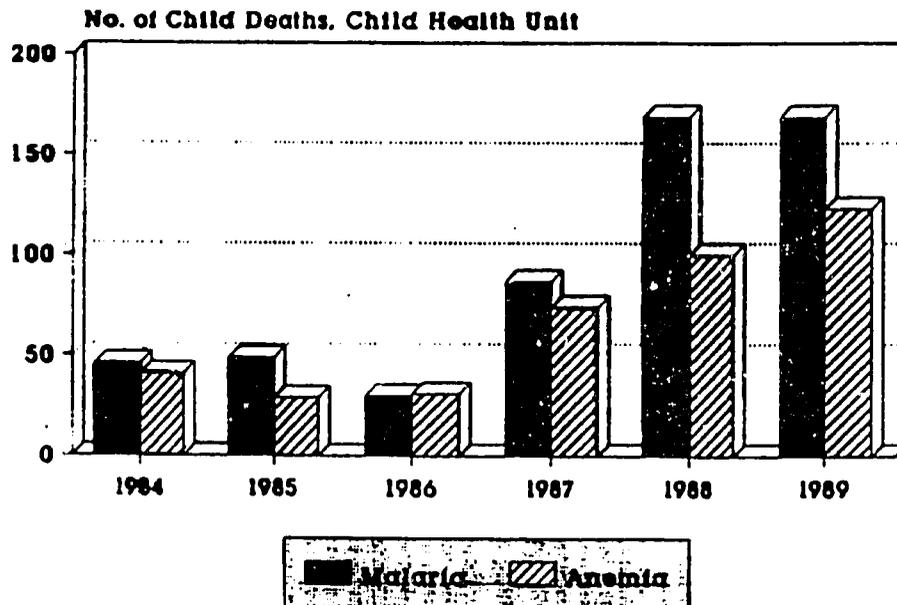


## IMPACT OF CHLOROQUINE RESISTANCE CASE FATALITY IN ZAMBIA: 1980-1986



Source: CCCD

## IMPACT OF CHLOROQUINE RESISTANCE CASE FATALITY IN TOGO: 1984-1989



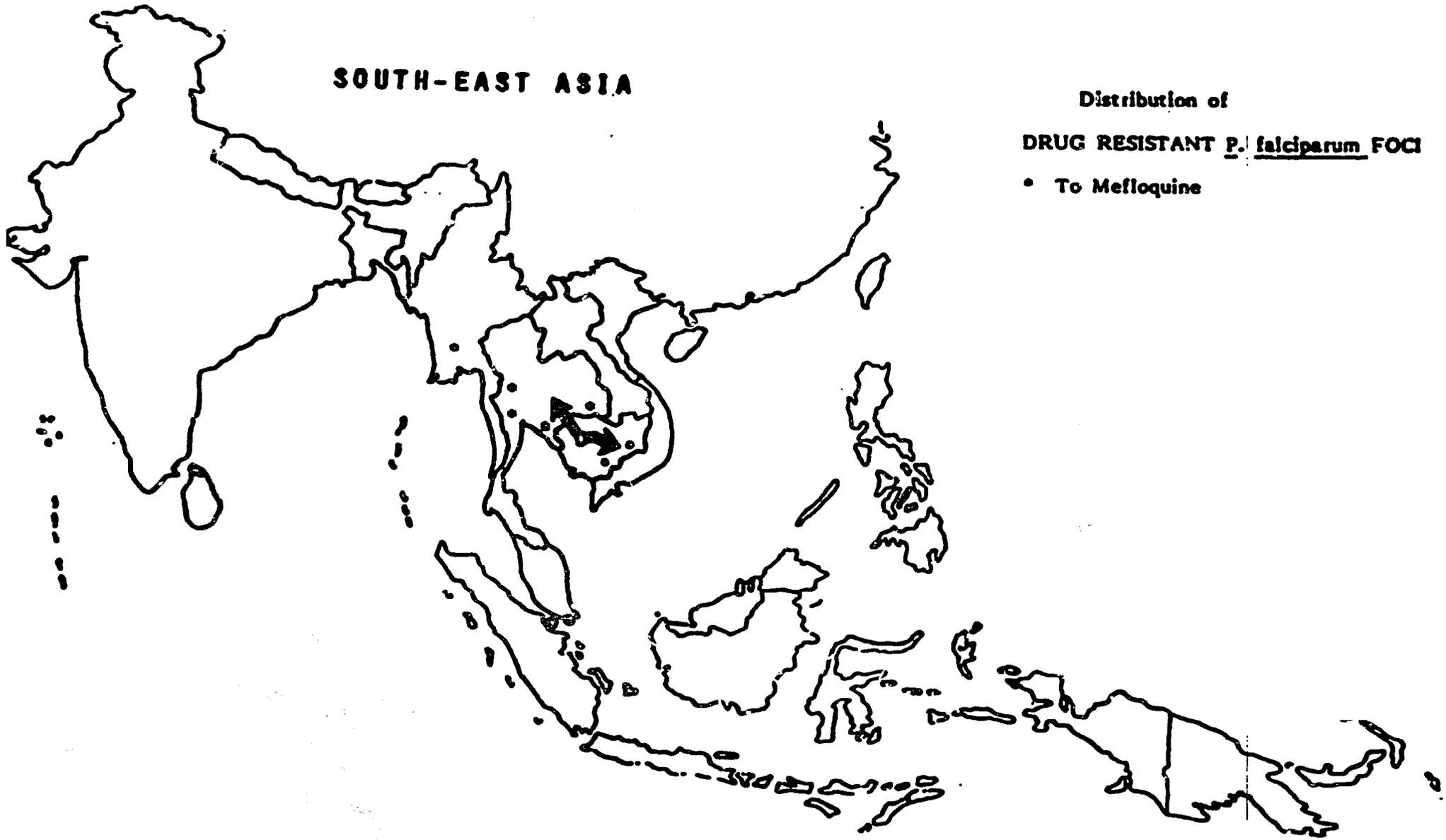
Source: CCCD

42

# SOUTH-EAST ASIA

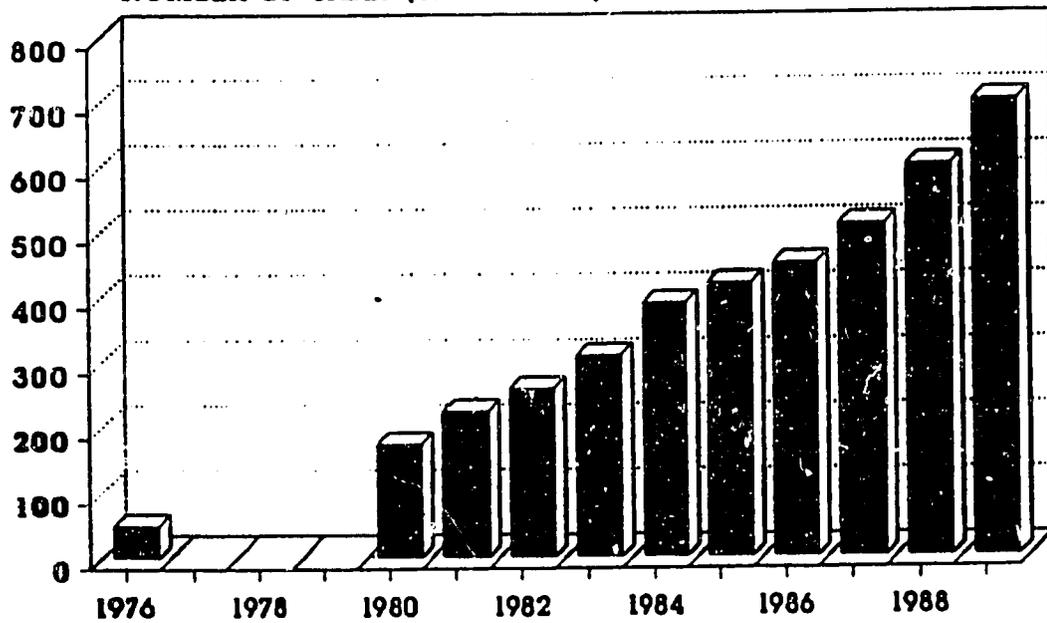
Distribution of  
DRUG RESISTANT P. falciparum FOCI

• To Mefloquine



# IMPACT OF DEVELOPMENT MALARIA IN THE AMAZON REGION

NUMBER OF CASES (THOUSANDS)



## **GENERAL STRATEGY**

- **PREVENTION** through the use of chemoprophylaxis and personal prevention devices
- **TREATMENT** by providing timely and effective diagnosis and care for malaria cases
- **CONTROL** through early detection or forecasting of epidemics and rapid application of control measures

