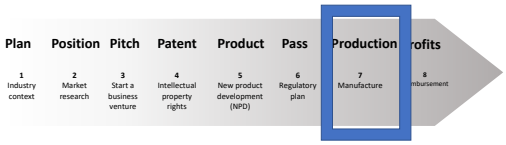
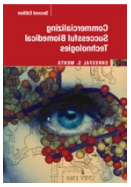


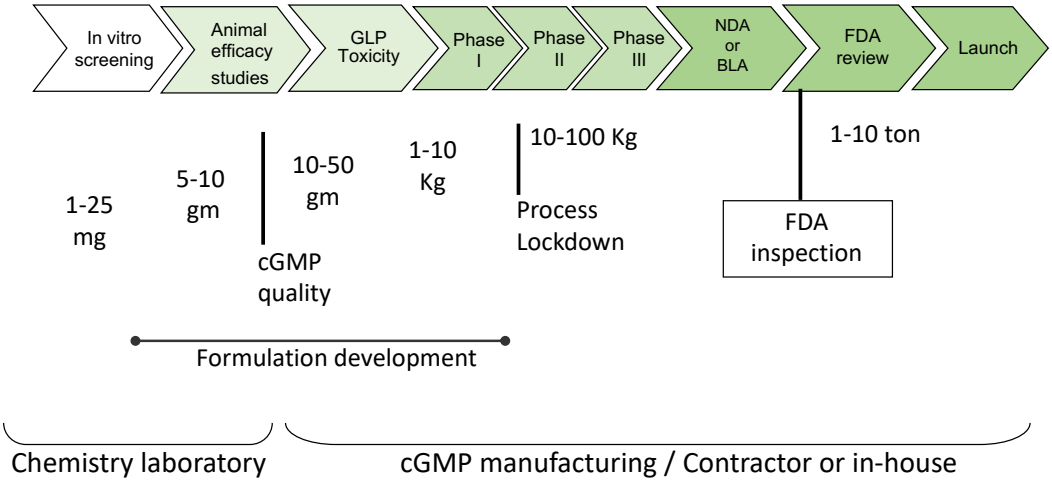


Chapter 7: Practical Tips and Notes on Manufacturing

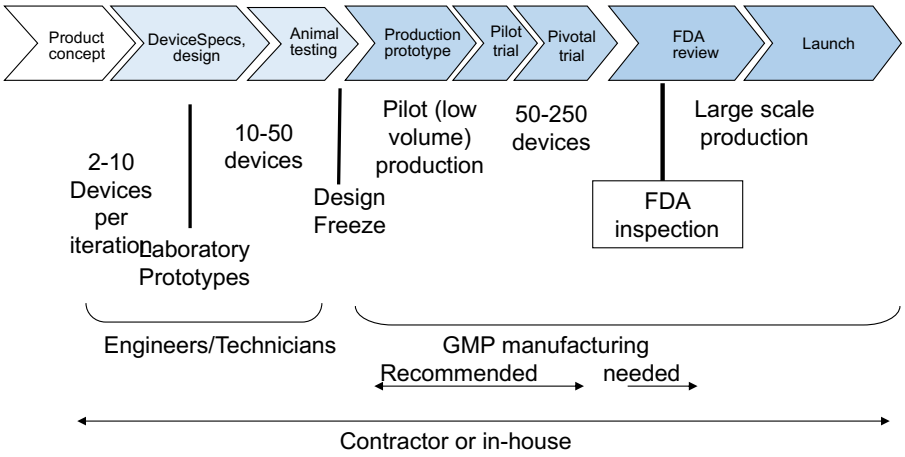
Q. When to scale and how much should I plan to manufacture during development?

- The figures below lay out the approximate quantities needed at various development stages (typically need GLP or GMP quality) for drugs and devices.

Manufacturing scale up during drug (biologics and small molecule) development:



Manufacturing scale up during medical device development:

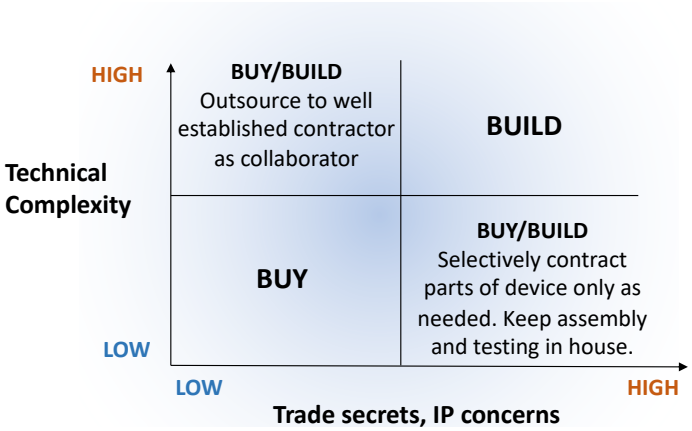


Q: What is the difference between Good Manufacturing Practices (GMP) and Good Laboratory Practices (GLP)?

- GLP and GMP regulations both govern quality in testing of a new product but have vastly different roles.
- The GLPs are designed to protect scientific data integrity, and to provide the EPA or FDA with a clear and auditable record of open-ended research studies. In contrast, the GMPs are intended to demonstrate to the FDA whether or not individual batches of a regulated product are manufactured according to pre-defined manufacturing criteria.
- In general, "lot release" or "lot conformance" testing of regulated products produced for sale, like finished pharmaceuticals, should be done under GMP. Safety testing and efficacy testing should be done under the GLP testing regulations.
- Current good manufacturing practices (cGMP) are defined as "a set of current, scientifically sound methods, practices or principles that are implemented and documented during product development and production to ensure consistent manufacture of safe, pure and potent products." GMP regulations are far-ranging and apply to not only testing but every step of the manufacturing process. The focus is on promoting consumer safety by preventing things like cross-contamination, microbial contamination, or lack of drug efficacy due to problems in the manufacturing process. GMP quality controls extend into every aspect of the manufacturing process from people to raw materials to processing and packaging.
- Good Laboratory Practices (GLP) – are a set of quality system standards that are recommended by various regulatory bodies including the FDA. In general, GLPs apply to premarket or preclinical research and testing..
- GLPs include numerous measures to promote the reliability of data. For example, each study must have a study protocol that is approved by the testing facility's management. Procedures and calibrations must be recorded, dated, and signed. Records must be retained securely for two years after completing the study
- A comparison for US and European (OECD) countries' GLP regulations are here: https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/fda-bioresearch-monitoring-information/comparison-chart-fda-and-epa-good-laboratory-practice-glp-regulations-and-oecd-principles-glp
- GMP regulations for medical device manufacturing are detailed here: https://www.fda.gov/medical-devices/quality-system-qs-regulationmedical-device-good-manufacturing-practices/medical-devices-current-good-manufacturing-practice-cgmp-final-rule-quality-system-regulation

Q. How to make the decision between contracting out manufacturing or building manufacturing internally ?

- A simple strategic analysis is shown in the graphic below:



- In manufacturing biomedical products, building one's own facility for a new product is a high-risk investment to make before the product is launched.

- Many companies start by using a contract manufacturing organization (CMO) (buying the capacity as needed) and once approval is obtained, start building their facility and transfer the process from the CMO.

- In general, the decision to build or outsource manufacturing has a lot of input considerations that need review and discussion, the above figure is only one set of considerations around the specific product. Table 7.2 in the text lists a number of other factors that must be evaluated, including capacity and costs.