Design Of Technology Transfer Of Drug Product From R&D To Manufacturing Site And Manufacturing Site To Manufacturing Site

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Abstract: In recent years, there is a growing awareness that an appropriate transfer of manufacturing technologies (technology transfer) is important to upgrade drug quality as designed during R&D to be a final product during manufacture as well as assure stable quality transferred for many reasons between contract giver and contract acceptor during manufacture. The drug quality, it is desired to make sure 5 W’s and 1 H, that is what, when and why information should be transferred to where and by whom and how to transfer, then share knowledge and information of the technology transfer each other between stake holders related to drug manufacturing. Transfer of Technology (TT) is defined as “a logical procedure that controls the transfer of an established process together with its documentation and professional expertise to a site capable of reproducing the process and its support functions to a predetermined level of performance. In most cases, scale-up occurs in several stages. Small-scale laboratory development from 0.5 to 2 kg can be scaled up to 5-10 kg and then 20-100 kg on a pilot scale. Production scale can typically range from 200 kg to greater than 1000 kg. The ultimate goal for any product as it advances through development is to produce a formulation and a process that will be robust enough for routine commercial manufacture. Technology transfer contributes Quality-by-Design (QbD) principles by identifying critical quality attributes, the key manufacturing parameters that affect those attributes, and ways to control those manufacturing parameters which has its own set of challenges. The development of a robust formulation and process through the use of design of experiments, as well as understanding the critical vs.

Keywords: Transfer of Technology, Quality-by-Design

Introduction: The ever-changing business strategies of pharmaceutical companies increasingly involve intra- and inter-company transfers of technology for reasons such as the need for additional capacity, relocation of operations or consolidations and mergers. Technology transfer is the practice of transferring scientific findings from one organization to another for further development so that new products such as medicines, educational tools, electronic devices, safety equipment and health services can become available to the public. Technology Transfer is the intersection between business, science, engineering, law and government. Technology transfer is the process by which basic science research and fundamental discoveries are developed into practical and commercially relevant applications and products. Whether a tablet, a transdermal patch, a topical ointment, or an injectable, the transformation of a pharmaceutical prototype into a successful product requires the cooperation of many individuals. Traditionally, technology transfer teams were charged with moving a physical process from research and development into production while that the role remains critical, today’s transfer team plays a larger part, helping the company attain its strategic goals throughout the product life cycle. The three primary considerations to be addressed during an effective technology transfer are the plan, the persons involved, and the process. A plan must be devised to organize the personnel and the process steps. Once prepared, the plan must be communicated to the involved parties in research, at the corporate level and at the production site. The success of any program is highly dependent on the effectiveness of the communication preceding its implementation. Whether from basic research to applied technology or from one firm to another, the transfer of technology is fundamentally a matter of the flow of human knowledge from one human being to another. This can be through education, the scientific literature, or direct human contact. At the legal level, one thinks about licenses dealing with legal rights to use the particular technologies in the particular context but it is the human level that dominates the managerial and economic reality.
1.1 Importance of technology transfer:

1. Effective Technology transfer can give standardized process, Recommend minimal base Documentation to support the technical transfer process, define key terms and consistent interpretation, Facilitate timely and cost effective technology transfers.

2. To elucidate necessary information to transfer technology from R&D to actual manufacturing.

3. To elucidate necessary information to transfer technology of existing products between various manufacturing places.

1.2 Why technology transfer is required?

The development and transfer of knowledge and technology has been and will continue to be critical to success in pharmaceutical industry. For putting the product on the shop floor to the market for public use involves integration of so many activities. If technology transfer isn’t done right than

- Process validation may be unsuccessful.
- Delayed regulatory approval and/or product launch.
- Flawed processing may result in High rate of batch rejections, costly schedule revisions, and excessive labour requirements.
- Analytical methods cannot support production.
- Incomplete documentation.
- Product does not perform as intended!

The Technology transfer integrates different key functions like project definition, team development, facility assessment, skill set analysis and training, analytical method transfer, raw material component evaluation, supply quality, equipment selection and transfer, process transfer, validation, data review, conclusion/ sign off and post transfer surveillance.