**TARGET STRENGTHENING INSTITUTIONAL CAPABILITIES**

1/25

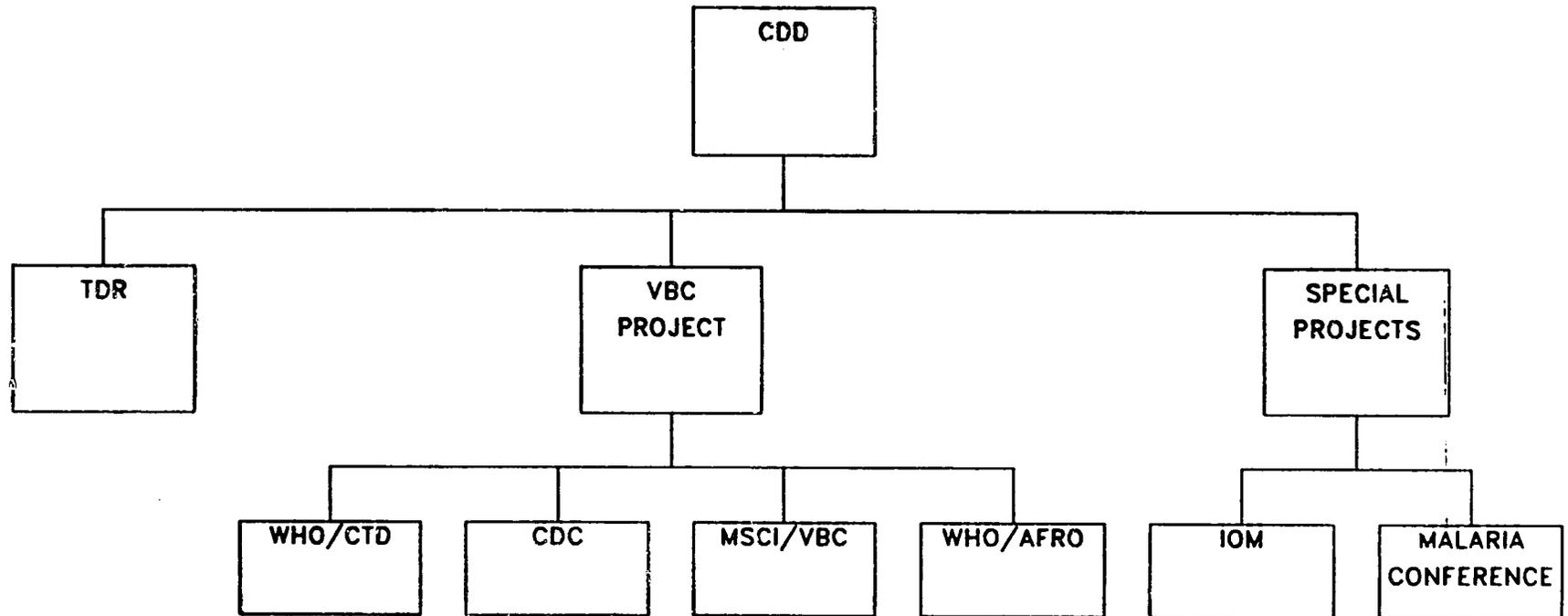
## **CAPABILITY TRANSFER**

- **SURVEILLANCE**
- **MANAGEMENT**
- **HEALTH EDUCATION**
- **OPERATIONS RESEARCH**

9/5

# R&D/H PORTFOLIO

## MALARIA PREVENTION AND CONTROL



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## TDR

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- **SUPPORTS 5000 TROPICAL DISEASE RESEARCHERS WORLDWIDE**
- **STRENGTHENS THE CAPACITY OF LDCs IN RESEARCH AND DEVELOPMENT**
- **TRAINS PEOPLE IN LDCs IN DETECTECTING AND RESPONDING TO THEIR MAJOR HEALTH PROBLEMS**
- **SUPPORTS THE DEVELOPMENT OF NEW DRUGS, VACCINES, DIAGNOSTIC TESTS AND CONTROL METHODS**

## **CDC PASA**

### **Objectives**

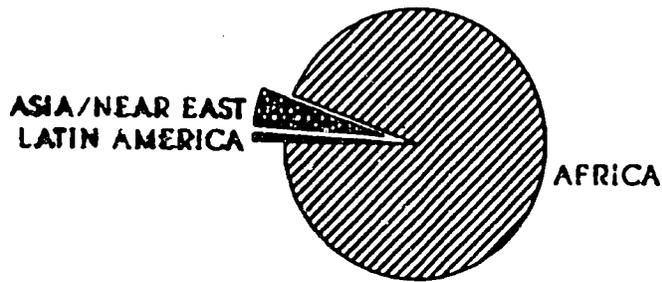
- Technical Assistance to A.I.D. assisted tropical disease control programs**
- b. Collaboration with the VBC project on directions, strategies, and priorities over the life of the VBC project.**
- c. Co-ordination with A.I.D. and CDC activities as they relate to tropical diseases.**
- d. To provide on request Laboratory Analysis of insecticides and pharmaceuticals to ensure quality.**

## **WHO/CTD GRANT**

### **Objectives**

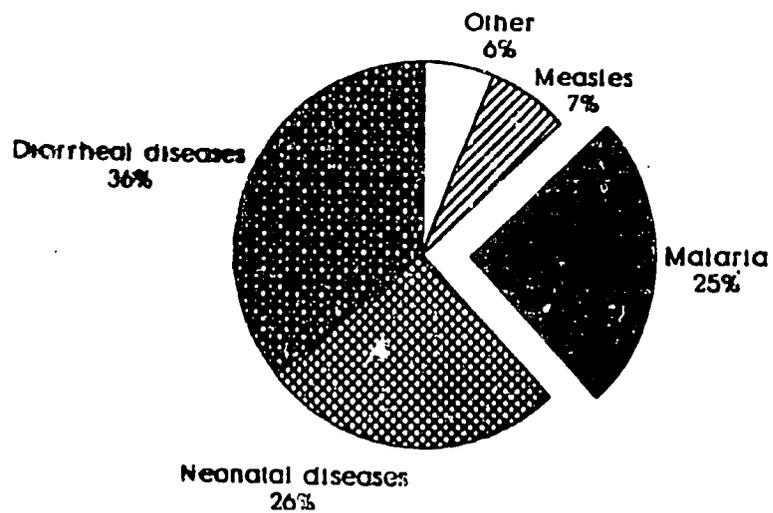
- **Technical Collaboration with national control programs**
- **Management Information Systems development**
- **Training of nationals**
- **Operations Research**
- **Environmental Management**

