OCCASION

This publication has been made available to the public on the occasion of the 50th anniversary of the United Nations Industrial Development Organisation.

DISCLAIMER

FAIR USE POLICY

CONTACT

Please contact publications@unido.org for further information concerning UNIDO publications.

For more information about UNIDO, please visit us at www.unido.org

UNITED NATIONS INDUSTRIAL DEVELOPMENT ORGANIZATION
Vienna International Centre, P.O. Box 300, 1400 Vienna, Austria
Tel: (+43-1) 26026-0 · www.unido.org · unido@unido.org

RESTRICTED

21623

DP/ID/SER.B/735/Add.1
4 July 1996
ORIGINAL: ENGLISH

DEVELOPMENT OF THE PHARMACEUTICAL INDUSTRY IN THAILAND

DP/THA/88/018

THE KINGDOM OF THAILAND

Terminal report*

Prepared for the Royal Government of Thailand
by the United Nations Industrial Development Organization,
acting as executing agency for the United Nations Development Programme

Based on the work of Mr. J. P. Beelen, Chief Technical Adviser and Dr. Prasan Dhumma-Upakorn, National Project Director

Project Manager: Zoltan Csizer, Chemical Industries Branch

*This document has not been edited.

V.96 84649

TABLE OF CONTENTS

Page

XII. ANNEXES

ABBREVIATIONS

BOD	Board of Directors of the Service Centre
CTA	Chief Technical Advisor
DTEC	Development of Technical and Economic Cooperation
ESCAP	Economic and Social Commission for Asia and the Pacific
FDA	Food and Drug Administration
FTI	Federation of Thai Industry
GATT	General Agreement on Tariffs and Trade
GLP	Good Laboratory Practices
GMP	Good Manufacturing Practices
GPO	Government Pharmaceutical Organization
HVAC	Heating Ventilation Air-Conditioning
IFPMA	International Federation of Pharmaceutical Manufacturers Association
MOI	Ministry of Industry
NPD	National Project Director
PIC	Pharmaceutical Industry Club
PPER	Project Performance Evaluation Report
PTSC	Pharmaceutical Technology Service Centre
QA	Quality Assurance
QC	Quality Control
QIT	Quality Improvement Team
R&D	Research and Development
RM	Raw materials
SME	Small-medium enterprises
SOP	Standard Operating Procedures
TPMA	Thai Pharmaceutical Manufacturer Association
TRIP	Trade-related aspects of Intellectual Property Rights
UNDP	United Nations Development Programme
UNIDO	United Nations Industrial Development Organization
VAT	Value-Added Tax
WFI	Water for Injection
WHO	World Health Organiztion
WIPO	World Intellectual Property Organization
WTO	World Trade Organization

I. OBJECTIVE

1. Problems to be solved

Some problems encountered by the local pharmaceutical industry include:

- Limited pharmaceutical technology.
- Lack of "know how" to improve product quality.
- Lack of skilled or qualified personnel in some areas of the pharmaceutical production.
- Lack of engineering consultants familiar or experienced with GMP regulations as applicable to plant layouts, material specifications or construction requirements.

The Food and Drug Administration (FDA) of Thailand in cooperation with the Industry and the Academic Institution, established the Quality Improvement Team (QIT) in 1987.

The QIT team visited about 60 pharmaceutical plants of which the majority were believed to be in need of technical assistance.

Plant visits were also conducted by a UNIDO mission and, during a subsequent meeting with some pharmaceutical executives of the Pharmaceutical Industry Club (PIC) and Thai Pharmaceutical Manufacturer Association (TPMA), several large volume manufacturers of drugs expressed the intention to renovate their existing plants or to relocate from the residential area to the industrial estates.

2. Type of technical assistance needed

The most immediate problems which had to be addressed by the pharmaceutical industry and for which different types of technical assistance was required include :

- Plant layouts in compliance with GMP guidelines.
- Effective environmental control and monitoring of production areas in terms of temperature, humidity, air pressure, dust and air ventilation.
- Clean Room technology.
- Development of comprehensive GMP training programmes for different levels of the plant personnel.
- Validation techniques applicable to production and QC operations.

- Manufacturing of Purified Water USP and Water for injection (WFI).

- Treatment of waste water at the plant site.

Different problems or constraints identified "***at the outset of the project***"were clearly stated in the project document.

The inputs and activities necessary to resolve these problems were summarized in the original workplan which covered a time frame of 15 months.

The perception of the different problems "***at the end of the project*** " which had to be solved did remain the same as at the *"**outset of the project**"* with the exception of the need of preparing a manual of GMP guidelines which was issued by the FDA, Thailand ***prior*** to the start up of the projects. It was also foreseen that the pharmaceutical companies, benefitted from the services provided by the Service Centre to be established by the project, would be charged reasonable fees for the services rendered by the Centre for its operation. The net resources of the Centre were in the period of January to August 1994 amounting to Baht 487,699. This clearly shows the sustainability of the Service Centre.

3. Development objective

The development objective of this project was to ensure that the quality of locally manufactured drugs meet the International Standards and thereby enhances their exportability.

II. PROJECT DESIGN and APPROACH

- As a result of the difficulties faced by the pharmaceutical industry in Thailand, the Royal Government, in conjunction with the United Nations Development Programme (UNDP), the United Nations Industrial Development Organization (UNIDO) and members of the Industry and the University of Chulalongkorn did set up the framework for a Pharmaceutical Technology Service Centre. ***(Annex 1)***

- The project was initiated by the Federation of Thai Industries (FTI) in close cooperation with the PIC who has close ties with the TPMA. Both associations have ***one*** and the ***same*** Executive Committee.

- The PIC represents the industry at Government levels and proposes measures for the advancement of its industry to the Ministry of Industry (MOI) in Thailand.

- The project was financed by the UNDP whereas UNIDO acted as the executing agency.

- The office of the FTI/PIC was selected as the counterpart organization.

- The National Project Director (NPD), who was appointed by the FTI/PIC, coordinated the project on the national side whereas the Chief Technical Advisor (CTA) represented UNIDO.

- The PIC was responsible to nominate the entire staff for the Pharmaceutical Technology Service Centre (PTSC) including the staff for QC laboratories and the National Experts.

- The project was carried out by the PTSC in very close cooperation with the Chulalongkorn University - Pharmaceutical Science Department and the PIC/TPMA Association.

- The PIC/TPMA appointed several industry representatives to facilitate the transfer of the available information regarding pharmaceutical technology to its members.

- The University provided adequate space for the laboratories and office for the Service Centre (PTSC).

- The Government of Thailand was represented by the Development of Technical and Economic Cooperation (DTEC) who closely monitored the implementation of this project.

- The project was carried out almost entirely by the PTSC and was designed to :

  (a) provide laboratory services to the industry;

  (b) organize consultancy services and provide technical assistance to the industry;

  (c) play important role as mediator or facilitator between the FDA and the industry.

- A workplan was prepared to schedule the activities required to achieve the results or outputs outlined in the project document, DP/THA/88/018.

- The active involvement of the industry was intended to facilitate the cooperation with the Service Centre and the counterparts of the industry as well as to ensure the financial sustainability of the project in the long term.

III. OUTPUT SOUGHT and PRODUCED

The status concerning the ***outputs sought and produced*** as applicable to the immediate objectives stated in the project document can be summarized as follows:

1. Immediate Objective 1

"Enable the local pharmaceutical companies to introduce 'Good Manufacturing Practices' in their production plants in order to ensure that the pharmaceutical products comply with the International quality standards."

1.1 Output to be achieved

Top managers, technicians and production personnel of 28 pharmaceutical production plants will be trained and able to introduce Good Manufacturing Practices at different levels.

1.2 Achievements and impact of the project

- A total of at least 105 pharmaceutical companies attended or participated the seminars/ workshops organized by the PTSC on several topics related to GMP aspects. Continued genuine interest has been shown by the industry as large as illustrated in ***Annex 2.***
- The industry has acquired a clear understanding of the different GMP aspects which must be implemented.
- The number of companies approved for GMP certification by the FDA, Thailand increased gradually from 95 to 125 plants which represents an increase of 30 companies . ***(Annex 3).***
- The FDA encourages the non-certified plants to contact the PTSC to obtain GMP training.

Results: Output Produced

1.3 Favourable factors

The main factors which facilitated the achievement of the above output are :

- The cooperation and interest demonstrated by the PIC/TPMA and its members towards all the activities initiated by the Centre to promote GMP training activities.

- The cooperation of the Department of Pharmaceutical Science at the Chulalongkorn University which provided the necessary physical space requirements and facilities to establish the Service Centre as per Contractual Agreement with the PIC/FTI Association .

- The technical and financial input provided by the UNIDO/UNDP to carry out the necessary programmes of activities as specified in the revised Workplan. ***(Annex 4)***

- The formal approval obtained by all participating partners (PIC/FTI/MOI/DTEC/UNIDO/UNDP) to extend the time period for completion of this project from ***15 to 36 months*** is considered a major factor of the success achieved as it enabled the PTSC to complete the outputs via step by step approach.

- The continued support and understanding exhibited by the Government Agencies such as Ministry of Industry (MOI) and DTEC whenever formal approval procedures had to be expedited to meet critical deadlines for many activities during this project (e.g. study tours, language tests, fellowships, changes in Workplan, budget line changes, hiring of international or national experts, etc.)

- The assistance and dedication demonstrated by the national experts from the University and the Industry who via different ***Task-Force Groups*** achieved good progress especially during the last 24 months.

- The atmosphere of mutual trust and respect which prevailed throughout the entire project between the international and national experts, the Industry and the Government Agencies ***(Annex 15)***.

2. Immediate Objective 2

Establish and operate a Service Centre for the Pharmaceutical Industry.

2.1 Outputs to be achieved:

A newly established Service Centre to provide the required technical services needed by the pharmaceutical industry.

2.2 Achievements and impact on the project:

- The Service Centre was officially inaugurated during April 1991 by the local UNIDO

Country Director in the presence of the University, Industry and Government representatives.

- The FTI/PIC, in close cooperation with the Pharmacy Science Department of the Chulalongkorn University in Bangkok provided, as stated in the project, adequate space for the Quality Control (QC) laboratory, and the offices for the Service Centre.

- The contractual agreement approved by both parties outlined the respective responsibilities and defined the composition of the Board of Directors which must control and monitor all activities of the Service Centre.

- The Board of Directors which are composed of representative of the University, PIC, FTI meet monthly to review activities and the progress made by the Centre.

- The National Director of the Centre has been appointed as the Secretary to the BOD meetings held on a monthly basis.

- A two-day seminar was organized by the PTSC for the Executives of the local pharmacies in order to stimulate the potential interest for the Centre.

- Suitable audio - visual training material and equipment was acquired for the GMP training of production personnel at the plant site or at the Centre.

- A comprehensive technical library has been set up which has available several international technical journal, GMP manuals and guidelines as well as textbooks on different related pharmaceutical technology subjects.

- The most needed laboratory equipment have been delivered to the Centre (***Annex 14).***

- The centre is often contracted by the industry for technical assistance in terms of plant layouts, QC testing methods and GMP training of personnel.

Results: **Output Produced**

However, additional efforts will be necessary in the QC laboratory to qualify for GLP certification by the FDA, Thailand which will be essential to attract more business from the pharmaceutical industry.

2.3 Favourable factors

- A contractual Agreement of Co-operation finalized between the FTI/PIC and the Pharmaceutical Science Department of Chulalongkorn University.

- The appointment of additional national experts approved by the Government and the UNDP/UNIDO.

- The continued support by the local pharmaceutical companies which encourage their technical staff to actively participate on several working committee at the Centre.

- The positive relationship and rapport developed between the Centre and the FDA. ***(Annex 5)***

3. Immediate Objective 3

To maintain quality assurance in the industry through a well documented Good Manufacturing Practices (GMP) Manual as well as a Manual on Standard Operating Procedures (SOP).

3.1 Output to be produced

A comprehensive GMP Manual and SOP Guidelines for the industry.

3.2 Achievements and impact on the project

- Several Committees have been set up to develop the manual of SOP's as it applies all many aspects of the pharmaceutical operations.

- Representatives of the University industry and the Service Centre meet at regular intervals to develop technical documents on subjects such as validation, SOP's - water treatment, Good Laboratory Practices, etc.

Results: Output Produced

Note : Manual of GMP was issued by the FDA *prior* to start up of the Centre.

3.3 Favourable factors

- The active participation and technical support provided by several local pharmaceutical companies to the Centre.

- The invitation extended by the FDA to the Centre to actively participate in their 5 years Development Programme towards the implementation of the GMP Guidelines. ***(Annex 5)***

- The support exhibited by the DTEC/UNIDO/UNDP towards the recommended revised Workplan which was extended from **15** to **36 months.** ***(Annex 4)***

- The approval granted by all participating partners to set up a comprehensive technical library.

IV. SUMMARY OF ACTIVITIES DURING THE LIFE SPAN OF THE PROJECT BETWEEN OCTOBER 1991 UNTIL SEPTEMBER 1994

	Total	Annex
Plant visits or inspections by the CTA	125	6
Workshops or Seminars	35	7
GMP Training sessions for plant personnel	12	
Working Sessions of PTSC/Industry/ University	92	8
Number of Study Tours	4	9
Fellowship Programmes	3	10
Participating Companies	105	2
Liaison Meetings with the FDA	4	
Meetings of Board of Directors	36	
Waste Water Treatment	1	
Regionalisation of the project	3	

The full list of activities organized by the Pharmaceutical Technology Service Centre which clearly shows its sustainability (see activities carried out in 1995 and 1996) is given in Annex 11.

Annex 12 gives the list of SOPs prepared by the Service Centre. The documentation amounts to 265 pages. A few SOPs as examples are also given.

V. MAJOR CONSTRAINTS

1. Hiring of CTA

- Difficulties experienced to identify a suitable Chief Technical Advisor (CTA) delayed the start up by about 8 months.
- Time period required in obtaining formal approval for the nomination of the CTA by all Government Agencies.

2. Introduction of VAT system

The increased cost of drugs resulting from the introduction of the VAT System (7%) has been absorbed by the local industry because of the fierce competition prevalent within the market places.

A decrease in the profit margins ***does not motivate*** the manufacturers to allocate new operating expenses for the implementation of GMP related projects. (GMP training - new equipment - hiring of additional personnel, etc.)

Routing Procedure for approval of changes to the original project document

- The routing procedure which must be followed to obtain approval of proposed changes regarding the "inputs" required several months (e.g. extension of the project from 15 to 36 months).
- Some activities could not be implemented unless a modification of the project was formally approved by all partners.

Volume and complexity of technical issues

Insufficient time was allocated at the ***outset of the project*** to ensure adequate completion of all activities, inputs and outputs.

The time required to overcome the attitude of "***Resistance to change***" and ***social and cultural*** constraints were underestimated.

Social and Cultural Environment

- Some cultural, social and academic practices prevented the hiring of a full time National Director from the University. The appointed professor ***must*** indeed continue to give lectures throughout the entire University calendar year and could therefore only devote his energies towards the Centre on a part time basis.

VII. COST EFFECTIVENESS OF THE PROJECT

It is rather difficult to estimate the monetary value of the ***many intangible and tangible benefits*** which will be derived from the implementation of this project.

Indeed, the financial benefits which will be derived from the production of high quality drugs is of ***unlimited*** value if one considers the positive impact that this project will continue to generate during many years. Many people with low income will have access to high quality drugs at reasonable prices.

The operating expenses for all the activities carried out by the Centre versus the outputs achieved at the end of the project are considered very ***cost effective*** especially if one considers the long term positive impacts this project will have on the production of high quality products by the local pharmaceutical industry in the future.

VIII. REMAINING ACTIVITIES OF PROJECT

QA/QC Laboratory

- Purchasing and installation of the additional equipment requested in February 6, 1994.
- Complete all QC documentation required for GLP compliance including adequate training of personnel.

Pharmaceutical Technology Services

- ***Complete*** the preparation of the technical manual documentation regarding the manufacturing of Purified Water and Water for injection.
- ***Prepare*** a technical manual regarding all aspects related to environmental control for sterile and non sterile production operation.(HVAC - Dust Control - Clean Room technology, etc.)
- ***Update*** on a continuos basis all reference technical information files regarding the validation of pharmaceutical operation.
- ***Continue*** the preparation of GMP training material for plant personnel.
- ***Develop*** technical documentation for workshops regarding plant layouts.

IX. EXPERIENCE GAINED THROUGH THE PROJECT

Communication Channels

- Several partners were involved in the decision making process related to this project as illustrated in ***Annex 13.***

- A specific routing procedure must therefore be followed to ensure that all partners remain properly informed about all important aspects of the project.

- Any breakdown did adversely affect the timely progress of certain inputs or activities.

Suggestion : Ad hoc meetings could be organized by the PTSC in order to expedite the distribution of important information necessary for early approval of new inputs or changes in the budget lines.

Employment of Qualified Staff

- Social and cultural practices currently prevalent within the working environment, represent a handicap whenever highly qualified personnel.

- Corrective action which sometimes is urgently acquired but that ***adversely*** affect the job security of the staff, tends to be delayed due to social and cultural practices.

Suggestion : A more cost effective approach should be investigated for the selection and hiring process in combination with the performance appraisal system compatible with the local social and cultural constraints.

X. FINDINGS / OBSERVATIONS

- Social, cultural and economic factors explain the reluctance exhibited by several local pharmaceutical manufacturers to implement GMP standards.
- The local FDA in Thailand does gradually impose stricter requirements for GMP compliance.
- Several companies at the end of the project intend to implement new plant layouts or upgrade their manufacturing facilities.
- The Government Pharmaceutical Organizations (GPO) supplies most of the drugs for the Government Health Institution. However, they are not subjected to similar FDA inspections for GMP compliance.
- The preparation of technical material for training session on all subject related to GMP topics depend greatly on the impact and cooperation of national experts of the industry with the Centre.
- It is anticipated that the approval of the QC laboratory to obtain a government GLP certificate, will require more time than anticipated.
- The FDA decision to invite the Service Centre to actively participate in their 5 year GMP Development Plan, represents a challenging opportunity to enhance the image and reputation of the Centre to the Government and Industry.
- All aspects regarding the financial management of the Centre are currently subjected to Government and University Regulations which prevents it to become an independent financial entity.