1.3 Scope

Definition of Technology Transfer: It’s an ability of a Receiving Unit to perform transferred technology, to the satisfaction of all parties and any, or all, applicable regulatory bodies. “Technology transfer can be considered successful if a Receiving Unit can routinely reproduce the transferred product, process or method against a predefined set of specifications as agreed with a Sending Unit and/or a Development Unit.”

Each time there is a change in scale, there is technology transfer. Technology transfer is critical for achieving rapid scale-up with control over how the manufacturing process is achieved. A general recipe can be converted into a master recipe for batch control in a specific plant at a given scale. “This conversion is a matter of identifying which recipe parameters are sensitive to scale and replacing class-based parameters with instance-based parameters.”

Ideally, development and manufacturing teams share a common information model for process definitions. “This model would capture process definitions and parameters in a machine-readable format that can be rendered into documents for human interactions.

REASONS FOR TECHNOLOGY TRANSFER

1) Lack of manufacturing capacity – The developer of technology may only have manufacturing equipment which is suitable for small scale operation, and must collaborate with another organization to do large scale manufacturing.

2) Lack of resources to launch product commercially - The original inventor of technology may only have the resources to conduct early-stage research such as animal studies and toxicology study, but doesn’t have the resources to take technology through its clinical and regulatory phases.

3) Lack of marketing and distribution capability - The developer of technology may have fully developed the technology and even have obtained regulatory approvals and product registrations, but it may not have the marketing and distribution channels.

4) Exploitation in a different field of application - Each partner may have only half of the solution i.e. the developer of the technology might be capable of exploiting the technology itself in the field of diagnostic applications and may grant exploitation right to commercial partner for the exploitation of therapeutics application.

2.1 MATERIAL AND METHOD

2.1.1 LIST OF EQUIPMENT USED IN PROCESS

<table>
<thead>
<tr>
<th>Sr.no</th>
<th>Equipment</th>
<th>Make</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Vibratory sifter</td>
<td>RP Products, Mumbai</td>
</tr>
<tr>
<td>2</td>
<td>Rapid mixer granulator(150 L)</td>
<td>Saral Engineering, Mumbai.</td>
</tr>
<tr>
<td>3</td>
<td>Fluid bed drier (60 kg)</td>
<td>Saral Engineering, Mumbai.</td>
</tr>
<tr>
<td>4</td>
<td>Pillar blender(150 L)</td>
<td>RP product, Mumbai</td>
</tr>
</tbody>
</table>
TABLE 1: List of Equipment

<table>
<thead>
<tr>
<th>No</th>
<th>Equipment</th>
<th>Vendor name</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>Co-mill</td>
<td>RP product, Mumbai</td>
</tr>
<tr>
<td>6</td>
<td>Rotator compression machine (20)</td>
<td>Cadmach, Ahmedabad</td>
</tr>
<tr>
<td>7</td>
<td>Combo deduster with metal detector</td>
<td>Technofour</td>
</tr>
<tr>
<td>8</td>
<td>Tablet inspection machine</td>
<td>Camopbell Electronics</td>
</tr>
<tr>
<td>9</td>
<td>Weighing balance machine</td>
<td>Mettle Electronics</td>
</tr>
<tr>
<td>7</td>
<td>HVAC System</td>
<td></td>
</tr>
</tbody>
</table>

TABLE 2: List of material

2.1.2 MATERIAL USED IN PROCESS

<table>
<thead>
<tr>
<th>Sr. No</th>
<th>Ingredients</th>
<th>Vender name</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Lisinopril Dihydrate equivalent to Anhydrous Lisinopril</td>
<td>Hetero drug</td>
</tr>
<tr>
<td>2</td>
<td>Mannitol</td>
<td>Roquette</td>
</tr>
<tr>
<td>3</td>
<td>Calcium hydrogen phosphate Dihydrate</td>
<td>Innophos</td>
</tr>
<tr>
<td>4</td>
<td>Corn Starch</td>
<td>Roquette</td>
</tr>
<tr>
<td>5</td>
<td>Starch Pregelatinised (Stach 1500 LM)</td>
<td>Colorcon</td>
</tr>
<tr>
<td>6</td>
<td>Purified Water</td>
<td>In house</td>
</tr>
<tr>
<td>7</td>
<td>Starch Pregelatinised (Stach 1500 LM)</td>
<td>Colorcon</td>
</tr>
<tr>
<td>8</td>
<td>Colloidal Silicon Dioxide</td>
<td>Degussa</td>
</tr>
<tr>
<td>9</td>
<td>Magnesium Stearate</td>
<td>Merck</td>
</tr>
</tbody>
</table>