# CASES OF MALARIA WORLD WIDE DISTRIBUTION



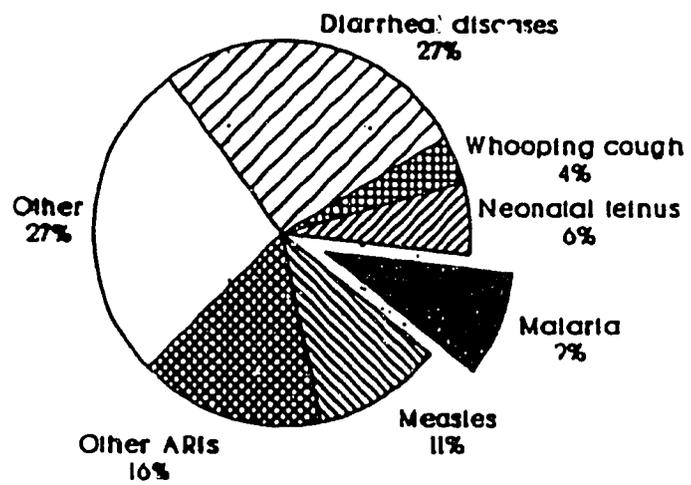
Source WHO

# CAUSES OF CHILDHOOD DEATHS SUB SAHARAN AFRICA



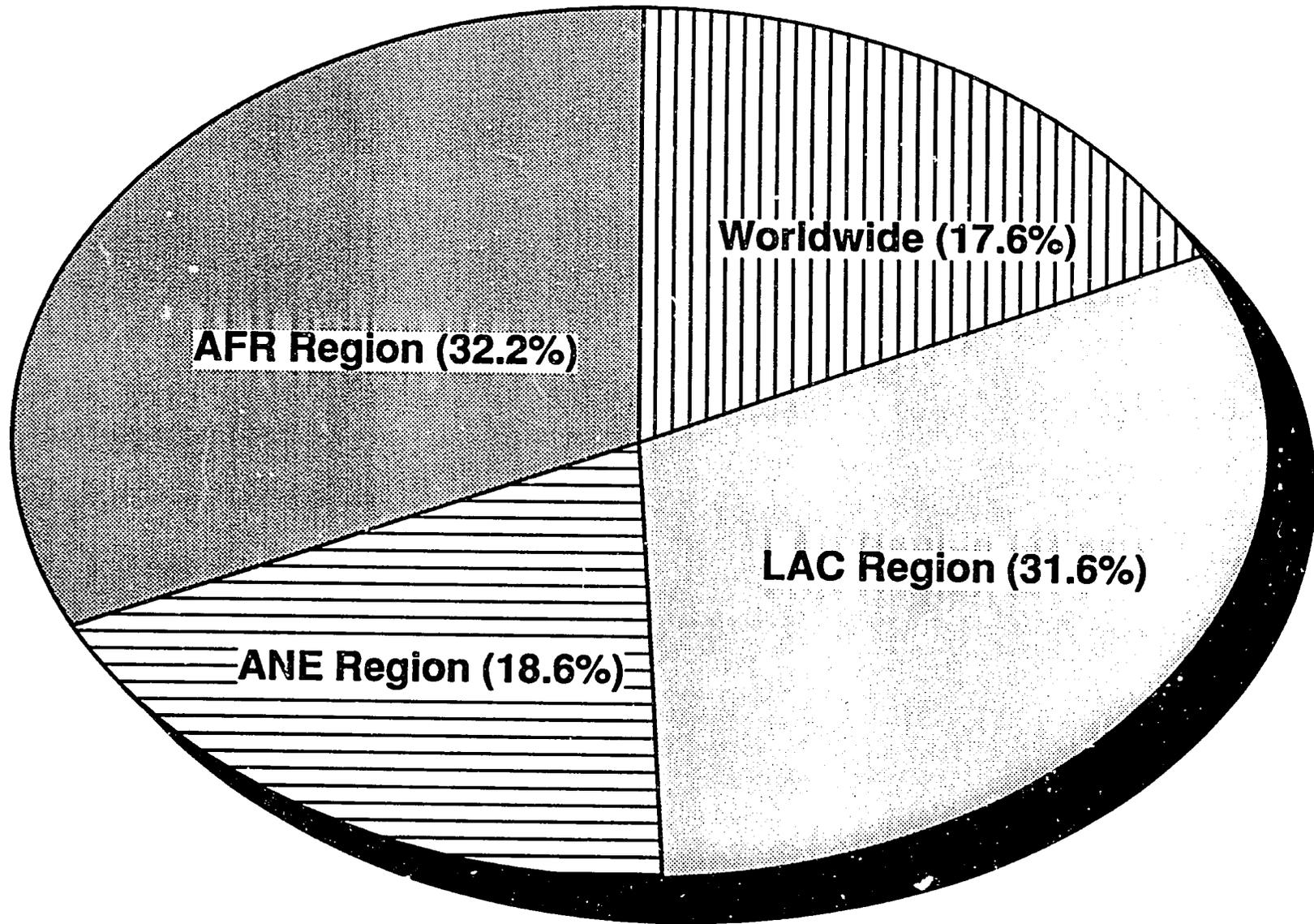
SOURCE: WHO