XI. RECOMMENDATIONS

Follow up Activities

- The shareholders are satisfied with the results achieved at the end of the workplan with this project.
- Some follow up activities by the BOD are however very important to ensure the continued growth and success of the PTSC on a medium and long term basis.

Recommendations to the PTSC / University

Expand	The physical facilities of the PTSC to accommodate an efficient library room, area for GLP training and additional space for the administration.
Develop	a comprehensive action plan to explore the possibility of funding a project on a regional basis (Vietnam - Laos).
Submit	as per standard procedure operating budgets for 1995 and 1996 to the BOD based upon planned activities or services which will be provided to the industry.
Investigate	together with the University the feasibility and merits to obtain the status of an "Independent Service Centre" as a financial entity.
Continue	to promote a harmonious report with the FDA, Thailand and participate actively in their 5 year GMP Development Plan.
Evaluate	the feasibility of hiring on a full time basis a qualified person for the preparation of all technical documentation and the review of technical journal and/or text books available in the library. (Water systems, SOP's, Plant layout, Validation, Manufacturing record, etc.)
Organize	at regular intervals visits of the Service Centre for the benefit of the executives of the Pharmaceutical, Cosmetic and Food Industries.
Circulate	to the industry at regular intervals the "Fee Schedule" for all Technical or Consultancy Services available at the Centre.
Issue	as soon as possible the purchase orders for the outstanding QC equipment allocated in the operating budget for 1994.
Give	top priority to meet GLP compliance in order to qualify for the FDA Certification.

Concentrate activities within the laboratory on training activities or workshops related to :

- GLP training
- Validation of QC equipment
- Operating instruction for QC equipment
- Routine testing of RM

Pursue the strategy of organizing activities which meet the urgent needs of the industry at large to ensure the financial sustainability of the Centre.

Recommendations to BOD/PIC/TPMA

Continue to encourage the PIC/TPMA members to utilize extensively the technical assistance of the Service Centre.

Promote the visibility of the PTSC via special information meetings between the Service Centre and members of the PIC/TPMA.

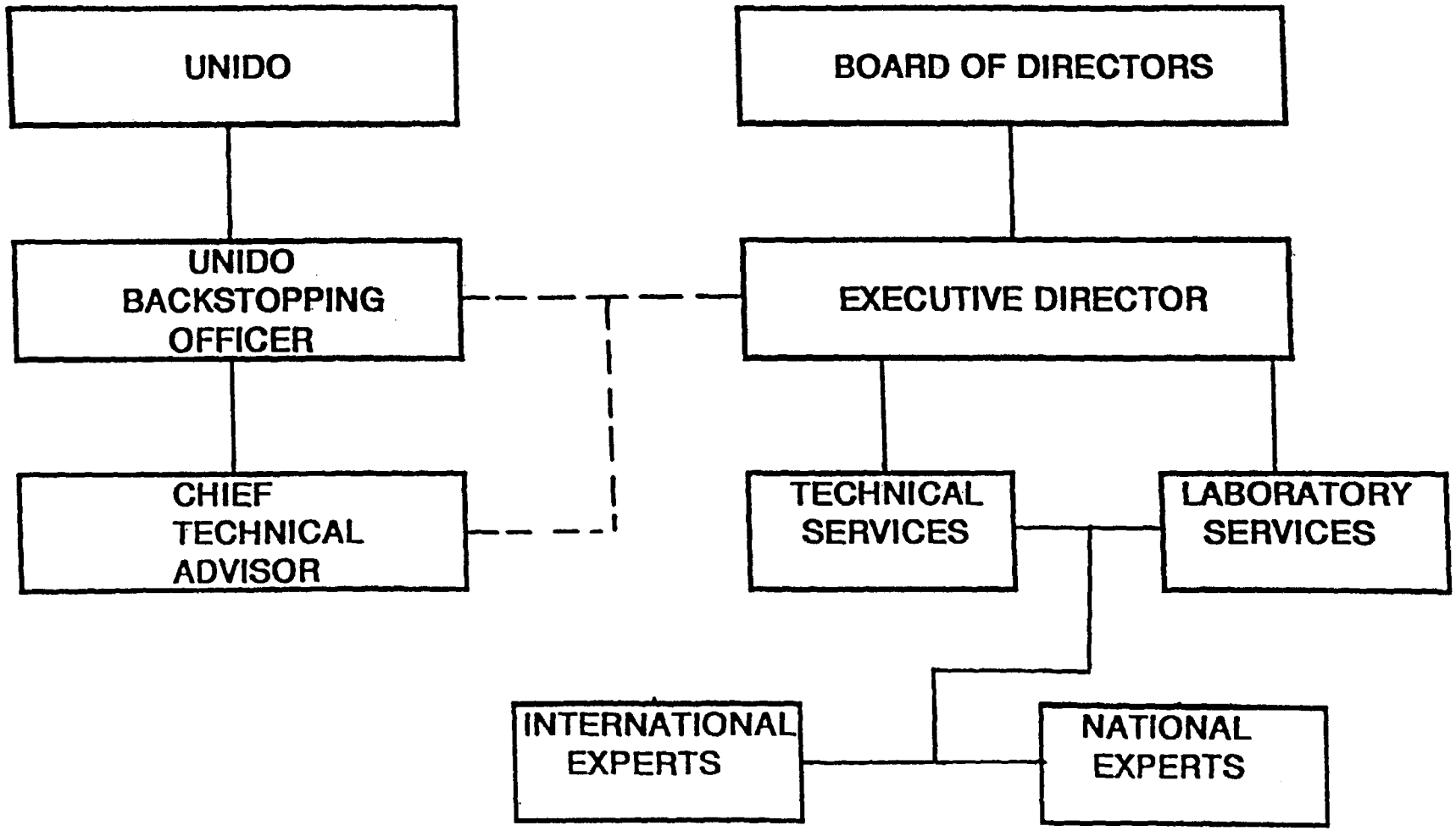
Provide continued management advice and support to the Service Centre and monitor the progress of activities designed to achieve all the established objectives.

Investigate the merits of rotating at regular intervals (e.g 2 years) the management team of the Service Centre between an Academic and a Business Director.

The above approach would facilitate the implementation of new business strategies or systems to assist the dynamic growth and expansion of the Centre.

XIII. ANNEXES

Organizational Chart for the Pharmaceutical Technology Science Centre



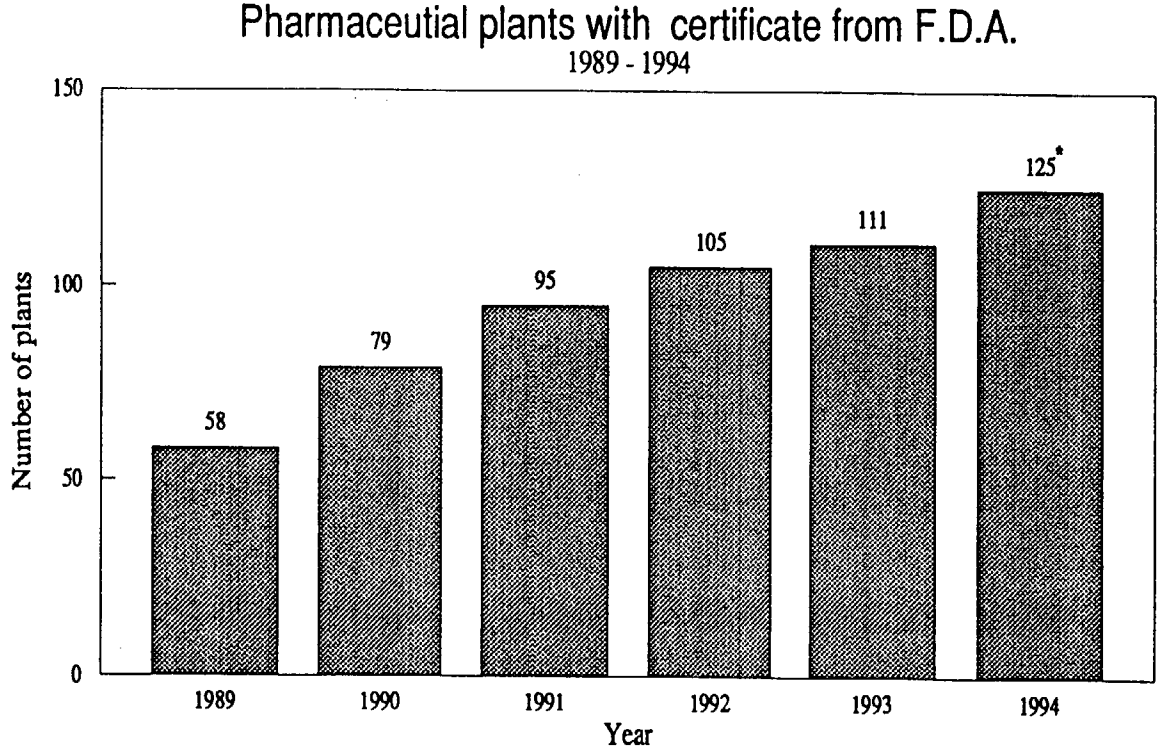
Companies participating in PTSC activities.

1. A.N.B. LABORATORIES CO.,LTD.
2. A.N.H. PRODUCTS
3. ACDHON CO.,LTD
4. AMORNKIAT TRADING LTD. PART.
5. ATLANTIC LABORATORIES CORP. LTD.
6. B.B.PHARMA CO.,LTD.
7. B.J. LIMITED PARTNERSHIP
8. B.L. HUA & CO.,LTD.
9. B.L. LIMITED PARTNERSHIP
10. BERLIN PHARMACEUTICAL INDUSTRY CO.,LTD.
11. BETERSCORF (THAILAND) CO.,LTD
12. BETTER PHARMA CO.,LTD
13. BIOLAB CO.,LTD.
14. BRYWOOD PHARMACEUTICAL LTD. PART.
15. BUKALO PHARMACY CO.,LTD
16. BURAPHA DISPENSARY CO.,LTD.
17. CATHAY CHEMICAL LTD,PART.
18. CHAROEN BHAESAJ LAB CO.,LTD.
19. CHEMEPHAND MEDICAL (FACTORY)
20. CHEW BROTHERS & CO.,LTD. PART.
21. CHINTA TRADING CO.,LTD.
22. COMBINE CO.,LTD
23. COMMUNITY PHARMACY PUBLIC COMPANY LIMITED
24. CONTINENTAL PHARM CO.,LTD
25. COX LABORATORIES LTD. PART.
26. DUMEX LIMITED
27. F.E.ZUELLIG (BANGKOK) LTD.
28. FACTORY OF PHARM CO.,LTD
29. FIVE PAGODAS PHARMACY CO.,LTD.
30. GENERAL DRUGS HOUSE CO.,LTD.
31. GLAXO-VIDHYASOM LTD.
32. GOLD MINTS PRODUCTS
33. GREATER PHARMA LTD. PART.

34. HI-PEX CO.,LTD
35. HOECHT PHARMACEUTICAL INDUSTRIES LTD.
36. JACK CHIA INDUSTRIES (THAILAND) LTD.
37. K.B. LABORATORY LTD.
38. KENYAKU (THAILAND) LTD.
39. KRUNGDHEB PHARMACY LTD. PART.
40. L.B.S. LABORATORY LTD, PART.
41. L.P. STANDARD LABORATORIES LTD.
42. LACHMANN CO.,LTD.
43. LAM THONG KARNPHATAYA PHARMACEUTICAL PRODUCTS
44. LART SINGH
45. LUPIN CHEMICALS (THAILAND) LIMITED
46. M & H MANUFACTURING CO.,LTD.
47. MEDICAL SUPPLY CO.,LTD.
48. MEDICAP LIMITED
49. MODERN MANY CO.,LTD.
50. NAKORN PATANA PHARM CO.,LTD.
51. NAM KOK DISPENSARY CO.,LTD.
52. NEOPLAST COMPANY LIMITED
53. NIDA PHARMA CO.,LTD
54. OLAN-KEMED CO.,LTD.
55. OLIC (THAILAND)LED.
56. OSOTH INTER LABORATORIES CO.,LTD.
57. OSOTHSAPHA (TECK HENG YOO)CO.,LTD.
58. P.P. LABORATORIES CO.,LTD.
59. PARAR LAB. LTD, PART.
60. PATANAKARN BHAESAI LTD, PART.
61. PHARMACARE CO.,LTD.
62. PHARMASANT LABS CO.,LTD.
63. POLIPHARM CO.,LTD
64. POND'S CHEMICAL (THAILAND) R.O.P.
65. PURE CHEM CO.,LTD.
66. RHONE-POULENC THAI INDUSTRIES LIMITED

67. ROTALABORATORIES CO.,LTD.
68. S.M. PHARMACEUTICAL
69. SCHERING CHEMICALS LTD.
70. SENG THAI COMPANY LTD. PART.
71. SEVEN STARS PHARMACEUTICAL CO.,LTD
72. SIAM BHEASACH CO.,LTD.
73. SIAM PHARMACEUTICAL CO.,LTD
74. SIAMERICAN PHARMACEUTICALS CO.,LTD.
75. SILOM MEDICAL CO.,LTD.
76. SOMCHITT DISPENSARY CO.,LTD.
77. SRIPRASIT PHARMA CO.,LTD.
78. SUPHON BHESAJ FACTORY
79. T.O. CHEMICALS (1979) LTD.
80. T.P. DRUG LABORATORIES (1969) CO.,LTD
81. T.P. DRUG LABORATORIES(1969) CO.,LTD
82. TAKEDA (THAILAND) LTD.
83. THAI MEIJI PHARMACEUTICAL CO.,LTD.
84. THAI NAKORN PATTANA CO.,LTD.
85. THAI NAKORN PATTANA CO.,LTD.
86. THAI OTSUKA PHARMACEUTICAL CO.,LTD.
87. THAI P.D. CHEMICALS CO.,LTD.
88. THAI PHARMED (1942) CO.,LTD.
89. THAIRED CROSS (SCIENCE DIVISION)
90. THE BOOTS MANUFACTURING CO(THAILAND) .TD.
91. THE BOOTS MANUFACTURING CO., (THAILAND) LTD.
92. THE FORTY-TWO LABORATORIES LTD.
93. THE GOLDEN CUP PHARMACEUTICAL CO.,LTD.
94. THE GOVERNENNT PHARMACEUTICAL ORGANIZATIO
95. THE JAWARAD CO.,LTD.
96. THE SERMMITR CO.,LTD.
97. THI OTSUKA PHARMACEUTICAL CO.,LTD.
98. TOPDERM CO.,LTD.
99. TRUST MAN PHARMAR L.P.

100. UDOMPHON (PHIHALAB) CO.,LTD
101. UNICHEM PHARMACEUTICALS CO.,LTD
102. UNION DRUG LABORATORIES LTD.
103. UNISON LABORATORIES CO.,LTD
104. UTOPIAN CO.,LTD.
105. VIDHYASOM CO.,LTD.



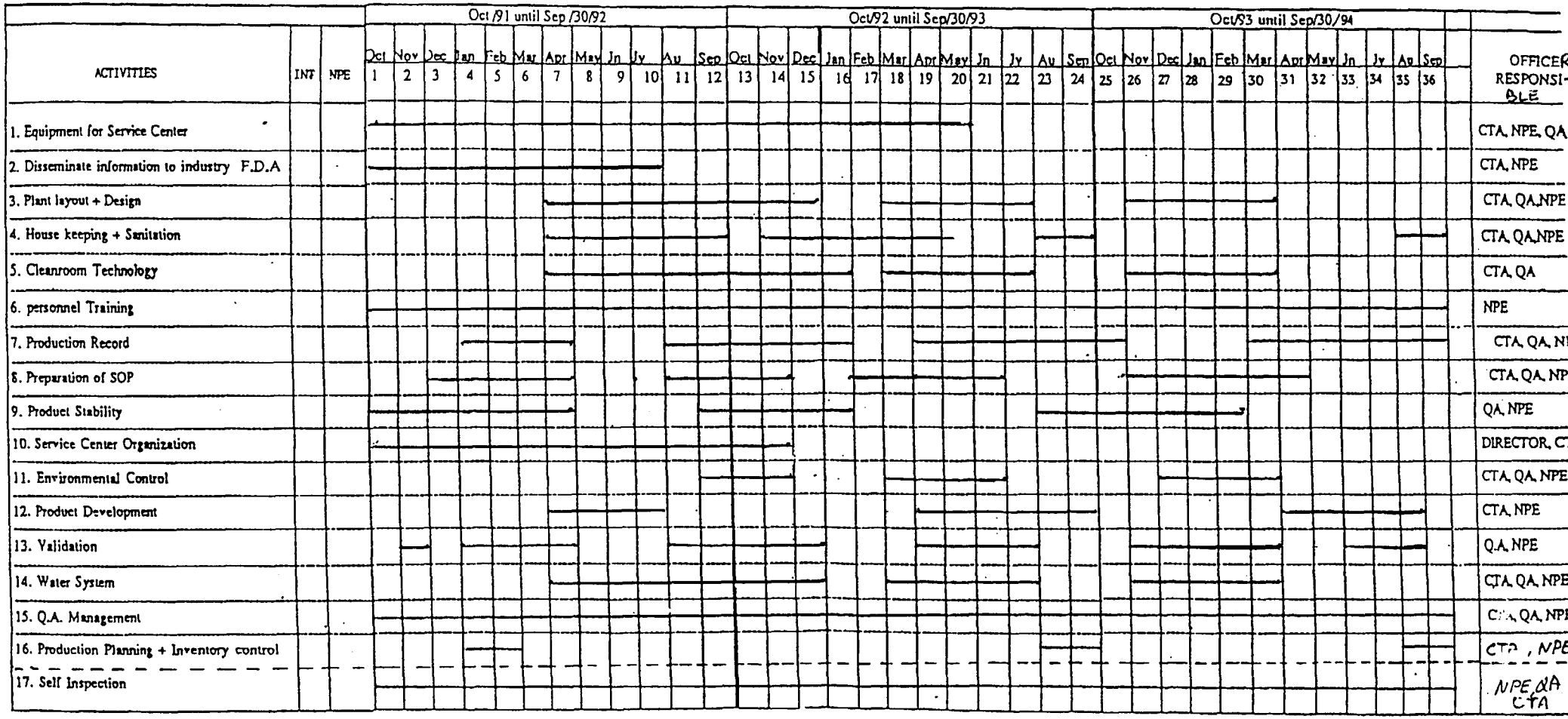
* The figure in 1994 is estimated by the end of the year.
As of the mid of August 1994, 119 plants have received GMP certificate.