2.1.3 Scale up efforts were directed with emphasis on following aspects –
A. Dispensing
B. Sifting
C. Dry mixing
D. Granulation
E. Drying
F. Sizing
G. Blending and lubrication
H. Compression
I. Tablet Inspection

2.1.4 Batch specification
The following batches were manufactured as a part of scale up study-
B.No.LT01, LT02 was manufactured using API with excipients, premixing, compaction, milling and blending time was optimized and blend homogeneity was evaluated. Compression of 2.5 mg strengths tablet was manufactured to evaluate the compression parameters, uniformity of dosage units, coating parameters and dissolution rate profile.

<table>
<thead>
<tr>
<th>product</th>
<th>Batch size</th>
<th>pack size</th>
<th>market</th>
<th>Shelf life</th>
<th>Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lisinopril 2.5 mg Tablets</td>
<td>400,000 Tablets</td>
<td>44.00 kg</td>
<td>20 T</td>
<td>24 months</td>
<td>Lupin Aurangabad</td>
</tr>
</tbody>
</table>
TABLE 3: Batch specification

2.2 Process optimization/Range justification studies –
Details of input materials -

<table>
<thead>
<tr>
<th>Sr. No</th>
<th>Ingredients</th>
<th>Specification</th>
<th>Function</th>
<th>LT01(kg)</th>
<th>LT02(kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Batch Size</td>
<td>Batch Size</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>44 kg</td>
<td>44 kg</td>
</tr>
<tr>
<td>1</td>
<td>Lisinopril Dihydrate equivalent to Anhydrous Lisinopril</td>
<td>Ph. Eur/ IH</td>
<td>Active Ingredient</td>
<td>1.000</td>
<td>1.106</td>
</tr>
<tr>
<td>2</td>
<td>Mannitol</td>
<td>Ph.Eur/IH</td>
<td>Diluents</td>
<td>17.600</td>
<td>17.600</td>
</tr>
<tr>
<td>3</td>
<td>Calcium hydrogen phosphate Dihydrate</td>
<td>Ph.Eur./IH</td>
<td>Diluents</td>
<td>8.800</td>
<td>8.800</td>
</tr>
<tr>
<td>4</td>
<td>Corn Starch</td>
<td>NF/EP</td>
<td>Granulating Agent</td>
<td>12.048</td>
<td>11.942</td>
</tr>
<tr>
<td>5</td>
<td>Starch Pregelatinised (Stash 1500 LM)</td>
<td>NF/EP</td>
<td>Disintegrant</td>
<td>1.600</td>
<td>1.600</td>
</tr>
<tr>
<td>6</td>
<td>Purified Water</td>
<td>BP</td>
<td>Binder solvent</td>
<td>8.000</td>
<td>5.500</td>
</tr>
<tr>
<td>7</td>
<td>Starch Pregelatinised (Stach 1500 LM)</td>
<td>Ph. Eur/ IH</td>
<td>Disintegrant</td>
<td>2.400</td>
<td>2.400</td>
</tr>
<tr>
<td>8</td>
<td>Colloidal Silicon Dioxide</td>
<td>NF/ EP</td>
<td>Glidant</td>
<td>0.220</td>
<td>0.220</td>
</tr>
<tr>
<td>9</td>
<td>Magnesium Stearate</td>
<td>NF/EP</td>
<td>Lubricant</td>
<td>0.332</td>
<td>0.332</td>
</tr>
</tbody>
</table>

TABLE 04: Detail Of Input Material

2.3 BRIEF MANUFACTURING PROCEDURE:
2.3.1 DISPENSING:
Dispensing all the raw materials required for manufacturing of scale up batch of Lisinopril tablets 2.5mg as per raw material requisition sheet.

