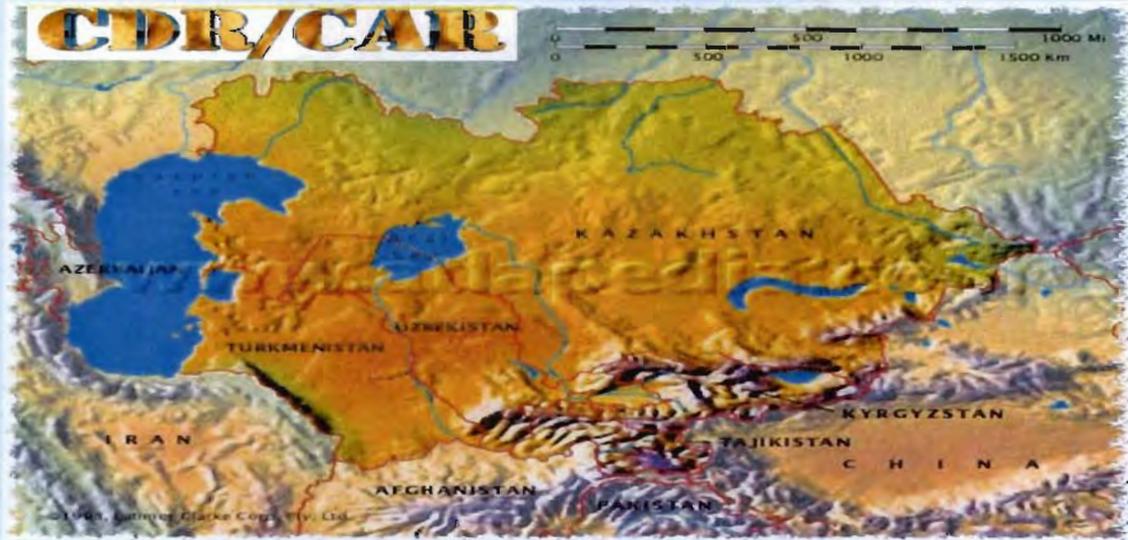




Embassy of the United States
Tel Aviv, Israel

Cooperative Development Research Program



Grant Agreement No.:

TA-MOU-06-C25-013

Participants:

Israel (BGU) and Thailand (AAGR)



U.S. AGENCY FOR INTERNATIONAL DEVELOPMENT
BUREAU FOR GLOBAL PROGRAMS, FIELD SUPPORT & RESEARCH
CENTER FOR ECONOMIC GROWTH
WASHINGTON, D.C.

[Copy 4 of 7]



Embassy of the United States of America

June 13, 2007

Prof. Moti Hershkowitz
Vice President & Dean for Research & Development
Ben Gurion University
P.O.B. 653, Beer Sheva 84105
Israel

Subject: **Grant No. TA-MOU-06-C25-013**

Dear Prof. Hershkowitz:

Pursuant to the authority contained in the Foreign Assistance Act of 1961, as amended, the Federal Grant and Cooperative Agreement Act of 1977, as amended, and the Interagency Agreement between the Agency For International Development and the U.S. Department of State of August 26, 2005, as amended, the U.S. Embassy/Tel Aviv (hereinafter referred to as "*Embassy*" or "*Grantor*") hereby grants to the Ben Gurion University of the Negev (hereinafter referred to as "*BGU*" or "*Grantee*") the sum of one hundred ninety nine thousand nine hundred three U.S. dollars (\$199,900) to provide support for a research program entitled "*Biotechnology to Produce Monosex Culture of the Giant Freshwater Prawn (Macrobrachium rosenbergii de Man)*" as more fully described in Attachment 2, entitled "Program Description", and the Grantee's proposal, as revised, which is made a part of the Grant and incorporated herein by reference.

This Grant is effective and obligation is made as of the date of this letter and shall apply to commitments made by the Grantee in furtherance of program objectives during the period beginning *July 1, 2007* and ending on or before *June 30, 2010*.

This Grant is made to the Grantee on condition that the funds will be administered in accordance with the terms and conditions as set forth in Attachment One, entitled "Schedule", Attachment Two, entitled "Program Description", Attachment Three, entitled "Payment Forms", Attachment Four, entitled "Performance Report - Guidelines", Attachment Five, entitled "Standard Provisions", and Attachment Six, "Interagency Edison", which have all been agreed to by your organization.

In order to comply with regulations applicable to this Grant, it is essential that all documentation provided as attachments to this letter be thoroughly reviewed. The Grantee is responsible for full understanding of, and compliance with, all applicable regulations. However, in some cases, information set forth in the attached is subject to interpretation and warrants specific guidance. Such additional information is set forth below.

I. SUBGRANTS

Grants are being awarded to Prime institutions to work in collaboration with Sub institutions. Notwithstanding actual billing and payment procedures, the full Grant amount and research activity is formally attributed to the Prime, or BGU in this case. The only legal relationship the U.S. Government has is with the prime institution.

The Grantee is required to establish a legal, binding relationship with the Subgrantee (Middle East Region and Developing Countries institutions) you intend to collaborate with. That relationship can be in the format essentially identical to this award document made by the U.S. Government, or in any other appropriate format.

A copy of each Subgrant agreement must be submitted to the Embassy within ninety (90) days after the start of the grant period.

Regardless of the Subgrant format chosen by the Grantee, care should be taken to ensure that required regulations have been applied. Subgrants may only be awarded to responsible institutions which possess the potential ability to perform successfully.

Since your institution will be held accountable for the grant in its entirety, it is important that the Subrecipient institution be held accountable by your institution. In this manner, the prime protects itself from unnecessary risk of disallowed costs.

However, in no case can a U.S. Government responsibility be claimed, construed, or inferred from the use of any Subgrant agreement by the Grantee.

II. AUDITS

In order to receive advance payments, all institutions (prime and sub) must have had a current audit performed by an independent external CPA firm in accordance with applicable regulations (i.e., those pertaining to the country where the institution is located as well as Government Auditing Standards developed by the Comptroller General of the United States). Any adverse findings contained in such audits, as determined by the Grant Officer or his designee, must have been adequately resolved. In the event an audit has not been performed recently, the Grantor (U.S. Government in the case of the prime, prime in the case of the sub) may elect to perform a limited financial review, conducted at the discretion of the Grantor, prior to authorizing advance payments. In this case, the Recipient of the advance must agree to comply with all future audit requirements.

III. STANDARD PROVISIONS

All Mandatory and Required as Applicable Standard Provisions indicated to be applicable in later sections of this Grant should be reviewed, understood, and adhered to. However, the following are considered to be most frequently applied to this program:

A. Revision of Grant Budget

In many cases, specific Grant Officer approval for budget changes is not required (if the need for a change is identified, the Grantee should refer specifically to the provision to determine whether or not Grant Officer approval is required). However, there may be other changes that should be discussed with the Project Officer, or his designee, to ensure continued agreement on the direction of the program. The Grantee should consider factors such as impact and reasonableness in determining which non-mandated changes should be brought to the attention of the Embassy. In no case will a change be approved which is contrary or detrimental to the original or detrimental to the objectives of the project as technically approved by the science review panel.

B. Air Travel and Transportation

Project Officer approval is required on all international travel. All air travel and shipments are to be made on U.S. flag air carriers when available. Exceptions to the requirement may be made if a U.S. flag air carrier cannot provide the foreign air transportation needed, or if use of such service will not accomplish the U.S. Government's mission (see circumstances outlined in the provision for specific allowable exceptions). Economic considerations do not override this provision. In the event U.S. flag carrier service is deemed to be unavailable, the Grantee must prepare and retain for audit purposes, a certificate of unavailability.

C. Procurement of Goods and Services

The Grantee must ensure high standards with respect to procurement. When possible, procurement should be competed to the maximum extent practicable. Technical needs should be determined, and all other factors being equal, purchase should be made at the lowest price available. Contracts meeting applicable thresholds should include appropriate legal remedies in case the subcontractor fails to perform. Wherever possible, the Grantee should use U.S. and small business sources.

D. Eligibility Rules for Goods and Services

The Grantee (and its Sub) may not purchase the following using U.S. Government funds: military equipment, surveillance equipment; police or other law enforcement commodities or services; abortion equipment or services; luxury goods or gambling equipment; or weather modification equipment.

The Grantee may not purchase from any source listed on the List of Parties Excluded from Federal Awards. To this end, the Grantee may rely on a self-certification provided by the supplier, unless there is any knowledge by the Grantee that the certification should not be accepted.

Specific prior, written approval from the Grant Officer is required prior to purchase of the following: agricultural commodities; motor vehicles; pharmaceuticals; pesticides; rubber compounding chemicals and plasticizers; used equipment; U.S. Government-owned excess property; or fertilizer. In the event the Grantee outlined a specific need for any of these goods in its proposal, and provided full disclosure of the reason, source, method of selecting the source, price comparisons, and other pertinent information, the Grantee may assume that approval of such specific goods is provided through award of this document. Any changes to requirements outlined in the proposal must be submitted for review and approval.

Also, attached is a partial list of authorized countries for acquisition of goods and services. In general, the order of preference is (1) U.S.; (2) Cooperating Country (i.e., country of location for prime and sub); (3) selected free world countries (see Code 941 countries, attached); and (4) special free world countries (Code 935, attached). These rules apply to source (place of purchase), origin (place of manufacture) and nationality (of supplier). When the Grantee uses other than U.S., documentation must be retained for audit purposes which indicates one of the following conditions: (1) procurement was of an emergency nature; (2) higher preference sources' prices are at least 50% higher; (3) impelling local political considerations preclude consideration of higher preference sources; (4) item is only available from the intended source; or (5) procurement from the identified source best promotes the objectives of the U.S. Foreign Assistance program.

IV. GRANT ADMINISTRATION AND CLOSEOUT

A. Responsibilities and Authority

1. Only the Grant Officer has the authority to modify the terms and conditions of this Grant. The Grantee must exercise care in considering various situations. In general, if any portion of the Grant must be changed to reflect the Grantee's intentions, the Grant Officer should be so notified, in writing with a copy to the Project Officer, or his designee. This correspondence should outline the change needed, the reason, and the impact (technical and financial), and should request approval to make such change.
2. The Project Officer, or his designee, is the Embassy's contact point for all issues not addressed to the Grant Officer. This includes, but is not limited to, technical clarifications, certain budget changes, voucher tracking, etc.

