



Rapid announcement of Inspectional observations < ORANGE* Letter >

Pharmaceuticals and Medical Devices Agency

* Observed **R**egulatory **A**ttention / **N**otification of **G**MP **E**lements

Importance of thorough management of outsourced activities

<< Related GMP Ministerial Ordinance** Clause: Article 11, Paragraph 5 >>

** GMP Ministerial Ordinance: Ministerial Ordinance on Standards for Manufacturing Control and Quality Control for Drugs and Quasi-drugs (MHLW Ministerial Ordinance No. 179 dated December 24, 2004)

Observation

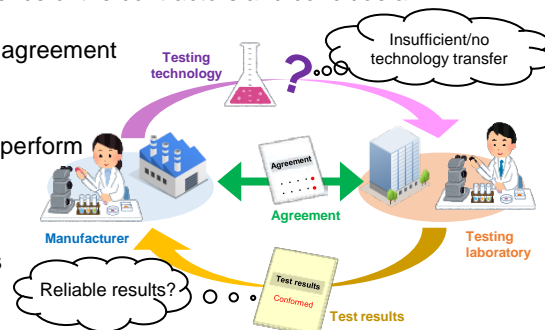
Suitability and competence of a testing laboratory are not adequately assessed, prior to outsourcing testing activities.

< Background >

- ◆ GMP Ministerial Ordinance provides that when a manufacturer outsources "part of manufacturing and quality control including testing," the manufacturer shall confirm suitability and competence of the contractors and conclude an agreement prior to the outsourcing.
- ◆ The manufacturer outsourced testings of drug products after signing an agreement with a testing laboratory.

< Actually observed situation >

- ◆ Prior to outsourcing testing activities, the manufacturer didn't sufficiently perform technical transfer of the testing methods to the testing laboratory, and it was not confirmed whether the tests to be outsourced could be properly implemented.
- ◆ An agreement between the manufacturer and the testing laboratory was concluded and the testing was started without confirming the suitability and competence of the testing laboratory.
- ◆ Similar operations were identified in the record of the already outsourced testings as well as in the planned outsourcing.



< Possible problem and risk >

- ◆ Even though the manufacturer and the testing laboratory are sharing same testing procedure, it can not exclude the risk of obtaining inappropriate results from the testing laboratory in the absence of appropriate technology transfer. This is because the conditions of the test environment (such as analytical equipment, reagent supplier, testing water, laboratory room temperature/humidity, etc.) and the organization system (including the proficiency level of the person in charge of testing and the management system of analytical equipment) may differ from those of the manufacturer.
- ◆ There is a possibility of releasing products based on inappropriate test results, that poses a risk of distribution of defective products that do not meet the intended quality.

(observed at a packaging/labeling/storage manufacturing site in Japan)

Check point



- ❑ Is the manufacturer confirming and assuring the performance of the testing laboratory such as below by appropriately conducting technical transfer and audit?
 - The testing laboratory has a system for appropriately performing assigned testing.
 - Analytical performance is appropriate and equivalence of the testing with that of the manufacturer is established.
- ❑ Is a necessary agreements concluded after clarifying the requirements that the contract acceptor must comply with, including the provisions of GMP Ministerial Ordinance?
- ❑ Does the manufacturer periodically confirm that the contract acceptor is carrying out outsourced activities properly and efficiently, and request improvements if any deficiencies are identified?

Operations can be outsourced, but "responsibilities" cannot be outsourced!!

- ✓ Prior to concluding an agreement, the manufacturer must assess the contract acceptor's qualification and competence to conduct the outsourced activities.
- ✓ It is important for the manufacturer to manage the contracted activities thoroughly such as (1) providing the contract acceptor with information and knowledge necessary for implementing the outsourced activities appropriately, (2) monitoring and reviewing of the contract acceptor's capability and performance of the outsourced activities, and (3) requesting improvements as necessary.
- ✓ It is also important for the contract acceptor to proactively acquire technical information and other relevant details from the contract giver in order to fulfill the outsourced activities appropriately!

