Contract manufacturer agreement

Author:
Max Lazar

Legal background

The contract manufacturer agreement is not a document that is voluntarily agreed between a contract giver and a contract acceptor, but is a requirement from the EU GMP Guide (see Figure 1).

In the USA, contracts are expected to exist as indicated within drug regulations and guidance and both the contract giver and contract acceptor are held responsible for conformance with drug GMP. The US FDA expects to see an executed Quality Agreement as a contract which specifically addresses all quality responsibilities between the contract giver and the contract acceptor. While the FDA does not discuss contract requirements in the same detail as found within the EU GMP Guide, such requirements still exist and are based upon the GMP principles expected under US law. It is a matter of a complex set of topics that is discussed and reviewed as part of supplier audits and the GMP inspection by the respective authorities in individual countries.

Figure 1 Legal background: EU requirements

Legal background - EU GMP Guide
Chapter 7 Contract manufacture and analysis Principle: "Contract manufacture and analysis must be correctly defined, agreed and controlled in order to avoid misunderstandings which could result in a product or work of unsatisfactory quality. There must be a written contract between the Contract Giver and the Contract Acceptor which clearly establishes the duties of each party. The contract must clearly state the way in which the Qualified Person releasing each batch of product for sale exercises his full responsibility."

Minimum requirements for contents

The contract manufacturer agreement should include as a minimum the items discussed below.

- Definition of responsibilities:
  This includes the responsibilities for the following operations:
  - manufacturing and packaging,
  - quality control,
  - problems of a pharmaceutical-technical nature,
  - release for dispatch/shipment and for sale.

The responsible persons should be listed by name and respective function with specimen signatures, if possible in an appendix to the contract.

- Scope of the contract acceptor's duties:
  This involves the agreement of the responsibilities for production, packaging, quality control and procurement. Since this part can sometimes turn out to be very large, it is advisable to define the duties and activities in an appendix along the lines of the list of signatures. The advantage of this is that if there are changes, only the appendices have to be adapted, rather than the whole contract. In this way, both parties can avoid a lot of administrative effort, since it is no longer necessary to review each individual page and the focus can be placed simply on the appendices.
- Documentation: Here it should be specified, which documents and records must be handed over by the contract acceptor to the contract giver after manufacturing is concluded. The retention of documentation (including the operating procedures) should also be agreed.

- Determination of the production site: Specifying a location prevents production of a preparation being changed to a sub-manufacturer without the contract giver being informed.
- List of preparations: Listing the preparations under contract in an appendix is profitable here too, as only one appendix will need to be adapted in case of additions.
- Prices and delivery dates
- Compliance with the legal provisions
- Agreements relating to additional analysis of starting materials
- Conformity of the manufacturing instructions: The contract giver is obliged to check and sign the contract acceptor's manufacturing instructions.
- Development batches: In particular, this section must describe the risk of a defective batch in the development and improvement phase.
- Liability: It often requires a lot of time to find a solution to this issue that is acceptable to both parties.
- Audits: The timing, frequency and scope of the audits should be established here. From a USA perspective, the contract giver should clearly have the authority to perform audits on an as needed basis should they become necessary for a specific reason. The contract acceptor would be expected to facilitate such requests should they become a regulatory need.
- Retention samples: The responsibility for the storage of the retention samples of manufactured goods, starting materials and packaging material should be established. The scope of the sampling for retention samples during routine production should also be established.
- Transport: The responsibilities during transport (potentially of starting materials from the contract giver to the contract acceptor and finished products from contract acceptor to contract giver) should be clearly defined.
- Release of artwork: Since the contract acceptor is not responsible for the content on the printed packaging material, all artwork must be approved by the contract giver.
- Deviations: The contract acceptor must inform the contract giver in the event of deviations from specifications and arrangements.
- Complaints: An action plan for handling of complaints should be established
- Change control: The contract acceptor must be informed if there is a change of supplier of starting materials or packaging material that is provided by the contract giver. This is important in that the contract acceptor often includes the permitted supplier or manufacturer in the manufacturing instructions or formulation.
- Regular review of the contract: The interval between reviews of the contract should not exceed 2 years.

A model contract for contract manufacture is shown in chapter 17.A.8 "Framework contract for contract manufacture and quality control" of the GMP MANUAL. This chapter is available as PDF file for download.

Author:

Max Lazar,
FDA Regulatory Compliance Consulting,
USA