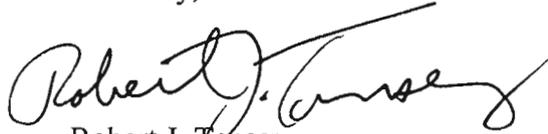
B. Closeout Procedures

1. The following definitions shall apply for the purpose of this section:
 - a. **Closeout:** The closeout of a Grant is the process by which the Embassy determines that all applicable administrative actions and all required work of the Grant have been completed by the Grantee and the Embassy.
 - b. **Date of Completion:** The date of completion is the date on which all work under the grant is actually completed, or the date on the award document, or any supplement or amendment thereto, on which the Embassy sponsorship ends.
 - c. **Estimated Completion Date:** The date contained in the Grant which is anticipated to be the "Date of Completion". This date may be modified to reflect delays or other reasonable circumstances which warrant extension of the time period. Requests for such revisions should comply with the above IV.A.1. requirements for Grant Officer approval, and should be submitted sufficiently (not less than 120 days) in advance of the estimated completion date contained in the Grant to permit evaluation and action prior to that time.

- d. **Disallowed Costs:** Disallowed costs are those charges to a Grant that the Grant Officer determines to be unallowable, in accordance with the applicable Federal cost principles or other conditions contained in the Grant.
2. The following outlines specific requirements which must be met prior to initiation of the closeout process:
 - a. Upon request, the Embassy shall make prompt payments to a Grantee for allowable reimbursable costs under the Grant being closed out.
 - b. The Grantee shall immediately refund any balance of unobligated (unencumbered) cash that the Embassy has advanced or paid and that is not authorized to be retained by the Grantee for use in other Grants.
 - c. The Embassy shall obtain from the Grantee within 90 calendar days after the date of completion of the Grant, all financial, performance, and other reports required as the condition of the Grant. The Embassy may at its discretion grant extensions when requested by the Grantee.
 - d. When authorized by the Grant, the Embassy shall make a settlement for any upward or downward adjustments, to the Embassy's share of costs after these reports are received.
 - e. The Grantee shall account for any property acquired with funds provided herein or received from the U.S. Government, as discussed in Attachment One, Schedule.
 - f. In the event a final audit has not been performed prior to the closeout of the Grant, the Embassy shall retain the right to recover an appropriate amount after fully considering the recommendations on questioned costs resulting from the final audit.

Please sign all copies of this letter to acknowledge receipt of this Grant. Keep **two** copies for your files and **one** for the Principal Investigator, and return the **original** and all remaining copies to this office.

Sincerely,



Robert J. Tansey
Grants Officer
American Embassy, Tel Aviv

ATTACHMENTS:

<u>No.</u>	<u>Title</u>
ONE	SCHEDULE
TWO	PROGRAM DESCRIPTION
THREE	PAYMENT FORMS
FOUR	PERFORMANCE REPORTS - GUIDELINES
FIVE	STANDARD PROVISIONS - MANDATORY & REQUIRED AS APPLICABLE
SIX	INTERAGENCY EDISON

ACKNOWLEDGED:

DATE: 1.7.07

INSTITUTION: **Ben Gurion University of the Negev**

AUTHORIZED INDIVIDUAL:

~~**Mrs. Einat Noy**
Head - International
Grants Management Section
Office of Sponsored research~~

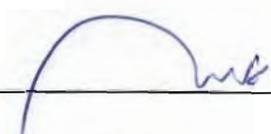
Prof. Moti Herskowitz
Vice-President & Dean for
Research and Development

SIGNATURE:

TITLE: _____

PRINCIPAL INVESTIGATOR: **Prof. Amir Sagi**

DATE: 25.6.07

SIGNATURE: 

TITLE: PI

COVER PAGE - Agreement

FISCAL DATA:

Proposal No.:	C25-013
Appropriation No.:	19-50113
Obligation No.:	4437665013
Amount Obligated:	\$ 142,170
Obligation No.:	4437664013
Amount Obligated:	\$ 57,630
Allotment No.:	4437
Function Code:	8550
Object Code:	4220
Total Obligated:	\$ 199,900
Estimated Amount:	\$ 199,900
Project Office:	U.S. Embassy Tel Aviv, ECON/AID
Voucher Paying Office:	RAMC/Bangkok

NUMERICAL LIST OF CURRENT AID GEOGRAPHIC CODESCode 935:SPECIAL FREE WORLD

Any area or country in the Free World* including the cooperating country itself.

Code 941:SELECTED FREE WORLD

Any independent country in the Free World*, excluding the cooperative country itself and the following:

Europe

Albania
Andorra
Armenia
Austria
Azerbaijan
Belgium
Bosnia and Herzegovina
Bulgaria
Belarus
Croatia
Czech Republic
Denmark
Estonia
Finland
France
Georgia
Germany
Greece
Hungary
Ireland
Italy
Latvia
Liechtenstein
Lithuania
Luxemburg
Macedonia**
Malta
Moldova
Monaco
Montenegro**
Netherlands
Norway
Poland
Portugal
Russia
San Marino
Serbia**
Slovak Republic
Slovenia
Spain
Sweden
Switzerland
Ukraine
United Kingdom
Vatican City

Others

Angola
Australia
Bahamas
Bahrain
Canada
Cyprus
Gabon
Hong Kong
Iceland
Japan
Kazakhstan
Kuwait
Kyrghyzstan
Mongolia
New Zealand
Qatar
Saudi Arabia
Singapore
South Africa
Taiwan**
Turkmenistan
United Arab Emirates
Uzbekistan

* "Free World" excludes the following areas or countries:

Afghanistan, Cambodia, Cuba, Iran, Iraq, Laos, Libya, North Korea, People's Republic of China, Syria, and Viet Nam.

** Has the status of a "geopolitical entity", rather than an independent country.

COVER PAGE - Agreement

E. Grant Participants:

Principal Investigator	Prof. Amir Sagi, Dept. of Life Sciences and Inst. For Applied Biosciences, Ben Gurion University of the Negev, P.O.B. 653, Beer Sheva 84105, Israel.
Co-PI	Dr. Boonyaratpalin, Aquatic Animal Genetics R&D Institute, Department of Fisheries Klong 5, Klonlaung, Pthumthanii 12120, Thailand
Co-PI	Dr. Uraiwan S. Aquatic Animal Genetics R&D Institute, Department of Fisheries Klong 5, Klonlaung, Pthumthanii 12120, Thailand
Co-PI	Mr. Ampolsak K. Aquatic Animal Genetics R&D Institute, Department of Fisheries Klong 5, Klonlaung, Pthumthanii 12120, Thailand
Project Officer	Mr. R. Tansey, EST&H Counselor, American Embassy, 71 Hayarkon St., Tel Aviv 63903, Israel

F. Reporting and Evaluation

Reports, the Principal Investigator's responsibility, must be sufficiently detailed to substantiate the findings and to permit a scientific evaluation of the research. Overseas collaborators shall be given fair credit for their participation in the research and a chance to review and comment on the Final Report before it is submitted. The principal investigator will share a draft of the Final Report with the Project Officer and USAID/EGAT for comments prior to the formal submission. All reports should include the following statistics:

- a list of publications resulting from the grant. Those joint publications which include both Grantee and Sub-Grantee target country investigators (including students) as authors on the same publication should be very clearly identified with this list.

- a list of Israeli/target country meetings and workshops actually funded by the grant (do not count attendance at a separate conference using grant funds for travel).

- a list of other cross-country visits or personnel exchanges between Grantee and Sub-Grantee participants. This list should include visits for the PI's and other scientists, as well as training of students, post docs, etc. from on country in another country's laboratory. No need for a detailed description, just a few words to describe the exchange, number of people, and approximate duration. For example:

- Prof. X from Israel to Ghana for 1 week consultation
- 2 grad students from Ghana for 2 months to learn .. techniques.. in Israel

Distribution of specific reports is outlined in individual report specifications, below.

All references to USAID/EGAT shall mean: U.S. Agency for International Development; Bureau for Economic Growth, Agriculture and Trade; Room 2.11-151 RRB, 1300 Pennsylvania Ave, NW; Washington, D.C. 20523-2110.

All references to RSP/NAS shall mean: Research Support Program for USAID; Policy and Global Affairs; National Academy of Sciences; 500 5th Street, NW, Mailstop W517; Washington DC 20001, USA.

All references to Project Officer shall mean: U.S. Embassy in Israel: ECON/AID Office; U.S. Embassy; 71 Hayarkon Street; Tel Aviv 63903, Israel (or via e-mail: ecoaidta@netvision.net.il).

1. **Performance Reports:** Required every six months. The principal investigator will submit reports stating what has been accomplished to date and detailing project management issues (also see Attachment IV). A Financial Status Report will be attached to each report. Reports are due within sixty (60) days after the end of each six-month period. One copy of each report is to be submitted to USAID/EGAT; one copy to the Project Officer; one copy to the USAID mission in the country of the collaborator; and two copies to NAS.
2. **Final Performance Report:** Within ninety (90) days after the estimated completion date of the Grant, the principal investigator will submit this report to the same recipients in the same quantities as specified above, and in addition sent to:

USAID Development Experience Clearing House; ATTN: Documents Acquisitions; 8403 Colesville Road, Suite 210; Silver Spring, MD 20910-6368 (or via e-mail: docsubmit@dec.cdie.org) One copy.

Publication of results in scientific journals is encouraged. Additional guidance on report preparation is given in the "Interim Guidelines on Projects", available from USAID/EGAT. Financial reports shall be in accordance with the applicable payment provision.

Failure to file the required progress and financial reports in a timely fashion will be grounds for suspension or termination of the grant.

