08-31-2001

101830223

R HEET

U.S. DEPARTMENT OF COMMERCE
Patent and Trademark Office

To the Honorable Commissioner of Paten ,ed original documents or copy thereof.

1. Name of conveying party(ies): 8.22-01

(1) Jonathan L. Vennerstrom, (2) Yuxiang Dong;

(3) Jacques Chollet; (4) Hugues Matile

Additional name(s) of conveying party(ies) attached? ☐ Yes ☒ No

2. Name and address of receiving party(ies)

Name: Medicines for Malaria Venture MMV International Centre Cointrin

Internal Address: Entrance G, 3rd Floor

Street Address: Route de Pre'-Bois 20,

Post Box 1826

CH-1215 Geneva 15

SWITZERLAND

Additional name(s) & address(es) attached? ☐ Yes ☒ No

3. Nature of conveyance:

☒ Assignment ☐ Merger
☐ Security Agreement ☐ Change of Name

☐ Other _____

Execution Date: (1, 2) 5/23/01; (3, 4) 5/15/01

4. Application number(s) or patent number(s):

If this document is being filed together with a new application, the execution date of the application is: _____

A. Patent Application No.(s)

09/886,666

B. Patent No.(s)

Additional numbers attached? ☐ Yes ☒ No

5. Name and address of party to whom correspondence concerning document should be mailed:

Name: Heidi S. Nebel

Internal Address: _____

Street Address: 801 Grand Avenue, Suite 3200

City: Des Moines State: Iowa Zip: 50309-2721

6. Total number of applications and patents involved: 1

7. Total fee (37 CFR 3.41).....$ 40.00

☒ Enclosed (If this amount is insufficient, please charge Deposit Account 26-0084)

☐ Authorized to be charged to deposit account

8. Deposit account number:

_____

(Attach duplicate copy of this page if paying by deposit account)

08/29/2001 TDIAZ1 00000106 09886666

01 FC:581 40.00 OP

DO NOT USE THIS SPACE

9. Statement and signature.

To the best of my knowledge and belief, the foregoing information is true and correct and any attached copy is a true copy of the original document.

Heidi S. Nebel
Name of Person Signing

Signature

8/20/01
Date

Total number of pages including cover sheet, attachments, and document: 25

Mail documents to be recorded with required cover sheet information to:
Commissioner of Patents & Trademarks, Box Assignments
Washington, D.C. 20231

H:\GROUPS\DHP\PATENT\ASSIGN\HUPRICH2.CVR

ASSIGNMENT - WORLDWIDE

For good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, each undersigned inventor has sold and assigned, and by these presents hereby sells and assigns as described in the "Agreement" by and between MMV, Board of Regents of the University of Nebraska, Swiss Tropical Institute, Monash University and F. Hoffmann-La Roche LTD dated June 14, 2000 attached herewith. Nothing herein shall convey any additional rights beyond the scope of the AGREEMENT, and to the extent any such rights exist those shall remain to the prior owner as if this assignment had not been executed:

Medicines for Malaria Venture MMV
International Centre Cointrin
Entrance G, 3rd Floor
Route de Pre'-Bois 20
Post Box 1826
CH-1215 Geneva 15
Switzerland

its successors and assigns, the entire right, title and interest so far as concerns the United States and the Territories and Possessions thereof and all foreign countries in and to the invention entitled SPIRO AND DISPIRO 1,2,4-TRIOXOLANE ANTIMALARIALS as set forth in this United States Patent Application

____ executed concurrently herewith

____ executed on _____

X Serial No. 09/886,666 filed June 21, 2001.

said application for United States Letters Patent, including all divisional, renewal, substitute, continuation and Convention applications based in whole or in part upon said inventions or upon said applications, and any and all Letters Patent and reissues and extensions of Letters Patent granted for said inventions or upon said applications and every priority right that is or may be predicated upon or arise from said inventions, said applications, and said Letters Patent; said Assignee being hereby authorized to file patent applications in any or all countries on any or all said inventions in the name of the undersigned or in the name of said Assignee or otherwise as Assignee may deem advisable, under the International Convention or otherwise; the Commissioner of Patents and Trademarks of the United States of America being hereby authorized to

