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# REPORT

UNIDO PROJECT No. DP / THA / 88 / 018
CONTRACT No. 93 / 169

REPORTED BY

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NATIONAL PROJECT DIRECTOR

DATE
20 DECEMBER 1994

## Background Information

The Royal Government in conjunction with UNDP/UNIDO acknowledged the need to develop the pharmaceutical industry in Thailand. Guidelines for GMP were issued by the Thai FDA, however, both the FDA and the Thai industries faced problems is the application of GMP. In 1989, 58 out of the 191 pharmaceutical factories or 30.4% were granted GMP certificates by the FDA in various dosage forms. Although this number has increased since, today it is still far from the FDA's goal which established that 100% of the pharmaceutical manufacturers will meet the GMP criteria targeted for the end of the year 1996. Some problems encountered by the local pharmaceutical industry which include such as, limited pharmaceutical technology, lack of "know how" to improve product quality, lack of skilled or qualified personnel in some areas of the pharmaceutical production. The most immediate problems which had to be addressed by the pharmaceutical industry and for which different types of technical assistance was required included :-

Development of comprehensive GMP training programs for different levels of the plant personnel. Validation techniques applicable to production & QC operations.

As a result of the difficulties faced by the Pharmaceutical industry in Thailand, the Royal Government in conjunction with UNIDO/UNDP, numbers of pharmaceutical industry and universities set up the framework for a Pharmaceutical Technology Service Centre ( PTSC ). On 17 of April 1991, the UNIDO Pharmaceutical Technology Service Centre was officially inaugurated. This centre was established at the Faculty of Pharmacy, Chulalongkorn university in Bangkok. The objectives established for the PTSC included a requirement for

improving local GMP levels, in order to meet international quality standards. The Centre would enable local pharmaceutical companies to introduce GMP's their production plants through training of company staff at the top, middle and production levels. Through seminars and workshops on GMP and/or pharmaceutical technology related topics, the Service Centre would serve to educate and inform local manufacturers, and would enhance its own reputation and credibility both within the industry, and the FDA authorities.

The Pharmaceutical Technology Service Centre became operational from October 1991. One of the Project's objectives is the development of human resources in the national pharmaceutical industry by providing training activities on Good Manufacturing Practices and Quality Assurance.

Since the start of the Project, contributions by National and International Experts on training and consultation activities have been considered of great importance for improving the quality standard of the pharmaceutical industry.

The subcontract was arranged for the recruitment of Thai Government officials as National Experts by the Pharmaceutical Technology Service Centre via Chulalongkorn University, Faculty of Pharmaceutical Sciences, on a part time basis.

## Scope of contractor Services

The technical support has in the provision of professional expertise in the following :-

- Quality Control and Good Laboratory Practices (GLP)
- Standard Operation Procedures (SOP)
- Good Manufacturing Practices (GMP)
- Validation Process
- Pharmaceutical Technology

The contractor recruited seven national experts with expertises in the areas mentioned above :-

The name of the experts are :

1. Dr.Chamnan Patarapanich
2. Dr.Kaisri Umprayn
3. Ms.Parunee Thanomkiat
4. Dr.Poj Kulawanich
5. Ms.Ruedee Saowakontha
6. Dr.Sirinart Vasanavathana
7. Ms.Waraporn Suwakul

Dr.Prasan Dhumma-upakorn
( National Project Director )

## Activities

## Quality Control and Good laboratory Practices

- Organization and implementation of QA management
- Organization and implementation of training activities
- Set up GLP
- Set up working groups for "Training the trainers"
- To assist the training activities of the PTSC in quality control and GLP

## National Experts responsibilities

Most of the activities were responsible by Dr.SIRINART, the leader in Quality Control and Validation and Dr.CHAMNAN leader in problems solving for testing and instrumentation. Dr.KAISRI gave suggestion and discussion about the testing of new products. The activities always cooperate with the other groups especially with the GMP and SOP's working groups.

## Preparation of SOP and Validation processes

Dr.SIRINART leader on Validation of Quality Control, set up working group conducted and prepared the documents for quality control, concentrated on Validation, 1-2 days meeting every month at the Centre since February 1993. ( 5-6 participants from universities and industries ). Some of the activities including :-

- Set up a protocol on Validation of pH measurement was proposed as a model for a real start on proceeding of the QC validation program.
- Set up a protocol on validation of spectrophotometer

- Set up the meeting and discussion with other validation groups for mutual understanding of the SOP written of SOP's for spectrophotometric validation.
- Set up meeting, discussion on how validation on HPLC instrument and system suitability test should be performed.
- Set up the document, VIDEO or slides for training and workshop.

The activities of quality Control - Validation working group ( see exhibit # 1 )

- The total activities January 1992 - September 1994 are 55 activities. The number of participants are 476 participants
- Set up 3 times one day seminar on Validation as a system approach to prevention, improvement and problem analysis & solving in the QA/QC program. ( 17 February, 26 April and 26 May 1994 )
- The PTSC produced 500 copies of a special training materials ( 103 pages )
- Set up 2 days seminar on general concept of Validation in QA/QC system and Operational Qualification of a pH meter and pH electrodes and validation of pH measurement.

Set up Good Laboratory Practices (GLP)

- Set up GLP and training laboratory equipments to serve both the Pharmaceutical and Cosmetic industries. Dr.CHAMNAN, leader and cooperation of problem solving for testing and instrumentation. Dr.KAISRI, also gave suggestion and discussion on the testing of new products and problem solving.

- Set up the SOP of the main analytical equipments in the PTSC. Cooperated with the chemist and technician in the centre.
- Set up a special training of analytical equipments for the LAO FDA ( 5 participants) at the PTSC
- Set up a special training on analytical equipments for the Thai FDA inspectors (35 participants) at the PTSC
- Training laboratory equipment for post graduate students: technique operations and maintenance of HPLC, FT-IR, Spectrophotometer, Coulter multisizer, Viscometer etc. (24 students)
- The PTSC organized a special project for testing of 54 pharmaceutical products from LAO FDA.

Audited and Calibration of the analytical Instruments

Many requests from the Pharmaceutical and Cosmetic companies for calibration of the analytical balances and other equipments ( 23 activities ).

Consulting,Problem solving for the Industries

Many requests from the industries for their problems e.g. method of analysis, identification of raw materials. Dr.CHAMNAN, Dr.KAISRI and Dr.SIRINART incooperation with the other national experts and NPD organized these activities.

- Organized and authorized testing of raw materials and finished products.
- Solving the problems and developing the analytical methods for combination drugs.
- develop methods of analysis for registration of new products.