G. Special Provisions

1. While in the country of collaborating institutions, the Grantee will keep the USAID field mission generally apprised of their work, but will not request administrative support except for the usual in-country introductions as may be appropriate. The Grantee will abide by Mission and host government regulations and customs as they apply to other AID supported in-country activity.
2. The principal and co-principal investigators of the Grantee and its primary sub-

grantee, and essential scientific staff which were identified as critical to the success of the program prior to award of this Grant will not be changed without the prior written approval of the Project Officer.

3. Mandatory and Required as Applicable Standard Provisions for Non-U.S. Non-governmental Grantees are set forth as Attachment 5 to this Grant.
4. Overhead Costs
As part of the application process, the Prime Grantee has agreed to absorb all indirect costs associated with this program in excess of the following which was agreed upon. Accordingly, overhead may be charged to this grant at a rate not to exceed 15%, of the Total Direct Costs for Israel and 6% for Thailand. This rate is considered fixed for the life of the Grant. If actual costs to the institutions are less than this ceiling rates, the Embassy shall only be requested to fund at the actual cost rates.
5. The title to all property acquired under this Grant will vest in the Grantee in accordance with applicable regulations contained herein. Property purchased for use by the collaborating institution shall vest in that institution. In light of the objectives of institutionalization within collaborating institution countries, equipment purchased for this use shall remain the property of that institution. Property titled to the Grantee shall be identified upon completion and disposition will be agreed upon. In general, the U.S. Government anticipates the transfer of this equipment to the Grantee if a valid continuation research activity is envisioned, particularly another under this CDR Program.
6. Compliance with Federal Guidelines and Regulatory Procedures:
 - a. The Grantee will implement this research activity in accordance with all relevant guidelines for U.S. Government funded research such as:
 - (1) The National Institutes of Health (NIH) guidelines for the ethical treatment of human subjects;
 - (2) Guidelines for the handling of radioactive materials;
 - (3) NIH and USDA guidelines for the handling of pathogenic microorganisms;
 - (4) USDA-APHIS procedures for animal and plant health inspection;

(5)
NIH Guidelines for Research Involving Recombinant DNA Molecules;

(6)
Procedures issued by the USDA, EPA, or other appropriate federal agency, regarding testing of genetically engineered organisms;

(7)
State Department's and AID's environmental procedures; and

(8)
Such other Federal guidelines and procedures as may apply during the course of research.

- b. All existing comparable guidelines of the host country in which the research is actually located must be followed also.
- c. Reports submitted under this activity to U.S. Embassy/Tel Aviv and AID/G/EGAT will address the cited regulatory issues. All modifications of protocols affecting these regulatory concerns must be reported. The investigators are responsible for reporting any difficulties encountered in implementing these protocols.

7. Laboratory Safety and Hazard Containment:

Research will be conducted following the protocols described in the Grantee's proposal, as revised, which insure the safety of persons involved in the research. All research shall be conducted following procedures issued by the U.S. Government and those issued by the government of the host country for the containment of these hazards.

If the protocols involving laboratory safety and hazard containment are revised, they must be re-reviewed by the investigator's institutional review committee(s) that approved the original protocol, and the Project Officer and AID/G/EGAT must be informed in writing before the revised protocols are used. The revised procedures must be consonant with the guidelines of the country in which the laboratory is located and of the United States. Copies of the approval of the revised protocols by the investigator's institutional review committee(s) should also be provided to the Project Officer and AID/G/EGAT.

Similarly, the research will be conducted in the facilities described in the Grantee's

proposal, as revised. If the research is moved to new facilities, or the facilities are modified in such a way to affect safety or hazard containment, a description of the new facilities must be provided to the Project Officer and AID/G/EGAT before the research is effected. Any applicable institutional reviews of the facilities must be repeated, and the re-certification must be provided to the Project Officer and AID/G/EGAT.

8. Humane Treatment of Experimental Animals:

- a. Principles for the Treatment of Vertebrates: The Grantee will adhere to the following principles for the utilization, care and transportation of vertebrate animals used in testing, research and training. For guidance throughout these principles, reference is made to the Guide for the Care and Use of Laboratory Animals prepared by the Institute of Laboratory Animal Resources, National Research Council.

(1)

Procedures involving animals should be designed and performed with due consideration of their relevance to human or animal health, the advancement of knowledge, or the good of society.

(2)

The animals selected for a procedure should be an appropriate species and quality and the minimum number required to obtain valid results. Methods such as mathematical models, computer simulation and in vitro biological systems should be considered.

(3)

Proper use of animals, including the avoidance or minimization of discomfort, distress, and pain when consistent with sound scientific practices, is imperative. Unless the contrary is established, investigators should consider that procedures that cause pain or distress in human beings may cause pain or distress in other animals.

(4)

Procedures with animals that may cause more than momentary or slight pain or distress should be performed with appropriate sedation, analgesia, anesthesia. Surgical or other painful procedures should not be performed on unanesthetized animals paralyzed by chemical agents.

(5)

Animals that would otherwise suffer severe or chronic pain or distress that cannot be relieved should be painlessly killed at the end of the procedure, or, if appropriate, during the procedure.

(6)

The living conditions of animals should be appropriate for their species and contribute to their health and comfort. Normally the housing, feeding, and care of all animals used for biomedical purposes must be directed by a veterinarian or other scientist trained and experienced in the proper care, handling, and use of the species being maintained or studied. In any case, veterinary care shall be provided as indicated.

(7)

Investigators and other personnel shall be appropriately qualified and experienced for conducting procedures on living animals. Adequate arrangements shall be made for their in-service training, including the proper and humane care and use of laboratory animals.

(8)

Where exceptions are required in relation to the provisions of these principles, the decisions should not rest with the investigators directly concerned, but should be made, with due regard to U.S. and host country regulations, by an appropriate review group such as an institutional animal research committee. Such exception should not be made solely for the purpose of teaching or demonstration.

- b. **Applicable Regulations:** The transportation, care and use of animals should be in accordance with the U.S. Animal Welfare Act (7 U.S.C. 2131 et. seq.) and other applicable U.S. Federal laws, guidelines, and policies. All research shall be conducted following procedures issued by the government of the host country for the humane treatment of experimental animals.
- c. **Compliance with Reviewed Protocols:** Research will be conducted following the protocols described in the Grantee's proposal, as revised, which insure the humane treatment of experimental animals.
- d. **Revision of Protocols:** If any protocol involving the experimental animals is revised, it must be re-reviewed by the investigator's institutional review committee(s) that approved the original protocol, and the Project Officer and AID/G/EGAT must be informed in writing before the revised protocol is used. The revised procedure must be consonant with the guidelines of the country in which the animals are affected, and of the United States. Copies of the approval of the revised protocol by the investigator's institutional review committee(s) should also be provided to the Project Officer and AID/G/EGAT.
- e. **Facilities for Animals:** The animals will be maintained in the facilities described in the Grantee's proposal, as revised. All animals shall be provided

facilities satisfying the requirements specified by the U.S. Government and those issued by the government of the host country for the humane treatment of experimental animals. If the animals are moved to new facilities or the facilities are modified in such a way to affect the animals, a description of the new facilities must be provided to the Project Officer and AID/G/EGAT before the change is effected. Any applicable institutional reviews of the facilities must be repeated, and the re-certification should be provided to the Project Officer and AID/G/EGAT.

9. Human Subjects

Research will be conducted following the protocols described in the Grantee's proposal, as revised, which insures the well-being and informed consent of human subjects. It will also be conducted in accordance with the applicable procedures issued by the U.S. Government to insure ethical treatment of human subjects, and by those issued by the government of the host country in which the human subjects are to be involved.

If any protocol involving human subjects is revised, it must be re-reviewed by the investigator's institutional ethical review committee, and the Project Officer and AID/G/EGAT must be informed in writing before the revised protocol is used. The revised procedures must be consonant with the guidelines of the host country and of the United States. If the patient's informed consent form is revised, a copy of the new form must be submitted to both the Project Officer and AID/G/EGAT. A copy of the approval of the revised form by the investigator's institutional ethical review committee must also be provided to the Project Officer and AID/G/EGAT.

In addition and prior to commencement of any experimentation involving human subjects, the Grantee shall make a judgment and communicate the same to AID/G/EGAT as to whether the regulations, procedures or facilities of the country in question are adequate to ensure the safety and free and informed consent of the human subjects. In the event such judgment is that they are not, the Grantee, the Project Officer, and AID/G/EGAT will consult and agree on the protocol to be applied to insure the safety and free, informed consent of the subjects.

10. Containment and Safe Disposal of Animal or Plant Pathogens or Pests

Research will be conducted following the protocols described in the Grantee's proposal, as revised, which insure the containment and safe disposal of animal or plant pathogens. All research shall be conducted following procedures issued by the U.S. Government and those issued by the government of the host country for the containment of these pathogens or pests.

If any protocol is revised, it must be re-reviewed by the investigator's institutional

review committee(s) that approved the original protocol, and the Project Officer and AID/G/EGAT must be informed in writing before the revised protocols are used. The revised procedures must be consonant with the guidelines of the country in which the laboratory is located and of the United States. Copies of the approval of the revised protocols by the investigator's institutional review committees should also be provided to the Project Officer and AID/G/EGAT.

Similarly, the research will be conducted in the facilities described in the Grantee's proposal, as revised. If the research is moved to new facilities or the facilities are modified in such a way to affect safety or hazard containment, a description of the new facilities should be repeated, and the re-certification should be provided to the Project Officer and AID/G/EGAT.

11. International Shipment of Organisms, Biologicals, or Controlled Materials or Equipment

Procedures for the international shipment of these materials must be in accordance with those approved in the permits cited in the Grantee's proposal, as revised. All such shipments shall be in compliance with International Import/Export Regulations for all countries to and from which regulated items are shipped. If the shipment procedures are varied from those specified for permits, permits for the revised procedures must be provided to the Project Officer and AID/G/EGAT before shipping commences.

12. Recombinant DNA

- a. Research will be conducted following the protocols described in the Grantee's proposal, as revised, which ensure the containment of recombinant organisms. If any such protocol is revised, it must be re-reviewed by the investigator's institutional review committee(s) that approved the original protocol, and the Project Officer and AID/G/EGAT must be informed in writing before the revised protocol is used. Copies of the approval of the revised protocol by the investigator's institutional review committees should also be provided to the Project Officer and AID/G/EGAT.