Annex 4

REVISED WORKPLAN 1991-1994

ACTIVITIES	INT	NPE	Oct/91 until Sep/30/92												Oct/92until Sep/30/93												Oct/93until Sep/30/94												OFFICER RESPONSIBLE
			Oct	Nov	Dec	Jan	Feb	Mar	Apr	May	Jn	Jy	Au	Sep	Oct	Nov	Dec	Jan	Feb	Mar	Apr	May	Jn	Jy	Au	Sep	Oct	Nov	Dec	Jan	Feb	Mar	Apr	May	Jn	Jy	Au	Sep	
			1	2	3	4	5	6	7	8	9	10	11	12	13.	14	15	16	17	18	19	20	21	.22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	
I. UNDP/UNIDO INPUTS :																																						
1. Chief Technical Adviser (CTA)	X																																					
2. Quality Assurance Expert (QA)+NPE*	X	X																																				
3. Controlled Air Con & Ref. Expert + NPE*	X	X																																				
4. Personnel Training + NPE*		X																																				
5. NATIONAL PHARM EXPERT (NPE)* R & D-SEMINAR-GMP TRAINING		X																																				
II. WORKSHOPS & SEMINARS																																						CTA, NPE
1. Top Management																																						
2. Middle level staff+Technical																																						
3. Mechanic-Electrical, Production personnel, Maintenance																																						25
III. FELLOWSHIPS																																						CTA-BOARD
1. Validation + Biology 1 person																																						
2. QA Management/Quality Assurance 1 person																																						
3. Production Technology/R & D/GMP 1 person																																						
III. STUDY TOUR																																						
1. FTI or (PIC/ITPMA) 2 Persons																																						
2. FDA & Medical Science 2 Persons																																						
3. SERVICE CENTER 2 Persons																																						

NOTE : ____ = INTERNATIONAL EXPERT ;---- = NATIONAL EXPERT (NPE)
A short term Consultant 2m/m will also be invited during the period of this project


Oct /91 until Sep /30/92
Oct/92 until Sep/30/93
Oct/93 until Sep/30/94
ACTIVITIES
INT
NPE
Oct Nov Dec Jan Feb Mar Apr May Jn Jy Au Sep
1 2 3 4 5 6 7 8 9 10 11 12
Oct Nov Dec Jan Feb Mar Apr May Jn Jy Au Sep
13 14 15 16 17 18 19 20 21 22 23 24
Oct Nov Dec Jan Feb Mar Apr May Jn Jy Au Sep
25 26 27 28 29 30 31 32 33 34 35 36
OFFICER RESPONSI-BLE
1. Equipment for Service Center
CTA, NPE, QA
2. Disseminate information to industry F.D.A
CTA, NPE
3. Plant layout + Design
CTA, QA, NPE
4. House keeping + Sanitation
CTA, QA, NPE
5. Cleanroom Technology
CTA, QA
6. personnel Training
NPE
7. Production Record
CTA, QA, NPE
8. Preparation of SOP
CTA, QA, NPE
9. Product Stability
QA, NPE
10. Service Center Organization
DIRECTOR, CTA
11. Environmental Control
CTA, QA, NPE
12. Product Development
CTA, NPE
13. Validation
Q.A, NPE
14. Water System
CTA, QA, NPE
15. Q.A. Management
CTA, QA, NPE
16. Production Planning + Inventory control
CTA, NPE
17. Self Inspection
NPE, QA CTA

Annex 5

No. 0802/ 14513

Food and Drug Administration
Ministry of Public Health
Devaves Palace, Bangkok 10200 Thailand

September 2 , B.E. 2535(1992).

Mr. Beelen
Pharmaceutical Technology Service Centre
Faculty of Pharmaceutical Sciences
Chulalongkorn University
Bangkok 10330

Dear Mr. Beelen,

Thank you very much for your letter of August 31, 1992, in which you explain the main objectives and activities concerning the Pharmaceutical Technology Service Centre at Chulalongkorn University.

Please find enclosed a copy of the English translation of the GMP 5-Year Action Program which the FDA authorities will enforce to achieve GMP compliance on a step by step basis throughout the entire pharmaceutical industry.

We are quite interested about your suggestion to arrange meetings at regular intervals between the Service Centre and the FDA authorities to discuss subjects related to GMP training.

ACTION PLAN OF PHARMACEUTICAL GMP FOR 1992-1996

Activities	Unit	Target (for budget year)					Total	Responsible Agency
		1992	1993	1994	1995	1996		
1. Inspect, advise and assess GMP compliance	plant	109	134	156	157	173		QIT & Inspection Div.
2. Seminars	time	1	1	-	1	-		Drug Control Div.
3. Training								
- Officials	time	-	2	1	1	1		Drug Control Div. & UNIDO
- Entrepreneurs	time	-	1	-	1	-		Drug Control Div.+ Faculty of Pharmacy, Mahidol U. + UNIDO
4. Make and publicize technical handbooks	subj.	4	←----4	-----→	←----4	-----→		Drug Control Div.+ commended persons from private sector + academia
5. Make slides and VDO on GMP	subj.	-	←----4	-----→	2	-		Drug Control Div.+ UNIDO
6. Oversea training on GMP for officials	person	2	2	2	2	2		Drug Control Div.+ UNIDO + Inspection Div. + Provincial Health Office + Health Consumer Protection Div.
7. Inspect and drug sampling from non-GMP manufacturers strictly according to the law	place	25	60	40	20	15		Inspection Div.
8. Revise GMP and amend Ministry's regulations	pc	←----1	-----→					Drug Control Div.
9. Suspension or non-renewal of license till corrections be made.				←-----	------	-----→		Drug Control Div.
10. PR on GMP data		←-----	------	------	------	-----→		Drug Control Div. + Public Relation & Advertisement Control Division
EXPECTED OUTCOME								
- More GMP compliance	plant	2	25	21	4	14	66	Drug Control Div. (QIT)
- Complaince with GMP in every category (increased)	plant	-	3	-	2	-		Drug Control Div. (QIT)
- Reassessment of GMP complying manufacturers	plant	107	109	131	155	150		Inspection Div.

The 5-Year GMP Action of the FDA assumes that the Service Centre will cooperate with the authorities to assure that a suitable GMP training program will be offered throughout the entire cycle of our Action Plan.

We very much appreciate the efforts made by the Service Centre in order to achieve all our common goals as it applies to the manufacturing of high quality products in Thailand

Yours sincerely,

Dr. Morakot Kornkasem
FDA Secretary-General

Plant Visits and Inspections by CTA and National Experts

Year	Number of Visits
1991 (Oct - Dec)	11
1992 (Jan - Sep)	51
1993 (Oct - Dec)	31
1994 (Jan - Oct)	42

	135
	=====

Seminars & Workshops

Year	Seminars	Workshops	Number of Participants	
1990	1	-	107	
1991	3	-	369	
1992	7	3	525	
1993	4	8	650	
1994	1	10	500	to date
	16	21	2,151	

Workshops with Industry/Center/University

Year	Total
1991	NIL
1992	12
1993	52
1994 (Jan – Sep)	28
	92

SCHEDULE
RE
STUDY TOUR/ CANADA
MAY 15 - 30 / 92

DAY	DATE	ACTIVITY	TIME
1.	15th-Fri	Departure : via CPA- Bangkok Arrival : Montreal/CANADA	08.30AM. 11.30PM.
2	16th-Sat	Weekend	
3	17th-Sun	Weekend	
4	8th-Mon	Holiday	
5	19th-Tue	- Hoechst Pharmaceuticals	10.00AM.
6	20th-Wed	-Bristol- Squibb	10.00AM.
7	21st-Thu	-ICN Pharmaceutical - Rougier Inc.	09.30AM. 02.00PM.
8	22nd-Fri	-Abbott -Cyanamid	10.00AM. 02.00PM.
9	23rd-Sat 24th-Sun	Weekend Weekend	
10	25th-Mon	-Rhone-Poulenc -Health Protection Branch	09.30AM. 02.00PM.
11	26th-Tue	-Schering Corporation -Burroughs Wellcome -University of Montreal	09.00AM. 02.00PM.
12	27th-Wed	-Merck-Frosst -Ciba - Geigy	09.30AM. 02.00PM.
13	28th-Thu	-Ayerst -Marion	09.30AM. 02.30PM.
14	29th-Fri	-Health Protection Branch	09.30AM.
15	30ths-Sat	Departure via CPA - Montreal Arrival in Bangkok on 31 st.	06.30 AM. 08.35 PM.

Report

STUDY TOUR TO MONTREAL, CANADA

15-30 MAY 1992

Organized by : UNIDO Pharmaceutical Technology Service Centre.

(Project : DP/THA/88/018 Development of Pharmaceutical Industry)

Dr.Prasan Dhumm-upakorn

Director of PTSC

5th October, 1992

cc. UNIDO Vienna
UNIDO Bangkok

Participants

1. Dr. Prasan Dhumma-upakorn,	DirectorPharmaceutical Technology Service Centre.
2. Dr. Pavich Thongroach,	Dean, Chulalongkorn University
3. Mr. Ruangsak Songpaisan,	Thai Pharmaceutical Manufacturers Association (TPMA)
4. Mrs. Montana Veerawattanan,	TPMA
5. Mrs. Sangthong Sawasdiphab,	Food and Drug Administration (FDA)
6. Mrs. Aungarb Wesgositt,	FDA
7. Mr. J.P. Beelen,	Chief Technical Adviser.

Tour Schedule : see attached.

Note : Dr. Prasan and Dr. Pavich visited the Dean of the University of Montreal at the 26th May, while the other participants were visiting Burroughs Wellcome.

Objectives of the Tour

- To provide more knowledge and better understanding regarding Good Manufacturing Practice, Good Laboratory Practice, Product Development, Validation and Plant Operation as it is applied to pharmaceutical companies abroad.

-To exchange the knowledge and experience in the manufacturing of pharmaceutical products, as well as among the participants as with representatives of the visited organizations

-To observe some modern equipment used for the manufacturing and control of pharmaceutical processes.

-To get more knowledge about personnel management by foreign pharmaceutical companies

-To get more information about the activities of government agencies regarding pharmaceutical issues

-To transfer the gained experience to local manufacturers and government drug control laboratories to improve their standards.

Experiences

a) *Companies*

- Although the majority of the visited plants have been built fo some years, they all meet GMP requirements by the implementatio of rational Standard Operating Procedures.

- Evidence of good housekeeping and sanitation were clearly seen Almost all companies reflected a practical plant design regardin the flow of materials.

- Because of the good observation to GMP-rules, drugs a cosmetic are allowed to be produced at the same production line in a company No seperation per product class is needed, as in Thailand.

- Most of the companies have implemented an intensive trainin program on GMP. Personnel receive a training course before starting to work in the manufacturing area, followed by trainin on-the-job and by lectures at specified intervals. GMP-principles are well understood through all layers of production management.

- To motivate the personnel, not only the salary is important but also the offering of social facilities. For instance the provision of a day nursery for the children of the personnel seemed to be a good stimulator.

- Several modern manufacturing systems have been observed of which many were computerized: e.g.check-weighers, continuous process of liquid preparation sterile liquid packaging system, coating processes, air handling and barcoding systems. Also an ultrafiltration system for the preparation of deionized water was shown. Several modern pieces of equipment of the QA laboratories were demonstrated.

One company showed a very well organized, efficient delivery system.

b) *Health Protection Branch*

Information was given about the organization and activities of the HPB. Only people who have enough knowledge about the manufacturing of pharmaceutical products can be qualified to become GMP-inspectors. For providing this knowledge,training sessions are held, sometimes together with people from the industry.

All the participants were very much impressed by the close cooperation betweeen the HPB and the pharmaceutical industry. Both parties work really together to achieve good quality products by using a practical approach.

c) *University*

The education of pharmacists in Canada and Thailand was discussed between Dr. Prasan, Dr. Pavich and the Dean of the University of Montreal. The relation between the University and the Canadian pharmaceutical companies seemed to be fruitful to develop the practical skills of the students; Master students and Ph. D's in Pharmaceutical Sciences are provided positions within the pharmaceutical industry to make research into manufacturing related subjects.

Conclusion

This study tour has broadened the pharmaceutical horizons of all participants intensively.

The gained knowledge, experiences and impressions seemed to all participants very important to share with their professional collegues. Not only for the improvement of the standard of their own activities, but also to improve the cooperation between the Pharmaceutical Industry, the University and the Food & Drug Administration in Thailand.

In the meantime the participants have informed their collegues about the gained knowledge and impressions from the tour. The cooperation between the three mentioned parties has indeed been improved; e.g. the Pharmaceutical Technology Service Centre has been invited by the FDA to actively participate in several aspects of the action plan, regarding GMP implementation. There is no doubt that the shared experiences during the study tour have made an important contribution to this achievement.

Annex 10

ศูนย์บริการเทคโนโลยีเภสัชอุตสาหกรรม
PHARMACEUTICAL TECHNOLOGY SERVICE CENTRE
คณะเภสัชศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย ปทุมวัน กทม. 10330 โทร. 2511871-7 ต่อ 273
FACULTY OF PHARMACEUTICAL SCIENCES CHULALONGKORN UNIVERSITY BANGKOK 10330 THAILAND

To	Mr.K.HANSELMANN	From	Dr.Prasan, NPD
	UNIDO, Vienna	Fax	662-255-8227
Fax	43-1-237280	NO. of pages(including this pages)	4
Date	February 8, 1994		

FILE REF. DP/THA/88/018

Ref. to the facsimile from HANSELMANN/ARAKELY from Vienna dated 3 February 1994 sent to DR. MEIXNER , UCD

- We send you again the Fellowship Program of :-
  - DR. PRASAN DHUMMA-UPAKORN
  - DR. SUREERAT CHAIAMNUAY
  - MR. SARUN GORSANAN

- Firstly, we would like to get UNIDO Letter informed that we get the fellowship.

- Please give top priority for the approval of the estimate cost to in order to buy the International flight tickets on time for MR.SARUN GORSANAN who will travel on March 12, 1994

Best regards.

Prasan Dhummapakorn

Dr.Prasan Dhumma-upakorn
Director of PTSC

cc. Dr. Meixner

Fellowship Program

- Name of Candidate : Dr.Prasan Dhumma-upakorn
- Institution/ Company :

  Health Protection Branch- HPB
  Toronto-Canada

  Hoechst Pharmaceuticals
  Montreal-Canada

  GMP Institute- U.S.A.

- Training Period

  week # 1 : May 3- 7th - Montreal
  week # 2 : May 9-14th - Toronto
  week # 3 : May16-21st- U.S.A.

- Travelling schedule

Departure ex Thailand	May1/94
Return to Thailand	May 22/94
Total number days	20 days

- Subjects to cover

  * Study GMP Guidelines of Canada
  * Gain experience from Plant Inspections
  * Review Methods of QA/QC Management Systems
  * Investigate Validation methods and application currently used in Canada
  * Obtain Guidelines and standard Techniques for preparation of SOP's
  * Study the set up and organization of the GMP Institute in U.S.A.

- Estimate Cost

Air fare	US$1500
Car rental & Insurance(3 weeks)	US$1400
Daily allowance(20 days)	US$3000
Miscellaneous	US$ 500
Total cost	US$6400

Pharmaceutical Technology Service Centre
Faculty of Pharmaceutical Sciences
Chulalongkorn University
Bangkok, Thailand.

Project : Development of Pharmaceutical Industry in Thailand.

DP/THA/ 88/ 018

Subject : Follow up report

Fellowship Program

for

Dr. Prasan Dhumma-upakorn

May 1 - May 21, 1994

Prepared by Dr. Prasan

Date : May 30, 1994

Content

Introduction

In accordance with the Fellowship program approved by the UNIDO and DTEC authorized for the above project, the undersigned was invited to complete three (3) study tours in Canada and USA based upon the agenda of activities outline in the attached exhibit # 1.

All activities were organized and coordinated by the CTA, Mr. J.P. Beelen in Canada.

Unforeseen incidence, however, required some minor change to the original agenda.

Objective

- Study GMP Guidelines of Canada.
- Acquire practical experience in inspection of pharmaceutical plants.
- Investigate standard technique and preparation of SOPs applicable use in Canada.
- Obtain informations regarding organizational set up and content of GMP training program in Canada or the USA.

Summary of Agenda

The study tour was delayed by two (2) days due to technical problem experienced by the THAI Airline upon departure.

The undersigned was held up in Hong Kong on May 1 - 3 and arrived in Montreal on May 3, 1994 at 11 p.m.

