BUREAU OF FOOD AND DRUGS
DEPARTMENT OF HEALTH
BUREAU OF FOOD AND DRUGS
Civic Drive, Filinvest Corporate City
Alabang, Muntinlupa City

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BUREAU CIRCULAR
No. 3 s. 2005

TO : ALL DRUG MANUFACTURERS

SUBJECT : **Submission of Site Information File**

To facilitate the evaluation and inspection of drug manufacturers' compliance to current Good Manufacturing Practice (cGMP) and other related regulations, you are hereby directed to submit your current site information file.

A Site Information File (SIF) is a document prepared by the manufacturer containing specific and factual information about the production and/or control of pharmaceutical manufacturing operation carried out at the site and any closely integrated operations at adjacent and nearby buildings. If only part of a pharmaceutical operation is carried out on the site, the site master file needed describe only those operations, e.g. analysis, packaging.

A site master file should be concise and must not exceed 25 pages in A4 size paper excluding annexes (see attached format)

Drug manufacturers with changes in their previously submitted SIF must prepare the necessary amendments thereto and submit the same to Regulation Division II on or before March 15, 2005.

For your information and guidance.

(Sgd) Prof. LETICIA-BARBARA B. GUTIERREZ, M.S.
Director

SITE INFORMATION FILE
(Drug Manufacturer)

1. GENERAL INFORMATION

1.1. Brief information on the firm (include, Name and Address); relation to other sites and particularly, any other information relevant to understanding the manufacturing operation.

In not more than one page, outline the firm's activities and other sites in addition to the site that is the subject of the document.

1.2. Manufacturing activities as licensed by the BFAD or if a license has not yet been issued, the activities included in the application for a Manufacturing License.

Quote the license document as issued by the BFAD, any conditions and or restrictions should be stated.

1.3. Any other (than Pharmaceutical products for human use), manufacturing activities carried out on the site.

1.4. Name and exact address of the site, including telephone, fax.

1.4.1. Name of Company
1.4.2. Telephone Number
1.4.3. Fax Number

1.5. Types of Pharmaceutical products manufactured in the site, and information about specifically toxic or hazardous substances handled, monitoring the way they are manufactured (e.g., in dedicated facilities or on a campaign basis)

1.5.1. Quote the type of actual products manufactured.
1.5.2. Note any toxic or hazardous substances handled (e.g., antibiotic, hormones, steroids, antineoplastics) note whether the products are manufactured in a dedicated facilities or in a campaign basis.
1.5.3. Mention if veterinary products are also manufactured on the site.

1.6. Short description of the site including size, location and immediate environment and the facilities for other manufacturing activities on the site. A short description of the site.

1.6.1. The location and immediate environment
1.6.2. The size of the site, types of buildings
1.6.3. Other manufacturing activities on the site.

1.7. Number of employees engaged in production, quality control storage and distribution.

1.7.1. Production
1.7.2. Quality assurance or quality control
1.7.3. Storage and distributions
1.7.4. Technical and engineering support services
1.7.5. Total of the above

1.8. Use of outside technical assistance in relation to manufacture.

1.8.1. Name and address of the company
1.8.2. Telephone Number
1.8.3. Fax Number
1.8.4. Brief outline of the activity being undertaken in not more than 100 words

1.9. Short description of the quality management system of the firms, including procedures for the release for supply of finished goods (see section 6 where more information is sought on the Quality Control System)

In not more than three pages.

1.9.1. State the firm's Quality Policy
1.9.2. Define the responsibility of the Quality Assurance function
1.9.3. Describe the elements of the quality system for example
1.9.3.1. Organizational structure, responsibilities, procedures, processes
1.9.3.2. Specifications, test methods and other quality related data collection
1.9.4. Describe audit programs (self inspection)
1.9.5. Describe how the results are reviewed to demonstrate the adequacy of the quality system in relation to the objective that is quality, efficacy and safety of the product. See also paragraph 6.1.2.
1.9.6. when suppliers of critical starting materials & packing materials, actives, excipients, containers and closures and printed materials are assessed, give details of how this done.
1.9.7. Describe the release for supply procedure for finished products.
1.9.8. Describe the product stability program.

1.10. Use of computers by the firm

2. SPECIFIC INFORMATION:

The following is an index of the major topics to be included

2. Personnel

2.1 Organization chart, showing the arrangements for quality assurance, including production and quality control

Organogram for quality assurance including productions and quality control record, senior managers and supervisor

2.2 Qualifications, experience and responsibilities of key personnel

Brief details of academe qualifications and work related qualifications and years relevant experience since qualifying.

2.3 Outline of arrangements for basic and in-service training and how records are maintained

2.3.1 Describe how training needs are identical and by whom
2.3.2. Give details of training relative to GMP requirements
2.3.3. State the form of training for example in-house, external and how practical experience is gained and which staff are involved.
2.3.4. Explain how the efficacy of the training is assed e.g. by questionnaires.
2.3.5. Explain how training needs are identified.
2.3.6. Give brief details of records kept.