# CAUSES OF CHILDHOOD DEATHS WORLD WIDE

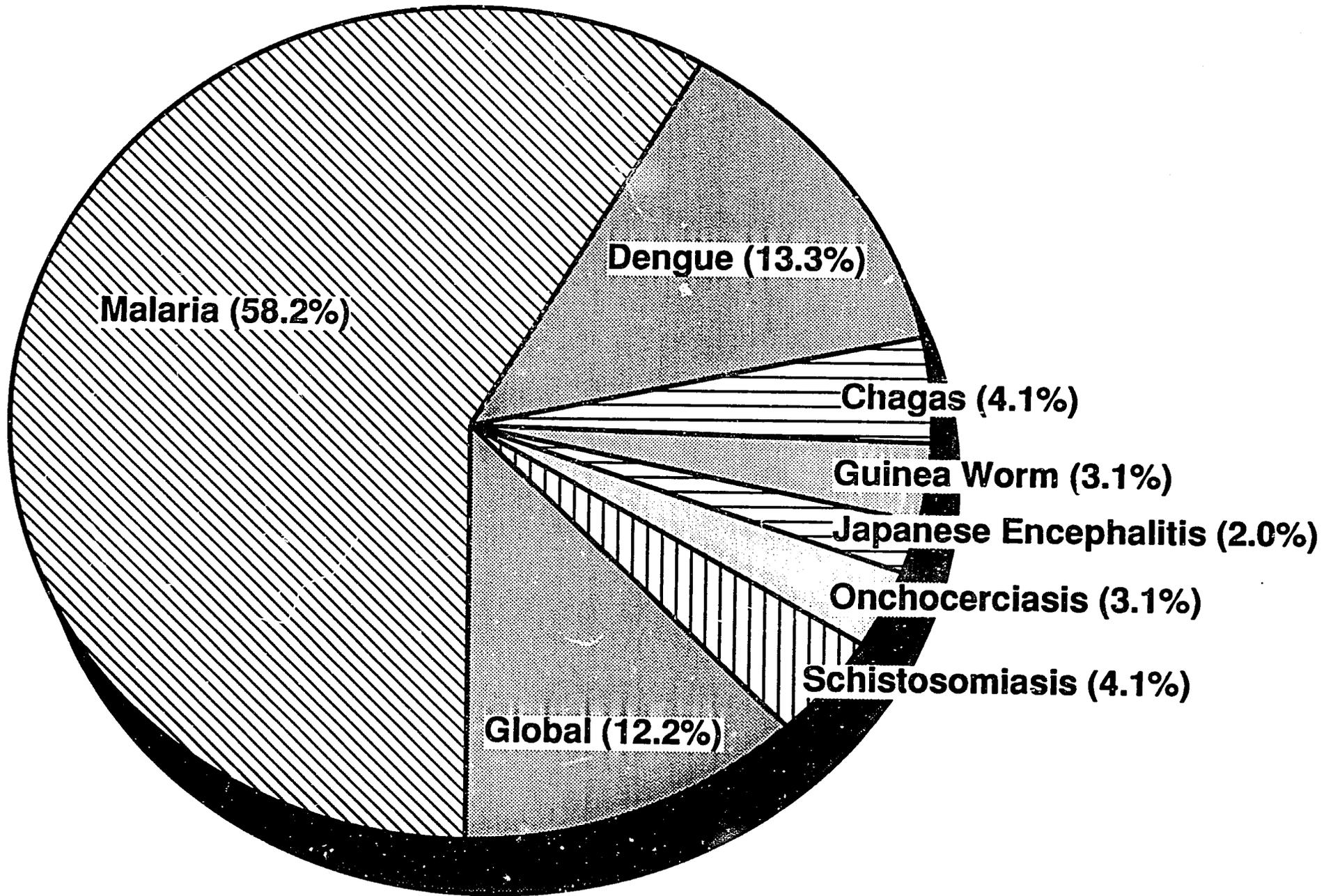


SOURCE: WHO & UNICEF ESTIMATES

# VBC II Project - Region Breakout

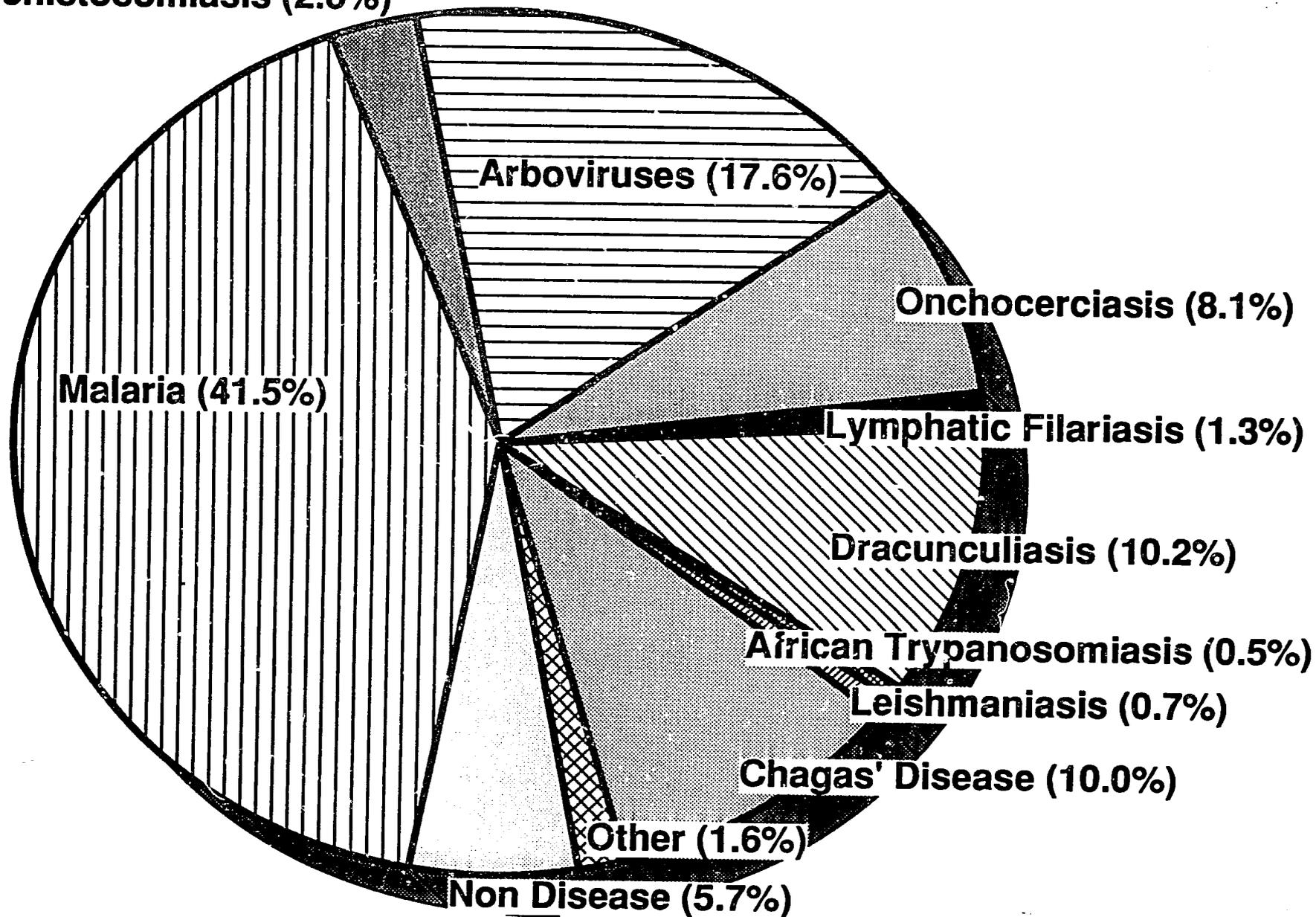