2.3.2 SIFTING:
1. Lisinopril dihydrate, Mannitol sifted through 60# S.S. sieve on vibratory sifter and collected in double polythene bag lined container.
2. Sifted corn starch through 60# S.S. sieve on vibratory sifter and collected in double polythene bag lined container.
3. Sifted Starch Pregelatinised and Calcium hydrogen Phosphate dihydrate through 40# S.S. sieve on vibratory sifter and collected in double polythene bag lined container.

2.3.3 DRYMIXING
Transferred the sifted materials of step (1), (2) and (3) in to bowl of Rapid mixer granulator (RMG) and mixed for 15 minutes by keeping impeller at “slow” speed and chopper “off”.

2.3.4 GRAUINATION
- Added 4.5L purified water into bowl of rmg of previous step 7.4.3. with the help of s.s. scoop& spatula.
- Started the rmg & mixed for 2 minutes keeping impeller and chopper at “slow” speed.
- Stopped the rapid mixer granulator and scrapped the contents from the side walls of bowls, blade, chopper and inside of lid with the help s.s. scoop and spatula.
- Again started the mixer and mixed for 02 minutes by keeping impeller and chopper at slow speed.
- Stopped the rapid mixer granulator and scrapped the contents from the side walls of bowls, blades, chopper and inner side of lid with the help scraper.
- Again started the mixer and mixed for 02 minutes by keeping impeller and chopper at fast speed. Checked the consistency of wet mass and required consistency was not obtained.
- Stopped the rapid mixer granulator and scrapped the contents from the side walls of bowls, blades, chopper and inner side of lid with the help scraper.
Additionally again started the mixer and mixed the content for 2 minutes by keeping impeller and chopper at fast speed. Checked the consistency of wet mass and desired consistency was obtained resulting in granulation end point. Ammeter reading of impeller at granulation and point was 10 amperes.

Unload the wet granules in two FBD bowls by keeping impeller and chopper at slow speed.

2.3.5 DRYING
- Place the FBD bowl containing wet granules of previous step under the retarding chamber and fitted it to the retarding chamber by operating the control panel.
- Intermittent racking was done.
- For lot-I, at the end of drying, outlet temperature and LOD of dried granules was 35.2°C and 3.0 to 4.0 % w/w.
- Total drying time required was 88 minutes.

2.3.6 SIZING
- Loaded the dried granules passed through #30 S.S. Sieve on vibratory sifter cum co-miller by using 1.0 mm screen of sifter and miller.
- Collected the sized granules into Pillar blender bin.

2.3.7 BLENDING AND LUBRICATION
Sifting of active and extra granular material:
- Sifting together Colloidal silicon dioxide and Starch Pregelatinised through 40 mesh S.S. sieve using vibratory sifter and collected into double polyethylene bag.
- Sifting Magnesium stearate through 40 mesh S.S. sieve using vibratory sifter and collected into double polyethylene.

Blending:
Added sifted material into the bin of Pillar blender (150 L) containing sized granules of previous step (a) and mixed for 20 minutes at 16 RPM

Lubrication:
- Added sifted material of into the bin of Pillar blender (150 L) of step (b) and mixed for 5 minutes at 16 RPM.
- Sampling: 200g of lubricated blend was withdrawn from bin of Pillar blender as a composite sample for assay analysis of API as per product release specification.
- 1.500g of lubricated blend was withdrawn from bin of Pillar blender for physical characteristics evaluation.

2.3.8 COMPRESSION
Compression was performed on Single Rotary Compression machine as per specification. Compressed tablets were passed through metal detector to remove tablets with any metallic piece. In process tests performed and recorded during compression.

1] Optimization of Compression for Lisinopril 2.5 mg:
In optimization of compression we can evaluate hardness challenge test and speed challenge test.