2.4. Health requirements for personnel engaged in production

2.4.1. Who is responsible for checking health of employees?
2.4.2. Is there a pre-employment medical examination?
2.4.3. Are employees routinely checked from time to time depending on nature of their work?
2.4.4. Is there a system for reporting sickness or contact with sick people before working in a critical area?
2.4.5 Is there a system of reporting back after illness?
2.4.6. Are there who work in clean areas (sterile manufacture) subject to additional monitoring?

2.5. Personnel hygiene requirements, including clothing

2.5.1. Are there suitable washing, changing and rest area?
2.5.2. Is the clothing suitable for the activity undertaken? Briefly describe the clothing
2.5.3. Are there clear instructions on how protective clothing should be used and when it should be changed?
Detailed procedures are not needed. Is in-house or external laundry used?

3. PREMISES AND EQUIPMENT

Premises:

3.1. Simple plan or description of manufacturing areas with dimensions.

3.1.1. Provide floor plan identifying each area with corresponding dimensions.

3.1.2. For sterile product areas indicate room and area classification and pressure differentials between adjoining areas of different classifications.

3.2. Nature of construction and finishes

3.2.1. To reduce narrative for a large complex plant, the details should be limited to critical areas.

3.2.2. There areas must include all processing and packaging & critical storage areas.

3.2.3. A narrative format is preferred.

3.3. Brief description of the air control system, indicating the quality of air filtration. More detail should be given for critical areas with potential risks of airborne contamination (schematic drawings of the system are desirable). Classifications of the rooms and used for the manufacture of sterile products should be maintained.

3.3.1. Designed criteria for example
Specific of the air supply
Temperature
Humidity
Pressure differential and air change rate
Simple pass or recalculation

3.3.2. Filter design and efficacy e.g.
Hepa 99.997% efficiency
Details of any alarms on the ventilation system should be given

3.3.3. The limits for charging the filters should be given

3.3.4. Give the frequency for revalidation of the system

3.4. Special areas for the handling of the highly toxic, hazardous and sanitizing materials

Follow the same layout as 3.1 above

3.5. Brief description of the process water system including sanitation. Schematic drawings of the system are desirable.

3.5.1. The schematic must go back to the city supply system

3.5.2. The capacity of the system (maximum quantity produced per hour)

3.5.3. Construction materials of the vessels must be given

3.5.4. Specification of any filters in the system must be given.

3.5.5. If water is stored and circulated, what is the temperature of the point of return.

3.5.6. The specification of the water produced.
Chemical
Conductivity

Microbiological

3.5.7. The sampling points and frequency of testing
3.5.8. The procedure and frequency for sanitation.

3.6. Maintenance – a description of planned preventative maintenance programmes and recording system
   3.6.1. Are there written procedures and suitable reporting form for maintenance and servicing? Do the documents record type frequency of services checks, details of service repairs and modifications?
   3.6.2. Are the maintenance routines that could affect product quality clearly identified?
   3.6.3. Are the reports made known to the users?

Equipment:

3.7. Brief description of major production and control laboratory equipment (List of equipment)

3.8. Maintenance – a description of planned preventative maintenance programmes and recording system
   3.8.1. Who is responsible for maintenance and servicing?
   3.8.2. Are there written procedures and contractual details for outside work?
   3.8.3. Are maintenance routines which could affect product quality clearly identified?
   3.8.4. Are records kept of:
      3.8.4.1 Type and frequency of service check;
      3.8.4.2. Details of service repairs and modifications?
   3.8.5. Are reports made known to the users?

3.9. Qualification and calibration, including the recording system.
   3.9.1. Briefly describe the company's general policy and records kept.

Sanitation and Pest Control

3.10. Cleaning and sanitation procedures for manufacturing areas and equipment.
   3.10.1. Are there written specifications and procedures for cleaning agents and their concentration for the method of cleaning and the frequency?
   3.10.2. Are cleaning agents changed from time to time?
   3.10.3. Have the cleaning procedures been validated and what was the method of evaluating the effectiveness of cleaning?
   3.10.4. Are cleaning methods monitored routinely by chemical and or microbiological methods?
   3.10.5. What are the cleaning methods and their frequency for the water supply system air handling system & dust extraction system?

3.11. Pest Control Measures

4. DOCUMENTATION

Noted: This section refers to all documentation used in manufacture. Manufacture involves all activities relating to the production and control of pharmaceutical products.

4.1. Arrangements for the preparation, revision, and distribution of necessary documentation for manufacture, e.g. batch records, SOP's.

4.1.1. Is there a description of the documentation system?

4.1.2. Who is responsible for the preparation, revision and distribution of documents?

4.1.3. Where are the master documents stored?

4.1.4. Is there a standard format and instructions of how documents are to be prepared?

Are there documents for:

- Product Process specifications
- Raw Material specifications
- Packaging component specification
- Standard process instructions including packaging
- Batch records including packaging
- Analytical methods
- QA release procedures

4.1.5. How is the documentation controlled?

4.1.6. For how long are documents kept after the release of the batch?

4.2. Any other documentation related to product quality, that is not mentioned elsewhere, e.g. microbiological controls on air and water.

