

AMERICAN PUBLIC HEALTH ASSOCIATION

International Health Programs
1015 Eighteenth Street, N.W.
Washington, D.C. 20036

**A REPORT ON THE
KIMIA FARMA ORAL CONTRACEPTIVE
PRODUCTION FACILITY IN
BANDUNG, INDONESIA**

A Report Prepared By:

HOWARD B. NELSON, M.S.

During The Period:

DECEMBER 4 THROUGH 15, 1977

Under the Auspices of The:

AMERICAN PUBLIC HEALTH ASSOCIATION

Supported By The:

**U. S. AGENCY FOR INTERNATIONAL DEVELOPMENT
OFFICE OF POPULATION, AID/pha/C-1100**

**AUTHORIZATION:
Ltr. POP/FPSD: 11/1/77
Assgn. No.: 1100-083**

**A REPORT ON THE
KIMIA FARMA ORAL CONTRACEPTIVE
PRODUCTION FACILITY IN
BANDUNG, INDONESIA**

I. INTRODUCTION

Reference is made to the letter dated November 18, 1977 from the American Public Health Association to me confirming arrangements for a visit to Indonesia to confere with officials of USAID, BKKBN and Kimia Farma. (Appendix A)

The nature of this report will have to be modified because certain aspects of the consultation could not be met. This is due to only 50 percent completion of the production facility. All production equipment and most of the laboratory equipment have not been received. (Appendix B) I believe, however, that the value of my trip is probably of greater benefit because I was able to discuss important aspects of the installation of the equipment and the type and depth of training of Kimia Farma key personnel to be provided by the U.S. supplier of raw materials. All of this will be discussed in detail in the sections of this report to which this information is pertinent.

I think it is important to characterize the cooperation of the personnel at Kimia Farma. This company had made an intensive effort to obtain the finest type of equipment and plant capability to produce the highest quality oral contraceptives (OC). All discussions were conducted with Mr. Utarto, Managing Director and the following key personnel:

Dra. Salama Adipura, Manager OC
Dr. Dadan Tjardhana, Production
Mr. Sabardi Berth, Administrator
Miss Dahniar Iskandar, Quality Control
Mr. Wahju Sumitra, Operations

All of the discussions were handled with utmost candor and the information provided to me covered all aspects of the completion of plant facilities, equipment installation, personnel requirements, training standards, personnel protection and potential completion dates for each step up to full capacity production of highest standard oral contraceptives.

There is some delay in Kimia Farma moving ahead because the BKKBN has not formalized the choice of the oral contraceptive formula. The key personnel training program is dependent upon competitive bid award of U.S. raw material supplier who, in addition to suppling raw materials, will be requested to train Kimia Farma key personnel in all aspects of production and quality control as well as to provide a production manager to Kimia Farma to supervise the trial run production, validate procedures, personnel protection programs and oral contraceptive production capability approval.

This training is required because Kimia Farma has had no experience in manufacturing drug productions with precise controls required for oral contraceptive production. The key personnel selected are competent to complete training required and upon return will have the necessary experience to establish Kimia Farma procedures for plant operational capability.

II. CURRENT STATUS

A. Plant

1. The plant for production of oral contraceptives is considered to be about 50 to 60 percent completed. This is the building structure only and other aspects of construction; such as roughing-in for equipment, special wiring and other utilities, will be put in place once the equipment is placed and service requirements and installation locations have been chosen.
2. The building has been well planned. The flooring and wall tile should be easy to clean and maintain. I have not seen superior tiles in any installation in my experience. The cubicles have large glass walls to provide good illumination and, since the production areas are isolated from the rest of the plant area, the glass areas will reduce the feeling of isolation.
3. The shower, clothing change room for personnel protection is in place and appears adequate.
4. The space for each production area is more than adequate and is large enough to accommodate installation of larger capacity equipment in the future when this is needed.
5. I was favorably impressed by all aspects of plant construction as to illustrated time and effort devoted to building and area planning for most effective use of available space.