Similarly, the research will be conducted in the facilities described in the Grantee's proposal, as revised. If the research is moved to new facilities, or the facilities are modified in such a way to affect safety or containment, a description of the new facilities must be provided to the Project Officer and AID/G/EGAT before the research is effected. Any applicable institutional reviews of the facilities should be repeated, and the re-certification should be provided to the Project Officer and AID/G/EGAT.

- b. Notwithstanding the above:

(1)

The Grantee and its subgrantees may not commence testing in any foreign location until written approval for testing is obtained from the Project Officer, AID/G/EGAT and the government of the country where testing is planned. Testing shall be conducted in accordance with all applicable regulations of that country.

(2)

In addition, however, and prior to commencement of any such testing, the Grantee shall make a judgement and communicate the same to the Project Officer and AID/G/EGAT as to whether the regulation, procedures or facilities of the country in question are adequate to ensure testing in an environmentally sound manner. In the event such judgement is that they are not, the Grantee, the Project Officer, and AID/G/EGAT will consult and agree on the conditions to be applied to the testing which will have such environmental effect.

(3)

Reports submitted under this activity to the Project Officer and AID/G/EGAT will address regulatory issues as above related to the activity.

13. Endangered Species

Research will be conducted following the protocols described in the Grantee's proposal, as revised, which insure the protection of endangered species. All research shall be conducted following procedures issued by the U.S. Government and those issued by the government of the host country for the protection of endangered species.

If any protocol involving these species is revised, it must be re-reviewed by the investigator's institutional review committee(s) that approved the original protocol, and the Project Officer and AID/G/EGAT must be informed in writing before the revised protocols are used. The revised procedures must be consonant with the guidelines of the country in which the species are to be affected, and of the United States. Copies of the approval of the revised protocol by the investigator's institutional review committees should also be provided to the Project Officer and AID/G/EGAT.

In addition, however, and prior to commencement of any such activity which may affect an endangered species, the Grantee shall make a judgment and communicate the same to the Project Officer and AID/G/EGAT as to whether the regulations, procedures, or facilities of the country in question are adequate to ensure the protection of those species. In the event such judgment is that they are not, the Grantee, the Project Officer, and AID/G/EGAT will consult and agree on the conditions to be applied to the activity which will protect that species.

14. Environmental Hazards

Research will be conducted following the protocols described in the Grantee's proposal, as revised, which insure that there are no unacceptable environmental hazards incident to the research. All research shall be conducted following AID and U.S. Department of State environmental guidelines and those issued by the government of the host country.

If any protocol involving environmental hazards is revised, it must be re-reviewed by the investigator's institutional review committee(s) that approved the original protocol, and the Project Officer and AID/G/EGAT must be informed in writing before the revised protocol is used. The revised procedure must be consonant with the guidelines of the country in which the research is located and of the United States. Copies of the approval of the revised protocol by the investigator's institutional review committee(s) must also be provided to the Project Officer and AID/G/EGAT.

In addition, however, and prior to commencement of any such activity which may create an environmental hazard, the Grantee shall make a judgment and communicate the same to the Project Officer and AID/G/EGAT as to whether the regulations, procedures or facilities of the country in question are adequate to ensure the protection of the environment. In the event such judgment is that they are not, the Grantee and the Project Officer and AID/G/EGAT will consult and agree on the conditions to be applied to the activity which will ensure environmental protection.

15. Intellectual Property Rights

Intellectual property rights stemming from the activities supported under this Grant will be apportioned as described in the Grantee's proposal, as amended. If the participants choose to modify that apportionment, the revised apportionment must be submitted to the Project Officer and AID/G/EGAT for approval before it takes effect.

Attachment Two

***Program Description
(Technical Work Plan - excerpts)***

ATTACHMENT TWO - Work Plan

Technical Work Plan

1. **Experimentation level 1: Monosex culture with the integration of manual segregation, selective harvest, claw ablation and economical analysis**

The experiments will be carried out to study monosex culture (Fig. 1 research level 1) under Fisheries Center conditions and in various selected farms. At least one Fisheries Experimental Center and three farms in the Northeast of Thailand will be selected for experimentation. Post larvae of *M. rosenbergii* will be obtained from the hatchery stock at the Aquatic Animal Genetics Research and Development Institute (AAGRDI) which have been culturing over 5 generations under the selective breeding program (Uraivan et al., 2003).

1.1. **Growth performance of monosex culture following manual segregation**

An experiment will be conducted in which manual sex segregation (sorted by male gonophores determination) will be applied three months of culture at the primary and secondary nursery in earthen ponds at a density of 15,000 individuals/800 m² until the age of 3 months. Shelters covering 60% of the pond's bottom area will be provided. The feeding strategy that will be used at this period of growth will be as follows: up to 2 months old the prawns will be fed with 40% protein small pellet, 10% of body weight, 4 times a day. Up to 3 months of age the prawns will be fed with 32% protein small pellet, 8% of body weight, 2 times a day.

Following the above 3 months hand segregated all male juveniles will be stocked in growout earthen ponds at a high stocking density (10-15 prawns per m²) and low stocking density (3-5 prawns per m²) in three replicates at random from each group in the experiments. Same age mix-sex juveniles at the same stocking densities will be stocked at the same time and location as the all-male culture and will serve as controls for the experiments. The feeding strategy that will be in use at this period of growth will be as follows: up to 4 months of age the prawns will be fed 32% protein pellets, 5% of body weight, 2 times a day. Up to 6 months of age the prawns will be fed 32% protein pellets, 3-5% of body weight, 2 times a day. Standard experimental methods of waste water monitoring will be used, APHA (Clesceri et al., 2001). Oxygen, pH and temperature will be checked twice a day. NH₃ and NO₂ will be checked every 3 days. Water alkalinity, hardness and transparency will be checked once a week. Water quality parameters will follow the following ranges: Oxygen > 4 ppm; PH= ~7.7; Ammonia <0.4 ppm; Nitrite <0.1 ppm; Alkalinity >50; Hardness >80; Transparency =30 cm.

Growth performance, survival rate, yield and profit of the experimental ponds will be checked monthly in comparison with the mix-sex culture ponds and statistically analyzed (analysis of variance ANOVA). Prawns will be reared until the harvest period (about 8 months). This part will be carried out under Fisheries Center conditions and in three selected local farms in the Northeast of Thailand in which prawn culture ponds are available.

Experiments with the same terms and conditions as described above will be conducted under combined rice/prawn culture conditions. The experiments will be carried until the harvest period

(depending on the rice production strategy), and growth performance, survival rate, yield and profit of the experimental combined culture will be checked at harvest time, since the combined strategy does not allow monthly follow-ups. Statistical analysis will be performed to compare the monosex treatment with the mix-sex culture control under rice/prawn conditions. Another comparison will be made with the performances under regular (no rice) culture strategy. This part will take place in three selected rice growing farms in the Northeast of Thailand.

The economical analysis will include budgeting all the investments (cost of post larvae, hand segregation, feed and other husbandry related investment) in relation to the income from the prawn yield and rice harvest in the case of rice/prawn culture.

1.2. Application of selective harvest and claw ablation on monosex culture

Manual hand segregated juvenile male prawns hatched at AAGRDI will be stocked at high and low densities (as described above C.1.1). Two sets in three replicates will be stocked at random in this experiment. Prawns will be reared until the harvest period (about 8 months). In one set, selective harvesting of the largest males reaching marketable size will be performed monthly. At each selective harvest claw ablation of terminally molted blue-claw males that did not reach marketable size will be applied and the ablated prawns will be released into the pond for further growth. The second set of ponds will be stocked with all male juveniles however they will not be subjected neither to the selective harvest or to claw ablation procedures, thus serving as controls for this phase of the research. Growth performance, survival rate, yield and profit of the above experimental all male cultures will be checked throughout the harvest procedure and at the final harvest. The cumulative and final results will be statistically analyzed in comparison with the control culture and compared to the results of the previous stage mix-culture.

Based on the results of the above experimental procedure, a set of aquacultural and economical recommendations will be generated serving as a base for local and regional workshops to proliferate the knowledge among selected farmers and extensionists.

2. Experimentation level 2: Microsurgical removal of the AG and sex reversal

This level of the research is divided into two phases: the first phase includes microsurgical removal of the AG to reverse the sex of juvenile males in order to produce 'neo-females'. This step presents the main bottle neck of the whole process since the success rate of sex reversal using AG ablation depends on complete removal of the AG in juvenile males at an early age and small size (PL 24-35, 0.1-0.25 g see our preliminary results Appendix B). However, at this age and weight the male gonophores are not fully distinguishable and selection is thus problematic enforcing the selection of larger individuals in which AG ablation results with low success rates in terms of full sex reversal (~1-2% see our preliminary results Appendix B). This step includes mating of suspected 'neo-females' with normal males (Fig. 1. level 2) and testing the sex ratio of their progeny. Following an extensive 'quality control' procedure, only 100% male progenies will be selected as success cases of the sex reversal and the creation of a proven 'neo-female'.

In the second phase we suggest a novel solution to this obstacle which will dramatically increase our ability to establish mass production of all male post larvae via 'neo-female' broodstock. This new approach includes the selection of proven 'neo-females' (with 100% male progenies following all the 'quality control' steps of the previous phase) that will be mated with normal males and their progeny will be dissected at a very small size and an early age without the need to previously check their masculinity. Since all the progeny of the latter crossings are males, the stage of male juvenile selection for dissection will be eliminated. Without the need to sort the juveniles the process will enable the intervention at the right size and age, more efficient and suitable for mass production of all male producing broodstocks to be transferred to the local backyard hatcheries.