# VBC I Project - Disease Breakout



# VBC II Project - Disease Breakout

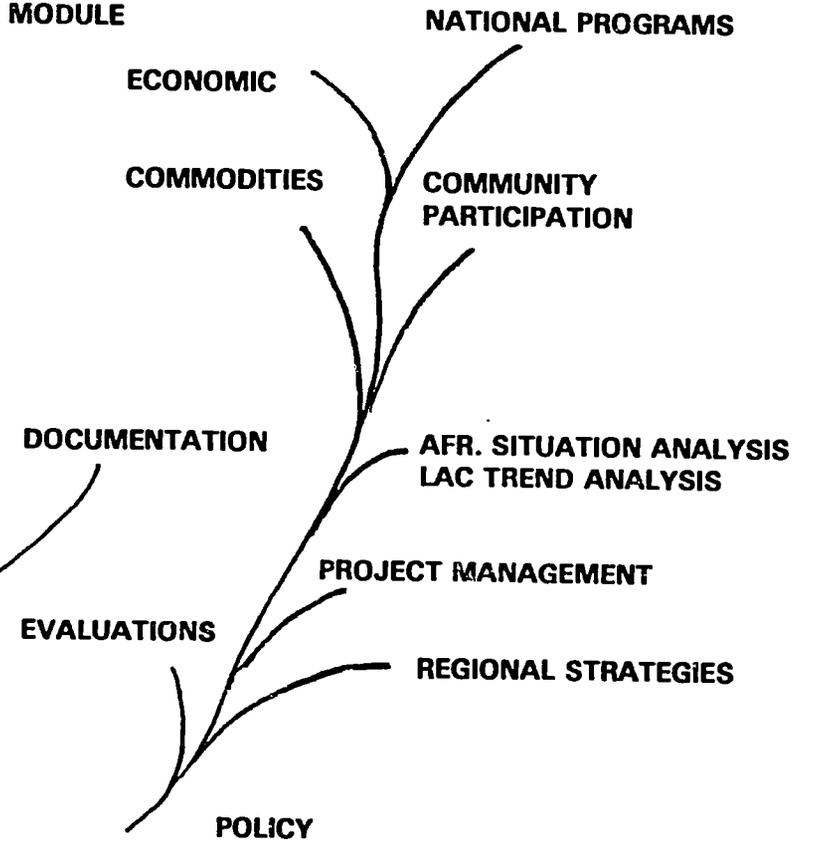
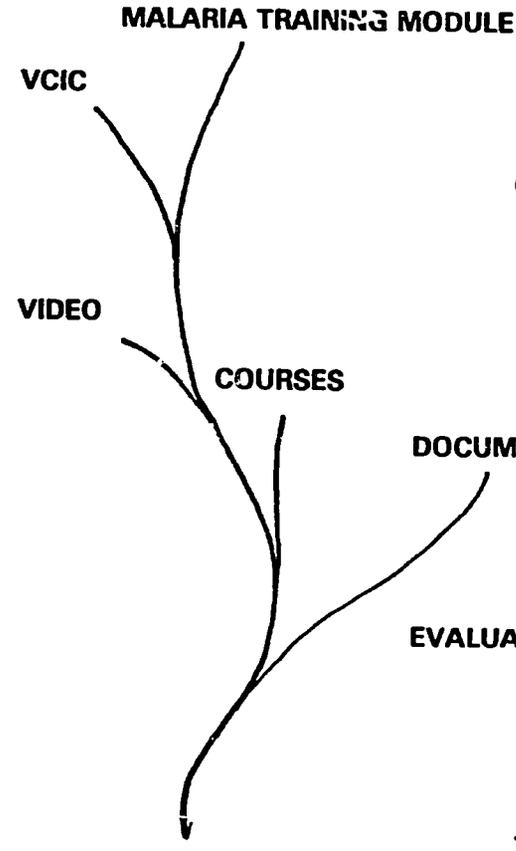
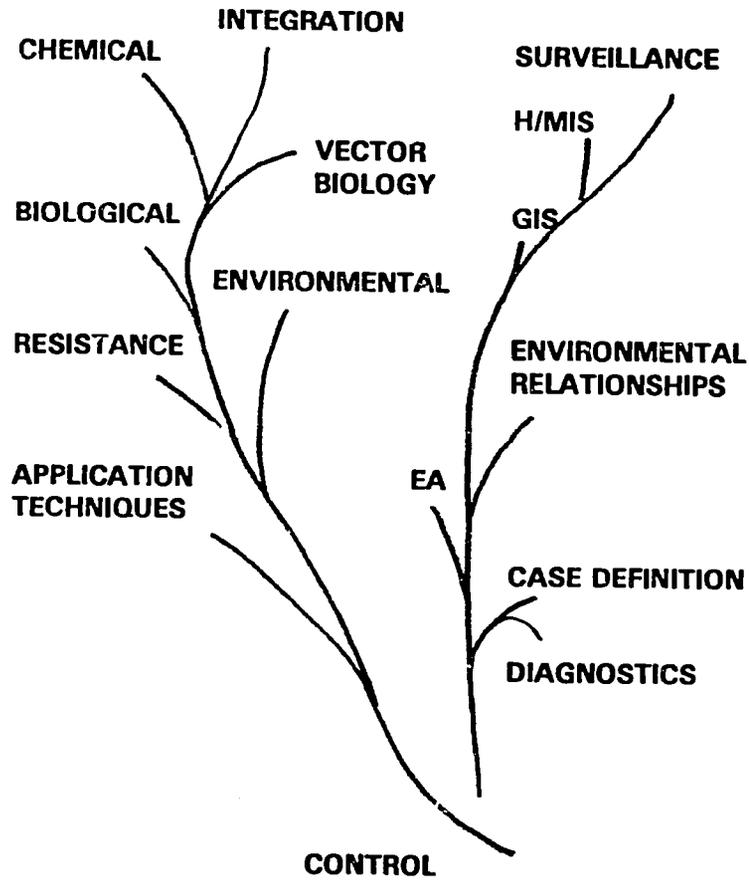
Schistosomiasis (2.8%)