As a result of the above delay some changes became necessary which affected the original agenda of activities. The revised agenda can be summarized as follows:

Week # 1 : May 4 - 7
- Montreal - plant visit, GMP institute
- Departure for Toronto

Week # 2 : May 9 - 16
- Toronto, Plant visit, GMP institute, HPB

Week # 3 : May 17 - 21
- Ottawa visit HPB, CIDA
- Montreal visit HPB, Plant visits
- Departure for Bangkok

Detailed Activities

The summary of the main activities completed during this fellowship program include plant visits, discussion on many aspects in detail concerning to the PTSC.

This program addressed three (3) distinct groups of institutes :

1. Government Health Protection Branch (HPB)
2. Institute of Pharmaceutical Technology
3. Pharmaceutical Industries

Government Health Protection Branch

The main topics discussed with the Canadian authorities (HPB) in Toronto, Ottawa and Montreal included the following issues :

- Organization set up of HPB in Canada
- Interpretation and implementation of GMP guidelines by the inspectors throughout the Pharmaceutical Industrises in Canada
- Harmonization program regarding GMP/QA, Validation guideline between Canada, USA and European countries.
- Feasibility and merit to organize a project to promote exchange of inspection methods between HPB authorities and FDA Thailand.

Institute of Pharmaceutical Technology

The institutes contacted during this study tour include :

1. Toronto Institute of Pharmaceutical Technology
2. Montreal Pharmaceutical Technology
3. GMP institute, Kentucky, Cincinnati, USA

The main issues addressed during and discussion with the above organizations include :

- Feasibility to develop a long term program of cooperation between the Training Centre and the PTSC
- Exchange of technical informations and/or documentations.
- Organization set up of the respective institution.
- Strategy and extend of training program which have been developed from the different target groups
- Detailed regarding the financial condition remain to be finalized.

Pharmaceutical Industries

The CTA (Mr. J.P. Beelen) managed to organize many more plant visits than the original plan.

The different companies visited during this study tour are :

1.	Syntex	Toronto
2.	Roche Hoffmann - La Roche Limited	Toronto
3.	Glaxo Canada Inc.	Toronto
4.	Connaught Laboratories Limited	Toronto
5.	Organon/ Pancap Inc.	Toronto
6.	Novopharm	Toronto
7.	Hoechst Canada Inc.	Montreal
8.	Merck - Frosst	Montreal
9.	Schering Canada	Montreal

The main objective of the plant visit included the following outlines : (both audit and discussion)

- Plant design
- Production processes
- GMP training program
- QA/ QC management
- Housekeeping / Sanitation
- Documentation (Process document, SOPs, etc.)

Note

During the visit of Toronto, Dr. Carpio, an international expert, Mr. J.P. Beelen, the CTA and Dr. Prasan, a National Project Director had a very good informative technical discussion regarding the following aspects :

- Extend activities of the PTSC become a regionalization of the training centre.
- Feasibility to identify where resource of funding for the PTSC (e.g. CIDA, World Bank and/or the PTSC only)
- Dr. Prasan and the CTA, Mr. J.P. Beelen visit and discussed with the CIDA authority (Mr. Michel Hardy) in Ottawa.

Conclusion

The study was proved to be very beneficial and successful in obtaining valuable technical information which will facilitate the task of the Director of the PTSC to establish training program for the pharmaceutical industry in Thailand.

The benefits and success must be extended his appreciation to the CTA, Mr. J.P. Beelen and Dr. M. Carpio for their assistance and arrangements during the study tour.

0

Fellowship Program

- Name of Candidate : Dr.Sureerat Chaiamnuay
- Institution/ Company :

  Glaxo Pharmaceutical Inc.
  Zebulon- NC- U.S.A.

- Training Period

  week # 1 - April 18 th - 22 th April/94
  week # 2 - April 25 th - 29 th April/94

- Travelling schedule

Departure ex Thailand	-	April 16th/94
Return to Thailand	-	April 30th/94
Total number days	-	15 days

- Subjects to cover

  How to prepare Validation Protocols for pharmaceutical dosage forms e.g. tablets, capsules, liquid, ointment, sterile products.

- Estimated Cost

Air fare	US$ 1600
Car rental & Insurance(2 weeks)	US$ 850
Daily allowances (15 days)	US$2250
Miscellaneous	US$ 300
Total cost	US$5000

Validation Techniques in Pharmaceutical Industry

Project DP/THA/88/018
Development of the Pharmaceutical Industry

BY

Dr.Sureerat Chaiamnuay

Training period : 16 th April 1994 -30 th April 1994

Place of Training : Glaxo , Zobulon , North Corolina

Training period : between 16 th - 30 th April 1994

Training Program

Table of Content

1. Air suit training and medical clearance
2. Tablet Manufacturing Visit
3. Packaging Visit
4. Discussion of process optimization
5. Discussion of process validation
6. Discussion of equipment qualification
7. Environmental Control
8. Q.C. Lab Visit and discussion of analytical methods validation
9. USP Water sytem design and validation
10. Cleaning validation

Fellowship Program

- Name of Candidate : Mr.Sarun Gorsanan
- Institution/ Company :
  - Health Protection Branch- HPB
    Toronto-Ontario-Canada
  - Merck Frosst Canada Inc.
    Montreal-Quebec -Canada
- Training Period

  week # 1 : March 14 to March 18/94
  at HPB- Toronto-Canada

  week # 2 : March 21 to March 25/94
  at Merck Frosst- Montreal/Canada

- Travelling schedule

Departure ex Thailand	:	12 March/94
Return to Thailand	:	26 March/94
Total number days	:	15 days

- Subjects to cover

  * Study Technique for preparation of SOP., Manufacturing Procedures,GMP Validation Techniques etc.
  * Obtain information how to prepare ValidationProtocol
  * Study Canadian GMP. Guidelines.
  * Obtain some information on procedure regarding product registration in Canada.

- Estimated Cost

Air fare		US$1500
Car rental & Insurance	(2 weeks)	US$ 850
Daily allowance	(15 days)	US$2250
Miscellaneous		US$ 300
Total cost		US$4900

REPORT

FELLOWSHIP TRAINING PROGRAM

CANADA

12 - 26 March 1994

UNIDO Pharmaceutical Technology Survice centre

Project : DP/THA/88/018-Development of Pharmaceutical Industry

TRAINING COURSE

SOP's, Manufacturing Procedure, GMP.,

Production Record, Housekeeping and Sanitation.

Report by : Sarun Gorsanan

(Mr. Sarun Gorsanan)

16th May, 1994.

: UNIDO Vienna

UNIDO Bangkok

FELLOWSHIP TRAINING PROGRAM

TRAINING COURSE : SOP's, Manufacturing Procedure, GMP., Production Record, Housekeeping and Sanitation

TRAINING SCHEDULE : 12 - 26 March 1994 (see attached)

NAME OF TRAINEE : Mr. Sarun Gorsanan

OBJECTIVE OF TRAINING :

- To study technique for preparation of sop, Manufacturing Procedure , GMP. etc.
- To obtain information how to prepare validation protocol.
- To study Canadian GMP. Guideline.
- To obtain some information or procedure regarding product registration in Canada.

*** - To collect new ideas as how to improve the quality of all technical documentation and will assist to establish the most efficient approach to teach associates in the industry how to write pharmaceutical documentation for the Pharmaceutical Technology Survice Centre and to transfer the gained experiences to local manufacturers and to improve their standard.

SCHEDULE OF TRAINING PROGRAM / CANADA

12 - 26 MARCH 1994

DAY	DATE	ACTIVITIES	
1	12th-Sat	Departure : via BANGKOK	10.00 AM.
		Arrival : MONTREAL/CANADA	10.30 PM.
2	13th-Sun	Weekend	
3	14th-Mon	Health Protection Branch	(OTTAWA)
4	15th-Tue	Health Protection Branch	(TORONTO)
5	16th-Wed	Warner Lambert (Adams)	"
6	17th-Thu	Baxter corporation	"
7	18th-Fri	Organon	"
8	19th-Sat	Weekend	
9	20th-Sun	Weekend	
10	21st-Mon	Merck-Frosst	(MONTREAL)
11	22nd-Tue	Merck-Frosst	"
12	23rd-Wed	Merck-Frosst	"
13	24th-Thu	Merck-Frosst	"
14	25th-Fri	Hoechst Canada Inc.	"
15	26th-Sat	Departure : via MONTREAL	07.00 AM.
		Arrival in BANGKOK on 27th-Sun	10.10 PM.

****

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	6	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

			PARTICIPANTS	
#	**DATE**	**TITLE**	**#**	**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/Univ ersity
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/Univ ersity/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/Univ ersity/FDA, Pr ivate sector
110	29/12/93	Validation of working group : "Quality Control"	4	Industry

1994

			PARTICIPANTS	
#	DATE	TITLE	#	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	6	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
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
164	20-21/94	Training on GMP & SOP of Colgate Palmolive Ltd. at the Imperial Queen Park Hotel	30	Industry
165	29/12/94	JMT Industry Ltd.(cosmetic) GMP & SOP audit	15	Industry

1995

166	17/1/95	Training on SOP Inspectors from FDA (cosmetic section) at the PTSC	14	FDA
167	24/1/95	SOP workshop at the PTSC (#12) (First day)	21	Industry
168	7/2/95	SOP workshop at the PTSC (Second day)	21	Industry
169	10,11,17 18,24,25 /2/95	Seminar & workshop on laboratory techniques at PTSC (6 days) first groups	12	Industry
170	11/2/95	Seminar & workshop GMP & SOP at Milott Co.,Ltd (cosmetic)	30	Industry
171	17/2/95	U.B.Chemical Industry Ltd. GMP &SOP audit	15	Industry
172	10,11,17 18,24,25 /3/95	Seminar & workshop on laboratory techniques at PTSC (6 days) second group	13	Industry
173	21/3/95	Seminar & workshop on GMP and SOP at Rubia Cosmetic Industry	3	Industry
174	22/3/95 27/3/95	Seminar & workshop on GMP & SOP for food at Friendship Co.,Ltd (2 days) first group	30	Industry
175	23/3/95 28/3/95	Seminar & workshop on GMP & SOP for food Industry at Friendship Co.,Ltd.(second group)	30	Industry
176	4/4/95 18/4/95	SOP workshop at the PTSC (group#13)	20	industry
177	8/4/95	Seminar on GMP and SOP for Food (Top management) at Friendship Co.,ltd.	8	Industry

178	25/4/95 26/4/95	Seminar &workshop on GMP &SoP for Government Hospital Pharmacists.	38	Hospital Pharmacist
179	27/4/95 28/4/95	Workshop or Enzyme activity testing	9	Industry
180	4/5/95 11/5/95	Seminar&workshop on GMP&SOP for Food at Friendship Co., ltd.(2 days)(Thirdgroup)	34	Industry
181	26/7/95 (6 days)	Semianr&workshop on laboratory Technique (3^{th} group)	13	Industry
182	6-20/6/ 95	Workshop on SOP	14	
183	23-24 /6/95	Seminar&workshop on GMP&SOP at colgate Palmolive	29	
184	7-22 /7/95	seminar&workshop on Laboratory Technique (4^{th} group)	13	
185	5/8/95	Audit,Seminar on GMP and SOP at Colgate Palmolive	25	
186	23-24	GMP Training WHO representation(3 participant) Bangladesh Sri lanka	3	
187	24/8/95	Join Seminar with FDA on GMP and ISO 9000 at Meridian President Hotel	37	Industry
188	18-2 /9/95	Seminar&workshop on laboratory Technique (5^{th} group)	7	
189	5/9/95	Seminar&workshop on Dissolution Technology and Application	27	Industry
190	4-7/9/95	First EUDRAGIT sales symposium South-East Asia Aguscies (11 nations)	18	International Participants
191	12/9/95	Seminar&workshop on HPLC Validation Process	58	University Government Industry
192	19/9/95	Seminar on Aseptic Filling Validation	60	University Government Industry
193	21/9/95	Seminar on GMP and SOP of Top management Siam Snack Co.ltd,.	8	Industry

194	25/9/95	Seminar&workshop on GMP and SOP at the plant Siam Snack co.ltd,.	19	Industry
195	4,16/10/95	Seminar and workshop on SOP at the PTSC	15	Industry
196	14/10/95	Seminar on GMP National starch & Chemical (Thailand)	19	Industry
197	7-10/11/95	Seminar and workshop on GMP&SOP. NSC (Thailand) Novotel Rayong	32	Industry
198	23-24/11/95	Seminar and workshop on GMP and SOP for Government Hospital in Bangkok	30	Hospital Pharmacists
199	27/11/95	Seminar on water treatment for Pharmaceutical and Cosmetic Industry	115	Industry
200	12-15/12-95	Seminar and workshop on GMP & SOP NSC (Thailand) Novotel Rayong	34	Industry

1996

201	16/1/96	Seminar on State of the Art in Planning, Engineering and Construction for New GMP Pharmaceutical Factory	120	Industry University
202	18-19/1/96	Seminar and workshop on GMP and SOP for Government Hospitals in Bangkok	30	Hospital Pharmacists

Annex 12

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

ศูนย์บริการเทคโนโลยีเภสัชอุตสาหกรรม
PHARMACEUTICAL TECHNOLOGY SERVICE CENTRE
คณะเภสัชศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย ปทุมวัน กทม. 10330 โทร. 2511871-7
FACULTY OF PHARMACEUTICAL SCIENCES CHULALONGKORN UNIVERSITY BANGKOK 10330 THAILAND

SOP # 65-0007

STANDARD OPERATING PROCEDURE

FOR

RAW MATERIAL INVENTORY CONTROL

INDEX

STANDARD OPERATING PROCEDURE

TITLE	SOP # .....65-0007.....
RAW MATERIAL **INVENTORY CONTROL**	Effective Date D ..... M ..... Y .....
	Page .....1..... of .....9.....

1. PURPOSE

Establish a "FIFO" inventory control system which ensures the accountibility and traceability of inventory items in compliance with the GMP Regulations and Company Policy.

2. SCOPE

This procedure is applicable for all active and inactive materials used for the production of semi-finished or finished goods.

3. RESPONSIBILITY

The Production and the Quality Assurance Managers are be responsible that this procedure is being implemented.

Prepared by :	Reviewed by :	Approved by :	Authorized :
Date :	Date :	Date :	Date :
Position :	Position :	Position :	Position :

Form # _____
Date _____

STANDARD OPERATING PROCEDURE

TITLE	SOP # .....65-0007.....
RAW MATERIAL INVENTORY CONTROL	Effective Date D ..... M ..... Y .....
	Page .....2..... of .....9.....

4. GENERAL GMP GUIDELINES

DO

- Maintain raw material storage area in neat, orderly and clean condition.
- Check carefully the accuracy of the different reference documents obtained from the Receiving and Q.A. departments.
- Identity clearly the content of each container.
- Alert the supervisor and Q.A. department about any discrepancy or error observed during the material handling operations.
- Record the justification for any variance of raw material as applicable for each lot number and advise QA and Supervisor.
- Process only one raw material at the time of the same lot number in order to avoid errors during the transaction operations.

DO NOT

- Accept or store in the warehouse dirty containers.
- Erase or use white ink to correct written errors on the documents but cross out and initial the correction !!!

Prepared by :	Reviewed by :	Approved by :	Authorized :
Date :	Date :	Date :	Date :
Position :	Position :	Position :	Position :

Form # _____
Date _____

STANDARD OPERATING PROCEDURE

TITLE	SOP # .....65-0007.....
RAW MATERIAL **INVENTORY CONTROL**	Effective Date D ..... M ..... Y .....
	Page .....3..... of .....9.....

5. FLOW CHART

Activities	Responsibility
1. SET UP a Sequential Numerical Inventory Control system.	Material Storage
↓	
2. OBTAIN the reference documents for each lot of raw material.	Material Storage
↓	
3. RECORD the reference data on the Material Receipt Record.	Material Storage
↓	
4. TRANSFER the raw materials to the allocated storage area.	Material Storage
↓	
5. DISPENSE the raw materials on a FIFO basis.	Material Storage
↓	
6. MONITOR the inventory variances for each lot of raw material.	Material Storage
↓	
7. COORDINATE the resampling procedure of each lot of raw material.	Material Storage

Prepared by :	Reviewed by :	Approved by :	Authorized :
Date :	Date :	Date :	Date :
Position :	Position :	Position :	Position :

Form # _____
Date _____

STANDARD OPERATING PROCEDURE

TITLE	SOP # .....65-0007.....
RAW MATERIAL INVENTORY CONTROL	Effective Date D M Y ....
	Page .....4..... of .....9.....

6. DETAILED INSTRUCTIONS

6.1 SET UP a Sequential Numerical Control System.

- Set up a Standard Inventory Control System which summarizes all the required reference information regarding each raw material transaction to ensure the accountibility and traceability of each lot number.

- Complete the required reference information which must be recorded on the inventory record to comply with the GMP Regulations as illustrated in EXHIBIT # 6

- P.S. set up, if necessary, a separate sequential numerical filing system for the active and non active ingredients which is based upon the Product Code Number.

6.2 OBTAIN the reference documents for each lot of material.

- Obtain a copy of the Receiving Report (EXHIBIT #1) and the Q.A. Sampling Report (EXHIBIT # 3) which includes all the necessary reference information for each lot of raw material.

- Keep all the above documents "on file" to justify the accuracy of each inventory record.

Prepared by :	Reviewed by :	Approved by :	Authorized :
Date :	Date :	Date :	Date :
Position :	Position :	Position :	Position :

Form # _____
Date _____

STANDARD OPERATING PROCEDURE

TITLE	SOP # .....65-0007.....
RAW MATERIAL **INVENTORY CONTROL**	Effective Date D ..... M ..... Y .....
	Page .....5..... of .....9.....

6.3 RECORD the required reference information.

- Record all the required reference from the Receiving report (EXHIBIT # 1) and the Sampling Report (EXHIBIT # 3) on the Receipt of Material Record (EXHIBIT # 6) for each lot number.