Phase 1: Sex reversal by microsurgical AG removal and 'quality control'

This part of the experiment will be initiated immediately after the first training of key members of the staff on the biology and microsurgical intervention in the AG in Thailand. This technique will be applied in the experiment as follows:

Post larvae from the experimental hatchery at the Aquatic Animal Genetics Research and Development Institute will be used. For successful operation, post larvae at an early age and the smaller size as possible, but with distinguishable masculine genital papillae will be selected. Juvenile males will be sorted out following examination of genital papillae development under a dissecting microscope. Microsurgical removal of the AG will be performed not later than PL 75 with preferences to males that could be identified at an earlier stage of development. In parallel to the AG ablation, the second left pleopod of the dissected juvenile (bearing the male sex character, Appendix masculina) will be removed. AG ablated and non-ablated populations will similarly grow in 4 concrete ponds. The feeding regime will be similar to that described above. Several steps of 'quality control' to test sex reversal success and remove 'failures' will be applied during the experiment. The parameters to be checked and used for the 'quality control' procedure will be as follows:

- a) *Growth performance* - weight, carapace and propodus lengths will be measured monthly.
- b) *Survival rate* - will be calculated at 24 hours, 1 week and 1 month after AG ablation and later on every month.
- c) *Presence of Appendix masculina on the regenerated versus the original second pleopod* - The second pleopod that have been ablated usually regenerates. Regenerated pleopod without Appendix masculina points on successful ablation of the AG and serve as important quality control criteria for the whole process. AG ablated juveniles will be examined under a dissecting microscope for the presence of Appendix masculina starting two months after AG ablation. Prawns regenerating Appendix masculina will be discarded.
- d) *Gonad development* - developed ovaries are orange in color which is clearly seen through the transparent cuticle and body wall of the prawns and enables the tracing of gonad development and maturation up to the lobe level. Prawns that are showing gonad development will be separated and monitored more frequently in order to assess their gonad maturation and development. When (and if) ready for mating the suspected 'neo-female' will be placed with a male in a mating tank for

mating.

e) *Females' genital openings development* - prawns that showed gonad development will be checked for female genital gonophores development in order to discard prawns with abnormal female gonophores or prawns that did not develop female gonophores at all.

f) *Spawning* - suspected 'neo-females' which passed all the quality control stages up to this point will be mated with normal males and will be kept separately until hatching in order to trace the larvae of each individual suspected 'neo-female'.

g) *Amount and quality of spawned larvae* - larvae from each suspected neo female will be grown separately and survival rate, larval staging, duration of each larval stage and time to metamorphosis will be determined and will be compared to larval development from batches of normal females.

h) *Progeny testing of post larvae* - from each 'neo-female' that spawned a sample of 1,000-1,500 post larvae will be kept separately up to the size and age that allows male gonophores recognition. Sex ratio will be determined and will serve as the final quality control step that assures the success of the sex reversal and the establishment of a functional 'neo-female' bearing 100% male progeny.

During the above 'quality control' steps, unsuccessful AG ablated prawns ('failures') will be discarded from the experiments. At the end of the experiment, all the above parameters in the experimental population ('neo-female') and the non-ablated population will be compared and will be statistically analyzed.

Testing the performance all-male population which are progeny of approved 'neo-females'

In order to evaluate the quality of the all male progeny in terms of proper growth and development, their performance will be compared to normal mix population progeny and hand segregated all male (experimental level 1) following the exact conditions described in C.1.1. In this experiment progeny of proven 'neo-females', normal females and groups of hand segregated males will be reared separately in three replicates under identical conditions as described in level 1. Growth performance, survival rate, yield and tentative profit will be compared and statistically analyzed between these three groups. At this part, the experiment could be examined also under the condition of selective harvest and claw ablation procedures based on the recommendations derived from the results of level 1 of the research.

Phase 2: Scale up of all-male population mass production

In order to scale-up the all male production and eliminate the major bottle neck, proven 'neo-females' from phase 1 will be selected and mated with normal males. Larvae and post larvae will be grown to serve as a stock of dissectible prawns. At this point the post larvae are assumed to be all males even without the clear identification of developed male gonophores. Thus, all the population from this stage could be AG ablated at a small size and early age (PL24-35 weighting 0.1-0.25 g). This procedure is relatively fast and could be done in high numbers without a need for previous exact gender identification and sorting. At least 4,000 post larvae are estimated as a dissected group in order to obtain approximately 200 functional 'neo-females' for a broodstock to be used for mass production of all male monosex progeny. Following AG removal the dissected prawns will be

grown separately with minimal quality control steps until sexual maturity is obtained. Following maturity, the successful egg bearing 'neo-females' will be selected to produce a large scale broodstock to be comprised of 'neo-females' and normal males. Progeny of the broodstock will be tested for aquaculture performances according to the procedures found favorable at level 1 of the project (see above 1.1).

Considerations of genetic principles

Monosex broodstock selection will not be done from the segregated and continuously harvested ponds, it to prevent the potential loss of genetic variability and selecting for slow grower individuals in the process. No selection, neither for age of appearance of male characteristics nor for size, will be performed during the first phase. The breeders will be randomly selected from various populations from different localities in Thailand to prevent founder effects.

Founder effects, leading to inbreeding and/or genetic drift during the microsurgical sex reversal (Tave, 1999) will be prevented. The potential 'bottle neck' during this step can be rectified, and the following strategy is suggested: Microsurgical removal of AG will be applied to samples of post-larval males from at least 10-20 single-pair matings. Parents will be taken at random from a large, genetically heterogeneous population. Proven neo-females will be identified among the offspring of each pair. These neo females will form the broodstock to be mated again with the most variable source of males (out crossing). The latter males will be collected from at least 3 different localities in Thailand to preserve a large portion of the genetic variation available in the original populations (Chevassus, 1989). Furthermore, use of non-sibling males as sires for producing the broodstock (males from different families, i.e. not brothers of the neo-females, or from a different population (out-crossing) will also contribute to the preservation or even increase of genetic variation.

3. Experimentation level 3: Elucidation of AG bioactive products

The experiment on elucidation of bioactive products (experimental level 3, Fig. 1) will be taken place in both Israel and Thailand. The training and part of the biotechnology related research will be done in Israel. The implementation will be taken place in Thailand, as well as the animals and material collection. Molecular and biochemical studies will be initiated in Israel and will be transferred gradually through training to Thailand.

Molecular approach based on AG's uniquely expressed genes

We will design primers based on sequences found to be uniquely expressed in the AG of *C. quadricarinatus* by the subtractive cDNA library developed by us (see appendix B2). We will check

if these sequences are also uniquely expressed in the AG of *M. rosenbergii* by using the above primers in a RT-PCR reaction. RNA from AGs and other tissues of mature *M. rosenbergii* males from the different morphotypes will be extracted using EZ-RNA Total RNA Isolation Kit. The concentrations of all the produced RNAs will be evaluated by spectrophotometry at 260 nm. cDNA will be obtained by a reverse transcriptase (RT) reaction from 1 µg of total RNA at 45°C for 1 h, in a volume of 20 µl, using 50 units of Expand Reverse Transcriptase and poly T reverse primer at a final concentration of 2.5 µM. The cDNA will then be amplified by PCR, using the primers that will be designed. The PCR program will include: one cycle at 95°C - 15 min; 35 cycles at 94°C - 1 min, 50-65°C - depends on the primers - 1 min, 72°C - 2min; one cycle at 72°C - 10 min. Each 25-µl reaction solution will contain 0.625 units of HotStartTaq DNA Polymerase, 0.2 mM of each d-nucleotide triphosphate, and 0.5 µM of primer concentrations, in buffer supplied with the DNA polymerase. Fragments that will be amplified only when using cDNA from the AGs will be cloned and sequenced in the Israeli laboratory.

Biochemical approach based on in vivo and in vitro bioassays

Extraction, characterization and application of androgenic factors from the AG

There is an ongoing effort to find chemical agents responsible for the regulation of the shifts from femaleness to maleness in order to control sexually plastic processes in important crustaceans and to determine the sex of offspring groups. Factors from the AG will be prepared as follows: 1. Crude AG extract - AGs will be homogenized and separated to lipoidal and proteinaceous extracts. 2. AG secretion - AGs will be incubated in a medium for 24 hours as described in Khalaila et al. (2002). Preliminary results in our laboratory from incubation of AGs from another decapod- *C. quadricarinatus*- showed that the medium contains secreted material from the AGs (see appendix B Fig. 3). We will use the same procedure with AGs of *M. rosenbergii* and the secreted material will be separated. 3. Preparations representing whole glands (either crude AG extract or AG secretion) that will be found to be active will be fractionated using RP-HPLC equipped with a C18 reverse-phase column (LiChroCART 250-4, LiChrospher 100 RP-18 (5 µm)). In addition it will be subjected to a lectin column, based on the assumption that the AGH has a sugar moiety.

All the above three avenues will be followed by testing the bioactivity of the preparations and/or fractions using various bioassays as suggested below.

In vivo bioassay

The aim of the experiment is to extract and identify bioactive factors from the AG and explore their effects on the development of male characters. The underlying hypothesis is that active androgenic factors from the AG induce masculinization, as was shown for AG implantation into female prawns that lead to the development of the appendices masculina, the male gonopore complex, mature masculine chelipeds and the initiation of spermatogenesis in the ovaries (Nagamine et al., 1980). A similar manipulation through the injection of AG extract is suggested here. Tested androgenic factors from the AG will be extracted according to the procedures detailed above. Each extract will be injected to groups of 20 *M. rosenbergii* juvenile females while 20 saline-injected prawns (i.e. vehicle-only) will serve as controls for each tested preparation. The above extracts, secretions or fractions will be injected according to the following procedures: injections of 4 AG-equivalents will be applied at a 3-day interval to the youngest and smallest identified female prawns for a period of 3 months. At this period the females will be weighted twice a month and will be checked for the development of the appendices masculina. When the females will arrive to sexual maturity, they will be examined for the development of primary and secondary male sex characters following the 'quality control' scheme described in experimental level 2.