issue or transfer all said Letters Patent to said Assignee in accordance herewith; this assignment being under covenant, not only that full power to make the same is had by the undersigned, but also that such assigned right is not encumbered by any grant, license, or other right theretofore given, and that the undersigned will do all acts reasonably serving to ensure that the said inventions, patent applications and Letters Patent shall be held and enjoyed by said Assignee as fully and entirely as the same could have been held and enjoyed by the undersigned if this assignment had not been made, and particularly to execute and deliver to said Assignee all lawful documents including petitions, specifications, oaths, assignments, invention disclaimers, and lawful affidavits in form and substance which may be requested by said Assignee, to furnish said Assignee with all facts relating to said inventions or the history thereof and any and all documents, photographs, models, samples or other physical exhibits which may be of said invention, and to testify in any proceedings relating to said inventions, patent applications, Letters Patent.

The undersigned hereby grant an authorized representative of Assignee the power to insert in this Assignment any further identification which may be necessary or desirable to comply with the rules of the U.S. Patent and Trademark Office for recordation of this Assignment.

NAMES AND SIGNATURES OF INVENTORS		
Inventor: Jonathan L. Vennerstrom	Signature: Jonathan L. Vennerstrom	Date: 5-23-2001
Witnessed by: Elaine L. Payne	Signature: Elaine L. Payne	Date: 5-23-2001
Inventor: Yuxiang Dong	Signature:	Date:
Witnessed by:	Signature:	Date:
Inventor: Jacques Chollet	Signature:	Date:
Witnessed by:	Signature:	Date:
Inventor: Hugues Matile	Signature:	Date:
Witnessed by:	Signature:	Date:
Inventor:	Signature:	Date:
Witnessed by:	Signature:	Date:

Note: Prima facie evidence of execution may optionally be obtained by execution of this document before a U.S. Consul or before a local officer authorized to administer oaths whose authority is proved by a certificate from a U.S. Consul.

GENERAL NOTARY-State of Nebraska
ELAINE L. PAYNE
My Comm. Exp. Oct. 15, 2003

issue or transfer all said Letters Patent to said Assignee in accordance herewith; this assignment being under covenant, not only that full power to make the same is had by the undersigned, but also that such assigned right is not encumbered by any grant, license, or other right theretofore given, and that the undersigned will do all acts reasonably serving to ensure that the said inventions, patent applications and Letters Patent shall be held and enjoyed by said Assignee as fully and entirely as the same could have been held and enjoyed by the undersigned if this assignment had not been made, and particularly to execute and deliver to said Assignee all lawful documents including petitions, specifications, oaths, assignments, invention disclaimers, and lawful affidavits in form and substance which may be requested by said Assignee, to furnish said Assignee with all facts relating to said inventions or the history thereof and any and all documents, photographs, models, samples or other physical exhibits which may be of said invention, and to testify in any proceedings relating to said inventions, patent applications, Letters Patent.

The undersigned hereby grant an authorized representative of Assignee the power to insert in this Assignment any further identification which may be necessary or desirable to comply with the rules of the U.S. Patent and Trademark Office for recordation of this Assignment.

NAMES AND SIGNATURES OF INVENTORS		
Inventor: Jonathan L. Vennerstrom	Signature:	Date:
Witnessed by:	Signature:	Date:
Inventor: Yuxiang Dong	Signature: W Dong	Date: 5/23/01
Witnessed by: Elaine L. Payne	Signature: Elaine L Payne	Date: 5/23/01
Inventor: Jacques Chollet	Signature:	Date:
Witnessed by:	Signature:	Date:
Inventor: Hugues Matile	Signature:	Date:
Witnessed by:	Signature:	Date:
Inventor:	Signature:	Date:
Witnessed by:	Signature:	Date:

Note: Prima facie evidence of execution may optionally be obtained by execution of this document before a U.S. Consul or before a local officer authorized to administer oaths whose authority is proved by a certificate from a U.S. Consul.

GENERAL NOTARY-State of Nebraska
ELAINE L. PAYNE
My Comm. Exp. Oct. 15, 2003

issue or transfer all said Letters Patent to said Assignee in accordance herewith; this assignment being under covenant, not only that full power to make the same is had by the undersigned, but also that such assigned right is not encumbered by any grant, license, or other right theretofore given, and that the undersigned will do all acts reasonably serving to ensure that the said inventions, patent applications and Letters Patent shall be held and enjoyed by said Assignee as fully and entirely as the same could have been held and enjoyed by the undersigned if this assignment had not been made, and particularly to execute and deliver to said Assignee all lawful documents including petitions, specifications, oaths, assignments, invention disclaimers, and lawful affidavits in form and substance which may be requested by said Assignee, to furnish said Assignee with all facts relating to said inventions or the history thereof and any and all documents, photographs, models, samples or other physical exhibits which may be of said invention, and to testify in any proceedings relating to said inventions, patent applications, Letters Patent.