B. Equipment

1. The excellent choice of production equipment has included items that will have capability of precise and dependable production of high potency drugs such as oral contraceptives.
2. All of the equipment is new so that a uniform level of performance is possible and, for at least one year or more, should operate within manufacturer's specifications for precision performance without serious problems.
3. In this regard Kimia Farma has not ordered spare parts for this equipment. I strongly recommend that they contact the suppliers of their equipment to determine the lists of spare parts that they have recommended for potential requirements for at least one year of operation.
4. The quality of water required for production of oral contraceptives

demands that Kimia Farma obtain a deionizer to treat their water for manufacturing, final washing and rinsing of equipment. A supply of distilled water is available for the near term demands, but it is essential to have adequate supplies of water and it will be necessary to install a deionizer water treatment system at the earliest possible date.

5. Air conditioning equipment specifications and air flow performance should be adequate to provide negative pressure in operating areas to facilitate effective removal of dust and other production contaminants. This performance specification should require testing to be made during manufacturing and contractors should be advised that final acceptance will be based on this requirement.
6. The production equipment chosen will produce on a one shift basis 18 million cycles per year with approximately a 10 percent safety factor. The capability for increasing this production on a two shift basis is not possible because equipment such as the drying oven can only be cycled on every 24 hours. It would be my strong recommendation that no increase of production be attempted during the first year of production and until all aspects of production achieve the highest level of confidence.
7. Generators for electrical power will not be in place until about June 30, 1978. The power requirements will be met with two generators in operation and one as a standby. The building to house the generators is about 60 percent complete and is located so as to eliminate distracting operating noise.
8. The blister packing machine is on order and is to be shipped during February 1978. The individual responsible for packaging will go to Italy for training and receive instructions for assembly and operation. The piece of equipment is one of the most acceptable packaging machines and is capable of exceeding production demands of 18 million cycles per year.

In this regard there will be catch-basin to hold water from cleaning and showering and it will hold this water until the solids have settled to bottom. The cleaning and disposal of oral contraceptives materials will require careful subsequent disposal. This problem has been fully discussed and Kimia Farma understands the special precautions necessary for cleaning catch-basins and proper disposal of contaminated solids.

III. PROJECTED TIMING FOR COMPLETION

A. Equipment in Place and Operational

1. Should be installed by May to June 30, 1978. Items such as the accelerator requires supplier installation and this could be a delaying factor which out of Kimia Farma's control.
2. All of the equipment, both production and quality control, requires action by the Indonesian Government to approve the tax-free importation. This can delay release to Kimia Farma by about 4 to 6 weeks.

3. All equipment must be in place to begin operations. The unexpected delay of one item can affect the time schedule for completion. Production is a step-by-step process and trial runs will be delayed until all is in readiness for production.

B. Plant Operation

1. This cannot take place until quality control equipment is installed and validated for accuracy.
2. The first trial runs of equipment can be scheduled when the key people who have finished their training in the plants of U.S. contractors have returned to Kimia Farma.

C. Key Personnel Training in U.S.

1. They will be trained in every aspect of production and quality control of oral contraceptives.
2. The contractor will assign trainees at the operations level and expect full competence for each step in manufacturing. This training should include written instruction, on-the-job-training, and then successful completion of an examination to assure understanding of all procedures before going to the next step in their training program.
3. The contractor will provide a statement at the end of the training period that these key personnel have satisfied the contractor's own standards of performance.

D. Contractor's Production Supervisor

1. About one month after the return of the fully trained key personnel to Kimia Farma the contractor will furnish a competent production supervisor to assist Kimia Farma to get into trial run production. He will validate performance of employees and develop adequate documentation for all steps in manufacturing.

His assignment will be completed when actual production of oral contraceptives proceeds uniformly and in full compliance with manufacturing and quality control procedures developed for Kimia Farma production.