In vitro bioassay

In female prawn *M. rosenbergii* the expression of the vitellogenin gene was detected in the R cells of the hepatopancreas (Jasmai et al., 2004). Primary cell culture of hepatocytes can be used as an *in vitro* bioassay by quantifying the activity of the factors from the AG through monitoring the expression of the vitellogenin gene in hepatocytes affected by these factors. Preliminary studies in our laboratory showed that AG implantation into young *C. quadricarinatus* females caused inhibition of the vitellogenin gene expression (Manor et al., 2004). Recently, we developed a tool for measurement of changes in the expression of the vitellogenin gene in tissue and primary cell cultures, using relative quantification RT-PCR. Our preliminary results showed that co-culture of hepatocytes with 2 AGs for 24 hours inhibited by 80% the expression of the vitellogenin gene in the hepatocytes measured by real time RT-PCR. Primary cell culture of hepatocytes from vitellogenic *M. rosenbergii* females will be obtained. Vitellogenic females will be selected as hepatocyte donors based on coloration and ovarian size observed through the transparent exoskeleton (O'Donovan et al., 1984; Chang and Shih, 1995). The selected females will be anesthetized by submerging in ice and dissected. Hepatopancreas will be removed and sectioned rapidly into small fragments (3-10 mg). Primary cell culture from hepatopancreatic tissue will be obtained using cell suspension achieved through a non enzymatic method as follows: The hepatopancreas fragments will be minced, in Ca²⁺ Mg²⁺ free prawn saline containing 1mM EDTA and protease inhibitor followed by 20 min stirring at room temperature and filtration through four layers of cheese cloth. The cell suspension will be centrifuged (600g, 5 min) and washed several times following seeding in pre-coated Petri dishes with 50% hemolymph and incubated in sterile Dulbecco's modified Eagle's medium (DMEM) with 4.5 g/l D-Glucose, without L-Glutamine, pH 7.4, supplemented with 1 % of bovine serum albumin (BSA) and adjusted to the hemolymph osmolarity of *M. rosenbergii*, as previously described

(Sagi et al., 1991). All incubations will be carried out at 28 C, with slight agitation under humid, oxygen-enriched atmosphere. Hepatocyte cell culture will be incubated for 24 hours, with 1 or 3 AGs or with a same sized sperm duct fragment control (n=6 for each treatment). For dose-response experiments, the above extracts, secretions or fractions will be added to each cell culture well with the following concentrations of AG extracts: 0.05, 0.5, 1, and 3 AG equivalent or equivalent amounts of carrier solution as control (n=6 for each treatment). At the end of the incubation period, RNA will be extracted from the hepatocytes as described above and vitellogenin gene expression will be evaluated by relative quantitative real time RT-PCR as follows: First-strand cDNA will be generated by an RT reaction (Reverse-iTTM 1st Strand Synthesis Kit - ABgene AB-0789) from 1 µg of total RNA at 47°C for 30 min with random hexamers as primers (20 ng/µl final concentration). Relative quantification of vitellogenin gene expression will be performed using primers that will be designed based on the sequence of *M. rosenbergii* vitellogenin gene (Okuno et al., 2002), 0.4 µM final concentration, and SYBR Green PCR Master Mix, with ABI Prism 7000 Sequence Detection System of Applied Biosystems (one cycle at 50°C - 2 min; one cycle at 95°C - 10 min; 40 cycles at 95°C - 15 s and 60°C - 1 min). Differences in levels of vitellogenin gene expression among the treatments will be statistically analyzed (one way ANOVA).

4. Workshops and technology transfer

Based on the results of level 1 of the experiment regarding the monosex culture, hand segregation and economical analysis, a set of aquacultural and economical recommendations will be generated serving as a base for local and regional workshops to proliferate the knowledge among selected farmers and extensionists. Practically the training done by Israeli and Thai experts will include: *M. rosenbergii* biology and population structure, gender recognition, morphotype recognition, monosex culture technology and basic economics of prawn aquaculture.

The second level of experimentation is based on the early identification of juvenile males and the microsurgical removal of the AG. This part of the experiment will be initiated immediately after the first training of key members of the staff on the biology and microsurgical intervention in the AG that will be taken place in Thailand. This technique will be the subject of a workshop. The best trainees will take part in its application during experimentation level 2 and in further technology transfer in the region and final workshops during the last year of the project involving other developing countries in Southeast Asia (according to the above list).

Technology transfer of scientific know-how related to research level 3 will be held continuously by the Israeli group both in Israel and Thailand. This will include the training of Thai representatives and students in the field of reproductive biology and related molecular and biochemical procedures that will enable capacity strengthening of the Thai institute for further biotechnological research. Practically, the training will include identification and dissection of AG and anatomical acquaintance with the reproductive system in decapods, RNA and DNA work, extraction of bioactive compounds, organ and primary cell culture.

Time Chart

Activities	Year 1			Year 2			Year 3		
	1-4	5-8	9-12	1-4	5-8	9-12	1-4	5-8	9-12
Experiment level 1.									
1.1 Spawning and larvae rearing	↔			↔					
1.2 Hand segregation	↔			↔					
1.3 Grow out under methods of selective harvesting and claw ablation	↔			↔			↔		
1.4 Comparison on growth and economic value between all male and mix sex culture	↔			↔			↔		
1.5 Data analysis and writing report				↔			↔		
Experiment level 2.									
2.1 Microsurgical AG removing training	↔			↔					
2.2 Spawning and larvae rearing	↔			↔					
2.3 Microsurgical AG removing	↔			↔					
2.4 Quality control steps of AG ablated prawns	↔			↔					
2.6 Spawning and larvae rearing of suspected neo females progeny				↔			↔		
2.5 Comparison of performances between experimental all male culture and mix sex culture				↔			↔		
2.6 Scale up neo females production				↔			↔		
2.7 Grow out under methods of selective harvesting and claw ablation	↔			↔			↔		
2.8 Data analysis and writing report	↔			↔			↔		
Experiment level 3.									
3.1. The molecular approach				↔			↔		
3.2. <i>In vitro</i> tests for bioactive material							↔		
3.3. <i>In vivo</i> tests of bioactive material							↔		
3.4. Data analysis and writing report	↔								
Training workshops									
4.1 Microsurgical training				↔					
4.2 AG Biochemistry, molecular workshop							↔		
4.3 All-male culture techniques to the Thai farmer							↔		
4.4 All-male culture techniques among the target countries							↔		

Attachment Three

Payment Forms

(Payment forms are also available by email upon request)

INSTRUCTIONS

1. Schedule

Financial Reports should be made on a quarterly basis unless otherwise agreed to by the Grant Officer (see attachment 1, page 11, Reporting and Evaluation). Advance payments should be requested for a period of up to three months only.

2. Use of Forms

It is essential that only the following forms be used when requesting Advance or Reimbursement type payments. **No other forms will be accepted for payment processing!**

Photocopy the forms for re-use or you can receive payment forms by e-mail. Please write to: ecoaidta@netvision.net.il (formatted for MS-Word or other; call us if you have any question)

- To request advance payment, use forms 1 & 3
- To request reimbursement, use forms 1, 2 & 4 (if applicable)
- Use a separate set of forms for each grant participant
- Each submitted report must include an original and one copy of the set of forms

3. Payment Information

Payments shall only be made to named grant participating institutions (**personal accounts are not allowed**). Payment information must be **detailed, accurate and complete** for each submission.

Payments can be made either by bank check or Electronic Funds Transfer (EFT).

Bank check can be sent through the Grantee's institution or directly to the Sub-grantee's institution. EFT can be sent directly to payee's account or via a correspondent bank.

- If EFT (Electronic Funds Transfer) is requested, please provide the following

ACCOUNT NAME
ACCOUNT NO.
BANK NAME & FULL ADDRESS
BRANCH NAME & NUMBER
SWIFT CODE

- If EFT via correspondent bank, please provide the following

ACCOUNT NAME	CORRESPONDENT BANK NAME & ADDRESS
ACCOUNT NO.	BRANCH NAME & NUMBER
BANK NAME & FULL ADDRESS	ACCOUNT NO.
BRANCH NAME & NUMBER	SWIFT CODE
SWIFT CODE	

- If check is requested, please provide the following

PAYEE NAME
PAYEE ADDRESS
ACCOUNT NO. (IF NEEDED)

Note: The method of payment should be clearly marked on the cover page (form 1), followed by accurate, full and valid bank details to allow funds to be transferred in a timely fashion.

For any questions, please do not hesitate calling us at 03-519-7360/2.

Embassy of the United States, Tel Aviv

(Payment forms: CDR & MERC)

REQUEST FOR PAYMENT COVER PAGE

(Please submit original and one copy from each SET OF FORMS PER PARTICIPANT)

From: _____
(Grantee/Subgrantee Institution's Name)

Grant No.: TA-MOU- - - -

To: Mr. Boaz Ayalon
American Embassy Tel Aviv
ECON/AID Section
71 Hayarkon Street
Tel Aviv 63903

Advance - Attached is a duly signed Form no. 3

Reimbursement - Attached is a duly signed Form no. 2

(Please select one of the above)

Period covering this request: from _____ to _____

Payment Information

(please provide relevant information only):

PAYMENT METHOD	<input type="checkbox"/> EFT	<input type="checkbox"/> Check	<input type="checkbox"/> Send to Prime Grantee
			<input type="checkbox"/> Send direct to Subgrantee
			<input type="checkbox"/> Send to Subgrantee via Prime Grantee
PAYEE NAME			
STREET and NUMBER			
CITY & POSTAL CODE			
COUNTRY			
BANK NAME & ADDRESS			
ROUTING NUMBER			
ACCOUNT NUMBER			
AMOUNT \$			
SPECIAL INSTRUCTIONS			
ADDITIONAL INFORMATION			

SIGNED: _____ NAME: _____

TITLE: _____ DATE: _____

ATTACHMENT THREE

FORM I

Embassy of the United States, Tel Aviv

(Payment forms: CDR & MERC)

FEDERAL CASH ADVANCE STATUS REPORT

(Please submit original and one copy from each SET OF FORMS PER PARTICIPANT)

Grantee/Subgrantee: _____ Grant No. TA-MOU- - - -

A. Period covered by this report: from _____ to _____ Grant Termination

Period covered by the next report: from _____ to _____

B. Cash Advance Use and Needs: (all in US dollars)

- 1. Cash advance on hand at the beginning of this reporting period \$
2. U.S. Treasury check advance(s) received during this reporting period \$
3. Interest earned on cash advance during this reporting period \$
4. GROSS cash advance available during this reporting period (lines 1,2, &3) \$
5. LESS, interest remitted to AID during this reporting period \$
6. NET cash advance available during this reporting period, including subadvances \$
7. Total disbursements during this reporting period, including subadvances \$
8. Amount of cash advances available at the end of this reporting period \$
9. Projected disbursements, including subadvances, for the next reporting period \$
10. Additional cash advance requested for the next reporting period \$
11. Total interest earned on cash advance from the start of the grant to the end of this reporting period, but not remitted to AID \$
12. Total cash advance to subgrantee, if any, as of the end of this reporting period \$

Footnotes

- 1. The Grantee shall submit a cumulative detailed report of disbursements by BUDGET Line item quarterly.
2. If the amount of disbursements in 7 is equal to or more than the advance amount in 6, the total must be 0!
3. The Grantee shall attach a Summary, by BUDGET Line item, of its projected disbursements for the next reporting period.