## Activities of working groups on Standard Operation Procedure ( SOP ) and Good Manufacturing Practice ( GMP )

The Standard Operating Procedure ( SOP ) training program has been launched in 1992. This training program is one of the required activities to facilitate the pharmaceutical industry as stated in the proposal. The chief technical advisor ( CTA ) is responsible that it is taught and implemented to the industry at middle level as well as lower level management.

The key to its success of the SOP training program is the committee members which are volunteers from the industry. They are required to come to the centre at least one full day in a month. Together, they will read and discuss the format, content or material and GMP guidelines of each SOP subject. The above informations are obtained from all around the world textbooks on GMP and good examples of well written in English are then handed in for typing.

In order to have this know-how transfer to the industry, a two-day SOP training program is conducted for a group of 12 - 16 attendants each month.

The National experts from the universities involved in the preparation of SOP and training or workshops are Dr. KAISRI, Dr. POJ, Asso.Prof. PARUNEE, Asso.Prof. WARAPORN and Dr. SIRINART incooperation with the NPD and the National experts from the industry.

List of SOPs on Pharmaceutical & Cosmetic Industry.

As shown in Exhibit 2 the PTSC have prepared some important SOPs for training. During 1992 - 1993 most of the participants came from pharmaceutical industry, however, since 1994 more participants from cosmetic and food industries are coming.

Since 1992 the PTSC organized workshops and seminar on SOP and GMP, both at the Centre and at the plant sites. There are 600 participants from companies.

The PTSC have organized seminar and workshop at the plant site for big pharmaceutical and cosmetic companies such as :-

- Thai Nakorn Patana Co.,Ltd. Pharmaceutical industry.
- Colgate Palmolive ( Thailand ) Ltd. Cosmetic industry.
- Lever Brother ( Thailand ) Ltd. Cosmetic industry.
- The S & J International Enterprises Co., Ltd. Cosmetic industry.
- Cosmetic Creation Co.,Ltd.
- International Laboratories Cosmetics ( ILC ) Ltd.

Set up a training on GMP and SOP for the Thai FDA inspectors ( 35 participants ) in Pharmaceutical industry and FDA inspectors ( 12 participants ) for Cosmetic industry at the PTSC.

Lecture on GMP and SOP

- Dr. PRASAN, the NPD with co-operation with Dr. KAISRI and other National experts were invited to give a lecture and discussion on GMP and SOP including the activities of the PTSC.
- On 30 May 1994, lecture and discussion on GMP and SOP for cosmetic industry organized by Thai FDA ( 220 participants )
- On 13 June 1994, lecture on GMP and SOP for 66 Government hospital pharmacists.

Evaluation and correction of all the reports ( SOP documents ) from the participants who joined the SOP workshop and were granted for the certificate ( 115 participants ).

## Activities in preparation of technical documentation on Validation process

The validation Protocol is one of the major activities of the PTSC. The centre set up 4 working groups on validations. One or two of the national experts from the subcontract organized a meeting with the representatives from the industries or from the university. They are required to come to the centre 1 - 2 days per month. Together, they will read and discuss the content or material, according to GMP for Validation protocols. The final draft or a complete validation process or protocols are written. Four working groups on Validation processes are ( see exhibit # 3 ):-

1. Working group on Validation of Quality control ( 4 - 6 participants ), Dr. SIRINART is responsible
2. Working group on Validation of Sterile process ( 3 - 5 participants ), Asso.Prof. RUEDEE and Asso.Prof. PARUNEE are responsible
3. Working group on Water system, validation of Water treatment system ( 4 - 6 participants ), Asso.Prof. PARUNEE is responsible
4. Working group on Validation of Tableting Process ( 4 - 6 participants ), Dr. POJ is responsible

The concept of the organization is similar to the SOP working groups. Each working group will set up a seminar or workshop and also participate in trouble shooting. The working groups always cooperate with the SOPs groups.

The activities of each group during February 1993 to December 1994 are concluded in the exhibit # 1

Asso.Prof. PARUNEE, a leader on the water system and Mr. KASEM, National expert from the industry set up a

meeting with other experts from the industry, preparing for a seminar on the water system.

The working group of the water system organized 2 days seminar on " Water system in the Pharmaceutical and Cosmetic industry " 16 - 17 August 1993, 145 participants.

The working group on water system joined with an expert on waste water treatment from Japan, Mr. YOSHIYUKI KOIKE, supported by JODC, Japan Overseas Development Co-operation. He stayed at the PTSC from 25 February to 26 March 1994.

Mr. KOIKE had ten days plant visit at the pharmaceutical industry and 1 day at the cosmetic industry. Waste water treatment in the pharmaceutical industry is on of the project of the PTSC.

The Validation groups on Validation Protocol continue their activities, Dr. SIRINART, the leader of the Validation of quality control incorporated with experts from the industry organized many activities, preparation of documents for seminar and workshop.( see exhibit 1 )

The working group of the validation of sterile process organized one day seminar on " Validation of Sterilization Process " 22 December 1993, 154 participants.

Dr. KAISRI, Dr. POJ and Dr. PRASAN, the NPD, meet two Pharmaceutical industries in order to organize a workshop and seminar on Validation and film coat technique on 27 November 1994. There were 142 persons participating in this workshop.

## Pharmaceutical Technology GMP and Related activities

The major activities are to assist in the training activities of the PTSC in Pharmaceutical Technology and GMP training. Dr. KAISRI, in cooperation with other national experts : Asso. Prof. PARUNEE, Asso. Prof. WARAPORN and also Asso. Prof. RUDEE provided the necessary technical assistance to the service centre on all aspects as in applies to product development. Preparation of training material and organization of seminars or workshops in close co-operation with the NPD; Dr. PRASAN, also arranged and conducted training for the development of new or modified drugs. However during April - June 1994, more co-operation with the cosmetic industries have been organized. The activity of the PTSC are very well known to the other industries, both for GMP training and more samples for testing from other industries.

( Activities organized by PTSC are concluded in exhibit # 1 )

## GMP and training activities

- The national experts in cooperation with international experts Dr. M. CARPIO, Mr. JOHN CLARK and CTA Mr. J. P. BEELEN and other experts from industry organized a plant visits where the training of lower managements, discussion with the middle and top management have been organized.

- Preparation of training materials for lower management or the workers. A cartoon pictures explaining the GMP in Thai, 72 pictures have been prepared, also the slides were developed. Video showing the activities of the workers or explaining the GMP in the plants are provided.