A] For Batch LT01
(1) Hardness challenge test
In hardness challenge test we can take 20 tablets in a hardness tester (Dr. Schleuniger of 8M model company Pharmatron) from low hardness, medium hardness and high hardness and checking the thickness and disintegration time. The tablets were compressed at different hardness and the parameters were recorded. Thickness can be checked in vernier where 20 tablets thickness can be measured. Disintegration test can be done on disintegration test apparatus. One tablet was placed in each 6 tube of the disintegration test apparatus and suspended in the beaker to move up and down for 15 minutes.

(2) Speed challenge test
In this test we can check the effect of speed on average weight, uniformity of weight, thickness, friability and disintegration time at low machine speed, optimum machine, and high machine speed in compression machine - cadmach-20 station (CTX-20).
Average weight can be checked in weighing balance (metler telledo) where 20 tablets can be weighed and its average can be calculated. Thickness can be checked in vernier where 20 tablets thickness can be measured. Disintegration test can be done on disintegration test apparatus. One tablet was placed in each 6 tube of the disintegration test apparatus and suspended in the beaker to move up and down for 15 minutes. Friability test can be done in Roche friabilator in it 20 tablets where taken and weighted in a weighing balance and then put it on friabilator and rotate at 25r.p.m speed for 4 minutes. After completing the 100 revolution in 4 minutes tablets where taken off from it and weighed it again and calculated from given formula:

\[ \% \text{Friability} = \frac{\text{Initial weight-final weight}}{\text{Initial weight}} \times 100 \]

The tablets were compressed at different machine speed and the parameters were recorded. The blend of the above step was compressed using 6.5 mm round shaped concave punches with 2.5 embossed on lower punch and breakline on upper punch.

B] For Batch LT02
(1) Hardness Challenge Test
In hardness challenge test we can take 20 tablets in a hardness tester (Dr. Schleuniger of 8M model company Pharmatron) from low hardness, medium hardness and high hardness and checking the thickness and disintegration time.
The tablets were compressed at different hardness and the parameters were recorded.
2) Speed Challenge Test

In this test we can evaluate the effect of speed on average weight, uniformity of weight, thickness, friability and disintegration time at low machine speed, optimum machine, and high machine speed in compression machine - cadmach-20 station (CTX-20). Average weight can be checked in weighing balance (metler telledo) where 20 tablets can be weighed and its average can be calculated. Thickness can be checked in vernier where 20 tablets thickness can be measured. Disintegration test can be done on disintegration test apparatus. One tablet was placed in each 6 tube of the disintegration test apparatus and suspended in the beaker to move up and down for 15 minutes. Friability test can be done in Roche friabilator and in it 20 tablets where taken and weighted in a weighing balance and then put it on friabilator and rotate at 25r.p.m speed for 4 minutes. After completing the 100 revolution in 4 minutes tablets where taken off from it and weighed it again and calculated from given formula:

\[
\%\text{Friability} = \frac{\text{Initial weight-final weight}}{\text{Initial weight}} \times 100
\]

The tablets were compressed at different machine speed and the parameters were recorded. The blend of the above step was compressed using 6.5 mm round shaped concave punches with 2.5 embossed on lower punch and breakline on upper punch.

2) Uniformity of Dosage units of tablets at different speeds of compression

Uniformity of Dosage units can be done by HPLC and calculation can be done by following formula-

A. Calculation: Percentage dissolved of label claim = \( \frac{\text{AT}}{\text{AS}} \times \frac{\text{AS}}{\text{AFT}} \times \frac{\text{P}}{100} \times \frac{1}{\text{Molecular weight of active}} \times \frac{\text{Molecular weight of active}}{\text{Molecular weight of active + salt}} \)

Where \( \text{AT} \) is Absorbance of sample solution; \( \text{AS} \) is Absorbance of standard solution; \( \text{AS} \) is Assay factor of STD solution; \( \text{AFT} \) is Assay factor of sample solution; \( \text{P} \) is Percent potency of sildenafil citrate; \( \text{C} \) is Label claim of tablet.

2.3.9 Tablet Inspection

It involves passing of compressed tablets through tablet Inspection machine for detected tablets.