C. Certification

The undersigned hereby certifies: (1) that the amount in paragraph B.9 above represents the best estimate of funds needed for the disbursements to be incurred over the period described, (2) that appropriate refund or credit to the grant will be made in the event of disallowance in accordance with the terms of the grant, (3) that appropriate refund or credit to the grant will be made in the event funds are not expended, and (4) that any interest accrued on the funds made available herein will be refunded to AID.

SIGNED: _____ NAME: _____

TITLE: _____ DATE: _____

Attachment Four

Performance Reports
-Guidelines-

**INTERIM GUIDELINES ON
PERFORMANCE REPORT PREPARATION FOR CDR PROJECTS**

GENERAL COMMENTS

Although reports are to be written by the Principal Investigator (P.I.), they should reflect the work of all project institutions involved in the research. Each report should be written in English and should be submitted according to the Grant Agreement, starting eight months after the project start date. This start date may not be changed without the specific, prior written approval of the granting office in the U.S. Embassy Tel Aviv.

TYPES OF REPORTS

Two types of performance reports are required:

- 1) Semi-Annual Progress Reports (expected within 60 days after the end of each six month period of the grant) summarizing progress during each six month period and highlighting constraints.
- 2) The Final Report (expected not later than 90 days after the end date of the grant period) summarizing all the project's accomplishments.

Semi-Annual Reports should be sent to the following distribution list:

1. USAID/EGAT: U.S. Agency for International Development; Bureau for Economic Growth, Agriculture and Trade; Room 2.11-151 RRB, 1300 Pennsylvania Ave, NW; Washington, D.C. 20523-2110. One copy
2. RSP/NAS: Research Support Program for USAID; Policy and Global Affairs; National Academy of Sciences; 500 5th Street, NW, Mailstop W517; Washington DC 20001 USA. Two copies
3. U.S. Embassy in Israel: ECON/AID Office; U.S. Embassy; 71 Hayarkon Street; Tel Aviv 63903, Israel (or via e-mail: ecoaidta@netvision.net.il) One copy
4. The USAID Office (Field Mission) in the non-Israeli CDR target-country. One copy

Final Reports should be sent to the above distribution list and in addition sent to: USAID Development Experience Clearing House; ATTN: Documents Acquisitions; 8403 Colesville Road, Suite 210; Silver Spring, MD 20910-6368 (or via e-mail: docsubmit@dec.cdie.org) One copy

SEMI- ANNUAL PROGRESS REPORT

The purpose of the Semi-Annual Report is to summarize significant scientific results from the previous six months' work and to describe advances in scientific capabilities in developing countries (Section I), along with managerial issues (Section II) that have arisen in the last six months. Semi-Annual Reports should be 6-10 pages long plus a Cover Sheet. Describe in detail any significant changes in the project.

Semi-Annual Reports should be prepared in the following format:

Cover Sheet: Identify as a SEMI-ANNUAL REPORT, Covering Period [Date to Date]; state that it is "Submitted to the U.S. Agency for International Development; Bureau for Economic Growth, Agriculture, and Trade"; give the TITLE OF PROJECT; Project Number and Award Number; identify the Principal Investigator, along with his/her institution, address, telephone number, and e-mail address; list each of the Co-Principals at each cooperating institution, along with his/her institution, address, telephone number, and e-mail address; and list the current contact information for the administrative officials at each institution. See sample cover page attached. **Note:** Be sure to provide current contact information for all investigators and institutions, since personnel and contact information may have changed since the original project was approved.

Executive Summary: Typed double-spaced on a separate page. No longer than three-fourths of a page. Use non-technical language. Describe the purpose of the project. Briefly describe the findings over the past six months and explain how these findings contribute to project objectives and to international development. Clearly describe the nature of collaboration during the last six months. **Note:** The Executive Summary is extremely important. It is the section of the report that policy makers normally use to assess the impact of USAID research programs. Write the Executive Summary so that the content is clear, concise, and understandable to a non-scientist.

Section I: Technical Progress

A) **Research Objectives:** A brief statement of project objectives. Do not include unnecessary background, history, or literature review. Focus on objectives covered since the previous Semi-Annual Report.

B) **Research Accomplishments:** Provide descriptions of results that are supported, if needed, with a few key tables and/or photos. Data should be clearly presented. If results have been published, attach reprints as appendices. Describe any project products or procedures that have been patented. Focus on accomplishments achieved since the previous Semi-Annual Report.

C) **Scientific Impact of Collaboration:** How have collaborating scientists participated in the project during the reporting year? How has the project contributed to the scientific strength of the developing-country partner(s)?

D) **Description of Project Impact:** Are results from the project being applied? If so, how? If not,

what are the anticipated uses?

E) Strengthening of Developing-Country Institutions: Describe any project investments such as facilities, equipment, or training that have been made. Summarize new research or managerial skills that have been acquired. Describe efforts to strengthen institutional partners in the target country.

F) Future Work: What remains to be done? Is the project on schedule? Has the work plan been revised? If so, describe the revision.

Section II: Project Management and Cooperation

A) Managerial Issues: Describe any project managerial issues that have arisen since the last Semi-Annual Report, including any administrative barriers to cooperation, budgetary concerns, staff changes, timetable changes, or research site changes. Describe and justify major changes to the budget, i.e., 10% or more in budget items. (Remember that any budget changes must have been pre-approved by U.S. Embassy Tel Aviv).

B) Special Concerns: Have any protocols that address "special concerns" (e.g. human subjects, intellectual property rights, etc.) changed? Attach any relevant documents, such as revised consent forms or patent disclosures.

C) Collaboration, Travel, Training and Publications: Briefly describe collaborative activities.

- 1) Provide a roster listing all the participants on the project; include each person's name and position (such as co-PI, technician, Ph.D. student, etc.).
- 2) Provide a list of completed travel and training since the last report. Indicate who was involved, the purpose of the travel or training, and when and where the activities occurred.
- 3) Provide a list of project publications that have appeared since the last report. Clearly identify any joint publications that included target-country and Israeli co-authors on the same manuscript.
- 4) Very briefly describe the anticipated activities in next 6 months.

Note: The information provided in this section is essential for CDR to be able to report to the U.S. Government on whether it is meeting its objectives in promoting meaningful scientific cooperation.

D) Summary of Requests for CDR Program Actions. Indicate requests made to the U.S. Embassy in Tel Aviv or USAID/EGAT staff in Washington for assistance in promoting project productivity.

Note: All specific requests for Embassy Tel Aviv or USAID to act must be sent separately from progress reports, by either letter or e-mail to the ECON/AID Office, U.S. Embassy Tel Aviv.

Note on Publications: USAID expects CDR investigators to publish their results in scientific journals, and especially encourages research that leads to publications jointly authored by researchers from Israel and developing countries. Joint publications in peer-reviewed international journals are important for researchers seeking new funding from USAID and other agencies. All new publications from work supported by the grant should be included in an appendix to the Semi-Annual Report.

The following Acknowledgment should be included in project-funded publications:

"This research was supported (in part [if applicable]) under Grant No. _____ funded by the U.S.-Israel Cooperative Development Research Program, Bureau for Economic Growth, Agriculture, and Trade, U.S. Agency for International Development."

FINAL REPORT

The purpose of the Final Report is to link all findings from the project so that the overall effectiveness and impact of the entire project can be assessed. Project effectiveness should be discussed both in terms of scientific accomplishments and relevance of findings to international development. Information in Final Reports may be published by USAID in non-technical publications. The Final Report should not be a repetition of Annual Reports. It is an overview of accomplishments from the entire project. The Final Report generally should be 10-25 pages long, and should include the sections below.

A) **Cover Sheet**: Identify as the FINAL REPORT, Covering Period [Date to Date]; state that it is "Submitted to the U.S. Agency for International Development; Bureau for Economic Growth, Agriculture, and Trade"; give the TITLE OF PROJECT; Project Number and Award Number; identify the Principal Investigator, along with his/her institution, address, telephone number, and e-mail address; list each of the Co-Principals at each cooperating institution, along with his/her institution, address, telephone number, and e-mail address; and list the current contact information for the administrative officials at each institution. See sample cover page attached. **Note**: Be sure to provide current contact information for investigators and institutions, since they may have changed since the original project was approved. Also provide current contact information for any investigators who have left the project.

B) **Table of Contents**

C) **Executive Summary**: On a separate page, and no longer than one page. Use non-technical language to review and summarize the entire project. The Executive Summary should clearly place project accomplishments in the overall context of international development. Also briefly describe any technical skills, innovation, or knowledge acquired by the developing-country partner as a result of the project. **Note**: The Executive Summary is extremely important and the section of the report that policy makers use to assess the impact of USAID research programs. Write this section so that the content is clear and concise.

D) **Research Objectives**: Describe why your project was conducted. What problem was addressed and why is the problem important to development? Briefly describe how the project fits into ongoing research by other scientists, and reference pertinent literature. Describe the innovative aspects of the project. Briefly explain how other organizations supported the project.

E) **Methods and Results**: Summarize how data were collected. Present data through use of tables, charts, photographs. When appropriate, data should be statistically analyzed. This section should

be presented as if for publication in a journal.