## The others related support activities of the PTSC

- Organized study tour for the top management to Europe

  Dr. KAISRI and Dr. PRASAN, NPD, incooperate with the tour company organized the study tour to Europe and Vietnam

  During 1 - 13 June 1991, ACHEMA' 91 in Germany and plant visits :-

  | | |
  |---|---|
  | England | - Smith Kline Beecham |
  | France | - Rhone Poulance |
  | Germany | - Rhome Pharma |

  During 1 - 12 May 1993, INTERPACK' 93 in Germany and plant visits :-

  | | |
  |---|---|
  | Belgium | - Janssen Pharmaceutica |
  | Netherland | - Pharmachemie Pharmaceutical Industry |
  | Italy | - Farmitalia Carlo Erba Industry |

  During 3 - 7 March 1994, Study Tour to Hanoi and Hochimin, Vietnam

  During 5 - 11 June 1994, ACHEMA'94 and plant visit in Germany.

- Preparation of the brochure of the PTSC
- Preparation of PPER submitted on 1993
- Preparation of TPR submitted on 1994
- Set up the seminar for the Syrian officials for 2 weeks at the PTSC ( 17 - 30 October 1994 )( see exhibit # 4 )

## Conclusion

The PTSC designs and administers training programs on quality assurance, GMP, SOP and process validation geared towards professionals working in the pharmaceutical and cosmetic industry. In addition, the PTSC ( in collaboration with the FDA and TPMA ) promotes GMP through conferences, seminar and workshop. The PTSC has been conducting a broad range of educational activities and programs for the Pharmaceutical and cosmetic industry. Its track record is impressive, as evidenced by the fact that a total of at least 115 pharmaceutical and cosmetic companies attended or participated the seminars or workshops organized by the PTSC on several topics related to GMP aspect which encompassed over 3900 participants ( see exhibit # 5 )

In addition, the PTSC acts as a focal point for technical advice on quality assurance, SOP formulation, GMP and analytical testing for the pharmaceutical and cosmetic industry. Through its training programs the PTSC provided working groups with hands on experience in a wide variety of applications.

The PTSC is making a significant contribution toward the attainment of the development objective as seen in exhibit# 6. There have been increasing number of pharmaceutical companies receiving GMP certificate from FDA. Also, lately the three cosmetic companies, where the PTSC have audited and trained on GMP at the plant received the GMP certificate. ( S&J International Enterprises Ltd., Lever Brothers ( Thailand ) Ltd. and Colgate - Palmolive ( Thailand ) Ltd.

The PTSC play an important role as mediator or facilitator between FDA and industry. This will facilitate the implementation of International GMP.

# LIST OF EXHIBIT

# Exhibit 1

## ACTIVITIES ORGANIZED BY PHARMACEUTICAL TECHNOLOGY SERVICE CENTRE

### 1990

| | | | PARTICIPANTS | |
|---|---|---|---|---|
| # | DATE | TITLE | # | SOURCE |
| 1 | Sep | Management of Pharm.Industry | 107 | Industry (top) |

### 1991

| | | | PARTICIPANTS | |
|---|---|---|---|---|
| # | DATE | TITLE | # | SOURCE |
| 2 | Mar | Stability of Pharmaceutical Products | 140 | Industry/FDA/ University |
| 3 | May | Analytical Instruments (Particle size analyzer) | 109 | Industry |
| | May | Study Tour | 27 | Industry |
| 4 | Nov | Evolution of Pharm. Technology Practical Implementation and Interpretation of GMP Regulations | 120 | Industry/FDA |

### 1992

| | | | PARTICIPANTS | |
|---|---|---|---|---|
| # | DATE | TITLE | # | SOURCE |
| 5 | Feb | How to Prepare SOP's | 40 | Industry |
| 6 | May | Technique for Preparation of SOP's | 30 | FDA |
| 7 | May | Technique for Preparation of SOP's | 34 | Industry |
| 8 | May | Study Tour Canada | 5 | Industry/FDA |

| | | | PARTICIPANTS | |
|---|---|---|---|---|
| # | DATE | TITLE | # | SOURCE |
| 9 | Jun | Stability of Vitamin Formulations | 120 | Industry |
| 10 | Jul | Good Manufacturing Practices | 25 | University |
| 11 | Aug | Technique for Preparation of SOP's | 32 | Industry |
| 12 | Aug | Preparation of one SOP | 7 | Industry |
| 13 | Sep | Validation of Pharmaceutical Process | 116 | Industry/ University |
| 14 | Sep | Validation of Pharmaceutical Process | 100 | FDA/ University |
| 15 | Sep | Preparation of one SOP | 6 | Industry |
| 16* | Nov | Technique for Preparation of SOP's | 12 | Industry |
| 17 | Nov | Preparation of one SOP | 6 | Industry |
| 18* | Dec | Technique for Preparation of SOP's | 16 | Industry |
| 19 | Dec | Preparation of one SOP | 5 | Industry |

## 1993

| | | | PARTICIPANTS | |
|---|---|---|---|---|
| # | DATE | TITLE | # | SOURCE |
| 20* | Jan | Technique for Preparation of SOP's | 13 | Industry |
| 21 | Jan | Preparation of one SOP | 5 | Industry |
| 22* | Feb | Technique for Preparation of SOP's | 12 | Industry/FDA |
| 23 | Feb | Preparation of one SOP | 4 | Industry |
| 24 | Feb | Guidelines for Validation | 26 | Industry/ University |
| 25 | Feb | Validation of Tableting Process | 5 | Industry/ University |
| 26 | Feb | Validation of Sterile Process | 3 | Industry/ University |
| 27 | Feb | Validation of Water Treatment System | 4 | Industry/ University |
| 28 | Feb | Validation of Quality Control | 9 | Industry/ University |
| 29 | Mar | Validation of Tableting Process | 5 | Industry/ University |

| | | | PARTICIPANTS | |
|---|---|---|---|---|
| # | DATE | TITLE | # | SOURCE |
| 30 | Mar | Validation of Sterile Process | 3 | Industry/ University |
| 31 | Mar | Validation of Water Treatment System | 6 | Industry/ University |
| 32 | Mar | Validation of Quality Control | 8 | Industry/ University |
| 33 | Mar | Validation of Tableting Process | 6 | Industry/ University |
| 34 | Mar | Validation of Sterile Process | 3 | Industry/ University |
| 35 | Mar | Validation of Water Treatment System | 4 | Industry/ University |
| 36 | Mar | Validation of Quality Control | 7 | Industry/ University |
| 37 | Mar | Validation of Sterile Process | 3 | Industry/ University |
| 38 | Mar | Validation of Quality Control | 5 | Industry |
| 39 | Mar | Validation of Quality Control | 4 | Industry |
| 40 | Mar | Technique for Preparation of SOP's | 14 | Industry/FDA |
| 41 | Mar | Technique for Preparation of SOP's | 110 | Industry |
| 42 | Mar | Validation wrap-up session | 16 | Industry/ University |
| 43 | Mar | Maximizing Your Profit Through GMP/Cost Effective Approach to QA Management | 220 | Industry |
| 44 | Apr | Preparation of one SOP | 3 | Industry |
| 45 | Apr | Stability study by computerprogram | 40 | Industry/ University |
| 46 | Apr | Stability study by computerprogram | 30 | Industry/ University |
| 47 | Apr | Validation of Quality Control | 5 | Industry |
| 48 | Apr | Validation of Water Treatment System | 5 | Industry/ University |
| 49 | Apr | Validation of Tableting Process | 3 | Industry/ University |
| 50 | Apr | Validation of Water Treatment System | 3 | Industry/ University |
| 51 | Apr | Validation of Sterile Process | 6 | Industry |
| 52 | May | Validation of Water Treatment System | 2 | Industry |