The undersigned hereby grant an authorized representative of Assignee the power to insert in this Assignment any further identification which may be necessary or desirable to comply with the rules of the U.S. Patent and Trademark Office for recordation of this Assignment.

NAMES AND SIGNATURES OF INVENTORS		
Inventor: Jonathan L. Vennerstrom	Signature:	Date:
Witnessed by:	Signature:	Date:
Inventor: Yuxiang Dong	Signature:	Date:
Witnessed by:	Signature:	Date:
Inventor: Jacques Chollet	Signature: Jacques Chollet	Date: 15 Janvier 2001
Witnessed by: Daniel Hunziker	Signature: D. Hunziker	Date: 15 Jan. 2001
Inventor: Hugues Matile	Signature: Hugues Matile	Date: 15 Janvier 2001
Witnessed by: Daniel Hunziker	Signature: D. Hunziker	Date: 15. Januar 2001
Inventor:	Signature:	Date:
Witnessed by:	Signature:	Date:

Note: Prima facie evidence of execution may optionally be obtained by execution of this document before a U.S. Consul or before a local officer authorized to administer oaths whose authority is proved by a certificate from a U.S. Consul.

Date Fourteenth day of June, 2000

(1) MEDICINES FOR MALARIA VENTURE

(2) BOARD OF REGENTS OF THE UNIVERSITY OF NEBRASKA

(3) SWISS TROPICAL INSTITUTE

(4) MONASH UNIVERSITY

(5) F. HOFFMANN-LA ROCHE LTD.

AGREEMENT

CMS Cameron McKenna
Mitre House
160 Aldersgate Street
London EC1A 4DD

T +44(0)20 7367 3000
F +44(0)20 7367 2000

BINDING HEADS OF TERMS

THIS AGREEMENT is made with effect from the fourteenth day of June, 2000.

1. PARTIES

1.1 MEDICINES FOR MALARIA VENTURE a foundation established in Switzerland under Swiss law whose principal place of business is c/o World Health Organisation, 1211 Geneva 27, Switzerland ("MMV");

1.2 THE BOARD OF REGENTS OF THE UNIVERSITY OF NEBRASKA doing business as THE UNIVERSITY OF NEBRASKA MEDICAL CENTRE whose principal place of business is at 986810 Nebraska Medical Centre, Omaha, Nebraska 68198-6810, USA ("University Nebraska");

1.3 SWISS TROPICAL INSTITUTE a public institution established under a local government decree of 1978 (revised 1992) under Swiss law whose principal place of business is at Socinstrasse 57, 4002 Basel, Switzerland ("STI");

1.4 MONASH UNIVERSITY, a body corporate established under the Monash University Act 1958 (Victoria) of Wellington Road, Clayton, Victoria 3168, Australia through its Victorian College of Pharmacy ("Monash University").

1.5 F. HOFFMANN-LA ROCHE LTD. a company established in Basel, Switzerlandunder Swiss law whose principal place of business is at Grenzacherstrasse 124, CH-4070 Basel, Switzerland ("Roche").

2. BACKGROUND

2.1 MMV is an entity funded by public institutions, philanthropic organisations and other sources in partnership with the pharmaceutical industry which is committed to undertake research and development of new therapies and prophylactics for malaria and to ensure their subsequent commercialisation.

2.2 MMV intends to operate on a virtual basis and to contract with third parties which will undertake such research, development or production / commercialisation.

2.3 MMV has invited research proposals directed at the conduct of a research programme the objective of which is the identification of lead compounds and subsequent lead optimisation studies up to the point of identification of robust development candidates such compounds providing a novel therapy (and possibly prophylactic) for malaria.

2.4 University Nebraska has identified a novel series of synthetic endoperoxides believed to be targets for a malarial drug discovery research programme more details of which are provided in the application dated the 18th June 1999 submitted by Dr J L Vennerstrom to MMV and at the date hereof has know how regarding their design and synthesis and other intellectual property and property rights protecting the same (" University Nebraska Background IPR").

