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28, September 2000

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Subject: Docket No. 00D-1418
Comments to ICH; Draft Guidance on
Good Manufacturing Practice for Active Pharmaceutical Ingredients

Gentlepersons:

Agvar Chemicals Inc. is a supplier of active pharmaceutical ingredients and a founding member of the Generic Pharmaceutical Association (GPhA). On September 25th, we submitted, on behalf of the Generic Pharmaceutical Association, the following comments to above subject draft guidance:

- The term "Significant structural fragment" in connection with the definition of "API Starting Material" should be more clearly defined and be part of the glossary.
- The glossary lacks a definition of the word "deviation", which is a very important term.
- With regard to point 4.22, the term "production area" is too broad. It should be more clearly specified as to the exact type of production area it refers to. For example, does it refer to production areas where a qualified HVAC system is in operation?
- Please be more specific as to what "GMP related computerized systems" mean.

We attach 10 additional comments which were recently received from GPhA members, to above subject Draft Guidance.

Thank you for your review and consideration of the GPhA's comments to above subject draft guidance.

Cordially yours,

AGVAR CHEMICALS INC.

Margaret Hsiao
Vice President

Attachments

00D-1418

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**COMMENTS ON THE ICH DRAFT
CONSENSUS GUIDELINE
GOOD MANUFACTURING PRACTICES GUIDE FOR
ACTIVE PHARMACEUTICAL INGREDIENTS**

(STEP 2 OF ICH, RELEASED - 19TH JULY 2000).

1. Refer 3.2 : Personnel Hygiene:

Please include sub-section on:

Health checks for all employees should be carried out by a competent medical professional, at least annually. This should also include test for Penicillin sensitivity (where penicillins are manufactured or handled) apart from other tests. Written procedures should be established and should be practiced. Such records should be maintained.

2. Refer 4 : Buildings and Facilities:

After 4.15, please include:

For special production areas / buildings, which are dedicated, a separate cafeteria may be provided for operating personnel to avoid cross-contamination.

3. Refer 4.2 : Utilities:

- a) The sub-section 4.2.4 may include:
Drains in production area may be disinfected with appropriate disinfecting agent.
- b) The sub-section 4.21 should include:
The schematics for Heating Ventilation and Air Conditioning Systems should be available describing air flow, circulation, velocity, filter types, distribution, etc.
- c) Written procedures for cleaning and maintenance of HVAC filters should be available and practiced.

4. Written procedures should be available for Sections 4.4, 4.6, 6.4, 6.6, 14.1, 14.2, 14.3, 14.4, 14.5, 16, 17.2

5. Refer 5.4 : Computerized Systems:

This section should cite requirements of compliance to 21 CFR Part 11.

6. Refer 6.1 : Documentation and Records:

Please include: Written procedures should be established for Rectification of Errors in Documentation and Records.

7. Refer 6.4 : Master Production and Control Records:

In sub-section 6.40, the Master Production Records should be approved by Quality Assurance.

8. Refer 6.6 : Laboratory Control Records:

Please include: Written procedures should be established for Recording of Analytical Data including rounding off decimals.

9. **Refer 12.6 : Periodic Review of Validation Systems:**

Please include the following:

Where periodic evaluation indicates revalidation, due to significant changes made to the system or process, revalidation shall be performed. Revalidation should follow the same approach as described in 12.4 (Approaches to Process Validation). This shall be either:

- Revalidation of Prospective Type – For significant impacting changes
- Revalidation of Concurrent Type – For significant non-impacting changes
- Revalidation of Retrospective Type – For insignificant non-impacting changes

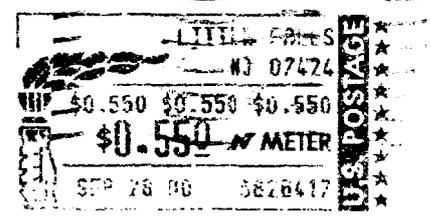
10. **Refer 20.0 : Glossary:**

Please include definition for "Objectionable Microorganisms" .

4gvar

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