| | | | PARTICIPANTS | |
|---|---|---|---|---|
| # | DATE | TITLE | # | SOURCE |
| 53 | May | Preparation of one SOP | 5 | Industry |
| 54 | May | Validation - SOP linkage meeting | 15 | Industry/ University |
| 55 | May | Study Tour | 30 | Industry |
| 56 | May | Validation of Quality Control | 6 | Industry |
| 57 | May | Validation of Water Treatment System | 5 | Industry/ University |
| 58 | May | Validation of Tableting Process | 4 | Industry/ University |
| 59 | Jun | Validation of Quality Control | 5 | Industry |
| 60 | Jun | Validation of Quality Control | 4 | Industry |
| 61 | Jun | Validation of Quality Control | 5 | Industry |
| 62 | Jun | Validation of Water Treatment System | 5 | Industry/ University |
| 63 | Jun | Validation of Water Treatment System | 5 | Industry/ University |
| 64 | Jun | Validation of Tableting Process | 4 | Industry/ University |
| 65 | Jun | Validation of Sterile Process | 4 | Industry/ University |
| 66 | Jun | Preparation of one SOP | 3 | Industry |
| 67 | Jul | Validation of Water Treatment System | 4 | Industry/ University |
| 68 | Jul | Validation of Water Treatment System | 4 | Industry/ University |
| 69 | Jul | Validation of Tableting Process | 3 | Industry/ University |
| 70 | Jul | Validation of Sterile Process | 5 | Industry/ University |
| 71 | Jul | Validation of Quality Control | 3 | Industry |
| 72 | Jul | Validation of Quality Control | 5 | Industry |
| 73 | Jul | Preparation of one SOP | 3 | Industry |
| 74 | Jul | "Certificate day" (SOP workshops) | 38 | Industry |
| 75 | Aug | Validation of Water Treatment System | 3 | Industry/ University |
| 76 | Aug | Validation of Tableting Process | 5 | Industry/ University |
| 77 | Aug | Validation of Tableting Process | 5 | Industry/ University |
| 78 | Aug | Validation of Tableting Process | 4 | Industry |

| | | | PARTICIPANTS | |
|---|---|---|---|---|
| # | DATE | TITLE | # | SOURCE |
| 79 | Aug | Validation of Sterile Process | 4 | Industry/ University |
| 80 | Aug | Validation of Sterile Process | 4 | Industry/ University |
| 81 | Aug | Validation of Quality Control | 4 | Industry |
| 82* | Aug | Seminar "Water Systems in the Pharmaceutical and Cosmetic Industry" | 145 | Industries, FDA, Med. Science, Universities |
| 83 | Aug | Preparation of one SOP | 3 | Industry |
| 84 | Sept | Preparation of one SOP | 3 | Industry |
| 85 | Sept | Validation of Sterile Process | 5 | Industry/ University |
| 86 | Sept | Validation of Sterile Process | 5 | Industry/ University |
| 87 | Sept | Validation of Quality Control | 4 | Industry |
| 88 | Sept | Validation of Quality Control | 5 | Industry |
| 89 | Sept | Validation of Tableting Process | 4 | Industry |
| 90 | Sept | Validation of Tableting Process | 6 | Industry, University |
| 91 | Sept | Validation of Tableting Process | 4 | Industry |
| 92 | Sept | Validation of Water Treatment System | 4 | Industry/ University |
| 93 | Oct | Validation of Tableting Process | 4 | Industry/ University |
| 94 | Oct | Validation of Tableting Process | 4 | Industry/ University |
| 95 | Oct | Validation of Quality Control | 4 | Industry |
| 96 | Oct | Validation of Quality Control | 4 | Industry |
| 97 | Oct | Validation of Sterile Process | 4 | Industry/ University |
| 98 | Oct | SOP's committee | 4 | Industry |
| 99 | 3/11/93 | Validation of Quality Control | 6 | Industry/Univ ersity |
| 100 | 10/11/93 | Validation of working group : "Tablet & solid-development" | 4 | Industry |
| 101 | 10/11/93 | Validation of working group: "Sterile products" | 5 | Industry/Univ ersity |
| 102 | 11/11/93 | Validation of working group: "Water Treatment" | 5 | Industry/Univ ersity |
| 103 | 12/11/93 | SOP working group | 5 | Industry |

| # | DATE | TITLE | PARTICIPANTS # | PARTICIPANTS SOURCE |
|---|---|---|---|---|
| 104 | 17/11/93 | Validation of Quality Control | 5 | Industry |
| 105 | 24/11/93 | Working group discussion on GMP and Validation with Dr.Z. Csizer | 15 | Industry/University |
| 106 | 25/11/93 | Special Lecture by Dr. Z.Csizer on "Pharmaceutical Industry in North America and Europe and its development related to Quality Assurance" | 46 | Industry/University/FDA |
| 107 | 1/12/93 | Validation of working group : "Quality Control" | 6 | Industry |
| 108 | 15/12/93 | Validation of working group : "Quality Control" | 6 | Industry |
| 109 | 22/12/93 | Seminar on: " Validation of Sterilization Processes" | 154 | Industry/University/FDA,Private sector |
| 110 | 29/12/93 | Validation of working group : "Quality Control" | 4 | Industry |