2.5 STI has the screens, assays and models, including animal models, necessary and useful for a malaria drug discovery research programme and at the date hereof has know how and other intellectual property and property rights protecting the same ("STI Background IPR").

2.6 Monash University has expertise in the monitoring of pharmacokinetic and metabolic properties of compounds useful for a malaria drug discovery programme and providing input into the design of compounds and at the

date hereof has know how and other intellectual property and property rights protecting the same ("Monash Background IPR").

2.7 Roche has know how and expertise in the area of malaria drug discovery and development including toxicology ("Roche Background IPR).

2.8 University Nebraska, STI, Monash University and Roche (collectively "Consortium" and individually "Consortium Member") have agreed to participate in a malaria drug discovery research programme under MMV funding and Consortium funding (by reason of Roche not seeking funding from MMV in respect of the utilisation of its resources and the other Consortium Members not seeking overhead payments from MMV.)

2.9 MMV has agreed to fund a Consortium malaria drug discovery research programme on such basis.

2.10 University Nebraska Background IPR, STI Background IPR, Monash University Background IPR and Roche Background IPR is collectively "Consortium Background IPR".

3. LEGAL NATURE OF THESE HEADS OF TERMS

3.1 MMV and the Consortium have agreed all the essential terms for the funding and conduct of a malaria drug discovery research programme and such terms are set out in these Heads of Terms ("Heads"). MMV and the Consortium have agreed that following execution of the Heads by all parties the MMV funding and the research programme shall commence on the terms set out in these Heads which shall come into full force and effect. The parties shall then use their best efforts to negotiate and agree in good faith the full terms of a research agreement which agreement shall contain the terms set out in the Heads together with any other terms normally found in agreements of this nature. The Parties shall use their best efforts to agree such full terms and execute the corresponding research agreement by 31st August 2000 at the

latest ("Closing Date"). If the Parties have not executed such full research agreement on or before the Closing Date these Heads shall remain in full force and effect as the terms governing the funding and conduct of the research programme.

4. CONDUCT OF THE RESEARCH PROGRAMME

4.1 The Consortium shall carry out the research programme set out in Schedule 1 hereto ("Research Programme") (as may be amended under the provisions of paragraph 4.3 below) and shall seek to achieve the goals set out in the Research Programme save as MMV shall otherwise agree in writing. Each Consortium Member shall carry out that part of the Research Programme allocated to it in the Research Programme or by the Research Committee (see paragraph 5.1 below) according to best practice laboratory procedures including compliance with best practice among research involving human subjects and the use of animals and general research safety. No Consortium Member shall have the right to sub-contract its obligations without the prior written agreement of MMV. Each Consortium Member shall ensure that only its employees are engaged on the Research Programme.

4.2 Each Consortium Member shall keep notebooks and other written records of the research conducted by it in accordance with good pharmaceutical industry practice. Each Consortium Member shall prepare not less than quarterly and not less than 21 days prior to each Research Committee meeting (see paragraph 5.3 below) a written report giving an overview in reasonable detail of its progress with the Research Programme during the previous quarter.

4.3 No later than 30 days prior to the date for the annual presentations to MMV Expert Scientific Advisory Committee in each year of the Research Programme the Consortium Members shall prepare a detailed written report giving a description of the work carried out by them as part of the Research

Programme during the previous year or since the commencement of the Research Programme if less than a year together with details of the results obtained and any related Programme IPR (see paragraph 7.2 below) and together with the suggested work programme for the Research Programme for the next year including priorities and goals. Subsequent to the presentation of the report the Consortium Members shall make the University Nebraska, STI and Monash University Principal Investigators (see paragraph 5.4 below) and the Roche Project Manager (see paragraph 5.5 below) available to MMV's Expert Scientific Advisory Committee (MMV ESAC) for the purposes of presenting the report and discussing it. Following such presentation MMV shall have the right to require in writing changes or modifications to the suggested work programme for the Research Programme or to the priorities and goals and such work programme priorities and goals shall thereafter be deemed to be part of the Research Programme.

4.4 When carrying out the Research Programme the Consortium Members shall discuss day to day progress with the MMV Project Manager (see paragraph 5.5 below) and shall give him / her such access to the premises at which their part of the Research Programme is being conducted and for the purposes of discussion with their personnel and such access to their laboratory records as he shall reasonably request. The Consortium shall take into account the comments of the MMV Project Manager which shall be transmitted to the University of Nebraska PI (or other such person identified by the consortium) in writing by the MMV CEO or his delegate.