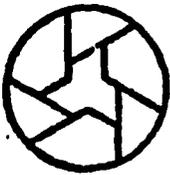
2. I would estimate the time require for key personnel training could be about 6 to 8 weeks in the plant of the U.S. raw material supplier. The contract supervisor to be sent to assist Kimia Farma should expect to be in the plant not less than four weeks. A certificate will be given by the contract supervisor that his responsibility has been discharged prior to returning to the U.S.
3. Time for first run capability.
 - a) First run of placebos. This should take place as soon as possible after return of key personnel. This training should not require more than one month.
 - b) Target date of placebo production should be scheduled to coincide with arrival of U.S. contract supervisor. The target date is for August or early September.

- c) First run of oral contraceptive production will follow immediately after validation of all procedures by contract supervisor. Target date will be October 1, 1978.
- d) Routine production of oral contraceptives at capacity should be October 15-November 1, 1978.
4. On Thursday December 8, 1977 I discussed with all of the foregoing information and my observations with:
 - all key personnel of Kimia Farma;
 - Mr. Thomas H. Reese III, Deputy Chief, Office of Population and Health, USAID/Jakarta
 - Dr. Awad, Consultant to BKKBN
 - Mr. Moebramsyah, Logistics Chief, BKKBN; and
 - Dr. Sayuti Hasibuan, BAPPENAS

IV. GENERAL CONCLUSIONS AND RECOMMENDATIONS

1. Kimia Farma can achieve oral contraceptive production equal in quality to U.S. production.
2. The timing is obviously an educated guess. From my experience with new production in a U.S. facility it would not vary much from these target projections.
3. From my inspection, interrogation and review of all documentation I recommend continuing USAID assistance and encouragement to achieve Indonesian capability to produce oral contraceptives.
4. After Kimia Farma has produced oral contraceptives satisfactorily for three months, I recommend that a study be authorized by BKKBN to test effectiveness of Kimia Farma oral contraceptives with identical formulations of other suppliers in the program. The test should involve controlled studies of not less than one year duration and require cross-over and double blind procedures to insure that no failure in contraception will occur if Kimia Farma's product is supplied in place of another identical oral contraceptive.

- References:
- 1) BKKBN report on Oral Contraceptives Production Project, November 14, 1977 and Annexes 1-5
 - 2) Letter dated November 1, 1977, subject AID Loan No. 497-U-045, Oral Contraceptive Loan Implementation Letter No. 4.



AMERICAN PUBLIC HEALTH ASSOCIATION

1015 Eighteenth Street, N.W., Washington, D.C. 20036 • (202) 467-5000

November 18, 1977

**Howard B. Nelson
2409 Lakevale Drive
Vienna, Virginia 22180**

Dear Col. Nelson:

This is to confirm arrangements previously discussed with you in regard to your forthcoming consultancy in Indonesia. This assignment is made in conformance with our agreement with the U.S. Agency for International Development, AID/pha/C-1100.

The purpose of your assignment is to review the Government of Indonesia plans and arrangements for the production of oral contraceptives with the input of U.S. finance and approved raw materials. This will also require a visit to the production site in Bandung. Key items of your work scope include:

1. Report to the National Family Planning Coordination Board (BKKBN) Jakarta and USAID/Jakarta for briefing, introduction and local itinerary.
2. Determine if design, specifications, equipment, procedures, etc. of the factory are suitable for oral contraceptive manufacture.
3. Evaluate handling, and safety precautions required for hormones in storage, mixing, manufacturing, etc.
4. Meet key production staff and assess proposed training for manufacturing procedure, batching, tableting, storage, quality control, etc.
5. Make recommendations and comments for production of quality and effective oral contraceptives and the various procedures and control related to their handling, mixing, formulation, manufacturing, packaging, stability, quality, storage, etc.
6. Produce a draft report or a draft Procedure Manual encompassing recommended procedures for manufacturing, controls, storage, etc. for discussion with BKKBN and USAID before departure from Indonesia o/a 14 December 1977.
7. Debrief BKKBN and USAID by presenting and discussing No.6, above.

