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General Requirements For Vacant Capsules

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Contents

Preface

This standard is drafted in accordance with GB/T1.1-2009.

This standard is administered by China National Pharmaceutical Packaging Association.

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Introduction

This standard applies to the production, process control and quality control of vacant capsules. The production and quality of vacant capsules should comply with the relevant technical requirements of this standard as well as in line with the national regulations on pharmaceutical excipients and the technical requirements of general chapters included in the current version of *Pharmacopoeia of the People's Republic of China*, to ensure the quality and safety of vacant capsules.

General Requirements for Vacant Capsules

1. Scope

This standard specified general principles, classification, nomenclature, production and quality management, applicability, stability, as well as packaging, storage and transportation of vacant capsules.

This standard is applicable to vacant capsules for oral capsules preparation.

2. General Principles

2.1 Vacant capsules are cylindrical, hard, elastic empty capsules, which consist of telescoping cap and body pieces. Vacant capsules should have a clean, smooth and uniformly coloured surface, odourless, well trimmed and shaped without deformation.

2.2 The functionality and applicability of vacant capsules should meet the requirements of filling substances.

3. Classification

3.1 By the source of raw materials

Vacant capsules can be classified as animal derived and non-animal derived capsules based on the source of raw materials.

3.2 By the film-forming materials

Vacant capsules can be classified as Vacant Gelatin Capsules, Vacant Hypromellose Capsules and Vacant Pullulan Capsules based on the primary film-forming materials.

3.3 By release characteristics

Vacant capsules can be classified as gastric vacant capsules and

enterosoluble vacant capsules based on contents released by the specific part of human body.

3.4 By transparency

Vacant capsules can be classified as transparent capsules (no opacifying agent in both pieces), half transparent capsules (opacifying agent in either pieces), opaque capsules (opacifying agent in both pieces) based on opacifying agents.

4. Nomenclature

4.1 The name at least include: "release characteristic" and "primary film-forming materials".

4.2 "Gastric soluble" can be omitted in gastric capsules.

For example: " enterosoluble vacant capsules ": where " enterosoluble " means the release of contents within the intestine, and "gelatin" means the primary film-forming material.

4.3 Nomenclature should reflect the primary film-forming material of the highest content in case of two or more "primary film forming materials" used.

5. Production and quality management

5.1 Formulation and raw materials control

The raw materials of vacant capsules usually consist of primary film-forming materials and other auxiliary materials. The primary film-forming materials mainly include gelatin, hypromellose, pullulan polysaccharide. The auxiliary materials include humectant, surfactant, etc. Colorants and opacifying agents can be added if necessary.

The manufacturer of vacant capsules should guarantee safety for drug products production and usage by assuring stable quality of raw materials and compliance with pharmaceutical or food safety

standards. The manufacturer should conduct suppliers audit regularly.

5.2 Auxiliary materials

5.2.1 Colorant

The use of synthetic colorant should be avoided or reduced during the production of vacant capsules. If synthetic colorant is required, evaluation of safety should be conducted and should comply with GB2760.

5.2.2 Ink

Safe ink free of benzene and benzene derivative should be chosen and suitable technical requirements and management guidance should be established in case of ink used.

5.3 Microbial control

5.3.1 Manufacturers should conduct overall control on the manufacturing process to avoid and reduce the microbial contamination. In principle, bacteriostat should not be used in the formula and terminal sterilization is not proposed.

5.3.2 Monitoring and safety evaluation should be conducted with residue limitation in case of terminal sterilization used.

5.3.3 Category of bacteriostat, quantity and residue limitation should be aligned with National pharmaceutical and food standard in case of bacteriostat added.

5.4 Control of Manufacturing Process

5.4.1 The manufacturer of vacant capsules should develop reasonable process parameters and conduct adequate process validation to ensure the stability of manufacturing process and the consistency of inter-batches.

5.4.2 Manufacturer of vacant capsules should take the initiative to carry out corresponding risk assessment and timely notify pharmaceutical manufacturers in case of major changes to formula, manufacturing process and specification that may affect the product quality.

5.4.3 Manufacturer of vacant capsules should control the production environment and carry out corresponding validation when the

main environment parameters are changed.

5.4.4 Strictly controlled system and operating procedures should be implemented in production to make sure no mixed batches.

5.4.5 Process evaluation and validation should be carried out to ensure product quality not impacted when the sterilization process or bacteriostat process is used. Effective concentration and residue of ethylene oxide should be controlled and validated if ethylene oxide is used.

5.5 Batch

The production batch should be identified based on the traceability and quality uniformity of the products.

Generally, production batch should be defined as products continuously manufactured at a certain interval with same formula, process and specification.

5.6 Inspection Items

Including but not limited to the following items: description, identification, compactness, friability, disintegration, loss on drying, residual on ignition, heavy metal and microbial limit.

Unless otherwise specified, above items for the vacant capsules should be determined according to the requirements of capsules preparation and tested according to the method in *Pharmacopoeia of the People's Republic of China*.

Specific identification method should be established and validated to effectively identify the primary film-forming materials of vacant capsules if not included in the *Pharmacopoeia of the People's Republic of China*.

6. Applicability Study

6.1 The applicability study of vacant capsules should be conducted in accordance with the concept of Quality by Design to ensure conformance to requirements of capsules preparation.

6.2 Vacant capsules are mainly used as carriers for drug products and can be filled with solid, liquid and semi-solid contents. The manufacturer of capsules preparation should carry out applicability study based on the characteristics of vacant capsules and its contents.

6.3 Manufacturer of capsules preparation should concern the possibility of cross-linking between vacant gelatin capsules, enterosoluble vacant gelatin capsules and its contents when applicability study conducted. Suitable dissolution medium could be selected in case of need.

6.4 The acid resistance ability and dissolution performance at different pH should be guaranteed for enterosolule vacant gelatin capsules.

6.5 Non-gelatin vacant capsules is suitable for water-sensitive drugs as its lower moisture compared to gelatin vacant capsules. Effect on drug dissolution and bioavailability should be concerned based on its longer disintegration.

6.6 Visual defect and dimension deviation of vacant capsules should be controlled for applicability in production of capsules preparation.

7. Stability

Shelf life should be determined for vacant capsules usually used as carriers and excipients for capsules preparation. Stability study and evaluation should be carried out in accordance with relevant requirements of *Pharmacopoeia of the People's Republic of China*.

8. Packaging, storage and transportation

8.1 Packaging of vacant capsules should ensure effective prevention of contamination and cross-contamination during storage and transportation.

8.2 The inner packaging materials which directly contact with vacant capsules should be pharmaceutical grade or food grade and should

not react with the vacant capsules; the outer packaging materials should keep a certain strength to protect vacant capsules from contamination or extrusion deformation that affect the usage during transportation and storage.

8.3 Vacant capsules should be stored and transported at appropriate temperature and humidity according to the requirements of different products, and in accordance with relevant national regulations.

Reference

1) Pharmacopoeia of the People's Republic of China (2015 edition).
2) Good Manufacturing Practice for Pharmaceutical Products (2010 revision) No. 79 Order of Chinese ministry of health.
3) GB2760-2014 National Food Safety Standard for Use of Food Additives.
4) China National Pharmaceutical Packaging Association standard YBX2000-2007 Vacant gelatin capsules.
5) Nomenclature Principles of General Name for Pharmaceutical Excipients in China (draft for comments).