4.5 If any Consortium Member wishes to suggest changes or modifications (including changes to the level of MMV funding) to the Research Programme these shall be proposed to the Research Committee and any such changes or modifications approved by the Research Committee shall be submitted to MMV which shall have 60 days to consider the same. If such changes or modifications are approved by MMV in writing within such 60 day period

the Research Programme and if necessary the Funding Budget (see paragraph 6.1 below) shall be changed as necessary. If such changes or modifications are not so approved by MMV the Research Programme shall proceed without such change or modification.

5. MANAGEMENT OF THE RESEARCH PROGRAMME

5.1 The Consortium Members shall establish a research committee comprising 8 members to manage and supervise the conduct of the Research Programme ("Research Committee") which shall consist of 2 representatives of each Consortium Member including the Principal Investigators from University Nebraska, STI and Monash University (see paragraph 5.4 below) and the Roche Project Manager (see paragraph 5.5 below). MMV shall not have a representative on the Research Committee. At least one Committee member from each institution or their alternates shall be its quorum.

5.2 Decisions of the Research Committee shall be unanimous. In the event of a dispute not capable of resolution the dispute shall be referred to MMV whose decision shall be final and shall be implemented by the Consortium Members.

5.3 The Research Committee shall convene quarterly (either by meeting or by telephone or video conference) and shall amongst other things consider the quarterly written reports provided by the Consortium Members under paragraph 4.2 above. Within 30 days of each such meeting the Research Committee shall ensure that minutes are prepared and such minutes together with the Consortium Members quarterly written reports shall be promptly supplied to MMV.

5.4 Each of University Nebraska, STI and Monash University shall have a principal investigator in charge of the part of the Research Programme being conducted by it ("Principal Investigator"). The Principal Investigators are:

University Nebraska	Dr. Jonathan Vennerstrom
STI	Dr. Reto Brun
Monash University	Dr. Bill Charman

5.5 Each of MMV and Roche shall have a project manager appointed by it in relation to the Research Programme ("Project Manager"). The Project Managers are:

MMV	Dr. Robert Ridley
Roche	Dr. Hugues Matile

MMV and Roche shall use all reasonable endeavours to keep the same Project Manager throughout the duration of the Research Programme but in the event of their resignation from MMV and Roche, or due to other circumstances, they each shall have the right to replace them on notification of the replacement to the other parties.

5.6 If a Principal Investigator resigns from his institution such Principal Investigator, the other Consortium Members and MMV shall promptly discuss the position and at MMV's sole discretion MMV shall have the right to terminate the involvement of such institution in the Research Programme upon giving 30 days written notice to such institution or renegotiate terms with such institution for its confirmed involvement with the Research Programmes. Such termination or renegotiation shall not affect the IPR position set out in paragraph 7 below;

6. RESEARCH PROGRAMME FUNDING

6.1 MMV shall pay to each of the Consortium Members the sums specified in the Research Programme funding budget set out in Schedule 2 ("Funding Budget").

6.2 Each Consortium Member shall submit a financial report to MMV in relation to each year of the Research Programme at the same time as submitting the report due under paragraph 4.3 specifying in detail how the monies received from MMV in respect of such year have been spent and identifying any surplus carried forward. Any surplus balance at the end of the Research Programme shall be returned to MMV on demand. MMV shall have the right to appoint an independent auditor to audit the Consortium Members' books and records concerning such expenditure and the Consortium Member shall permit the same. Such books and records shall be kept for a period of 7 years following completion of the Research Programme.

7. INTELLECTUAL PROPERTY

7.1 Each Consortium Member shall give each other Consortium Member a licence under its Consortium Background IPR solely to carry out the Research Programme.

7.2

7.2.1 Any and all results of the Research Programme and any and all related intellectual property, know how and other property ("Programme IPR") which are identified as having an actual or potential therapeutic or prophylactic application(s) for malaria shall be owned by MMV (MMV Programme IPR). The parties shall adhere to the patent filing protocol set out in Schedule 3 for the MMV Programme IPR ("Patenting Protocol") and MMV shall be responsible for all costs and expenses relating to the application, prosecution and maintenance of such patent rights.