## 1994

| # | DATE | TITLE | PARTICIPANTS # | PARTICIPANTS SOURCE |
|---|---|---|---|---|
| 111 | 5/1/94 | Special Seminar of the working group by CTA ( JP.Beelen) about "Validation" | 24 | Industry/University |
| 112 | 11/1/94 | Workshop on SOP (first day) | 13 | Industry |
| 113 | 12/1/94 | Workshop on SOP at the plants (first day) | 29 | Industry |
| 114 | 18/1/94 | Workshop on SOP "advance course" | 13 | Industry |
| 115 | 20/1/94 | Working group on: "Water Treatment discussion with CTA" | 5 | Industry |
| 116 | 25/1/94 | Workshop on SOP (second day) | 13 | Industry |
| 117 | 26/1/94 | Workshop on SOP at the plant (second day) | 29 | Industry |

| | | | PARTICIPANTS | |
|---|---|---|---|---|
| # | DATE | TITLE | # | SOURCE |
| 118 | 8/2/94 | Workshop on SOP at the plant (first day) | 29 | Industry |
| 119 | 17/2/94 | Validation QA/QC (1) | 34 | Industry |
| 120 | 21/2/94 | Group dicussion on GMP | 3 | Industry |
| 121 | 3-6/3/94 | Study Tour to Vietnam | 26 | Industry |
| 122 | 3/3/94 | Validation working group participants | 5 | Industry |
| 123 | 16/3/94 | Validation working group participants | 3 | Industry |
| 124 | 16/3/94 | Working on SOP | 13 | Industry |
| 125 | 21-23/3/94 | GMP, SOP Seminar for the FDA (Inspectors) | 25 | FDA |
| 126 | 25/3/94 | Evaluation of the JODC | 12 | Industry |
| 127 | 30/3/94 | Validation working group participants | 6 | Industry |
| 128 | 9/4/94 | GMP and SOP Seminar for cosmetic Industry | 111 | Industry |
| 129 | 21-22/4/94 | GMP and SOP Seminar for cosmetic Industry Colgate-Palmolive | 25 | Industry |
| 130 | 26/4/94 | Validation as a Systematic Approach to Prevention, Imporvement, and Problem Solving in the QA/QC Program | 51 | Industry |
| 131 | 18/5/94 | Validation working group participants | 3 | Industry |
| 132 | 26/5/94 | Validation as a Systematic Approach to Prevention, Imporvement, and Problem Solving in the QA/QC Program | 62 | Industry |
| 133 | 08/6/94 | Seminar FDA (Cosmetic) on GMP + SOP | 12 | Industry |
| 134 | 09/6/94 | Meeting National Experts at PTSC | 5 | Industry |
| 135 | 14/6/94 | Lecture on GMP and SOP Hospital Pharmacist | 66 | Industry |
| 136 | 15/6/94 | Validation working group participants | 4 | Industry |
| 137 | 18/6/94 | Seminar GMP and SOP Lever Brother (Cosmetic) | 37 | Industry |

| | | | PARTICIPANTS | |
|---|---|---|---|---|
| # | DATE | TITLE | # | SOURCE |
| 138 | 21/6/94 | SOP workshop (Firstday) at PTSC | 25 | Industry |
| 139 | 23/6/94 | SOP Committee Schedule | 4 | Industry |
| 140 | 28/6/94 | SOP workshop (Firstday) at PTSC | 24 | Industry |
| 141 | 5/7/94 | SOP workshop (Secondday) at PTSC | 20 | Industry |
| 142 | 12/7/94 | SOP workshop (Secondday) at PTSC | 25 | Industry |
| 143 | 22/7/94 | Lever Brother GMP & SOP audit and consult | 12 | Industry |
| 144 | 26-27/7/94 | Seminar on Validation of Quality Control at the GPO | 60 | GPO |
| 145 | 3/8/94 | Lever Brother GMP & SOP audit and consult | 15 | Industry |
| 146 | 4/8/94 | SOP Committee Schedule | 4 | Industry |
| 147 | 6/8/94 | GMP & SOP Training Cosmetic Creation | 27 | Industry |
| 148 | 9/8/94 | Plant layout (new plants) Colgate | 6 | Industry |
| 149 | 11/8/94 | GMP & SOP audit Colgate | 5 | Industry |
| 150 | 22/8/94 | Lever Brother GMP & SOP audit | 12 | Industry |
| 151 | 25/8/94 | Colgate Palmolive GMP & SOP audit | 10 | Industry |
| 152 | 27/8/94 | Presentation of SOP Certificate | 63 | Industry |
| 153 | 1/9/94 | Colgate Palmolive GMP & SOP audit | 12 | Industry |
| 154 | 10/9/94 | Seminar GMP & SOP International Laboratories Ltd. (Cosmetic) | 150 | Industry |
| 155 | 12/9/94 | Colgate Palmolive GMP & SOP audit | 10 | Industry |
| 156 | 30/9/94 | GMP & SOP workshop at the ILC | 30 | Industry |
| 157 | 14/10/94 | GMP & SOP workshop at the ILC | 30 | Industry |
| 158 | 17-30/10/94 | Training Syrian Officials on GMP, SOP, plant visits & Management | 7 | Industry |
| 159 | 7/11/94 | Audit at P & G cosmetic company in Philippines | | Industry |
| 160 | 22/11/94 | Semianr on Tablet coating technique with Aqueous Polymer | 120 | Industry & university |

| | | | PARTICIPANTS | |
|---|---|---|---|---|
| # | DATE | TITLE | # | SOURCE |
| 161 | 25/11/94 | Training on GMP & SOP at the plant of ILC company | 33 | Industry |
| 162 | 26/11/94 | Validation working group participants | 4 | Industry |
| 163 | 7/12/94 | U.B.Chemical Industry Ltd., GMP and SOP audit ( cosmetic company ) | 15 | Industry |

