

SFDA published Regulation of Strengthening Supervision on Pharmaceutical Excipients

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To: Food and Drug Administration in each provinces, autonomous regions, and municipalities

In order to strengthen the supervision on manufacturing and use of pharmaceutical excipients, ensure drug quality, SFDA established *Regulation of Strengthening Pharmaceutical Excipients Supervision* based on *The Drug Administration Law of People's Republic of China*, its implementation rules and other laws and regulations.

State Food and Drug Administration

August 1st, 2012

Regulation of Strengthening Supervision on Pharmaceutical Excipients

Pharmaceutical excipient is important component of drugs. Excipients directly impact the quality of drugs. In order to strengthen the supervision on manufacturing and use of pharmaceutical excipients, ensure drug quality, SFDA established rules as below based on *The Drug Administration Law of People's Republic of China* and its implementation rules, *State Department Special Rules on Strengthening Supervision on Safety of Food and other products*, *Management Rules on Drug Manufacturing Supervision*, *Management Rules on Drug Registration*, *Drug Good Manufacturing Practice* and other laws and regulations.

I. Drug manufacturers must ensure the quality of purchased pharmaceutical excipients

(1) Drug manufacturers is responsible for the the quality of drugs. Must strengthen the management on drug manufacturing and quality to make sure the quality and safety of drugs. Must strictly manage the use of pharmaceutical excipients, use the excipients which meet the requirements to produce drugs according to the formula and manufacturing process approved by Drug Administration. Drug manufacturers must take the major responsibility if there's drug quality issue caused by excipients use which violate the law and regulation.

(2) Drug manufacturers must improve quality management system. Need make sure quality department effectively implement quality assurance and quality control responsibilities. Company management people and people in other departments must not interfere or prevent quality depart implement the responsibilities. Ensure excipient suppliers are audited, suppliers are approved by quality department.

(3) Drug manufacturers must strengthen the audit on excipients suppliers. According to the related requirements in *China Drug Good Manufacturing Practice (2010 revision)*, need periodically conduct quality evaluation on excipient suppliers, conduct quality audit and

retrospective analysis on excipient suppliers' quality system, and set up quality file for purchased excipients and the suppliers.

(4) Drug manufacturers must strictly control the quality of excipients used in drugs. Must conduct test for purchased excipients according to approved excipient specification in drug registration to make sure the excipients meet the requirement to use in drug. For excipients already with China national drug standard, must comply with requirements in China national drug standard (note: such as ChP)

(5) Drug manufacturers need sign quality agreement with major excipient suppliers. Drug manufacturers need timely know the change status of excipients in use, study and evaluate the impact of the change on drug dosage forms, need do related registration according the requirements in *Management Rules on Drug Registration*.

II. Pharmaceutical excipient manufacturers must ensure product quality

(6) Excipient manufacturers must be responsible for product quality. Need strictly implement *Excipients Good Manufacturing Practice*, improve quality management system, strengthen the supplier audit for raw materials used for manufacturing, strict control raw materials quality. Need produce excipients according to the approved formula/manufacturing process when product registration, manage the rules for product batch number, make sure the stability of product quality. For excipients don't have approved license but were used in existed drugs due to historical reason, these excipient manufacturers need produce products according to the agreed quality agreement with drug manufacturer.

(7) Excipient manufacturers must ensure product quality. Need conduct FULL test for each batch of product according to specification approved in excipient license or the specification aligned with drug manufacturers, qualified products can be stored and sold. For excipients already with China national drug standard, must comply with requirements in China national drug standard. All manufacturing documents and records including test data must be reviewed by quality department and must meet requirement before product release, products not meet requirements can not be released.

(8) Excipient manufacturers need cooperate to accept the audit from drug manufacturers. When the change of manufacturing process/raw material origins may impact excipient quality, excipient manufacturers need proactively evaluate the impact, timely inform drug manufacturers.

III. Drug administration implement management on excipients based on classification

(9) Implement management on excipients based on classification.

For **novel excipients and excipients with high safety risk**, implement approval management, these excipient manufacturers need get Drug Manufacturing License, and these excipient products need get excipient registration approval. For other excipients, implement filing management,

which means filing for the manufacturer and the products. SFDA will set up the list of excipients for approval management, and will publish the excipient lists batch by batch.

For excipients need approval management, manufacturers need submit related documents according to requirement. Provincial FDA will conduct on-site inspection and random test according to *Excipients Good Manufacturing Practice*. The excipient product will be approved after pass SFDA review. SFDA will link the excipient registration review with the registration of drug dosage forms using this excipient.

