Scope of Work Tool for Technology Transfers - APIs

Background Information

1. Why is the process being transferred?
2. What safety issues have been identified with the process?
3. What portion of the process has been transferred before? Was that transfer successful?
4. What is the maximum scale at which the API has been produced?
5. What is the expected scale for the proposed transfer?
6. What are the known vulnerabilities of the API synthetic process?
7. What steps of the process appear to be operator-dependant for achieving acceptable results?
8. How many times has the process been replicated, and at what scale?
9. Which steps have been examined using a statistical design approach?
10. What persistent impurities have been identified?
11. Which steps have been examined with intentional spiking experiments to determine the fate of, and purging ability for, known or potential impurities?
12. Which raw materials have known instabilities, or a history of borderline quality attributes?
13. Which raw materials have likelihood for containing regioisomers or stereoisomers as impurities?
14. Which raw materials, raw material precursors, intermediates, or related impurities possess potential genotoxicant alert structures?
15. What level of vendor qualification has been performed for raw material suppliers?
16. Which process wastes may pose a significant problem for disposal?

Technical Process Considerations

1. What critical process parameters have been identified (e.g., time, temperature, stoichiometry, concentration, mixing, etc.)?
    a. What are the current setpoints for these factors?
    b. What are the proven acceptable ranges for these factors?

   c. What setpoint values have resulted in failures? What specific process or product attribute failures were observed in these cases?

2. What is known about the effect of moisture upon the process / product?
3. What is known about the mass balance for the process?
4. What are the known catalyst poisons (if catalysts are used)?
5. What in-process control testing has been applied?
   a. What reaction sampling issues have been identified (e.g. sampling inhomogeneity, instability, quenching protocol needed)?
   b. What in-process analytical methods are currently in place, and are those methods qualified or validated?
   c. Are qualified reference standards of intermediates and final products available for performing in-process control tests?
6. What process hold-points have been identified? Have hold times been qualified experimentally?
7. What purification processes are employed?
   a. Crystallization – metastable zone width identified?
   b. Chromatography – “OK pool” and “rich-cut” specifications set?
   c. Distillation – fractionation specifications set?
8. What cleaning methods have been validated for the process?

Expectations

1. What constitutes a successful transfer of this process?
   a. Product Purity – what specifications must be met?
   b. Product Yield – what is the expected yield, and what is the acceptable lower limit?
   c. Product Physical Form – what particle size, bulk density, and polymorphic form specifications must be met?

Timeline and Budget

1. What is the timeline for completion of the transfer?
2. What is the overall budget for completing this transfer?