- Indicate clearly the sequence in which each lot has been received on the Raw Material Record to facilitate the usage of raw materials on a FIFO basis or based upon the shortest expiry date (EXHIBIT # 1).

6.4 TRANSFER the Raw Materials to the allocated storage area.

- Proceed with the storage of the raw materials in accordance with the storage location system which has been established by the Company.

- Identify clearly each container and/or pallet regarding the "Q.A. Release Status" (e.g. Quarantine/Released) prior to storage and apply the appropriate sticker. (EXHIBIT # 4 and # 5)

- Segregate the active and non active ingredients within the storage area as deemed neccessary.

- Use a sequential numerical storage system to facilitate the location and retrieval of raw materials which is based upon the Product Code Number.

- Keep on file the most updated standard location layout for all raw materials.

Prepared by :	Reviewed by :	Approved by :	Authorized :
Date :	Date :	Date :	Date :
Position :	Position :	Position :	Position :

Form # _____
Date _____

STANDARD OPERATING PROCEDURE

TITLE	SOP # .....65-0007.....
RAW MATERIAL INVENTORY CONTROL	Effective Date D M Y ....
	Page .....6..... of .....9.....

6.5 DISPENSE the raw materials on a FIFO basis.

- Indicate on the "Material Usage Record" (EXHIBIT # 7) which specific lot number is being used for dispensing as illustrated on EXHIBIT # 7 (lot # 920017)

- Dispense the raw materials on a First in/ First out (FIFO) basis in order to comply with the GMP Regulations. Except, whenever a lot with the shortest expiry date is on hand.

- Record prior to start up of the weighing operations each lot number of the raw material which has been allocated for each Manufacturing order (EXHIBIT # 8). In the event that two different lot numbers are required clearly indicate on the Formula Sheet the "exact quantity" weighed for each lot.

- Indicate clearly the balance of the gross weight for each container partially filled. (EXHIBIT # 9)

- Attach the above record to the partially filled container.

Prepared by :	Reviewed by :	Approved by :	Authorized :
Date :	Date :	Date :	Date :
Position :	Position :	Position :	Position :

Form # _____
Date _____

STANDARD OPERATING PROCEDURE

TITLE	SOP # .....65-0007.....
RAW MATERIAL INVENTORY CONTROL	Effective Date D M Y ....
	Page .....7..... of .....9.....

6.6 MONITOR the inventory variances for lot of raw materials.

- Calculate the inventory variance upon depletion of each lot number of raw material. (EXHIBIT # 7 : Usage of Materials Record)
- Investigate the cause of the variance and clearly indicate the justification on the "Usage of Materials Record" (EXHIBIT # 7).
- Report any inventory variances to the supervisor and the inventory control department in order to adjust the inventory and accounting records.

6.7 COORDINATE the resampling procedure of each lot of raw material.

- Set up an effective monitoring system to ensure the timely retesting of raw materials which must be completed at least 4 months prior to the expiry date (SOP # 60-0015)
- Contact the Q.A. department to initiate the resampling procedure in accordance with the existing SOP #60-0007 for Sampling of Raw Materials.

Prepared by :	Reviewed by :	Approved by :	Authorized :
Date :	Date :	Date :	Date :
Position :	Position :	Position :	Position :

Form # _____
Date _____

STANDARD OPERATING PROCEDURE

TITLE	SOP # .....65-0007.....
RAW MATERIAL INVENTORY CONTROL	Effective Date D M Y ....
	Page .....8..... of .....9.....

7. GLOSSARY OF TERMS

QUARANTINE :
Effective restriction of the availability of material for use until released by a designated authority.

LOT :
A quantity of any drug in dosage form, a raw material, or a packaging material, homogeneous within specified limits, constituting all or part of a single batch and identified by a distinctive lot number (Receiving Control Number)

RECEIVING CONTROL NUMBER (LOT NUMBER) :
Any combination of letters, figures, or both, by which any material can be traced prior, during or after the production cycle (e.g. Distribution).

SCOPE :
Range of action

Prepared by :	Reviewed by :	Approved by :	Authorized :
Date :	Date :	Date :	Date :
Position :	Position :	Position :	Position :

Form # _____
Date _____

STANDARD OPERATING PROCEDURE

TITLE	SOP # .....65-0007.....
RAW MATERIAL INVENTORY CONTROL	Effective Date D ..... M ..... Y .....
	Page .....9..... of .....9.....

8. EXHIBITS

Exhibit # 1	Receiving Report
Exhibit # 3	Sampling Report
Exhibit # 4	Quarantine Label
Exhibit # 5	Released Label
Exhibit # 6	Material Receipt Record
Exhibit # 7	Material Usage Record
Exhibit # 8	Master Formula Sheet
Exhibit # 9	Container Record

Prepared by :	Reviewed by :	Approved by :	Authorized :
Date :	Date :	Date :	Date :
Position :	Position :	Position :	Position :

Form # _____
Date _____

STANDARD OPERATING PROCEDURE

TITLE	SOP # 25-0001/ 1.....
	Effective Date from ....
OPERATION AND MAINTENANCE OF A PACKAGED AIR CONDITIONING UNIT	to ....
	Page 1 of 4

1) PURPOSE

To establish a procedure to ensure the correct operation and maintenance of air handling plant in the production environment,including full records and history of the equipment such that any progressive deterioration in performance can be identified and corrected.

2) SCOPE

This document contains guidelines for the operation and maintenance only. It is not intended to be implemented before full validation and handover to the owner of the air handling equipment. The operating parameters of the equipment must be based upon the validation documentation.

3) RESPONSIBILITY

The Production Manager is to ensure that this procedure is being implemented by the maintenance staff before commencing production. The engineering manager is directly responsible for carrying out this procedure.

4) DESCRIPTION OF INSTALLATION

The system comprises two principal sections, the inside room fan coil unit, and the external refrigerant condensing unit.

The room fan coil unit consists of a steel casing containing the room air circulating fan, the cooling coil with associated drain pan and refrigerant expansion valve, electric heating coil, air filter and room thermostat.

The external condensing unit consists of a weatherproofed steel housing containing the refrigerant compressor, refrigerant condensing coil, condensing coil cooling fan, compressor starter and electrical controls, high and low pressure switches, and refrigerant gas charging valves

The two sections are connected by refrigerant pipework and control and power wiring. The refrigerant pipework is run in copper tube,the smaller diameter pipe is the hot liquid line from the condenser to

Prepared By:	Reviewed By:	Approved By:	Authorized By:
Date:	Date:	Date:	Date:
Positon:	Positon:	Positon:	Positon:

STANDARD OPERATING PROCEDURE

TITLE	SOP # 25-0001/ 1.....		
	Effective Date from	D	M	Y
OPERATION AND MAINTENANCE OF A PACKAGED AIR CONDITIONING UNIT	....	....	....
	to	....	....
	Page 2 of 4		

the expansion valve, the larger diameter insulated pipe is the cold gas line from the cooling coil (evaporator) to the compressor.

The system is powered by a three phase electrical supply, which is connected to the external condensing unit. Single phase power to the internal fan coil unit is run from the control box in the external unit to the connection terminals in the fan coil section.

5) DOCUMENTATION

The Building Manager is to prepare a log book for the purpose of recording all activities relating to this equipment. This logbook is to be kept for reference with the manual and data recorded during validation of the equipment.

6) EQUIPMENT START-UP

To restart the equipment after a shut-down for maintenance:

1) Check that all electrical safety covers have been replaced.
2) Check that all external equipment casings are properly secured.
3) Check that the room side air filter is correctly fitted.
4) Check that the room fan speed control is in the 'OFF' position
5) Turn on the main electrical isolator adjacent to the condensing unit
6) Turn the room side fan speed control to the required position
7) Check that the room thermostat is at the correct setting to maintain the required temperature
8) Check the refrigerant sight glass is flooded, i.e. there is sufficient refrigerant in the system for correct operation.
9) After the equipment has run for 1 hour,take measurements of room conditions as described in the validation procedure, compare the data with the validation performance data. If the operating conditions are not in accordance with the validated requirements, switch off the plant and investigate for malfunctions in accordance with the manufacturers operating manual.

7) MAINTENANCE PROCEDURES

All maintenance is to be carried out with the equipment electrically isolated.

Prepared By:	Reviewed By:	Approved By:	Authorized By:
Date:	Date:	Date:	Date:
Positon:	Positon:	Positon:	Positon:

STANDARD OPERATING PROCEDURE

TITLE	SOP # 75-0008/1		
	Effective	D M	Y
ORGANIZATION OF	date from	20 3	93
VALIDATION SET UP	to	20 3	95

Prepared by	Reviewed by	Approved by	Authorized by
Position	Position	Position	Position
Date	Date	Date	Date

1.PURPOSE

To establish a validation program to assure that all manufacturing and/or testing activities are performed in a reliable manner.

2. SCOPE

This SOP applies to validation of pharmaceutical products, processes, facilities, equipment and personnel working in Production and Quality Control.

3. RESPONSIBILITY

The validation task leader (VTL) is responsible for the implementation of the validation program in accordance with this SOP. The VTL is responsible for the organization of validation projects, the coordination and/or supervision of validation teams, validation plans, validation protocols and SOP's.

Please note that the VTL could have many other nominations in accordance with the organizational structure of each company.

4. GENERAL GUIDELINES

* Set up a validation program assisting the establishment of overall control over the entire operation.

  Additionally, validation
  - provides a high degree of Quality Assurance
  - optimizes inventory control
  - increases safety
  - reduces costs, due to
    . more efficient processes (less waste, less production time, less in process controls, less

failures, less breakdowns)
. reduced re-work
. reduced number of complaints
. reduced re-testing
. reduced number of recalls

5. FLOW CHART

	ACTIVITIES	RESPONSIBILITY
1. ESTABLISH	and ORGANIZE internal training program	plant management
2. SET UP	validation team	plant management
3. DEVELOP	strategic plan	VTL
4. PREPARE	documentation	VTL
5. CALIBRATE	instruments	VTL
6. IMPLEMENT	pilot project (*)	VTL
7. DOCUMENT	data	VTL
8. EVALUATE	test results	VTL
9. DOCUMENT	conclusions	VTL
10.CERTIFY	the validated process	VTL
11.TRAIN	key personnel	VTL
12.APPROVE	additional documentation	VTL, QA
13.REPLICATE	and EXTEND validation process to other areas	VTL
14.ASSESS	and PLAN validation program for the entire operation	VTL, QA
15.IMPLEMENT	process validation	VTL

(*) Pilot project is recommended for companies which are new in implementing validation processes ("first-timers")

6. DETAILED INSTRUCTIONS

6.1 ESTABLISH and ORGANIZE internal training program

* Establish and organize — an internal training program on QA in which the importance of validation, as part of Quality Assurance, is explained
* Point out — the importance of documentation and the responsibility of every person in the company to assist complying with this documentation
* Encourage — personnel to propose, adjust or generate documentation for critical processes, in accordance with company policies
* Prepare — an SOP, outlining the training program. State the responsible person(s) for the development and implementation of the training program.
* Train — personnel on the performance of validation activities

6.2 SET UP validation team

* Establish — the validation team, depending upon the company size and technical disciplines available, including representatives from Quality control (chemical, physical, microbiological testing), production, engineering, research & development, statistical analyis, safety, purchasing, regulatory affairs.

  The team will be coordinated and/or supervised by one person, the VTL, who has been recognized and officially appointed as responsible for the implementation of this task

6.3 DEVELOP strategic plan

* List — all critical manufacturing and testing processes and equipment to be considered for validation studies

* Set — validation priorities, in accordance with company policy and strategic objectives, based on e.g. product sells, needs (e.g. regulatory compliance), availability of resources

6.4 PREPARE documentation

* Provide — an SOP on Documentation Management for the validation process

* Prepare — a validation protocol, outlining in detail test procedures and acceptance criteria for each process. The protocol should include:
- validation project number
- introduction/purpose of the project
- description of the system to be validated, including location
- identification of process/specific equipment involved
- characteristics to be investigated
- test methods
- test requirements
- acceptance criteria
- reference to SOP's or any other documentation
- maintenance information, including purchasing order, drawings, service conditions, information on spare parts
- signature for approval, including date

The protocol should be signed for approval before initiating the validation activity.

6.5 CALIBRATE instruments

* Ensure — the instruments used for the validation process are calibrated. Calibrate the instruments in accordance with their SOP.

6.6 IMPLEMENT pilot project

* Decide — on a pilot project in accordance with the list of validation priorities

* Review	all documentation and adjust, as necessary, for this particular project
* Approve	the documentation
* Implement	the project. Fulfill all steps, laid down in the protocol.

6.7 DOCUMENT data

* File	all data directly in the protocol. Data should be clearly written, including units of measure. Changes must be reflected in the protocol.
* Summarize	test results in the validation report

6.8 EVALUATE test results

* Study	the data in combination with the acceptance limits, stated in the validation protocol
* Ensure	that all testing requirements were achieved

6.9 DOCUMENT conclusions

* State	in the validation report that the process has been validated, based on the test results

6.10 CERTIFY the validated process

* Identify	the validated system by a certificate (Exh.# 50), if possible

6.11 TRAIN key personnel

* Demonstrate	the validation method by using the necessary documentation
* Demonstrate	the way in which data should be collected, analyzed and interpreted
* State	the person to be contacted if clarification is required

6.12 APPROVE additional documentation

* Write and Approve	all necessary documentation before replicating the validation method to other areas

6.13 REPLICATE and EXTEND validation process to other areas

* Apply	the method of approach to other processes within the company's operations

6.14 ASSESS and PLAN validation program for the entire operation

* State	in an SOP the frequency and/or the situation for which the project has to be validated again, by using the same protocol.
* Revalidate	in case of a major change, e.g to any of the following parameters: - batch size - manufacturing equipment - manufacturing location - manufacturer of raw materials - method of formulation - formula - analytical method In case of processes for which visual inspection plays an important role, new inspection personnel has to be validated. For revalidation projects, new protocols have to be prepared.

6.15 IMPLEMENT process validation

* Validate	all processes in accordance with the validation program

7. GLOSSARY OF TERMS

* **Validation**	: establishing documented evidence that a process does what it purports to do
* **Revalidation**	: validation of a validated process, in which a major change has been implemented (will be revised)
* **Validation report**	: a final document on a validation project. It is recommended to use the following headings: - ABSTRACT - PLAN OF STUDY - EXPERIMENTS - RESULTS - CONCLUSION - LITERATURE OF REFERENCE - SIGNATURE/DATE for approval, by QA

8. EXHIBITS

EXHIBIT # 50	certificate for validated processes/equipment

STANDARD OPERATING PROCEDURE

TITLE	SOP # 25-0001/ 1.....			
	Effective Date from	D	M	Y ....
OPERATION AND MAINTENANCE OF A PACKAGED AIR CONDITIONING UNIT	to	....	....	....
	Page 3 of 4			

Should these instructions in any way conflict with the manufacturers recommendations, refer to the engineering manager for guidance.

EVERY DAY

Record the room conditions and external conditions in the logbook

Check that theoperator controls are at the correct settings, reset if necessary.

EVERY WEEK

Inspect the air filter. If an exessive build-up of dust occurs, clean outside the room and investigate the cause.

Check the refrigerant sight glass. If the glass shows excessive gas, check pipework for damge and leaks.

EVERY MONTH

Remove casing and remove the room air filter from the equiipment. Remove from the room and clean. If the filter becomes damaged, replace.

Ensure drain pan condensate drain is sealed by flushing with water, to fill trap.

EVERY THREE MONTHS

When carrying out the filter clean, vacuum clean the inside of the casing and the surface of the cooling coil.

Attach a pressure gauge to the refrigerant charging valves, record refrigerant pressures. Check against validation documentation

Clean cooling coil drain pan to prevent the build-up of any contaminant.

8) <u>BREAKDOWNS</u>

If the equipment ceases to function:

1) Check that the isolator adjacent to the condensing unit is not turned off.
2) Check that the main fuse or circuit breaker has not fused or tripped. If the safety device has been activated, check the equipment for electrical fault in accordance with the manufacturers instructions.

Prepared By:	Reviewed By:	Approved By:	Authorized By:
Date:	Date:	Date:	Date:
Positon:	Positon:	Positon:	Positon:

STANDARD OPERATING PROCEDURE

TITLE	SOP # 25-0001/ 1.....
OPERATION AND MAINTENANCE OF A PACKAGED AIR CONDITIONING UNIT	Effective Date from .... to ....
	Page 4 of 4

3) Check that the refrigerant high or low pressure switches have not stopped the equipment If the safety device has been activated, check the equipment for refrigeration circuit fault in accordance with the manufacturers instructions.
4) Check the room thermostat for correct operation. Replace if defective.

9) SPARES LIST

A spares list was requested with the order for the installation,and is kept with the manufacturers literature for this equipment. This must be examined and any item not already held in stock must be evaluated, as to the effect on production if a breakdown of this component occurs. All spares held must be catalogued and clearly labelled and stored in a central location, not in the production area.

Prepared By:	Reviewed By:	Approved By:	Authorized By:
Date:	Date:	Date:	Date:
Positon:	Positon:	Positon:	Positon:

STANDARD OPERATING PROCEDURE

TITLE	SOP # 25-0003/ 1.....			
	Effective	D	M	Y
SPECIFYING ENVIRONMENTAL CONDITIONS IN PHARMACEUTICAL MANUFACTURING PLANTS.	Date from	....	....	....
	to	....	....	....
	Page 1	of	4	

1) PURPOSE

To ouline the steps to take to ensure that specifiers of factory facilities communicate the HVAC requirements effectively.