Col. Howard B. Nelson
November 17, 1977
Page Two

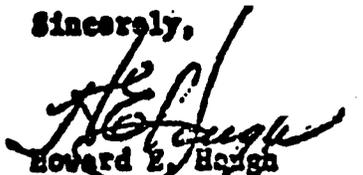
8. Submit to APHA a report and/or a Procedures Manual for use by BKBN as per No. 6, above not later than 31 December 1977.

This assignment is made for a period of up to three weeks starting in Jakarta on or about December 5, 1977. Your passport, with a visa for Indonesia, and your airline tickets are enclosed. As you can see from the itinerary, no reservations were made for your return flight and we suggest that you make the necessary arrangements as soon as your work itinerary will permit. The USAID Mission in Jakarta have been advised of your ETA and were requested to arrange for your accommodations there.

The enclosed memorandum describes our arrangements for the payment and reimbursement of consultants and other conditions pertinent to your assignment. Copies of the forms on which you must submit the information necessary for your payments are also enclosed. In this respect, we are enclosing a check in the amount of \$900.00, which represents an advance on your anticipated travel per diem. The amount will, of course, be taken into account when final reimbursement is made for your travel expenses. Please review the enclosed memorandum carefully and if you have any questions, we hope you will call (202/467-5028).

I wish to take this opportunity to express our appreciation for your cooperation and assistance in this project. We hope that you have a safe and successful visit and look forward to receiving an interesting report of your activities.

Sincerely,


Howard E. Haugh
Project Coordinator
International Health

Enclosures

LIST OF EQUIPMENT

VIII. MACHINES AND EQUIPMENT

Balances; Berkel (Holland):

- Ø semi automatic, E 250 (15 Kg)
- 2 bench dial, 75 S (60 Kg)
- 2 floor dial, 75 M (120 Kg)
- 1 Loedige mixer FM 130-D/1Z, max 90 lt. (Germany)
- 1 Glatt Fluid-bed spray drier granulator, WSG 30, max 50 K (Germany)
- 1 Double arm Kneader, CY-DWK-10, max 100 lt. (Taiwan)
- 1 Drying oven for granulates and powders, JC/DO/B (Taiwan)
- 1 Manesty Betapress, 23 stations, max 2000/min (UK)
- 1 Manesty Rotapress MK II, 61 stations, max 11000/min (UK)
- 1 Manesty Accela-Cota, 48", max 170 lt., 150 K (UK)
- 1 IMA Blister packing machine, IMA-C 60 (Industria Macchina Automatiche Italy)
- max 190 blisters, 64 cartons/min.
- 3 Caterpillar generators (Hongkong)
- 1 A7C, Westinghouse (Hongkong)

IX. LABORATORY

Balances, Mettler:

1 semi micro analytical

1 micro analytical

1 micro m.p apparatus

1 Electronic polarimeter

Drying oven, Heraeus:

1 vacuum, model VT 5042 K

1 Heating and drying, model T 5042 K

1 potentiometric Titration apparatus

1 Thin-layer chromatography set

1 Spectrophometer, UV and visible, Beckmann model 25

1 Spectrophometer, infra-red, Beckmann acculab VI, BTN

2 Hardness Tester, Erweka

2 Tablet digestability Tester, Erweka

1 Tablet abrasion Tester, Erweka

1 Magnetic stirrer and hot plate

1 Rotary vacuum pump

1 Ultrasonic cleaner and rapid glass drier

1 Cooled thermostatic bath

1 Tube furnace

Glassware (breakers, flasks, pipettes, burettes, tubes, volumetric flasks, cylinders, desiccators, racks, stands, bottles, etc.).