7.2.2 Subject to the provisions of clause 7.2.3 MMV shall grant to the Consortium Member(s) whose employees were responsible for the relevant part of the Research Programme the right to exploit any

non-malarial applications for the MMV Programme IPR save that such licence shall not extend to:

any compound if such is identified as having a potential malarial application unless and until MMV determines not to pursue the development of such compound for malarial application; or abandons any such development.

7.2.3 Where University Nebraska, STI or Monash University generate income through the licensing or other exploitation of MMV Programme IPR MMV shall be entitled to 50% of such income.

7.2.4 If Roche wish to develop any product derived from MMV Programme IPR then any licence for such development shall be negotiated in good faith with the relevant parties.

7.3

7.3.1 The Programme IPR excluding MMV Programme IPR shall be owned by the Consortium Member(s) whose employees were responsible for the relevant part of the Research Programme and those Consortium Member(s) shall solely be responsible for any decision to apply for patent protection and also for the costs incurred in applying for, and/or prosecuting and/or maintaining any such patent protection. Provided that if the Consortium Member(s) in relation to any such element of the Programme IPR do not seek patent protection, or abandon patent protection or fail to make reasonable steps to exploit the relevant invention the Consortium Member(s) shall assign all rights to that element of the Programme IPR to MMV and if MMV generate income through the licensing or other exploitation of the Programme IPR MMV shall pay the relevant Consortium Member(s) a total of 5% of all income received by it.

7.3.2 Where any Consortium Member(s) generate income through the licensing or other exploitation of Programme IPR (excluding MMV Programme IPR) MMV shall be entitled to 5% of such income.

7.3.3 Insofar as it shall be necessary MMV shall be entitled to a perpetual non-exclusive, world-wide royalty-free licence under any Programme IPR (excluding MMV Programme IPR) to enable it to develop and market products with a therapeutic or prophylactic malarial application.

7.4 Where MMV generates income through the licensing or other exploitation of MMV Programme IPR in relation to the conduct of research or development or marketing of products for the therapy or prophylaxis of malaria University of Nebraska, STI and Monash University shall be entitled to 5% of such income resulting to MMV and the respective shares of each of the institutions shall be University of Nebraska - 40% and STI and Monash University - 30% each.

7.5 If any of the Consortium Member(s) wishes to develop any compound comprised within the Programme IPR for an application other than one for the therapy or prophylaxis of malaria the relevant Consortium Member(s) shall have an exclusive, perpetual, irrevocable, world-wide sub-licensable licence under Consortium Background IPR (but excluding Roche Background IPR) to develop, make, have made, use, import, market, distribute and sell the product in question which shall include access to the Consortium Background IPR.

7.6 Prior to completion of the Research Programme under the provisions of paragraph 7.3 the Consortium Members shall have no right to use the MMV Programme IPR to conduct research or development into products other than products for the therapy or prophylaxis of malaria without the prior written consent of MMV.

7.7 If at any time MMV shall abandon the development of any product based upon the MMV Programme IPR MMV shall assign all rights to the MMV Programme IPR to the Consortium Member(s) who are responsible for the relevant part of the Research Programme provided that if any Consortium Member(s) generate income through the licensing or other exploitation of the MMV Programme IPR they shall pay MMV 5% of all income received by them.

8. PUBLICATION POLICY

8.1 Before any Programme IPR is published or otherwise disclosed (as set out in paragraph 8.2) the Consortium Members shall use all reasonable endeavours to keep the same secret and confidential and not to disclose the same to any third party other than as permitted under the Heads. Each Consortium Member shall ensure that its employees who may generate such Programme IPR are made aware of this obligation of confidence and shall instruct them not to disclose the same to any such third party (including other scientists and researchers at University Nebraska, STI, Monash University or Roche not engaged on the Research Programme) and otherwise to treat the same as confidential.

8.2 Each Consortium Member shall procure that when any of its employees who has generated any Programme IPR is ready to publish or otherwise disclose such Programme IPR in a presentation or in any other way whatsoever (other than previously published Programme IPR) they shall send to the Research Committee a final completed manuscript of the proposed journal publication or a full description of the unpublished results forming part of Programme IPR to be presented or otherwise disclosed. If the Research Committee decides that publication should occur it shall send the manuscript or description (amended as the Research Committee may have agreed) to MMV. On receipt of any proposed publication or description MMV shall within 45 days review the same. If the Consortium either receives approval

for publication from MMV or no response at all within such 45 day period then publication may proceed. MMV shall not unreasonably withhold approval but if MMV informs the Research Committee that it does not approve publication then publication may not proceed. Upon the expiry of 180 days from any refusal of approval the Research Committee may renew a request for approval in which case the same procedure shall be followed.