EPIDEMIOLOGY-CONTROL

HRD AND INFORMATION

POLICY MODIFICATIONS AND ID



TRAINING

INFORMATION

NEEDS ASSESSMENTS

PROACTIVE  
REACTIVE

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**VECTOR BIOLOGY AND CONTROL PROJECT**  
**Major Areas of Emphasis (1992 - )**

- o Understanding and exploiting environmental relationships
- o Implementing Malaria Training Module
- o Surveillance H/MIS and GIS
- o Vector control
  - management/efficiency/cost
  - new control tools
  - integration
- o Information dissemination
- o Policy development
  - national planning
  - regional programs
  - economic analysis

# **Vector Biology and Control Project**

## **MALARIA CONTROL TRAINING MODULE**

### **Units within Module:**

**Unit 1. Planning, Organizing, Monitoring and Evaluating**

**Unit 2. Collection of Planning Data (Surveys)**

**Unit 3. Implementation of Curative Services**

**Unit 4. Implementation of Preventive Services**

**Unit 5. Collection/Analysis of Data for Monitoring/Evaluation**

**Unit 6. Simulation Unit**

**Unit 7. Training of Trainers**

## Procedures for the Protection of Human Subjects

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- ❖ Cooperative Agreements
- ❖ Clinical trials
- ❖ CDC field studies in Kenya
- ❖ Field studies in Papua New Guinea (PNG) conducted by the Institute of Medical Research (IMR)

## Procedures for the Protection of Human Subjects

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### FIELD STUDIES IN PNG

- ❖ Requested a Multiple Project Assurance from OPRR
- ❖ Dialogue continued (September 1991)
- ❖ Recommendations of evaluation team

## Procedures for the Protection of Human Subjects

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### **NEW FEDERAL POLICY FOR PROTECTION**

“Whenever the U.S. Agency for International Development or the Agency’s awardees or contractors conduct or support research involving human subjects in foreign countries, the research must be carried out in compliance with the new **Common Federal Rule — Protection of Human Subjects for Research Risks.**”