* two days activity

**Exhibit 2**

*LIST OF SOPs PREPARED BY THE SERVICE CENTRE*

| # | SOP Title | Area | Code No. | P. |
|---|---|---|---|---|
| 1 | Dispensing an weighing of raw material | Manufacturing | 15-0001 | 17 |
| 2 | Cleaning of manufacturing equipment | | 15-0003 | 12 |
| 3 | Preparation and use of batch manufacturing record | | 15-0020 | 12 |
| 4 | Gowning procedure for non-clean areas | | 15-0023 | 3 |
| 1 | Guideline for preparation of SOPs | Quality Assurance | 60-0000 | 5 |
| 2 | Raw material specification document | | 60-0001 | 10 |
| 3 | Sampling of raw materials | | 60-0002 | 14 |
| 4 | Guidelines for review, revision and deletion of SOPs | | 60-0003 | 6 |
| 5 | Assignment of product code number | | 60-0007 | 5 |
| 6 | Returned goods policy | | | 4 |
| 7 | Stability program | | 60-0013 | 9 |
| 8 | Preparation of master formula and manufacturing method | | 60-0017 | 12 |
| 9 | Handling of product complaints | | 60-0018 | 4 |
| 10 | Sampling of water system | | 60-0029 | 2 |
| 1 | Receipt of raw materials | Warehousing | 65-0007 | 8 |
| 2 | Assignment of receiving control numbers ( lot numbers ) | | 65-0005 | 6 |
| 3 | Raw material inventory control | | 65-0007 | 9 |
| 1 | Gowning procedure for clean areas | Sterile production | 70-0001 | 5 |
| 1 | Organization of validation set-up | Validation | 75-0008 | 5 |
| 2 | Calibration of instruments | | 75-0013 | 12 |
| 3 | Organization of retrospective validation program | | 75-0014 | 5 |
| 4 | Organization of prospective validation program | | 75-0015 | 7 |
| 5 | Prospective validation of pre blending process of Ethiny Estradiol 10 µg tablets | | 75-0016 | 5 |
| 6 | Validation of spectrophotometer | | 75-0017 | 14 |
| 7 | Installation Qualification of Equipment and Instruments | | 75-0018 | 6 |
| 8 | OQ of pH meter # Electrode / PG of pH measurement | | 75-0019 | 12 |
| 9 | Validation of High Performance Liquid Chromatography and system suitability | | 75-0020 | 27 |
| 1 | Measurement of pH | Quality control | 80-0002 | 10 |
| 1 | Operation and maintenance of a packaged air conditioning unit | Air Handling Systems | 25-0001 | 4 |
| 2 | Preparation of maintenance of procedures for air handling systems in pharmaceutical applications | | 25-0002 | 7 |
| 3 | Specifying environmental conditions in pharmaceutical applications | | 25-0003 | 4 |
| 4 | Procedure for the leak testing of HEPA filters in clean room installations | | 25-0004 | 4 |

Exhibit 3

# Quality Control Validation

## Topics to consider for validation

1. Validation of Analytical Methodology
   - Method selection criteria
   - Reference standards
   - Reagents
   - Water specifications
   - Equipment
   - Analytical test procedures
   - Operators
   - Samples (Handling and receiving)
   - Critical support system
   - Working environment
   - SOP
   - Training
   - Documentation
   - Evaluation of the results
   - Method of evaluation
   - Validation of data
   - Criteria of acceptance
2. Equipment
   - Glassware
   - Instruments and accessories
   - Calibration
   - Performance checks
   - Preventive maintenance program
   - Critical support system
     - Electrical
     - Humidity
     - Temperature
   - Cleaning and Lubricating
   - History file
   - Personnel training
   - SOP
   - Documentation
3. Training
   - Topics
   - Target groups
   - Frequency
   - Methodology
   - Evaluation
4. Audit Functions
   - Objectives
   - Team
   - Methodology
   - Frequency
   - Problems solving
   - Documentation
   - Evaluation

## Validation of Analytical Methodology

**Purpose :** - to determine the suitability of a measurement system for providing useful analytical data
- to valuely judge the performance parameters of the method according to the requirements for the analytical data.

**Criteria of Method Selection :**
- simple, feasible, reliable and reproducible
- appropriate and suitable for use under conditions of the existing laboratory

- analyzing a sufficient number of reference samples and comparing the results to the expected or certified values.
- approach II: infer the appropriateness of methology from measurements on analogous reference materials.
- approach III: use spiked samples and surrogates as reference samples. This approach is less desirable and less satisfactory because of the difficulty in the reliable preparations of such samples and because artificially added materials such as spikes and surrogates may exhibit matrix effects differing from those of natural samples.

**Numbers of tests required :**

The test method should include atleast three levels of concentration - the extremes and the midrange of the compositions expected. Associated risk : a method that is valid in one situation could be invalid in another.

**Statistical considerations :**

At least six degrees of freedom ( or seven measurements ) should be involved at each decision point.

## Validation of Samples

**Purpose of sample validation :**

- to accept an individual sample as a member of a population under study
- to admit samples to the measurement process
- to minimize later questions on sample authenticity
- to provide an opportunity for resampling when needed

**Criteria for acceptance of a sample :**

- positive identification
- conformance with physical/chemical specifications
- a valid chain of custody

**Rejection of a sample can be based on**

- knowledge that a sampling system was not in control at the time a sample was obtained
- erroneous or conflicting data on the identity or character of a sampler
- questions about a sample that cannot be resolved
- any information that would cast doubt on the status of a sample as a member of the population of interest.

## Validation of Data

**Purpose :** To filter and accept or reject a data or a group of data based on a set of criteria.

**Remark :** Data validation can be facilitated if the analyst is fully informed on the nature of the problem, the end use of the data, and even the expected results.

**Criteria of acceptance :**

Statistically supported limits of uncertainty should be estimated.

**Lists of possible checks :**

The following checks should be made to eliminate blunders to the extent possible.

- checks for proper identification
- checks for transmittal errors
- checks for internal consistency
- checks for temporal and spatial consistency

**Checking Techniques :**

- intercomparisons with similar sample data
- checks for reasonableness of values with respect to a priori and/or a posteriori limits
- data plots
- regression analysis
- tests for outliers.

The checks may range from spot checks of randomly selected data to a total data analysis.

# Validation of Sterile Product Process

a. Aseptic production process
b. Sterilization process

## □Topics to consider for validation□

1. Environmental considerations
   - Air systems
   - temperature monitoring equipment
   - ventilation
   - filtration
   - sanitization
   - nonviable particles
   - viable particles
2. Utilities
   - gases
   - vacuum systems
   - electrical systems
   - steam systems
   - water systems
3. Facilities and Equipment
   - washing machine
   - sterilizing equipment
   - steam sterilization - autoclave
   - dry heat sterilization - hot air oven
   - ethylene oxide sterilization
   - aseptic processing filters
   - lyophilizer
   - filling machine
   - container sealing machine
4. Component Preparation Process
   - rubber closure
   - glass component
5. Operating personnel in aseptic area
   - well-trained
   - well-dressed
   - gowns materials and procedures

# Tableting Process Validation

## Outlines :

a. Process validation
   1. Weighing and Blending
      - homogeneity
         - sampling and statistic of mixing
         - mixing of [illegible]
   2. Granulation, screen wet granulation
      - characterization of granulation
      - evaluation of tablets
      - use and care of the tools
      - preformulation testing
   3. Drying, screen dry granulation
      - size reduction
      - powder characterization
      - particle size analysis
      - compression
      - measurement of compression force
   4. Tablet compression
      - compressed tablet by wet granulation
      - manufacturing problems
      - compressed tablet by direct compression
      - tablet production design validation
   5. Process optimization

b. In-process testing
   - calibration of equipment
   - review of sampling procedures
   - review of testing procedures
   - validation of data recording

c. Equipment validation
   - balance
   - wet mixer
   - dry mixer
   - tableting machine
   - capsule filling machine
   - powder filling machine

d. Environmental conditions
   - removal of dust
   - removal of organic solvents
   - treatment of exhaust gases from coating processes