9. WARRANTIES

9.1 University of Nebraska, STI, Monash University and Roche shall jointly or severally ensure that the Programme IPR vests in the Institution(s) employing the researchers rather than any one or more of the individuals whom the institution may employ to undertake the research and shall also severally indemnify MMV against any negligent act either on behalf of the Institution or any person engaged by the Institution to undertake the research.

10. TERMINATION

The Research Programme shall be funded by MMV and conducted by the Consortium on the terms of these Heads for an initial period of 3 years provided always that if MMV in its sole discretion determines that it should be terminated for whatever reason MMV shall be entitled to terminate this agreement on 100 days notice to each Consortium Member. Save as otherwise specified herein no Consortium Member shall have the right to terminate its involvement in the Research Programme and cease to perform its obligations hereunder.

11. OTHER PROVISIONS

11.1 The validity, construction and interpretation of the Heads and any determination of the performance which it requires shall be governed by English law.

11.2 All disputes, controversies or claims arising out of or in connection with the Heads (other than disputes on the Research Committee which shall be handled under the provisions of paragraph 5.2 above) shall be finally settled in accordance with the UNCITRAL Arbitration Rules as at present in force. The tribunal shall consist of 1 arbitrator as appointed by the appointing authority. The appointing authority for the purpose of the UNCITRAL Rules shall be the London Court of International Arbitration. The place and seat of the arbitration shall be London and the language of the arbitral proceedings shall be English.

11.3 Save as expressly provided in the Heads nothing herein takes away from any party or constitutes a waiver by any party of any of its rights or remedies under common law, statute or otherwise.

11.4 The Heads constitute the entire agreement and understanding between the parties and supersede all prior oral or written understandings, arrangements, representations or agreements between them relating to the subject matter of the Heads provided that this does not remove any right of action by any party in respect of any fraudulent misrepresentation, fraudulent concealment or other fraudulent action.

11.5 All formal notices to be given pursuant to the Heads shall be in writing and shall be delivered by hand to the address of the parties set out above (or such other address as may be notified by a party to the others from time to time) with a confirmation copy being sent by post. Notices shall be deemed to have been received at the time of delivery by hand.

11.6 The activities of the parties contemplated pursuant to the Heads shall not constitute a partnership and no party has the authority to bind the other parties in anyway except as provided in the Heads.

11.7 Each party shall bear its own legal costs and other expenses incurred in the negotiation, preparation, execution and implementation of the Heads.

11.8 Any press releases to be made by any party relating to the Heads will require the prior written approval of the other parties.

SCHEDULE 1
Research Programme

This programme is based on:

a) Submission made to MMV ESAC July 19-21 1999
b) Reply letter from MMV to Dr. Jonathan Vennerstrom of August 1999

The components of the research over two years are outlined in the documentation. Over the first two years the work includes:

University of Nebraska

- Chemistry to optimise lead trioxalane and further develop SAR
- Scale up chemistry where necessary for further analysis
- Studies to attempt to relate antimalarial activity with molecular interaction with haematin to assist with SAR

STI

- Testing of compounds against *P. falciparum* in culture and against *P. berghei* to determine the efficacy of compounds.
- More detailed evaluation of potential candidate compounds in animal models and against a variety of *P. falciparum* strains.
- Attempts to demonstrate that trioxalanes can cure animals with fewer doses over fewer days than artemisinin derivatives. This has special consequences for these compounds to be superior to artemisinins in the field and to cure within three days treatment.

Monash

- Preliminary characterisation of parameters relating to developability characteristics (metabolism, pharmacokinetics, physical chemical properties) to direct chemical synthesis.
- Assistance in developing appropriate SAR around these parameters.
- Detailed characterisation of selected compounds, particularly with respect to pharmacokinetics and metabolism.

Roche

- Provision of consultancy on antimalarial testing and evaluation.
- Provision of pilot toxicology testing where appropriate, including early assessment of neurotoxicity. If due to priority reasons Roche cannot fulfil this task within a reasonable time Roche will assist with study design and outsourcing.
- Provision of advice and expertise with respect to medicinal chemistry and project evaluation.