## A.I.D. MVDP PI/Industry Relationships

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### CURRENT STATUS

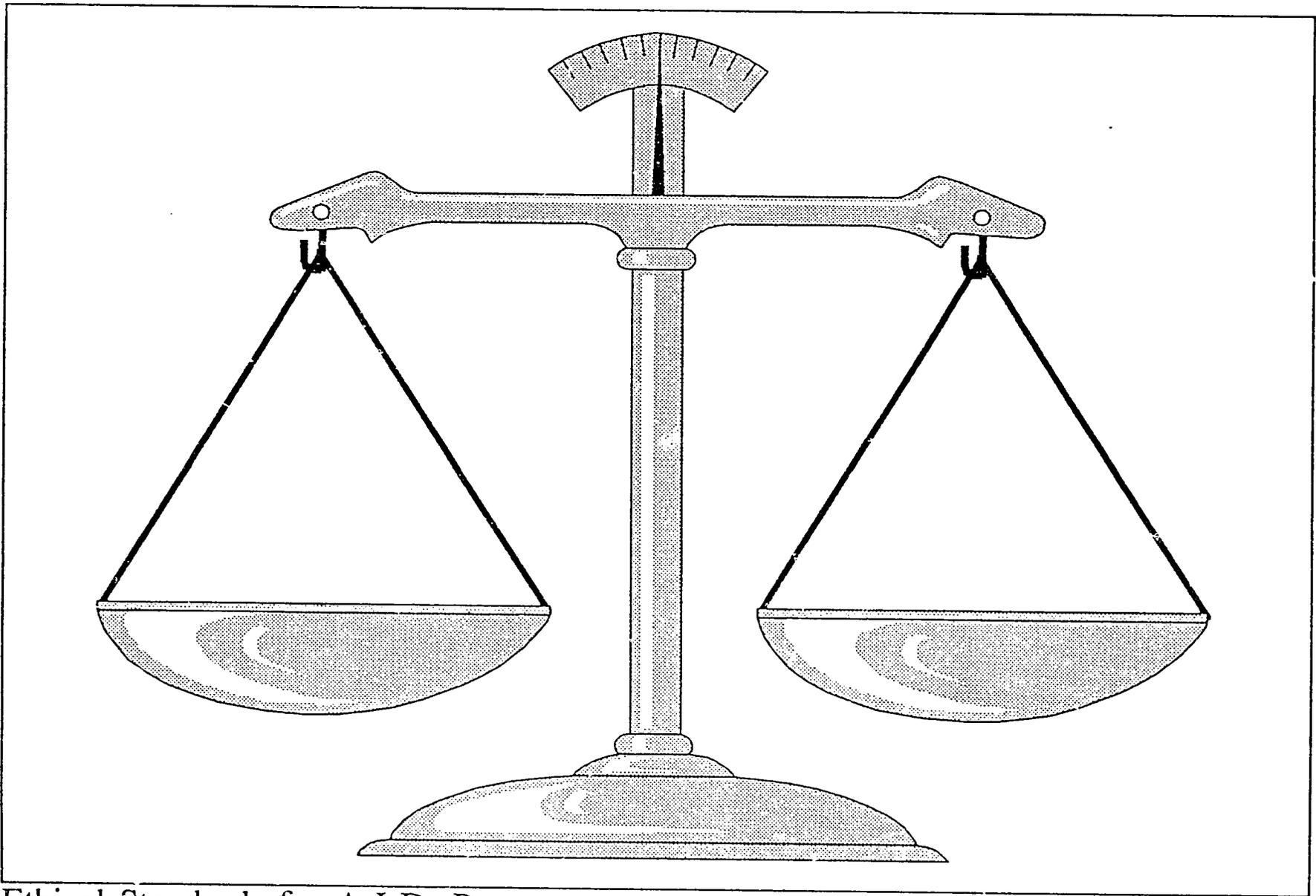
- ❖ US Government Policy/A.I.D. options regarding patents
  - PIs own patent rights on inventions;
  - Decision to submit patent applications (at own expense) rests with PI; and
  - A.I.D. can submit patent applications (at Government expense) if PI declines.
  
- ❖ MVDP posture towards PI/industry relationships
  - PIs expected to develop industrial collaboration to produce clinical grade vaccines;
  - PI or PI institution can use licensure to company as incentive;
  - A.I.D. requires “formula price” clause as part of collaborative agreement
    - ▲ if industrial collaborator develops vaccine as part of collaboration
    - ▲ if A.I.D. supports evaluation of vaccine developed independently by industry; and
  - A.I.D. has “march in rights.”

## A.I.D. MVDP PI/Industry Relationships

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### RECENT TRENDS

- ❖ A.I.D. moving to NIAID/DoD ad hoc collaboration model
  - Direct A.I.D. MVDP negotiations with industry ;
  - May involve expediting PI/industry agreements; and
  - Clinical/field trial potential provides incentive.
  
- ❖ Coordination with industry essential for MVDP planning
  - To avoid parallel development of similar constructs (*viz.*, gp195 by CHIRON); and
  - To better define companies' agendas (*viz.*, Roche attitude towards MAPs).



Ethical Standards for A.I.D. Programs

**(Excerpted from the  
Code of Ethics for  
Government Service)**

Any Person in

Government Service

Should -

Seek to find and employ  
more efficient and  
economical ways of  
getting tasks  
accomplished.

601

**Make no promises of any kind binding upon the duties of office, since a Government employee has no private word which can be binding on public duty.**

**Engage in no business with the Government, either directly or indirectly, ... inconsistent with the conscientious performance of his public duties.**



**Never use any  
information coming to  
him confidentially in the  
performance of  
governmental duties as  
a means for making  
private profit.**

112

**Expose**

**corruption**

**wherever**

**discovered.**

*Any Person in Government Service Should -*

**Never discriminate unfairly by the dispensing of special favors or privileges to anyone, whether for remuneration or not; and never accept, for himself or his family, favors or benefits under circumstances which might be construed by reasonable persons as influencing the performance of his governmental duties.**