F) Impact, Relevance, and Technology Transfer: How will findings be useful in the developing country? Describe the project's impact on individuals, laboratories, departments, and institutions. Will results be used? If so, how, by whom, when? Are larger scale trials warranted? What difference has the project made; now that the project is complete, what new capacity, equipment or expertise will be acquired by the developing country? How have the scientific capabilities of the CDR target country scientists been improved?

G) Project Activities/Outputs:

- 1) List the meetings held over the course of the entire project; include time, location, attendance.
- 2) List the training that occurred over the course of the project. Indicate who was trained, the purpose of the training, and when and where the activities occurred.
- 3) List the publications and patents for the entire project. Clearly identify all joint publications that included co-authors from Israel and the CDR target country on the same manuscript.

H) Project Productivity: Did the project accomplish all of the proposed goals? If not, why not?

I) Future Work: Will the project lead to future work? Describe.

J) Literature Cited: Provide a list of references cited throughout the report.

Note on Publications: USAID expects CDR investigators to publish their results in scientific journals, and especially encourages research that leads to publications jointly authored by researchers from Israel and developing countries. Joint publications in peer-reviewed international journals are important for researchers seeking new funding from USAID and other agencies. All publications from work supported by the grant should be included in an appendix to the Final Report.

The following Acknowledgment should be included in project-funded publications:

"This research was supported (in part [if applicable]) under Grant No. _____ funded by the U.S.-Israel Cooperative Development Research Program, Bureau for Economic Growth, Agriculture, and Trade, U.S. Agency for International Development."

Note: Prior approval of the granting office in the U.S. Embassy Tel Aviv is required for any changes in the project's workplan, budget, management or cooperation structure, or terms of agreement. Inclusion of information in progress reports does not negate this requirement to obtain prior permission from the embassy via a separate request.

SEMI-ANNUAL REPORT

Covering period from: (Date to Date)

Submitted to the U.S. Agency for International Development; Bureau for Economic Growth,
Agriculture and Trade

TITLE OF PROJECT

Project Number (e.g. C24-000) and Award Number (e.g. TA-MOU-0000)

Principal Investigator: [NAME]

Grantee Institution: [NAME]

Address:

Telephone Number:

FAX Number

E-mail address:

Co-Principal Investigator #1: [NAME]

Institution

Address:

Telephone Number

FAX Number

E-mail address:

Co-Principal Investigator #2:

Etc.

Administration Official: [NAME]

Institutional Affiliation:

Address:

Telephone Number

FAX Number:

E-mail address:

Administration Official: [NAME]

Institutional Affiliation:

Address:

Telephone Number

FAX Number:

E-mail address:

ATTACHMENT SIX



The following Internet-based system, *Interagency Edison*, should be used by both Grantees and Sub-Grantees to report their patentable inventions that are developed using USAID funding.

Internet Address: < <http://www.iedison.gov/> >

Interagency Edison provides Federal grantee/contractor organizations and participating federal agencies with the technology to electronically manage extramural invention portfolios in compliance with federal reporting requirements.

Interagency Edison was developed by the Office of Policy for Extramural Research Administration, National Institutes of Health, Bethesda, Maryland.

What is Interagency Edison?

Interagency Edison supports a "Common Face" for Invention Reporting to the Government. The system has been designed to facilitate grantee/contractor institutions with the compliance of laws and regulations mandated by the Bayh-Dole Act whose purpose is to ensure transfer of technology from the research laboratory to the commercial/public sector.

What are the steps necessary to become an Interagency Edison user?

To become an efficient and effective Interagency Edison user, follow these steps:

1. Read the ["Introduction to Interagency Edison"](#).
2. Familiarize yourself with the [functions and features of Interagency Edison](#).
3. [Create a test account](#) and practice using Interagency Edison in a test environment.
4. [Create a formal account](#) and access the secure production server.
5. If you have a large database of invention information, read the ["Special Instructions for Organizations that have Large Databases"](#).
6. If you have any additional questions, read ["Frequently-Asked-Questions \(and answers\)"](#).

USAID is one of the participating Government agencies in Interagency Edison

While it is the responsibility of grantee/contractor institutions to comply with the Bayh-Dole Act, as stewards of federal funds, and to provide assistance with compliance, Interagency Edison has been designed to streamline the invention reporting process mandated by the Code of Federal Regulations:

[37CFR Part 401](#) with particular emphasis on the Standard Patent Rights Clauses, [Section 401.14](#).

Grantees/contractors of USAID may utilize the system to satisfy invention reporting requirements.

What are the major Invention Reporting requirements mandated by the Bayh-Dole Act?

The following checklist contains the major invention reporting requirements which are mandatory for compliance with the Bayh-Dole Act. This checklist is based on the 37 CFR 401.14:

- Employee Agreements [401.14(f)(2)]
- Invention Disclosure [401.14(c)(1)]
- Election of Title [401.14(c)(2)]
- Filing of Patent Application [401.14(c)(3)]
- Utilization Report [401.14(h)]
- Non-Election of Title [401.14(d)(1)]
- Foreign Filings [401.14(c)(3)]
- Flowdown of Requirements [401.14(g)]
- Acknowledgement of Government Support [401.14(f)(4)]
- Preference for U.S. Industry and Small Business [401.14(i)]
- March-In Rights [401.14(j)]
- Special University Provisions [401.14(k)]
- Decision to Discontinue Patent Prosecution [401.14(f)(3)]
- Utilization of License Revenue [401.14(k)(3)]

Following are the Sec. 401.14 Standard patent rights relevant clauses mentioned above:

(c) Invention Disclosure, Election of Title and Filing of Patent Application by Contractor

(1) The contractor will disclose each subject invention to the Federal Agency within two months after the inventor discloses it in writing to contractor personnel responsible for patent matters. The disclosure to the agency shall be in the form of a written report and shall identify the contract under which the invention was made and the inventor(s). It shall be sufficiently complete in technical detail to convey a clear understanding to the extent known at the time of the disclosure, of the nature, purpose, operation, and the physical, chemical, biological or electrical characteristics of the

invention. The disclosure shall also identify any publication, on sale or public use of the invention and whether a manuscript describing the invention has been submitted for publication and, if so, whether it has been accepted for publication at the time of disclosure. In addition, after disclosure to the agency, the Contractor will promptly notify the agency of the acceptance of any manuscript describing the invention for publication or of any on sale or public use planned by the contractor.

(2) The Contractor will elect in writing whether or not to retain title to any such invention by notifying the Federal agency within two years of disclosure to the Federal agency. However, in any case where publication, on sale or public use has initiated the one year statutory period wherein valid patent protection can still be obtained in the United States, the period for election of title may be shortened by the agency to a date that is no more than 60 days prior to the end of the statutory period.

(3) The contractor will file its initial patent application on a subject invention to which it elects to retain title within one year after election of title or, if earlier, prior to the end of any statutory period wherein valid patent protection can be obtained in the United States after a publication, on sale, or public use. The contractor will file patent applications in additional countries or international patent offices within either ten months of the corresponding initial patent application or six months from the date permission is granted by the Commissioner of Patents and Trademarks to file foreign patent applications where such filing has been prohibited by a Secrecy Order.

(d) Conditions When the Government May Obtain Title

The contractor will convey to the Federal agency, upon written request, title to any subject invention--

(1) If the contractor fails to disclose or elect title to the subject invention within the times specified in (c), above, or elects not to retain title; provided that the agency may only request title within 60 days after learning of the failure of the contractor to disclose or elect within the specified times.

(f) Contractor Action to Protect the Government's Interest

(2) The contractor agrees to require, by written agreement, its employees, other than clerical and nontechnical employees, to disclose promptly in writing to personnel identified as responsible for the administration of patent matters and in a format suggested by the contractor each subject invention made under contract in order that the contractor can comply with the disclosure provisions of paragraph (c), above, and to execute all papers necessary to file patent applications on subject inventions and to establish the government's rights in the subject inventions. This disclosure format should require, as a minimum, the information required by (c)(1), above. The contractor shall instruct such employees through employee agreements or other suitable educational programs on the importance of reporting inventions in sufficient time to permit the filing of patent applications prior to U.S. or foreign statutory bars.

(i) Preference for United States Industry

Notwithstanding any other provision of this clause, the contractor agrees that neither it nor any assignee will grant to any person the exclusive right to use or sell any subject inventions in the United States unless such person agrees that any products embodying the subject invention or produced through the use of the subject invention will be manufactured substantially in the United States. However, in individual cases, the requirement for such an agreement may be waived by the Federal agency upon a showing by the contractor or its assignee that reasonable but unsuccessful efforts have been made to grant licenses on similar terms to potential licensees that would be likely to manufacture substantially in the United States or that under the circumstances domestic manufacture is not commercially feasible.

(j) March-in Rights

The contractor agrees that with respect to any subject invention in which it has acquired title, the Federal agency has the right in accordance with the procedures in 37 CFR 401.6 and any supplemental regulations of the agency to require the contractor, an assignee or exclusive licensee of a subject invention to grant a nonexclusive, partially exclusive, or exclusive license in any field of use to a responsible applicant or applicants, upon terms that are reasonable under the circumstances, and if the contractor, assignee, or exclusive licensee refuses such a request the Federal agency has the right to grant such a license itself if the Federal agency determines that:

- (1) Such action is necessary because the contractor or assignee has not taken, or is not expected to take within a reasonable time, effective steps to achieve practical application of the subject invention in such field of use.
- (2) Such action is necessary to alleviate health or safety needs which are not reasonably satisfied by the contractor, assignee or their licensees;
- (3) Such action is necessary to meet requirements for public use specified by Federal regulations and such requirements are not reasonably satisfied by the contractor, assignee or licensees; or
- (4) Such action is necessary because the agreement required by paragraph (i) of this clause has not been obtained or waived or because a licensee of the exclusive right to use or sell any subject invention in the United States is in breach of such agreement.

(k) Special Provisions for Contracts with Nonprofit Organizations

If the contractor is a nonprofit organization, it agrees that:

- (1) Rights to a subject invention in the United States may not be assigned without the approval of the Federal agency, except where such assignment is made to an organization which has as one of its primary functions the management of inventions, provided that such assignee will be subject