## Water System Validation

**Outlines :**

1. Background of water purification
2. Distribution and utilization of water
3. Classification of impurities, characteristics types of water
4. Purification process
5. Disinfection and sterilization and pyrogen removal
6. Purified water practice and storage
7. Overview of water system validation
8. Types and classification of water system
9. Maintenance
10. Equipment of choice and maintenance

**Exhibit 4**

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**FACSIMILE TRANSMISSION**
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Drafted by/Contact persou: Z.Csizer/el

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Tel/Ext. : 21131 3948
Reference :DP/THA/88/018
Date : 8 December 1994
Transmission No:
No. of pages: 6

FROM CSIZER FOR PRASAN

PLEASE FIND ATTACHED A COPY OF REPORT ON THE FACILITIES PROVIDED BY PHARMACEUTICAL TECHNOLOGY SERVICES CENTRE (PTSC) CHULALONGKORN UNIVERSITY, BANGKOK. IN THIS REGARD I WOULD LIKE TO EXPRESS MY GRATITUDE TO YOU AND YOUR STAFF FOR THE OUTSTANDING PERFORMANCE. THANK YOU AND REGARDS.

YOUSSEF/UNIDO/VIENNA

RREPORT ON THE FACILITIES PROVIDED BY PHARMACEUTICAL TECHNOLOGY SERVICE CENTRE (PTSC) CHULALONGKORN UNIVERSITY - BANGKOK.

The experience was gained over a two week period 17 - 30 October 1994 during a Study Tour of seven Syrian delegates to Thailand supported by UNDP/UNIDO within the project DP/SYR/92/008.

The Study tour was set up in order that the Syrian delegates should gain first-hand knowledge of the development of Pharmaceutical Industry in a nation at a similar stage of industrialisation to that of Syria. Additional similarities exist in that both countries operate their Pharmaceutical Industry as a mixture of public sector, private sector and military factories.

The study program compiled by the NPD was intense and comprehensive, comprising lectures by PTSC staff and visiting UNIDO STCs., lectures by officers of the independent Thai Pharmaceutical Manufacturer's Association (TPMA), visits to the factories of general and specialist pharmaceutical manufacturers including the Government Pharmaceutical Organisation (GPO), a visit to the principal Thai manufacturer of pharmaceutical machinery, and the facilities of the Ministry of Health. Additionally a most generous social program was provided by PTSC, by the manufacturers whose factories were visited, and by the TPMA.

The study program was conducted completely in the English language, and at times presented problems to some of the Syrian delegates. However, since the subject matter was also provided in print at the closing session of the program, each delegate is able to review the course content at leisure and to refer to it in Syria. It is not possible to provide an objective measure of the level of understanding achieved by the delegates, but by their questions after the lectures and during the factory visits, it was clear that they gained much benefit from what was presented to them. It was equally clear that the delegates were much more comfortable when dealing with substantive topics such as water and air treatment, than they were when struggling to relate to the conceptual matters related to the establishment of a logical and systematic approach to preparing Standard Operating Procedures. Overall, it is estimated that about 80% understanding was attained by the delegates.

Personal and professional relationships between the participants were excellent and it is likely that some long term contacts have been developed, to the benefit of all.

Of particular relevance to the Syrian delegation was the organisation of the Thai FDA (Federal Drug Administration) and its associated Drug Testing Laboratories which have provided an excellent model for the Syrian authorities.

A wide range of topics was covered (see attached list) in the blackboard sessions but principal attention was focussed upon Management systems and motivation, Water Treatment, Air Treatment systems, and SOPs. The latter represented a synopsis of many man-months of work at DTEC by both its own staff and International Experts. To convey to the Syrian Delegation more than the briefest explanation of the results to date was not possible in the available time. However, the main thrust of the work was clearly identified and well supported by printed material which was provided to the Syrian group at the end of the session.

Additionally, papers were presented on the concepts of "Qualification" and "Validation". These concepts are proving difficult to promote in Thailand and are of academic interest only in the current situation in Syria. However, the Syrian group is now familiar with the terminology and aware that this is another facet of GMP which will need to be addressed at some time in the future.

The study tour is rated an outstanding success which will long be remembered by all who participated. It will remain a motivational experience to the Syrian group when they commence installation of similar systems in their own facilities.

REPORT FOR Dr.PRASSAN DHUMMA-UPPAKORN RESULTING FROM THE RECENT VISIT (NOV.17 -30 1994) OF A UNIDO STUDY TOUR FOR SYRIAN OFFICIALS ACCOMPANIED BY J.T. BROWN UNIDO STC.

The study tour is classified as an outstanding success by the Syrian group. See attached Report which will become part of the Final Report of the second Mission to Syria DP/SYR/92/008

The following brief report is provided for the express use of Dr. Prassan in the ongoing support of the Centre.

In context of the technologies provided, with UNIDO assistance, at PTSC, these are of top quality and currently exceed the available laboratory space. However, continued expansion of the facility is imperative if it is to continue to provide the increasingly sophisticated services demanded by pharmaceutical industry. There should be no doubt that a demand for services offered by PTSC do exist, both in Thailand and in the neighbouring countries.

There are, however, four principal constraints upon the maximisation of use of the PTSC:

i) the fact that it is not operated and managed as a commercial entity,

ii) the fact that its salary structure is unable to attract sufficient numbers of post doctoral candidates to its workforce,

iii) the fact that it provides sophisticated services to industry, at non-commercial rates,

iv) the fact that it is seen to be an isolated facility within the Faculty of Pharmacy, in-stead of having the interfaculty connections which are vital to its ongoing success, and which will provide the cross-fertilisation of ideas which are a necessary part of leading edge technology.

The PTSC is a centre of excellence within the ASEAN region and it must function as such or ultimately it will stagnate into just another under-funded laboratory doing academic work and struggling for recognition and survival. Inevitably stagnation in the Centre would serve to make recruitment of scientists even more difficult than it currently is.

Currently, PTSC is in a dilemma; it is under-utilised, yet it is unwilling to seek more work since it cannot recruit the necessary skilled staff to meet an increased work-load, within a time scale which will satisfy prospective customers.

As the only laboratory of its kind in the region, PTSC is a potential earner of Foreign Exchange. It has the opportunity to significantly influence the development of technology, drug delivery systems, and innovative molecules regionally and globally.