2) SCOPE

This procedure applies to all factories, clean rooms, sterile areas, packaging halls, laboratories, warehouses or other construction intended for use in accordance with GMP guidelines. .It is intended to be used by purchasers and specifiers of pharmaceutical installations and provides a check list of design, construction and commissioning requirements which might or might not be relevant. Detailed recommendations are not given concerning the level or control of contamination but allows for them to be agreed by the interested parties.

3) RESPONSIBILITY

The purchaser is responsible for ensuring that all information outlined below is made available to the supplier if necesary in consultation with the user and/or supplier.

4) GENERAL GUIDELINES

Prepare a 'General Arrangement' drawing of the facility, showing production equipment, machinery, vessels, ovens, autoclaves etc.

Show on the G.A. drawing peripheral areas such as product and personnel airlocks.

Conduct a survey of the facility to identify where air handling equipment can be located, inside and outside of the building.

Discuss with production departments and maintenance departments essential requirements of the system, and additionnal desirable but not essential qualities to be considered, such as provision for future expansion, etc.

Prepared By:	Reviewed By:	Approved By:	Authorized By:
Date:	Date:	Date:	Date:
Positon:	Positon:	Positon:	Positon:

STANDARD OPERATING PROCEDURE

TITLE	SOP # 25-0003/ 1.....			
	Effective Date from	D	M	Y ....
SPECIFYING ENVIRONMENTAL CONDITIONS IN PHARMACEUTICAL MANUFACTURING PLANTS.	to	....	....	....
	Page 2	of	4	

Compile a design brief describing system requirements in detail, based on the elements listed in this SOP.

Review design brief with production and maintenance managers.

5) INFORMATION TO BE INCLUDED IN THE DESIGN BRIEF

a) Standards, referenced by originating source, number, date and title, to which the facility is to be constructed. e.g. U.S. Federal Standard 209E, September 1992, 'Airborne Particulate Cleanliness Classes in Clean Rooms and Clean Zones'.
b) The required class or classes relevant to this installation. If part or all of the facility is to be unclassified, this must be stated.
c) The purpose for which each space is to be used, the operations to be carried out, and any constraint imposed by the operating criteria.
d) The General Arrangement layout.
e) All critical dimensions, including those relating to available space for plant, and production space.
f) Special ventilation services required, e.g. dust extract, fume cupboards etc.
g) Responsibility for witnessing and performing commissioning tests and procedures.
h) Specify environmental parameters: Temperature ^{o}C+/-^{o}C,
Relative Humidity %+/-%
Ventilation and Air Change Rate,
Room Pressure Pa (indicate whether relative to adjacent room or atmosphere)
j) Requirement for determining environmental cleanliness at sampling positions additionnal to those required by the standards specified in items a) and b).
k) Requirement for periodic or continuous monitoring and associted alarms if required.
l) Special filtration requirements, e.g. laminar flow area above outlet from sterilising oven

Prepared By:	Reviewed By:	Approved By:	Authorized By:
Date:	Date:	Date:	Date:
Positon:	Positon:	Positon:	Positon:

STANDARD OPERATING PROCEDURE

TITLE	SOP # 25-0003/ 1.....			
	Effective	D	M	Y
SPECIFYING ENVIRONMENTAL CONDITIONS IN PHARMACEUTICAL MANUFACTURING PLANTS.	Date from	....	....	....
	to	....	....	....
	Page 3	of	4	

6) DETAILED INSTRUCTIONS

a) Standards can be national, international, of foreign origin, or an internal company standard. .The purchaser and specifier must ensure that the supplier is aware of the source of the standard so that he may obtain a copy for reference.

b) Class must be indicated for each room, including the occupancy state, e.g. as built, at rest or operational. .The purchaser should fully understand the implications the selection of occupancy state will have for the supplier in designing, constucting and testing the clean room.

c) The purpose for which each space is to be used, e.g. changing room, quarantine, autoclave loading, finished goods store. Any constraints imposed by operating requirements, e.g. hazard due to solvent, explosive or toxic vapours, room to be gas sterilised, etc.

d) The General Arrangement should include all available information regarding equipment positions, power supply, room heeights, materials of construction and where possible mechanical and electrical services to be provided by others nd coordinated with the HVAC services.

e) The dimensions of all openings,doors, pass-through hatches, conveyor transits, windows should be made known to the supplier as soon as possible. In the case of openings which are to be determined by installed equipment, sufficient information must be given to the supplier for him to be able to make an assessment of the effect on room conditions caused by the opening.

f) The data must include whether special ventilation services run continuously or intermittently, constant or variable volume.

g) The purchaser may require the supplier to include in his estimate for the services of an independent testing and commissioning specialist. The purchaser must specify to the supplier the extent of testing to be carried out, with clearly stated acceptance criteria.

h) An example of additionnal continuous monitoring which could be required is the particle counts to be taken adjacent to filling needles on a sterile injectable vial or ampoule filling machine.

j) Any monitoring limits or alarm limits specified must be established before the detailed design of the air handling system, so as to be within the capabilities of that system.

k) The purchaser must specify control points and tolerances for internal temperature, relative humidity, room pressures for each zone or room. The purchaser must advise the supplier of any heat & moisture generated in the room, the location of heat & moisture sources, and the nature of any .dynamic variation.

Prepared By:	Reviewed By:	Approved By:	Authorized By:
Date:	Date:	Date:	Date:
Positon:	Positon:	Positon:	Positon:

STANDARD OPERATING PROCEDURE

TITLE	SOP # 25-0003/ 1.....			
	Effective Date from	D	M	Y ....
SPECIFYING ENVIRONMENTAL CONDITIONS IN PHARMACEUTICAL MANUFACTURING PLANTS.	to	....	....	....
	Page 4	of	4	

7) DOCUMENT ISSUE

Based on the above information the design brief is to be prepared, then circulated to production, maintenance, and Q.A. for comment. A review meeting shall be held at which the design brief shall be revised and approved. The design brief is then to be issued to all tendering suppliers of the HVAC installation.

Prepared By:	Reviewed By:	Approved By:	Authorized By:
Date:	Date:	Date:	Date:
Positon:	Positon:	Positon:	Positon:

STANDARD OPERATING PROCEDURE

TITLE	SOP # ..25-0002/ 1.....
	Effective Date from .... D .... M . Y
PREPARATION OF MAINTENANCE PROCEDURES FOR AIR HANDLING SYSTEMS IN PHARMACEUTICAL APPLICATIONS	to ....
	Page 1 of 5

1) PURPOSE

To outline the steps to be followed when a SOP is established for the operation and maintenance of air handling plant., in compliance with GMP guidelines and company policy.

2) SCOPE

This procedure applies to all SOP's relating to air handling equipment in Pharmaceutical Facilities. This document contains guidelines for the operation and maintenance only. It is not intended to be implemented before full validation and handover to the owner of the air handling equipment. The operating parameters of the equipment must be based upon the validation documentation.

3) RESPONSIBILITY

The QA manager is responsible that the instructions in this SOP are followed when SOP's are prepared.

4) GENERAL GUIDELINES

- Refer to SOP #_____"SOP Guidelines" for detailed instructions for the preparation of SOP documents.
- Establish a central indexed filing system for all manufacturers literature, certified drawings, installation drawings, wiring diagrams, control schematics, commissioning data and test certificates.
- Maintain a planned maintenance program, for all items of mechanical plant throughout the factory.
- Keep an inventory of all spares held in stock.

Prepared By:	Reviewed By:	Approved By:	Authorized By:
Date:	Date:	Date:	Date:
Positon:	Positon:	Positon:	Positon:

STANDARD OPERATING PROCEDURE

TITLE	SOP # ..25-0002/ 1.....
PREPARATION OF MAINTENANCE PROCEDURES FOR AIR HANDLING SYSTEMS IN PHARMACEUTICAL APPLICATIONS	Effective Date from .... D .... M . Y to ....
	Page 2 of 5

- Maintain an up-to-date list of original equipment suppliers with contact names and telephone numbers.
- Set up a reporting system to record and act upon any equipment malfunctions.
- Monitor system performance regularly, to note and rectify any change in plant performance.
- Update record drawings commissioning records to show any modifications to the installed systems.

5) FLOW CHART

	ACTIVITIES	RESPONSIBLE
1.	IDENTIFY all systems for which SOP to be prepared	Engineering Manager
	⇓	
2.	RECORD SOP titles	Q.A. Manager
	⇓	
3.	DESIGN standard layout	Q.A.Section
	⇓	
4.	WRITE SOP	Engineering Section
	⇓	
5.	REVIEW and APPROVE SOP	Engineering Manager
	⇓	
6.	AUTHORIZE SOP	Q.A. Manager
	⇓	
7.	ESTABLISH review survey of SOP's	Q.A.
	⇓	
8.	LIST Exhibits	Engineering Manager
	⇓	

Prepared By:	Reviewed By:	Approved By:	Authorized By:
Date:	Date:	Date:	Date:
Positon:	Positon:	Positon:	Positon:

STANDARD OPERATING PROCEDURE

TITLE	SOP # ..25-0002/ 1.....
PREPARATION OF MAINTENANCE PROCEDURES FOR AIR HANDLING SYSTEMS IN PHARMACEUTICAL APPLICATIONS	Effective Date from .... . . to ....
	Page 3 of 5

9. SET UP glossary of terms — Engineering Manager
⇓
10. DISTRIBUTE SOP — Q.A. Manager
⇓
11. REVIEW SOP — Engineering Section
⇓
12. DON'T REVISE/REVISE/DELETE SOP — Q.A. Manager
⇓
13. FILE SOP — Q.A. Manager
⇓
14. ISSUE New SOP — Q.A. Manager

6. DETAILED INSTRUCTIONS

6.1 ESTABLISH a filing index

- List all air handling systems and activities for which SOP's have to be written (e.g. Sterile unit-injectables-HEPA filter change)
- Allocate to each system or activity a unique number.

6.2 RECORD SOP - titles

- State on which topics SOP must be written
- Select the most appropriate title which reflects the topic (e.g. HEPA filter changing for sterile systems)
- Index all titles of SOP's by allocating each a unique 6 digit number;
  first two digits: refer to the system;
  last four digits: sequential number.

Prepared By:	Reviewed By:	Approved By:	Authorized By:
Date:	Date:	Date:	Date:
Positon:	Positon:	Positon:	Positon:

STANDARD OPERATING PROCEDURE

TITLE	SOP # ..25-0002/ 1.....
	Effective D M Y
PREPARATION OF MAINTENANCE PROCEDURES FOR AIR HANDLING SYSTEMS IN PHARMACEUTICAL APPLICATIONS	Date from .... .
	to ....
	Page 4 of 5

6.3 USE standard layout

- Obtain standard SOP layout from Q.A.
- Include the following items: the company name
  purpose, scope and title of SOP
  unique SOP number
  authorizing persons, the preparer and their signatures
  date of review
  revision number
  reason for revision
- Number the pages (of total number of pages)

6.4 WRITE SOP

- Decribe — briefly the system to which the SOP applies.
- Quote — manufacturersdrawing numbers and operating manual references.
- Describe — all individual components in the system, their function and location.
- Indicate — associated systems upon which the operation of this system is reliant e.g. chilled water system for air handling unit, cross referencing this SOP to the associated system SOP's.
- State — responsible functionaries for implementing the SOP
- List — the operations to be carried out for each component of the system
- Summarise — the activities in a chronological order, tabulating them on a bar(Gant) chart. Highlight earliest and latest dates for each function. or activity.

Prepared By:	Reviewed By:	Approved By:	Authorized By:
Date:	Date:	Date:	Date:
Positon:	Positon:	Positon:	Positon:

STANDARD OPERATING PROCEDURE

TITLE	SOP # ..25-0002/ 1.....
	Effective Date from ....
PREPARATION OF MAINTENANCE PROCEDURES FOR AIR HANDLING SYSTEMS IN PHARMACEUTICAL APPLICATIONS	to ....
	Page 5 of 5

- Describe the instructions in detail in the imperative.
- Writing and language used must be consistent and clear.
- Design exhibits and refer to them to clarify the meaning of the text.
- Fill in and sign the Document Review Form.
- Sign the SOP

6.5 REVIEW and APPROVE SOP

Review approve and authorize theSOP in accordance with the SOP Guidelines SOP#_____

During the effective period

Ensure that operations are carried out according to written procedures

Revise the SOPwhen any modifications to the air handling system are carried out. A revised SOP reflecting the plant changes must be in place before the plant revisions can be accepted by maintenance or production departments

Update manufacturers and contractors record drawings and manuals to show all changes to the systems.

Prepared By:	Reviewed By:	Approved By:	Authorized By:
Date:	Date:	Date:	Date:
Positon:	Positon:	Positon:	Positon:

STANDARD OPERATING PROCEDURE

TITLE	SOP # 25-0004/ 1.....			
	Effective	D	M	Y
PROCEDURE FOR THE LEAK TESTING OF HEPA FILTERS IN CLEAN ROOM INSTALLATIONS	Date from	....	....	....
	to	....	....	
	Page 1	of	4	

1) PURPOSE

To establish a standard for the testing of HEPA filters in Clean Room installations.

2) SCOPE

This procedure applies to all HEPA filter installations in clean rooms. The procedure is to be read in conjunction with the appropriate standard to which the installation is required to comply.

3) RESPONSIBILITY

The engineering manager is responsible for ensuring that this procedure is followed when filters in clean rooms are tested.

4) GENERAL GUIDELINES

A copy of the 'General Arrangement' drawing of the facility, showing all ventilation supply and exhaust grilles and diffusers shall be obtained. Each HEPA filter shall be assigned a unique identification number for the purpose of recording test data.

5) PREPARATORY MEASUREMENTS

5.1 Room Pressures

Before beginning any leakage detection tests, the difference in air pressure between the controlled space under test and any adjacent areas of lower classification including void spaces, shall be undertaken. The results of the pressure tests shall be recorded and comparison made with the specification for the room. If any deviation of greater than or equal to +/- 5Pa is detected the room shall be rebalanced and the test for air pressure repeated.

5.2 Air Velocity Measurement

Air flow velocity through the HEPA filters or workstations being tested should be measured using a calibrated hot wire or vane type anemometer accurate to within +/-3% of full scale.

Prepared By:	Reviewed By:	Approved By:	Authorized By:
Date:	Date:	Date:	Date:
Positon:	Positon:	Positon:	Positon:

STANDARD OPERATING PROCEDURE

TITLE	SOP # 25-0004/ 1.....			
	Effective	D	M	Y
PROCEDURE FOR THE LEAK TESTING OF HEPA FILTERS IN CLEAN ROOM INSTALLATIONS	Date from	....	....	....
	to	....	....	....
	Page 2	of	4	

The air flow velocity through each filter should be no greater than +5% above the manufacturers recommended maximumair flow velocity, and no greater than -5% below the manufacturers recommended lower air flow velocity limit.

All air flow velocities should be recorded and a review of the overall results undertaken to confirm uniformity of velocity for the filters in each room.

6) INTRODUCTION OF AEROSOLS

6.1 Where possible aerosols should be introduced upstream of individual filters in such a manner as not to affect other filters on the air distribution system.

6.2 Where it is not possible to introduce an aerosol in accordance with item 6.1, it shall be introduced in the air handling unit fan section preferably immediately in front of the fan to ensure adequate mixing of the aerosol with the air stream.

6.3 The test aerosol shall consist of particles with the following size distribution:

More than 20% by mass of particles less than 0.5×10^{-6}m
More than 50% by mass of particles less than 0.7×10^{-6}m
More than 75% by mass of particles less than 1.0×10^{-6}m

7) PROCEDURE

7.1 Disperse the test aerosol upstream of the filter to produce a uniform challenge concentration across the filter and sealing frame.

7.2 Maintain this concentration throughout the test, and measure it at a point as close as possible to and ideally not more than 150mm from the filter face.

7.3 Adjust the aerosol generator so that the challenge concentration at the upstream filter face is at a level such that the photometer can be set and maintained at a stable reading of 100%.

7.4 Set the photometer at 100%. For all measurements the photometer shall be set to use the logarithmicscale in order to minimise background or,

STANDARD OPERATING PROCEDURE

TITLE	SOP # 25-0004/ 1.....			
	Effective	D	M	Y
PROCEDURE FOR THE LEAK TESTING OF HEPA FILTERS IN CLEAN ROOM INSTALLATIONS	Date from	....	....	....
	to	....	....	....
	Page 3	of	4	

7.5 Using the same photometer, scan all of the downstream face and perimeter of the filter including the sealing device with the sampling probe. Hold the probe approximately 25mm away from the area being tested and pass it over the entire area in slightly overlapping strokees, at a traverse rate of not more than 0.05m/s. Make separate passes around the entire periphery of the filter, along the bond between the filter pack and the frame and around the seal betweeen the filter and retaining device.

7.6 Record the location of any steady repeatable reading of the photometer which exceeds the value set by the standard for the relevant class of environmental cleanliness.

7.7 Where an unacceptableconcentration is detected, the filter including all recesses shall be cleared of all aerosol using a vacuum cleaner. A narrow nozzle shall be used so that aerosols which may have collected in stagnant or inaccesible points around the filter assembly can b adequately cleared.

7.8 The scanning procedure will be repeated in accordance with 7.5 after a period of 30 seconds has elapsed following the cleaning in accordance with 7.7.

a) if no concentrations above the permissible level are detected the filter will be deemed to be acceptable.

b) if an aerosol concentration above the permissible level detected the actions in 7.7 are to be repeated.

7.9 If after repeating the above procedures 3 times an unacceptable aerosol concentration is still detected its position (or positions) is to be noted so that remedial action as described below can be carried out.

7.10 Prior to further investigation, the remaining filters and filter assemblies are to be tested before detailed actions taken to pinpoint a leak.

