आईएफटीएम विश्वविद्यालय, मुरादाबाद, उत्तर प्रदेश

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Topic: Granularity Of TT Process (API, Excipients, Finished Products, Packaging Materials)

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2024

Granularity of TT Process (API, excipients, finished products, packaging materials)

Starting materials

The specifications of the starting materials (APIs and excipients) to be used at the RU should be consistent with reference batches (development batches, bio batches or batches manufactured at the SU). Any properties which are likely to influence the process or product should be identified and characterized.

Active Pharmaceutical Ingredients (API)

The SU should provide the drug master file (DMF) and any relevant additional information on the API to the RU to be checked against the specifications of the API. The following information should be provided:

- manufacturer;
- flow chart of synthetic pathway, outlining the process, including entry points for raw materials, critical steps, process controls and intermediates;
- definitive form of the API (including photomicrographs and other relevant data) and any polymorphic and solvate forms;

- solubility profile;
- partition coefficient (including the method of determination);
- intrinsic dissolution rate (including the method of determination);
- particle size and distribution (including the method of determination);
- bulk physical properties, including data on bulk and tap density, surface area and porosity as appropriate;
- water content and determination of hygroscopicity, including water activity data and special handling requirements;
- microbiological considerations (including sterility, bacterial endotoxins and bioburden levels where the API supports microbiological growth) in accordance with regional pharmacopoeial requirements;
- specifications and justification for release and end-of-life limits;
- summary of stability studies conducted in conformity with current guidelines, including conclusions and recommendations on retest date;
- listing of potential and observed synthetic impurities, with data to support proposed specifications and typically observed levels;

• information on degradants, with a listing of potential and observed degradation products and data to support proposed specifications and typically observed levels;
• potency factor, indicating observed purity and justification for any recommended adjustment to the input quantity of API for product manufacturing, providing example calculations; and
•special considerations with implications for storage and/or handling, e.g. safety and environmental factors and sensitivity to heat, light or moisture.

Excipients

The excipients to be used have a potential impact on the final product. Their specifications as well as the DMF should, therefore, be made available by the SU for transfer to the RU site. The following information should be provided for all types of excipients:

• description of functionality, with justification for inclusion of any antioxidant, preservative or any excipient above recommended guidelines;
• manufacturer;

- specifications, i.e. monographs and additional information that may affect product processing or quality for compendia excipients, or a complete listing of specifications, including analytical methods and justification for release limits for non-compendial excipients. For excipients used for the first time in a human drug product or by a new route of administration, the same level of detail as for a drug substance should be provided;
- special considerations with implications for storage and/or handling, including but not limited to safety and environmental factors (e.g. as specified in material safety data sheets) and sensitivity to heat, light or moisture solubility; and
- regulatory considerations, i.e. compendial status and appropriate regulatory information for non-compendial excipients; information on residual solvents or organic volatile impurities; and documentation to support compliance with transmissible animal spongiform encephalopathy certification requirements (where applicable).

Finished Products Depending on the type of dosage form, the SU should provide relevant information on physical properties of excipients to the RU, including:

- definitive form (for solid and inhaled dosage forms);
- solubility profile (for solid, inhaled and transdermal dosage forms);
- partition coefficient, including the method of determination (for transdermal dosage forms);
- intrinsic dissolution rate, including the method of determination (for transdermal dosage forms);
- particle size and distribution, including the method of determination (for solid, inhaled and transdermal dosage forms);
- bulk physical properties, including data on bulk and tap density, surface area and porosity as appropriate (for solid and inhaled dosage forms);
- compaction properties (for solid dosage forms);
- melting point range (for semi-solid/topical dosage forms);
- pH range (for parenteral, semi-solid/topical, liquid and transdermal dosage forms);

• ionic strength (for parenteral dosage forms);
• specific density/gravity (for parenteral, semi-solid/topical, liquid and transdermal dosage forms);
• viscosity and/or viscoelasticity (for parenteral, semi-solid/topical, liquid and transdermal dosage forms);
• osmolarity (for parenteral dosage forms);
• water content and determination of hygroscopicity, including water activity data and special handling requirements (for solid and inhaled dosage forms);
•moisture content range (for parenteral, semi-solid/topical, liquid and transdermal dosage forms);
• microbiological considerations in accordance with regional pharmacopoeial requirements (for parenteral, semi-solid/topical, liquid, inhaled and transdermal dosage forms); and
• information on adhesives supporting compliance with peel, sheer and adhesion design criteria (for transdermal dosage forms).

Packaging

• Information on packaging to be transferred from the SU to the RU include specifications for a suitable container/closure system, as well as any relevant additional information on design, packing, processing or labeling requirements needed for qualification of packaging components at the RU. For quality control testing of packaging components, specifications should be provided for drawings, artwork, material.

Documentation: The documents used in technology transfer are presented in table.

Documentation for transfer of technology (TOT)

Key task	Documentation provided by SU	Transfer documentation
Project definition	Project plan and quality plan (where separate documents), protocol, risk assessments, gap analysis	Project implementation plan TOT protocol
Quality agreement Facility assessment	Plans and layout of facility, buildings (construction, finish) Qualification status (DQ, IQ, OQ) and reports	Side-by-side comparison withRU facility and buildings; gap Analysis Qualification protocol and report
Health & Safety assessment	Product-specific waste management plans Contingency plans	

Skill set analysis and training	SOPs and training documentation (product-specific operations, analysis, testing)	Training protocols, assessment results
Analytical method transfer	Analytical method specifications and validation, including in-process quality control	Analytical methods transfer protocol and report
Starting material Evaluation Equipment selection and transfer	Specifications and additional information on APIs, excipients Inventory list of all equipment and systems, including makes, models, qualification status (IQ, OQ, PQ). Drawings, manuals, logs, SOPs (e.g. set-up, operation, cleaning, maintenance, calibration, storage)	Side-by-side comparison with RU equipment (makes, models, qualification status) Gap analysis. Qualification and validation protocol and report

Process transfer: manufacturing and packaging	**Reference batches (clinical, dossier, bio-batches) Development report (manufacturing process rationale),History of critical analytical data Rationale for specifications, Change control documentation, Critical manufacturing process Parameters Process validation reports Drug master file. API validation status and report(s) Product stability data Current master batch manufacturing and packaging records List of all batches produced Deviation reports, Investigations, complaints, recalls Annual product review**	**History of process development at RU, Experiences at RU should be recorded for future reference Provisional batch mfg document (RU to develop) Provisional batch packaging document (RU to develop) Description of process at RU (narrative, process map, fl ow chart) Process validation protocol and report**
Cleaning	Cleaning validation, Solubility information; therapeutic doses; category (toxicology); existing cleaning SOPs; validation reports chemical and micro; agents used; recovery study	Product- and site-specific cleaning SOPs at RU Cleaning validation protocol and report

THANK YOU