The goal of this research within 2 years is a development candidate that has a relatively low cost of goods, is orally bioavailable and can provide a cure within 3 days of treatment. Within one year it is expected to have focused on a limited series of compounds for assessment and further SAR development, that are superior to artemisinin derivatives with respect to eliciting a complete cure in the *P. berghei* model.

SCHEDULE 2

Funding Budget

Funds will be provided in 6-monthly instalments. A sum of 50% of personnel and consumables budget plus the full equipment and travel budget will be supplied at the beginning of each year's funding. The remainder will be provided after 6 months upon appropriate demonstration of the satisfactory disbursement of previous funds.

The budget for year 1 is as follows:

University of Nebraska	
Personnel	$280,000
Consumables	$ 50,000
Equipment	$ 90,000
Travel	$ 8,500
Swiss Tropical Institute	
Personnel	$295,000
Consumables	$ 65,000
Equipment	$ 25,000
Travel	$ 8,000
Monash University	
Personnel	$200,000
Consumables	$ 60,000
Equipment	$ 20,000
Travel	$ 8,500
Hoffmann-La Roche	
No cost	
Outsourced Toxicology studies	$100,000
(to be retained by MMV until required and provided subject to approval of studies)	
Total	$1,210,000

The budget for year 2 is provisionally proposed to be $1,100,000 (which assumes no equipment costs).

The budget for year 3 is provisionally proposed to be $1,100,000 (which assumes no equipment costs).

SCHEDULE 3

Patenting Protocol

1. Whilst MMV shall determine at its sole discretion whether to seek to apply for, prosecute and maintain patent protection in any jurisdiction for inventions comprised within the MMV Programme IPR it is MMV's intention to focus patenting activities on mature series of chemical compounds of proven efficacy against malaria, using cellular and animal models, and where there is a strong likelihood that a compound from the series is likely to be selected as a development candidate.

2. All costs in connection with preliminary advice, searches, preparation of patent applications, patent prosecutions and maintenance shall be borne by MMV subject only to all such expenditure being approved in advance by MMV.

3. All patent applications shall initially be made in the United States and MMV shall retain the services of a patent attorney nominated by University Nebraska and approved by MMV and such other patent attorneys outside the United States as MMV may nominate from time to time. Nothing herein shall prevent MMV from engaging the services of other patent attorneys for the purpose of reviewing MMV's patent strategy and the implementation of it.

4. Immediately upon becoming aware that a patent invention may have been made each Consortium Member shall notify both MMV and the Research Committee in writing. The Research Committee may itself make a recommendation to MMV as to whether the invention should be patented. However, no cost incurred in relation to obtaining third party advice shall be payable by MMV unless and until authorised by MMV.

5. If MMV decides to proceed to seek patent protection for an invention the patent attorney nominated by University of Nebraska and agreed by MMV shall be requested to provide advice, undertake searches and/or prepare a patent application. Where required the Consortium Members shall provide all necessary assistance to the patent attorney to enable the patent attorney to provide the advice and/or prepare an application for filing.

6. Upon filing a patent application each relevant Consortium Member shall assign its entire right, title and interest in the patent application to MMV and if required shall procure that its employees who may have been involved in the making of the invention shall do likewise.

7. MMV and the Consortium Members shall ensure that all communications and disclosures in relation to any invention that is potentially patentable shall be undertaken under obligations of confidence so as to ensure that the right to patent is in no way jeopardised.

8. MMV shall keep the Research Committee informed as to decisions and progress in relation to the filing and prosecution of patent applications and the maintenance of any patent(s) granted.

9. MMV shall not abandon any right to apply for patent protection or any pending patent application or any granted patent without first providing not less than 30 days' notice to the Consortium Members of its intention to do so.

SIGNED by
for and on behalf of
MEDICINES FOR
MALARIA VENTURE

SIGNED by
for and on behalf of
THE BOARD OF REGENTS OF THE
UNIVERSITY OF NEBRASKA

SIGNED by
for and on behalf of
SWISS TROPICAL INSTITUTE

SIGNED by
for and on behalf of
MONASH UNIVERSITY

SIGNED by
for and on behalf of
F. HOFFMAN LA ROCHE Ltd.