8) LEAK LOCATION

8.1 If the primary scans of a suspect filter indicate a failure of the media the filter shall be rescanned. If a point failure is found, the upstream aerosol concentration shall be checked for compliance

Prepared By:	Reviewed By:	Approved By:	Authorized By:
Date:	Date:	Date:	Date:
Positon:	Positon:	Positon:	Positon:

STANDARD OPERATING PROCEDURE

TITLE	SOP # 25-0004/ 1.....			
	Effective	D	M	Y
PROCEDURE FOR THE LEAK TESTING OF HEPA FILTERS IN CLEAN ROOM INSTALLATIONS	Date from	....	....	....
	to	....	....	....
	Page 4	of	4	

wih the specification, and if the challenge is within limits then the filter has failed and must be replaced with a new filter.

8.2 If a failure is located at the edge of the filter a small diameter nonozzle shall be used to detect the axact position of the leak. Static or slow scanning< .01m/sare acceptable.

Once the position of the leak is detected the upstream aerosol concentration shall be checked for conformance, and a report issued.

9) TEST REPORT

The test report shall include at lest the folowing:

a) Number and date of the standard to which the clean room is to comply.

b) Title of the test method.

c) Class of environmental cleanliness and occupancy state.

d) Result, i.e. whether or not the installation was deemed to leak.

e) The location of any leak.

f) The nature of the challenge aerosol.

g) Name and address of the testing authority.

h) Any special conditions relating to the test, or departures from the test method.

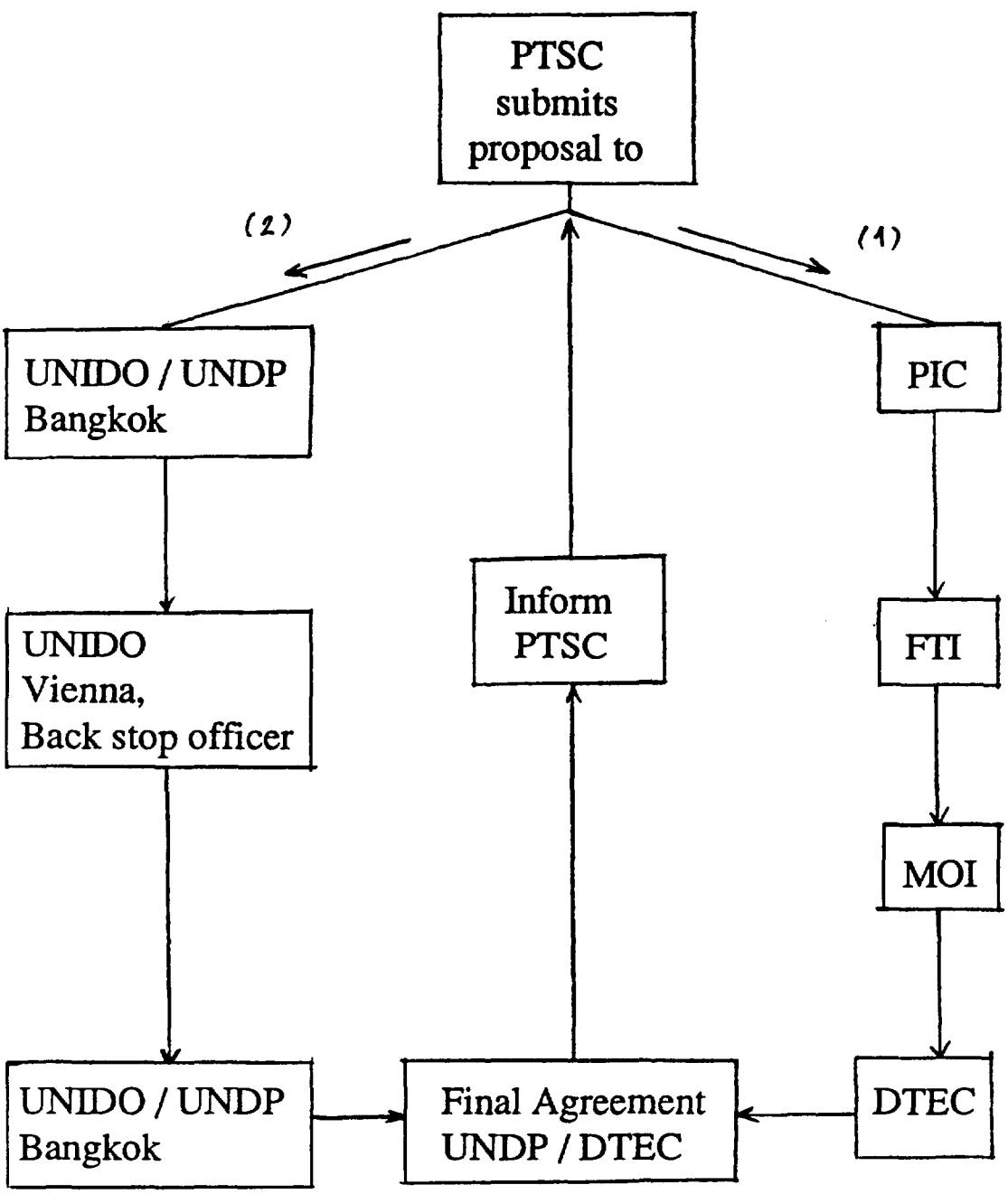
I) Date on which the test was carried out.

j) An identification for the controlled space tested.

k) Details of apparatus used, together with those of the apparatus calibration certificate, showing the date of calibration.

Prepared By:	Reviewed By:	Approved By:	Authorized By:
Date:	Date:	Date:	Date:
Positon:	Positon:	Positon:	Positon:

Routing Channel of Communication of PTSC and Participating Organizations



UNITED NATIONS INDUSTRIAL DEVELOPMENT ORGANIZATION
NON-EXPENDABLE PROPERTY CONTROL RECORD

Project No. DP/THA/88/018
Country THAILAND

PRICE MORE THAN US$5,000.-

Purchase order Number	Item No.	Description	Stock-on-hand in US$	Cond	Qty on Hand	Remarks
		1 set of HPLC *				
15-0-00427	1	WATER MULTIPLE-PUMP GRADIENT HPLC COMPLETE WITH : U6K INJECTOR.	1,884.00	G	1	
15-0-00427	2	M5 10 SDS 100-240 50/60 SERIAL# 510139906, 510139878	11,320.00	G	2	
15-0-00427	3	M680 AGC CONTR 100-240V SERIAL # 680008154	3,189.00	G	1	
15-0-00427	4	M490 PMD 220V	10,909.00	G	1	*
15-0-00427	5	470 FLUOROMETER W/MANUAL	7,010.00	G	1	
15-0-00427	6	746 SINGLE CHANL DATA MOD.	2,629.00	G	1	
15-0-00427	7	WISP M712 100/240 50/60HZ SERIAL # 712007457	10,514.00	G	1	
15-0-00427	8	ACCESSORIES	3,854.00	G	1	

UNITED NATIONS INDUSTRIAL DEVELOPMENT ORGANIZATION
NON-EXPENDABLE PROPERTY CONTROL RECORD

Project No. DP/THA/88/018
Country THAILAND

Purchase order Number	Item No.	Description	Stock-on-hand in US$	Cond	Qty on Hand	Remarks
15-0-00428	1	AUTOMATIC TITRATOR	19,018.00	G	1	
		1 Set of Coulter Multisizer Particle *				
15-0-00428	2	COULTER MULTISIZER PARTICLE ANALYZER WITH ACCUCOMP SOFTWARE *	47,102.00	G	1	*
15-0-00428	3	ACCUCOMP SOFTWARE COULTER 9904421 *	1,874.00	G	1	
15-0-00428	4	VACUUM OVEN CAPACITY	8,320.00	G	1	
15-0-00428	5	TABLET HARDNESS TESTER	6,497.00	G	1	
15-0-00428	6	DISSOLUTION APPARATUS 6-STATION, HANSON SR 2.	7,437.00	G	1	
15-0-00428	7	LAMINAR FLOW CABINET, BASSAIRE MODEL A6HB	8,449.00	G	1	

UNITED NATIONS INDUSTRIAL DEVELOPMENT ORGANIZATION
NON-EXPENDABLE PROPERTY CONTROL RECORD

Project No. DP/THA/88/018
Country THAILAND

Purchase order Number	Item No.	Description	Stock-on-hand in US$	Cond	Qty on Hand	Remarks
		1 set of Spectrophotometer *				
15-0-00592	1	DU-68 SPECTROPHOTOMETER W/INTERFACE 230 V S/N 0004293098	11,790.00	G	1	*
15-0-00592	2	AUTO 7 SAMPLER	1,665.00	G	1	
15-0-00592	3	ACCY, PRINTER FX85-230V.	945.00	G	1	
15-0-00592	4	ASSY, D2 LAMP DU-70.	1,062.00	G	2	
15-9-01986	1	GENMARK/HERAEUS-VOETSCH CLIMATIC (HUMIDITY) TEST CABINET MODEL HC 7005	21,527.00	G	1	
19-0-09259	1	(MACKINTOSH, APPLE LASER WRITER) COMPUTER	16,000.00	G	1	

UNITED NATIONS INDUSTRIAL DEVELOPMENT ORGANIZATION
NON-EXPENDABLE PROPERTY CONTROL RECORD

Project No. DP/THA/88/018
Country THAILAND

PRICE LESS THAN US$ 5,000.-

Purchase order Number	Item No.	Description	Stock-on-hand in US$	Cond	Qty on Hand	Remarks
15-0-00428	1	VISCOMETER WITH UL ADAPTER FOR LOW VISCOSITY	4,365.00	G	1	
15-0-00428	2	CONSTANT TEMPERATURE BATH SIMILAR TO MODEL EX 200 BUT WITH COOLER AND ACC. NO. WK14-1DS	2,461.00	G	1	
15-0-00428	3	OVEN TEMPERATURE CONTROL DIGITAL TEMPERATURE READ-OUT ACCURACY 0.1 DEGREE CELSIUS CAPACITY ABOUT 115 LITER BINDER MODEL B 115	3,928.00	G	4	
15-0-00428	4	ANALYTICAL BALANCE CAPACITY 205 G METTLER AE 200 S	2,362.00	G	1	
15-0-00428	5	TOP LOADING BALANCE, METTLER MODEL PM 1200	2,490.00	G	1	

List of locally purchased Laboratory Instruments

PRICE MORE THAN 5000 US $

#	Item	Quantity	Supplier	Purchase no.	Condition (*)	Price (US $)
1	Infrared Spectrophotometer	1 set	Perkin - Elmer (Thailand) Ltd.	93 / 09	G	53,050
2	Cryoscopic Osmometer "Osmomat 030"	1 set	Scientific Promotion Co. Ltd	93 / 05	G	7,614
3	Accupyc 1330 Gas Pycnometer	1 set	Engineering & Science Assoc.Co. Ltd.	93 / 10	G	12,566

(*) G = Good

UNITED NATIONS INDUSTRIAL DEVELOPMENT ORGANIZATION
NON-EXPENDABLE PROPERTY CONTROL RECORD

Project No. DP/THA/88/018
Country THAILAND

Purchase order Number	Item No.	Description	Stock-on-hand in US$	Cond	Qty on Hand	Remarks
15-0-00428	6	STANDARD SIEVE FOR PARTICLE ANALYZER RETSCH TYPE VIBRO ORDER NO. 355	635.00	G	1	
15-0-00428	7	STERILITY TEST UNIT "SARTORIUS"	967.00	G	1	
15-0-00428	8	LABORATORY VACUUM PUMP	692.00	G	1	
15-0-00592	1	DISSOLUTION TUBING KIT	1,634.00	G	2	
15-2-01370	1	TOYOTA COROLLA 1300CC, 4-DOOR STD. SEDAN/ COOLER	3,621.00	F	1	TRANSFERRED FROM DP/THA/ 86/010
15-9-01987	1	MISTRAL 3000E CENTRIFUGE	4,228.00	G	1	

List of locally purchased Laboratory Instruments

PRICE LESS THAN 5000 US $

#	Item	Quantity	Supplier	Purchase no.	Condition (*)	Price (US $)
1	Accessories for Coulter Multisizer II	1 set	Meditop Co., Ltd	93 / 11	G	715
2	Desiccator Model D-BOX	1 set	Sithiporn Assoc. Co., Ltd	93 / 08	G	548
3	Fume Hood, size 1.2x2.35x0.85 m^3	1 set	Bangkok Chemart	93 / 06	G	4,648
4	Silicon Automation Voltage Stabilizer	3 units	J.S. General Supply Co., Ltd	93 / 07	G	1,289
5	Computer with printer for Coulter Multisizer II	1 set	Sahaviriya OA Group	93 / 13	G	1,786
6	Computer "NOAH" Model 386 and printer Epson Model LQ 1170	1 set	J.S. General Supply Co., Ltd	93 / 12	G	2,930

(*) G = Good

Accessories for alternatives HPLC column (6 columns) not received yet.

July 1993

List of locally purchased Training Equipment

#	Item	Supplier	Purchase no.	Condition (*)	Price (US $)
1	Video Camera Recorder (SHARP, Model VL-MX98GY)	SHARP Thebnakorn Co. Ltd	92 / 14	G	1,091
2	Video Cassette Recorder (SHARP, Model VC-95HT)	SHARP Thebnakorn Co. Ltd	92 / 14	G	555
3	Colour Television (SHARP, Model 25N42-E1)	SHARP Thebnakorn Co. Ltd	92 / 14	G	754
4	Photocopy Machine (Model SF-7800)	SHARP Thebnakorn Co. Ltd	92 / 009	G	2,344
5	Electronic Typewriter (NAGAJIMA, Model AX-60)	O.M.A. Ltd	92 / 10	G	547
6	Overhead Projector (KODAK, Ektalite L-5)	Chai Sayam Trading Co., Ltd	92 / 11	G	714
7	Slide Projector (KODAK, Caroussel S-AV 1030)	Chai Sayam Trading Co., Ltd	92 / 11	G	926
8	DA-LITE Tripod Screen 60 x 60	Chai Sayam Trading Co., Ltd	92 / 11	G	174

G = Good

List of locally purchased Training Equipment

#	Item	Supplier	Purchase no.	Condition (*)	Price (US $)
1	Video Camera Recorder (SHARP, Model VL-MX98GY)	SHARP Thebnakorn Co. Ltd	92 / 14	G	1,091
2	Video Cassette Recorder (SHARP, Model VC-95HT)	SHARP Thebnakorn Co. Ltd	92 / 14	G	555
3	Colour Television (SHARP, Model 25N42-E1)	SHARP Thebnakorn Co. Ltd	92 / 14	G	754
4	Photocopy Machine (Model SF-7800)	SHARP Thebnakorn Co. Ltd	92 / 009	G	2,344
5	Electronic Typewriter (NAGAJIMA, Model AX-60)	O.M.A. Ltd	92 / 10	G	547
6	Overhead Projector (KODAK, Ektalite L-5)	Chai Sayam Trading Co., Ltd	92 / 11	G	714
7	Slide Projector (KODAK, Caroussel S-AV 1030)	Chai Sayam Trading Co., Ltd	92 / 11	G	926
8	DA-LITE Tripod Screen 60 x 60	Chai Sayam Trading Co., Ltd	92 / 11	G	174

G = Good

List of locally purchased Laboratory Instruments

PRICE LESS THAN 5000 US $

#	*Item*	*Quantity*	*Supplier*	*Purchase No.*	*Price (US$)*
1	E 55013 MINIPLUS 3 MODEL MP 8 GILSON PERISTALTIC PUMP, 220-240 V/50 HZ WITH STANDARD	1 SET	QUALITECH INSTRUMENTS CO.,LTD.	94/01	3,098
2	PN. 537094 PUMP CONTROL BOARD	1 SET	QUALITECH INSTRUMENTS CO.,LTD.	94/01	1,215
3	PN. 598274 RS 232 C INTERFACE	1 SET	QUALITECH INSTRUMENTS CO.,LTD	94/01	745
4	IMMERSION MEASURING CELL K = 0.8	1 SET	SCHMIDT SCIENTIFIC (THAILAND) LTD.	94/02	422
5	TEMPERATURE SENSOR	1 SET	SCHMIDT SCIENTIFIC (THAILAND) LTD.	94/02	186
6	ULTRASONIC BATH	1 SET	SAHAVIRIYA PURE SCIENCE CO.,LTD.	94/03	1,476
7	ULTRAVIOLET LAMPS MODEL UVGL-58	1 SET	SAHAVIRIYA PURE SCIENCE CO.,LTD.	94/04.1	440
8	CAPILLARY DISPENSER	1 SET	DIETHELM & CO.,LTD	94/04.2	690.40
9	NANOMAT	1 SET	DIETHELM & CO.,LTD	94/04.3	1,184
10	15 MICRON APERTURE TUBE WITH CALIBRATION STANDATD	1 SET	MEDITOP CO.,LTD.	94/07	1,145

List of locally purchased Laboratory Instruments

PRICE LESS THAN 5000 US $

#	*Item*	*Quantity*	*Supplier*	*Purchase No.*	*Price (US$)*
11	280 MICRON APERTURE TUBE WITH CALIBRATION STANDATD	1 SET	MEDITOP CO.,LTD.	94/07	725
12	ERWEKA DISINTEGRATION TESTER	1 SET	HAVE LINK LTD.	94/10	2,200
13	MELTING POINT APPARATUS	1 SET	SAHAVIRIYA PURE SCIENCE CO.,LTD.	94/11	1,480
14	POLARIMETER MODEL D2	1 SET	BANG TRADING 1992 CO.,LTD.	94/12	4,569

" ON ORDER " as of Sep 25/94

List of locally purchased Laboratory Instruments

PRICE MORE THAN 5000 US $

#	*Item*	*Quantity*	*Supplier*	*Purchase No.*	*Price (US$)*
1	TSP : CONSTA METRIC FLUID METERING PUMPS MODEL CM 3200	1 SET	SCITRONIC CO.,LTD.	94/06	6,000
2	GAS CHROMATOGRAPHY TREMETRIC USA	1 SET	SCITRONIC CO.,LTD.	94/08	24,108
3	TSP : VARIABLE - WAVELENGTH U/VIS DETECTOR MODEL SM 3200	1 SET	SCITRONIC CO.,LTD	94/09	6,500

" ON ORDER " as of Sep 25/94

Correspondence of evaluation by pharmaceutical companies concerning the technical services provided by the PTSC.