4.2.1. Equipment specification

4.2.2. Specifications for disposable i.e. cleaning materials

4.2.3. Standard operating procedures

4.2.4. Quality Control Procedures

4.2.5. Training procedures

4.2.6. Computer program specifications (if applicable)

4.2.7. Documentation control of process deviations.

4.2.8. Calibration and test documents (see paragraph 3.9.5)

4.2.9. Validation documents (see paragraph 3.9 and 5.4)

4.2.10. Reconciliation of batches of raw materials, major packaging components i.e. product-contract and printed materials

4.2.11. List and briefly explain the use of any additional standard documentation used routinely.

4.3. Batch numbering system

5. PRODUCTION:

5.1. Briefly description of production operations using, wherever possible, flow sheets and charts specifying important parameters, (See list of products manufactured at Annex I)

- This narrative should be kept to a minimum and generalized schematic layouts used where possible. The following points should be addressed.
- Describe the operations capable of being carried out at the site with the existing facilities and specify the types of drug products (see paragraph 1.5.1 and annex II for types of products manufactured)
- When packaging only is undertaken, give a brief description only e.g. labeling, filling, etc. and the nature of containers used e.g. sachets, blisters packing, transfer proof glass containers.
- Describe the production operations using flow charts if possible Technical details are not required.
- Describe how products are identified during production and how in-process strange is organized.

5.2. Arrangements for the handling of starting materials, packaging materials, bulk and finished products, including sampling, quarantine, release and storage.

- Identification of supplier's lot number with the company's lot number
- Sampling labeling e.g. by using labels or by computer
- Issue of materials to manufacture and package
- The control of weighing
- Checking methods
- How are the materials being used for manufacture identified and release?

5.2.1. Control of bulk manufacture

- Checks on key parameters during manufacture e.g. blend, timer, filter integrity tests
- Records of key parameter
- In process checks
- Records of in-process checks

5.2.2. Packing

- Release of bulk, semi-finished products, packaging materials
- Confirmation of identity and line clearance checks
- In-process checks

5.2.3. Quarantine and release of finished products

5.3. Arrangements for the handling of rejected materials & products

5.3.1. Are reject materials & products clearly labeled? Are they stored separately in restricted areas?

5.3.2. Describe arrangements for sentencing the materials and their disposal. Is destruction recorded?

5.4. Brief description of the general policy for process validations

An outline of process validation protocol only is required (see paragraph 3.9.3)

6. QUALITY CONTROL:

6.1. Description of the quality control system and the activities of the quality control department. (See also section 1.9 where information is sought on the firm's quality management system)

6.1.1. Briefly describe the activities of analytical testing, packaging component testing, biological & microbiological testing.

6.1.2. If the review of batch documentation and release of final documentation takes place in the department; give details (see also paragraph 1.9.5)

6.1.3. Outline the involvement in the arrangements for the preparation, revision and distribution of documents in particular those for specification test methods and release criteria if not mentioned elsewhere (see also paragraph 1.9 and chapter 4, Documentation)

7. CONTRACT MANUFACTURING AND/OR ANALYSIS

7.1. Description of the way in which the GMP compliance of the contract manufacturer is assessed.

7.2. Are there written agreements with all contract acceptors, specifying GMP responsibilities.

8. DISTRIBUTION/COMPLAINTS & PRODUCT RECALL

8.1. Arrangements and recording system for distribution.

8.1.1. Is the warehouse secure?

8.1.2. Is it environmentally controlled?

8.1.3. is there refrigerated storage? (food room)

8.1.4. How are the materials stored e.g. pallet racking?

8.1.5. How is the status of products controlled e.g. by computer, by label?

8.1.6. What are the methods of distribution to customers?

8.1.7. Does the dispatch order ensure first in first out and identify the lot number?

8.2. Arrangement for handling complaints and products recalls

8.2.1. Complaints

8.2.1.1. Is there a written complaint procedure?

8.2.1.2. Who is responsible for:

- Logging

- Classifying
- Investigating complaints

8.2.1.3. Are written reports prepared?
8.2.1.4. Who reviews those reports?
8.2.1.5. For how long are complaints' records kept?

8.2.2. Product Recalls
8.2.2.1. Is there a written procedure which describes the sequence of actions to be followed including?
- Retrieval of distribution data;
- Notification of customers;
- Receipt segregation inspection of returned products;
- Investigation/reporting of cause;
- Reporting corrective action

8.2.2.2. Who is responsible for coordinating product recalls?
8.2.2.3. Who notifies the BFAD of complaints
8.2.2.4. Is the BFAD involved in complaints & decision to recall?

9. SELF INSPECTION:

9.1. Short description of the self inspection system

9.1.1. Describe how the self-inspection system verifies that those activities that have a bearing on quality comply with the planned arrangements

9.1.2. Are the quality system effective?

9.1.3. Are there documented procedure for the self inspection system and for the follow up actions?

9.1.4. Doest he system ensure that those responsible for the area of activity take timely corrective action on the deficiencies found.

ANNEX 1

- If a product is only partially processed, state the step of manufacture carried out at this facility.
- If products are blistered packed or stripped by others, state the company name.
- State whether sterile products are aseptically prepared or terminally sterilized.