Technology Transfer from a CDMO Perspective

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Key Definitions

CDMO – Contract Development/Manufacturing Organization, a company that is paid to provide pharmaceutical dosage form development services to support early to late-phase clinical trials all the way to commercialization. Services can include but are not limited to: clinical trial material manufacturing, relevant analytical testing, and regulatory affairs guidance.

Technology Transfer – *"The goal of technology transfer activities is to transfer product and process knowledge between development and manufacturing, and within or between manufacturing sites to achieve product realization"* (ICH Q10 [1], paragraph 3.1.2)

Key Definitions (continued)

Sending Unit – *"The involved disciplines at an organization where a designated product, process, or method is expected to be transferred from"*

Receiving Unit – *"The involved disciplines at an organization where a designated product, process, or method is expected to be transferred and executed"*

(Both definitions above from ISPE Good Practice Guide: Technology Transfer, 2nd Edition)

Common Examples of Technology Transfer (of Oral Solid Dosage Forms)

- Pre-formulation complete, need to develop dosage form
- Dosage form development underway, but need to manufacture clinical supplies (Case Study #1)
- Scale-up for late-phase clinical supplies (Case Study #2)
- Inter-site transfer of approved commercial product (life-cycle management)

Case Study #1 – Virtual Pharma

- Sponsor has limited or no OSD expertise and no facilities of their own to manufacture drug product under cGMP's (…and very little time to get to the clinic!)
- Sponsor has licensed compound believed to be an Active Pharmaceutical Ingredient (API)
- Sponsor supplied with abbreviated technical package for API: some basis for QTPP, limited analytical method information, incomplete API characterization or limited formulation info

CS #1 – Where do we start?

- Complete the characterization of API (typically requires collaboration between sending and receiving units)
- QbD Assessment (CQA, Risk Assessment)
- Non-GMP prototype manufacturing by Pharm Dev (limited scale, typically ~1kg batch size)
- Analytical Dev will use prototypes for methods development

CS #1 – What is the next step?

- CDMO Pharm Dev will report/present outcomes of prototypes with focus on QbD mindset, with phase-appropriate risk assessment
- Pharm Dev would manufacture confirmation batch to be placed on abbreviated stability in most cases
- CDMO Analytical Dev will have methods in place to be validated with phase-appropriate considerations for execution

CS #1 – What is the end point?

- Following obtaining acceptable drug product stability information, sponsor agrees to move to GMP manufacturing/testing/release of clinical trial material
- Clinical trial material dosed in a limited-population Phase I study
- Reality check: Are we ready to scale up? How deeply do we dig back into QbD when we do? …
- Collaboration between sponsor and CDMO on phase-appropriate development reports

Case Study #2 – Medium/Big Pharma

- Sponsor transferring a formulation/process developed in-house (or at a 3rd-party) at a smaller scale with phase appropriate QbD already underway
- Analytical methods have been validated in a phase-appropriate manner
- Drug product has already been manufactured under GMP and dosed in a Phase I study (…and safety profile is acceptable)
- Sponsors typically have in-house subject-matter experts

CS #2 – Where do we start?

- Sponsor and CDMO review existing technical packages prepared by sending unit and agree on strategy for transfer to receiving unit
- Sponsor and CDMO identify gaps in capabilities between the sending and receiving units (This is critical…)

CS #2 – What are the next steps?

- Plan for Pharm Dev experimentation developed with QbD mindset, targeting Pilot/Commercial scale work
  - Quality Target Product Profile must already be established
  - Critical Quality Attributes should be in place
  - Risks identified and agreed upon
  - Deliverables to include identification of both Critical Process Parameters and Design Space
- Analytical work will center on drafting of and agreement to a transfer protocol highlighting phase-appropriate validation of methods

CS #2 – What is the end point?

- Successful completion of Pharm Dev experimentation will conclude with registration batch manufacturing by receiving unit
- Full support of release and stability testing by analytical team from receiving unit
- Then… Sponsor and CDMO collaborate on submission-ready reports covering Pharmaceutical and Analytical Development activities (These reports tend to be much more lengthy than those generated in CS #1)

Technology Transfer Discussion Points (from the perspective of CDMO)

1) CDMO is obliged to offer a compliant pathway for execution of Technology Transfer, mitigating risk to Sponsor
2) Sponsors have budgets
3) Points 1 and 2 above are seldom harmonized
4) Negotiations around risk assessment often result in truncating the compliant pathway…

Questions?

- How long does technology transfer take?
- How much does it cost a sponsor?
- What types of technology transfers do I prefer the most?

THANK YOU!

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