For excipients need filing management, excipient manufacturers need submit related documents to provincial FDA for records. Provincial FDA will conduct on-site inspection and random test when it's necessary.

The requirement for excipients approval and filing will be set up separately. Imported excipients need follow this regulation, submit related files to SFDA for approval or filing.

(10) Increase the requirements for drug registration documents.

Drug manufacturers need submit the information of excipient name, excipient supplier, specification and excipient supplier audit results, etc. in drug registration.

For supplementary application to change excipient type, need evaluate and study, submit study documents and supplier audit results to SFDA for review and approval before begin to use the excipient.

When excipient supplier changes but excipient type doesn't change, drug manufacturers need submit study documents and supplier audit results to provincial FDA for record before start to use it in drugs.

(11) Strengthen the management on Pharmaceutical excipients standard. SFDA organize China Pharmacopeia committee to draft and revise pharmaceutical excipient quality standard, and publish pharmaceutical excipients national drug standard, study to draft pharmaceutical excipients recommended standard. Each level of Drug administration department will supervise and inspect according to national drug standard.

IV. Drug regulatory authorities must strengthen whole-process supervision on the production and use of pharmaceutical excipients

(12) Local drug regulatory authorities of all levels shall implement regulatory responsibilities. Routine supervision on drug manufacturers shall be reinforced in respective administrative regions, with focuses on whether drug manufacturers produce products in accordance with approved manufacturing process and formulations; whether pharmaceutical excipient manufacturers are audited in accordance with supplier audit requirements; whether the excipients used are tested in accordance with the corresponding quality standards; whether change excipient in formulation without approval; whether records are made filling the change in accordance with requirements when change suppliers.

(13) Local drug regulatory authorities of all levels need enhance supervision on excipients manufacturing. Routine supervision on excipients manufacturers need be conducted in respective administrative regions, or extend the inspection on excipient manufacturers when find problems during the supervision and inspection on drug manufacturers. Inspection focuses on whether the production of pharmaceutical excipients complies with *Pharmaceutical Excipient Good Manufacture Practice*; whether quality of raw materials are strictly controlled; whether production is conducted in line with approved or filed manufacturing process; whether batch management systems and factory inspection systems are set up. The excipients produced by such manufacturers as refuse to be inspected shall not be used by drug manufacturers.

(14) Local drug regulatory authorities of all levels need strength supervision and random inspection on excipients. According to inspection result, identify key inspection points and specify inspection range and requirements. Random inspections shall cover excipient manufacturers and drug manufacturers which use pharmaceutical excipients. Random inspections need be conducted more frequently and strictly on those manufacturers which with problems have been identified during previous supervisions and inspections.

(15) Drug regulatory authorities of all levels need strengthen inspection and implement more severe punishment. Such drug manufacturers and pharmaceutical excipient manufactuers as breach law and regulations in terms of production and use of pharmaceutical excipients along with their persons-in-charge shall be investigated and punished pursuant to *The Drug Administration Law of People's Republic of China*, *Special Rules of the State Council on Strengthening the Supervision and Management on Safety of Food and other products* and other regulations. Cases of gross violation shall subject to severe punishment. Cases identified as crime shall be transferred to public security organs, and criminal liabilities shall be investigated under the law.

V. Emphasis on database establishment, set up credibility management mechanism.

(16) Set up pharmaceutical excipient database. Drug manufacturers need fill in the information on excipients used in their products in accordance with use information of excipients approved by drug regulatory authorities, and notify relevant excipient manufacturers to assist them with filling in the excipient information, submit information to respective provincial drug regulatory authorities. State Food and Drug Administration and provincial drug regulatory authorities consolidate the relevant information and build up pharmaceutical excipient databases with comprehensive dynamic information of production and use of excipients.

(17) Set up credit files of excipient manufacturers. Drug regulatory authorities of provincial level shall set up credit files for excipient manufacturers, make the results of inspections and random inspections on excipient manufacturers public for drug manufacturers' references when selecting and using excipients.

(18) The public shall be encouraged to participate in the supervision. Industry associations,

third-party organization and the public shall be supported in supervising and reporting violations in terms of the production and use of excipients, for the purpose of jointly maintaining quality safety of drugs and excipients. Relevant industry associations shall enhance industrial self-discipline, promote construction of industrial integrity, boost classification management and guide drug manufacturers and excipient manufacturers to operate under law with integrity.

The rule shall be executed from **February 1, 2013** and State Food and Drug Administration shall be responsible for interpretation.

Chinese version is available at <http://www.sfda.gov.cn/WS01/CL0844/73959.html>