BIOLAB CO., LTD.

625 Soi 7A Bangpoo Industrial Estate
Samutprakarn 10280, Thailand.

Telephone : 317-7773, 317-2456, 3240715-7
Cable : BIOPHARM BANGKOK
Telex No. 87278 BIOPHAR TH

Ref : ADM001/94 January 27th, 1994

Attn : Mr. Joseph Beelen, Chief Technical Advisor
Pharmaceutical Technology Service Center
Faculty of Pharmaceutical Sciences
Chulalongkorn University
Bangkok, Thailand

From : Mr. Rachod Thakolsri
Director of Administration of Biolab

I would like to congratulate you for the impressive and outstanding training and advises that you provided to us during your ten day sessions You have not only informed and advised my colleagues on the knowledge that they required but you have changed their attitude about how to work together and the real concept of Good Manufacturing Practices which you could not have done if I would have send my colleagues to the center.

You have gained our acceptance and we honor you as the first technical and managerial advisor for our factory. We hope that the center will concentrate on such services for the industry and keep the magic going.

Sincerely Yours,

Rachod Thakolsri

Mailling Address:
G.P.O. Box 401 Bangkok 10501. Thailand.
Office Address:
384 Soi 6. Pattana 3 Road.
Bangpoo Industrial Estate.
Samutprakarn 10280. Thailand.
Tel: 324-0681. 324-0847-8
Tlx: 22575 GEEPEE TH Fax: (662) 324-0451
324-0537

MEDICAP LTD.

REF: MKT/ML-93-064

March 29, 1993

Dr. Prasan Thamaupakorn
Pharmaceutical Technology Service Centre
Faculty of Pharmaceutical Sciences
Chulalongkorn University
Bangkok 10330 Thailand.

Dear Dr. Prasan,

We are proud to inform you that Medicap Ltd. has received GMP Compliance from Australia and Denmark. Our company is grateful to you and your team for the help and training provided to us, without which we would not have been able to achieve international standards.

We hope that you will continue to provide new services and training programme for the benefit of pharmaceutical and health industry in Thailand.

Thanking you.

Yours sincerely,

Vivek Dhawan
Managing Director

หจก. โรงงานเวชภัณฑ์ แอล.บี.เอส. แลบบอเรตอรี่
英咪億製藥廠兩合公司
L.B.S. Laboratory Ltd.,Part.

Jan 21, 1994.

Dear Dr. Prasan,

We would like to express our sincere appreciation towards Mr. J.P Beelen, chief technical advisor of UNIDO, for his dedication to our company during his plant visits and audits from Dec. 14/93 - Jan 21/94.

His efforts to evaluate our company's system and procedures together with plant design and layout proved very beneficial.

His advice for corrective actions was extremely practical and will undoubtedly also contribute towards the long-term success of our company in several areas of our plant operations.

We would very much appreciate to arrange another opportunity to welcome Mr. Beelen in order to benefit from his consultancy services.

Best Regards,

Piya Tiragarn
President of L.B.S. Laboratory

602 ซอยพานิชอนันต์ สุขุมวิท 71 กรุงเทพฯ 10110 โทร. 3924082 (6 คู่สาย) โทรเลขย่อ "ฮ็อคโซน" กรุงเทพฯ
602 Panichanant, Sukhumvit 71 Rd., Bangkok 10110 Thailand. Tel. 3924082 (6 Lines) Cable "HAWKSONE" Bangkok, Telex: 21966 POLAR TH, Fax: (662) 3917123

BERLIN BERLIN PHARMACEUTICAL INDUSTRY CO., LTD.

January 27, 1994

Dear Mr. Beelen,

We would like to express our appreciation for your valuable assistance in providing your support to our company in various aspects applicable to the plant operation.

We feel that your "on site" plant visits and training sessions have greatly contributed to improve our GMP and QA standards within our plant. These plant visits are very effective as they allow us to investigate the specific areas for improvement and permit valuable discussions both in scope and depth.

We thank you very much for all the technical support and are looking forward to your next visit in Thailand in order to benefit again from the UNIDO consulting services.

Sincerely yours,

Vanida Chainuvati

Vanida Chainuvati

Managing Director

OFFICE:
352-361 NEW ROAD
BANGKOK 10100
THAILAND

OFFICE
TELEPHONE:
2231011-2

OFFICE TELEX.
BERLIN

OFFICE FAX:

FACTORY:
63 ROMKLOA ROAD
BANGKOK

FACTORY
TELEPHONE:
3267741-4

FACTORY
FAX:
(662) 3267745

Annex 16

ศูนย์บริการเทคโนโลยีเภสัชอุตสาหกรรม
PHARMACEUTICAL TECHNOLOGY SERVICE CENTRE
คณะเภสัชศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย ปทุมวัน กทม. 10330 โทร. 2511871-7 ต่อ 273
FACULTY OF PHARMACEUTICAL SCIENCES CHULALONGKORN UNIVERSITY BANGKOK 10330 THAILAND

May 28, 1996.

Z. Csizer
Director, UNIDO
Vienna
Austria

Subject : DP/THA/88/018 - Development of Pharmaceutical Industry.

Dear Mr. Csizer:

I received your fax of May 20, 1996 last week and tried hard to collect the information on obtaining the GLP certificate for our Centre as you need. Detail is as follows.

1. The GLP certificate has not been awarded to any laboratories. This is because the Department of Medical Science, Ministry of Public Health which is the organization responsible for accreditation all laboratories in order to award such certificate has not released the standard guildline to follow for a GLP yet. Source of information stated that it might be available next year. Our Centre can do nothing at the present time, however, we will prepare ourselves.

2. Our Centre is going to move in order to expand the activities for exporting the drug - products. The new place about 150 sq. m. located on the fourth floor of Pharmacy Building. It is well designed expecting to meet the requirements for a GLP. The construction and decoration will start within the next two months under the support of the Department of Promotion for Export, Ministry of Commerce.

Our activities are well progressive both services and transferring technologies. We just finished arranging an exhibition tour to attend the Interpack at Düsseldolf, Germany and visitting the pharmaceutical manufacturing companies, namely, Hoechst AG and Merck KGaA in Germany, and NV Organon in Netherland during May 7-15, 1996. Our laboratory are assaying about 30 items of drug-products to assure their quality for Ministry of Health, Lao PDR under the provision of World Bank. Moreover, we are preparing an intensive training program on Good Manufacturing Practice (GMP), a short training course for 2 inspectors from Drug Control Division, Food and Drug Department, Ministry of Health, Lao PDR, during July 1-31, 1996 in Bangkok.

Thank you for your kindness, I will inform you as soon as possible whenever I have any information on obtaining the GLP certificate for our Centre.

With best regards.

Sincerely,

Uthai Suvanakoot, Ph. D.
Director.

Annex 17

Comments of the Project Manager/Substantive Backstopping Officer

One of the main goals to be achieved by the pharmaceutical industry, as a general aim of the industry both in the developed and the developing countries, is to compete successfully in the domestic and eventually in the international market and at the same time to provide a wide range of the needed products of consistent quality at a reasonable price. The pharmaceutical industry in the developing countries falls mostly in the category of the small and medium size industry, it can hardly reach the critical size to become a research-based industry. With the exception of a few developing countries, e.g. China, India, etc. the pharmaceutical industry in the Third World can mainly be characterized by the formulation and packaging industry (secondary pharmaceutical industry). Even in those countries with a well established domestic industry the pharmaceutical manufacturing has up to the recent times been based on reproductive technologies and reproductive research and development. The Uruguay Round Agreements has, however, had serious implications for the reproductive type of pharmaceutical industry.

In the mid-1980s, the World Intellectual Property Organization (WIPO), with the aim of implementing of the recommendations received from several industrialized countries with respect to the inadequacy of the Industrial Property System established by the 1883 Paris Convention, started a diplomatic exercise for the preparation of a convention on the harmonization of patent legislation that would eventually be agreed and signed worldwide.

WIPO's exercise was however overtaken by a more ambitious negotiation in the General Agreement on Tariffs and Trade (GATT). The 1984 and 1988 reforms of the United States Trade Act and the launching of the GATT's Uruguay Round in 1986, brought into the agenda of international trade a very important topic, that is the Trade-Related Aspects of Intellectual Property Rights (TRIPs).It should be noted that international discussions in this theme started at the end of the Tokyo Round when GATT received a mandate to analyze the feasibility of the preparation of an international code on the trade of counterfeit goods.

Signed in 1994 by the relevant ministers of the GATT countries, the Final Act of the Uruguay Round includes the TRIPs Agreement. It also established, as of 1 January 1995, the World Trade Organization (WTO) which by providing a single institutional entity, replaced the GATT. As of April 1995 the Final Act was ratified by 76 countries. The Geneva-based International Federation of Pharmaceutical Manufacturers Associations (IFPMA) noted with satisfaction those provisions that have implications for pharmaceuticals. The most important among these provisions is that the pharmaceutical **products will be patentable**. Most importantly the imported and locally manufactured pharmaceutical products are equally treated, and there is no discrimination between technologies, the TRIPs Agreement strictly limit the granting of compulsory licenses in order to permit local manufacture of patented products.

Of the substantive Agreements, Understanding, Ministerial Declarations and Decision adopted in Marrakesh, Morocco in April 1994 as a part of the Final Act Embodying the Results of the Uruguay Round of Multilateral Trade Negotiations, the only one of direct relevance to the pharmaceutical sector is the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPs). The TRIPs Agreement contains seven parts:

Part I : General provisions and basic principles which govern the Agreement;

Part II: Substantive, minimum standards for seven intellectual property rights (IPRs);

Part III: Procedures and measures for enforcement;

Part IV: Acquisition and maintenance procedures;

Part V: Arrangements for the prevention and settlement of disputes;

Part VI: Transitional arrangements; and

Part VII: Other final provisions for the implementation of the Agreement.

The seven IPRs are as follows : copyright and related rights, trademarks, geographical indications, industrial designs, patents, layout-designs of integrated circuits and undisclosed information (trade secrets). The term of a patent, under the TRIPs Agreement, shall be at least 20 years from the filing date. The transitional arrangements permit to delay the implementation of the TRIPs Agreement. The developing and transitional economy countries have five years to bring their legislation in compliance with the TRIPs Agreement (i.e. by 1 January 2000). However, if a country does not introduce pharmaceutical product patent protection by the end of this initial five-year period, the implementation of the Agreement may still be delayed for another five years.

The TRIPs provisions only apply to inventions where a patent application has been filed after 1 January 1995 and therefore entirely prospective excluding products in the pipeline. For the research-based pharmaceutical industry, pipeline protection is a vital component of anew patent law because of the long period of time between when a NCE is patented by the inventor and when it receives the license from the national control authorities to be marketed.

Mailbox protection under the TRIPs Agreement implies that a country which chooses to delay the introduction of a patent law consistent with the TRIPs Agreement, and which currently does not offer product patent protection, has to provide for a mechanism to accept patent applications for products invented after the Agreement entered into force, i.e. 1 January 1995. These applications will sit unprocessed in a mailbox until the day the country introduces its new patent law with product patent protection.

The TRIPs Agreement may have a severe impact, especially in high technology sectors such as the pharmaceuticals, working to the disadvantage of developing countries in two main respects: domestic manufacturers wishing to produce and commercialize products covered by patents will be forced into licensing agreements involving royalty payments to patent holders; while R&D activities may be hindered since the TRIPs Agreement is likely to inhibit "reverse engineering" - the process by which research-based industry products are copied and adapted for developing country usage. The copies are sometimes produced by different processes which might even be patent protected as process patent.

One of the most significant industries of concern to TRIPs is the pharmaceutical industry. At the beginning of the Uruguay Round almost 50 countries did not have product patents provisions governing pharmaceuticals. The lack of such provisions probably had more to do with the a lack of

need rather than an intent to allow domestic firms to produce pharmaceutical products in violation of a foreign patent. Most developing countries satisfied domestic consumption by importing, primarily from developed countries. More than 80 % of world production of pharmaceutical products occurs in developed countries; and almost 75 % of the production of that does occur in developing countries occurs in only six countries. As a result, there are only a few developing countries that have a big stake in the application of TRIPs to pharmaceutical products currently. The real importance lies in the future and the implications for research and development in this area. And in most developing countries with domestic production, a significant share of the local products is by foreign owned firms; in some cases domestic and foreign owned firms share the domestic market.

Enforcement of TRIPs will seriously affect those few developing countries with significant production of domestic firms (excluding foreign owned firms). Those domestic firms producing frontier products subject to patent protection will be required to negotiate licensing agreements, and pay royalties, or withdraw from the production of frontier products and shift their efforts to the production of generic pharmaceuticals. In total their costs for these products will increase in terms of both consumer prices (owing to monopoly pricing) and foreign exchange costs of imports. Monopoly pricing can be minimized by the inclusion of "compulsory licensing" provisions in national intellectual property legislation. In those developing countries that do not have domestic production, current consumer prices and foreign exchange costs may be excessive. TRIPs will not make these matters worst. However, TRIPs might discourage new domestic firms from forming.

The degree of patent protection covered pharmaceutical products was, in general, strongly related to the level of development of the domestic pharmaceutical industry. Recently, due to bilateral and multilateral cooperations using technology transfer from developed countries, the situation has changed. In those countries with well-established domestic industry based on reproductive R&D, the local enterprises strongly favor a weak product patent protection. The absence of product patent protection makes it easier for the domestic companies to copy patented drugs on the basis of alternative processes. This explains why much of the resistance to TRIPs, which continues even after the Agreement, comes from countries of well-developed pharmaceutical industry, e.g. Argentina, India, etc.

In the above presented very briefly country reviews an attempt has been made to illustrate that in long term the TRIPs Agreement has significant advantages to the pharmaceutical industry. In the developed world, in addition to providing an increased patent life of 20 years, which seems to be reasonable to recover R&D expenditures, the Agreement helps to promote the generics industry. In developing countries with high level of R&D, the product patent system will provide motivation to bridge the gap between academic and applied research as well as to increase the efficiency of R&D for moving from product prototype to commercialization. Countries in the Asia-Pacific region, e.g. China, India, Republic of Korea, Singapore have a sophisticated, and significantly strong domestic pharmaceutical industry, R&D capabilities and financial resources to develop an export-oriented financially sustainable industry at global scale. Some other countries with less developed pharmaceutical industry and financial resources should go for development with less ambitious way. These countries should seek for some sort of long term cooperation, preferably from an industrial partner. Joint venturing or licensing agreements could be the recommended forms of cooperation, however, companies with more resources might develop contract manufacturing.

The pharmaceutical industry in Thailand is a very competitive, dynamically growing sub-sector. In addition to the Government Pharmaceutical Organization (GPO), which has the largest share of the domestic market, there are more than 150 pharmaceutical enterprises, among them one can find the

subsidiaries of all major multinational companies. The industry is well organized and represented by the local professional associations, e.g. The Federation of Thai Industries (FTI), The Thai Pharmaceutical Manufacturers Associations (TPMA) and The Pharmaceutical Industry Club (PIC). The national Food and Drug Administration (FDA) is a major driving force to improve quality and to meet the requirements of the international regulations.

The Pharmaceutical Technology Service Centre (PTSC) was set up in an agreement between the FTI, the TPMA and the Chulalongkorn University as a programme of the Thai Government and UNDP, and was implemented by UNDO. The PTSC was founded in 1991, and from this time it worked in very close cooperation with the FDA in assisting domestic pharmaceutical industry to comply with the current Good Manufacturing Practice (GMP). It should be noted that the Centre has enjoyed since its conception the generous support of the domestic industry. Furthermore it is worthwhile to mention that the local subsidiaries of the multinational companies were among the first to use the services of the Centre and by doing so they created a strong a loyal clientele to support directly and indirectly its activities.

The Centre delivered high quality services through which it facilitated to obtain export certification to several local companies. As a major outcome of the Centre's activities, it gained regional reputation and has established itself as a regional centre of excellence for pharmaceutical technology, which to date is the only one of its kind in South East Asia. Several countries of the region, e.g. Laos, Viet Nam, etc. directly and through ESCAP have received the services of the Centre. As the newest development, the Centre is providing quality control testing of about 30 pharmaceutical products for the Ministry of Health, Lao People's Democratic Republic financed by the World Bank.

With the continuous support of the Faculty of Pharmaceutical Sciences of the Chulalongkorn University the Centre has become financially self-sustained and it is developing well since the formal completion of the UNDP/UNIDO project. The contacts with UNIDO are living, and UNDO does its utmost to create business opportunities for the Centre, e.g. it successfully organized a two-week intensive training programme for a high level pharmaceutical industry delegation from Syria in 1994. UNIDO has also encouraged the representatives of WHO and IFPMA to visit the Centre and use its facilities and services in their relevant programmes. The sustainability of the Pharmaceutical Technology Service Centre can also be demonstrated by the fact that based on its very sensitive role played in promoting the export of local pharmaceutical products, the Department of Promotion for Export, Ministry of Commerce has decided to provide support for the expansion of the Centre and the construction of a new location in compliance with the requirements for GLP. Last but not least it should be noted that based on the experience gained with PTSC, UNIDO is developing similar programmes in other developing countries within its priority thematic programmes. In order of importance these are as follows:

Thematic priority 4: Innovation, productivity and quality for international competitiveness - Component C: Quality management;

Thematic priority 5: Industrial information, investment and technology promotion - Component C: Technology promotion;

Thematic priority 3: Small and medium enterprises: Policies, networking and basic technical support - Component B: SME support systems and institutions.