As such, the facility should be given maximum support by the UN system, by the Thai authorities, and by national and regional pharmaceutical organisations.

Exhibit 5

# NUMBER OF PARTICIPANTS JOINED THE PTSC's SEMINARS

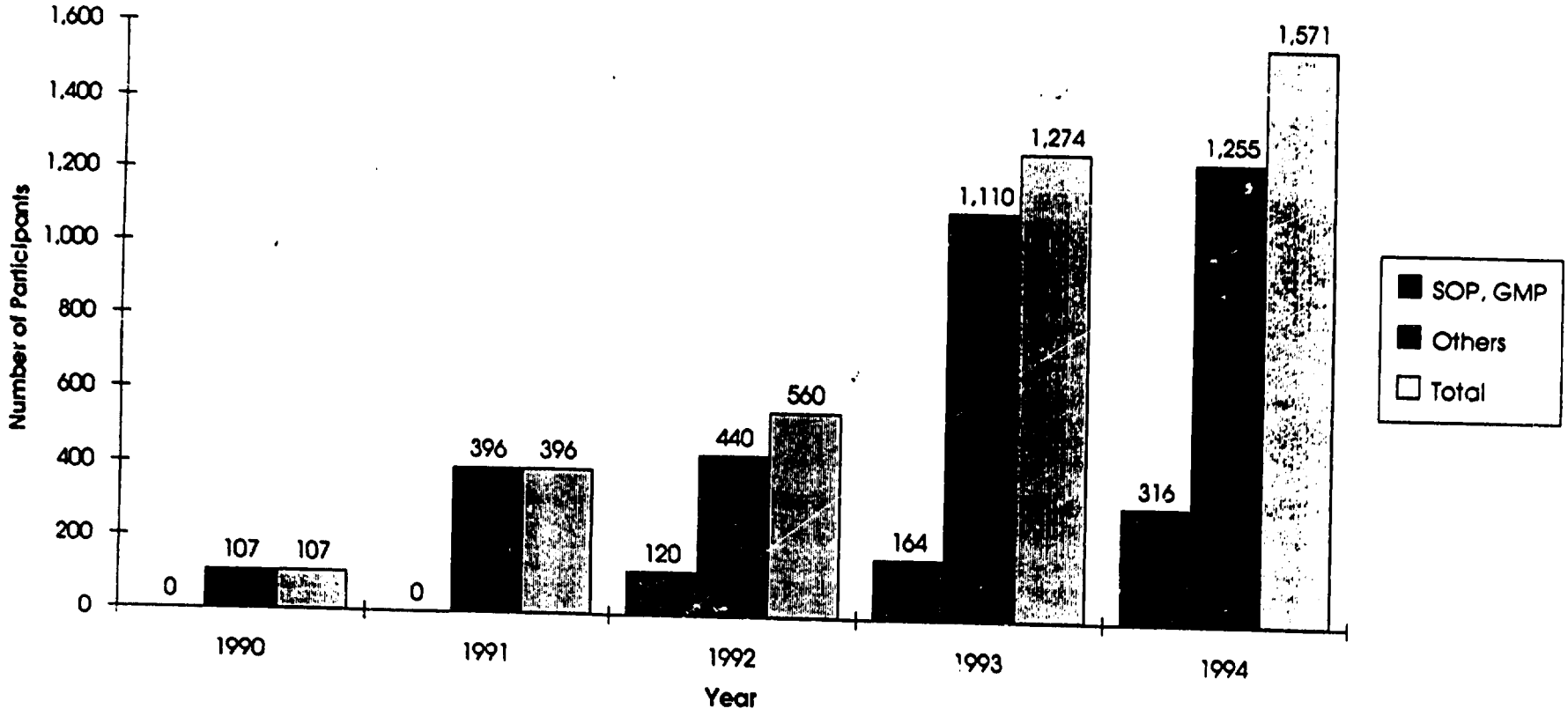
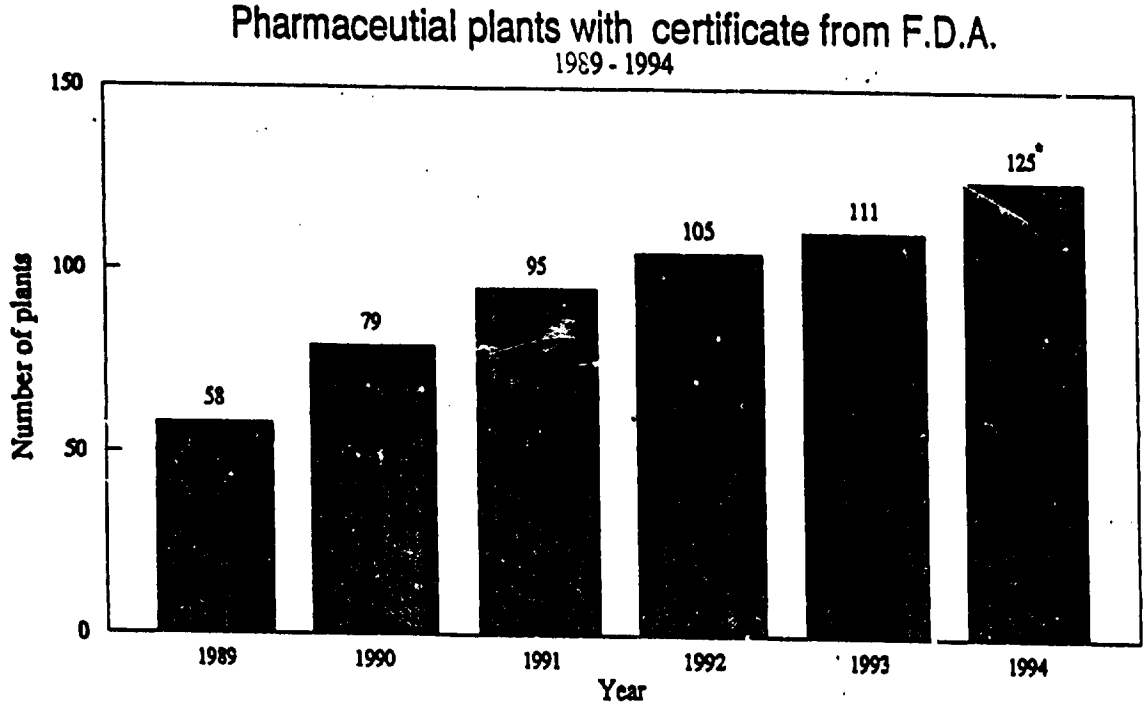


**Exhibit 6**




* The figure in 1994 is estimated by the end of the year.
As of the mid of August 1994, 119 plants have received GMP certificate.