2.3.10 Product details:

<table>
<thead>
<tr>
<th>3.4.1</th>
<th>Label Claim</th>
<th>Each uncoated tablet contain: Lisinopril dihydrate Ph. Eur Equivalent to anhydrous Lisinopril …………………. 2.5 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.4.2</td>
<td>Overage (%w/w)</td>
<td>Nil</td>
</tr>
<tr>
<td>3.4.3</td>
<td>Shelf life</td>
<td>24 Months</td>
</tr>
<tr>
<td>3.4.4</td>
<td>Active percentage Pharmaceutical Ingredient</td>
<td>2.27 %</td>
</tr>
</tbody>
</table>

2.4.0 Exhibit Batch

After success of scale up batches of the product, manufacturing of exhibit batches was performed. Exhibit batches are processed for filing purposes with different regulatory agencies and confirming that the exhibit batch will run as freezed scale up value.

Two batches of 2.5mg strength and same quantity as in the scale up batches were processed on the same values which were freezed on scale up batches and samples were evaluated. All the results were found under limit condition and then we perform holding time studies and moisture uptake studies for regulatory filing.

2.4.1 Holding time studies

In this study final blend, core tablets and coated tablets were subjected to holding time study by keeping them in well closed containers at temperature NMT 27°C & relative humidity of NMT 50% and samples were analysed after 30 days. The samples were tested for assay, related substances, dissolution and water content.

To evaluate the holding time of tablets, 10 mg strength was selected.

2.4.2 Moisture Uptake Studies

Tablet blend kept in Petri dish with perforated cap was exposed to temperature NMT 25°C & humidity condition of NMT 60% RH in order to assess the moisture uptake tendency. The moisture gain was calculated from the weight gained by the blend after periodic interval.

3.0 SUMMARY AND CONCLUSION:

3.1 Summary

Based on the manufacturing details processing, results of blend analysis, data generated by carrying out the in process checks during tablet compression and finished product analysis. It is evident that the product Lisinopril tablets 2.5mg can be successfully manufactured with given set of equipments, environmental conditions and the process.
It is observed that no material retained on the sieve after sifting and sieves are intact before and after the sifting. The dry mixing time for all 2 batches was 15 minute respectively at 11 RPM blender speed. The blend uniformity at 20 minute primarily found to be within the acceptance criteria.

Blending and lubrication time for all batches are 5 minute respectively at 14 RPM (Blender speed). The blend uniformity at 3 minute, Lubricant and in-process taste of complete blend was found to be within the acceptance criteria. The yield obtain at lubricant stage was acceptance limit.

In compression the same punch set was used for all 2 batches and the observation for the in-process parameter like description, group mass of tablets, average mass, uniformity of mass, thickness, hardness, disintegration time, friability and analytical data like disintegration, assay and related substance were found to be found within acceptance criteria. The yields obtained at compression stage for all 2 batches were obtained within limit.

4.0 Conclusion:
The above results of two batches of LT 01 & LT02 tablets, found to be within the predefined acceptance criteria. Process parameter will be assessed and conclusion will be drawn.

<table>
<thead>
<tr>
<th>Sr. no.</th>
<th>Processing Stage</th>
<th>Assessment Parameter</th>
<th>Set value</th>
<th>Observation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Blending</td>
<td>Blender RPM</td>
<td>11 RPM</td>
<td>LT01</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Dry mixing time</td>
<td>15 minutes</td>
<td>LT02</td>
</tr>
<tr>
<td>2</td>
<td>Lubrication</td>
<td>Blender RPM</td>
<td>14 RPM</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mixing time</td>
<td>3 minutes</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Compression</td>
<td>RPM</td>
<td>To be recorded</td>
<td>20-25</td>
</tr>
</tbody>
</table>

TABLE 5 : 26 Process parameter of 2.5mg strength

REFERENCES

3. International Convention and Exhibition, Toronto, Canada, 2006
8. Rauner F, Salari D. Cultural determinants of technology transfer - a case study in human resources planning for steel production. AI & society 2003
9. Reamer A; Icerman Larry; Youtie, Jan. Technology Transfer and Commercialization: Their Role in Economic Development. 2003
11. Technology Transfer Principle & Strategy Chapter
25. Anderson, M., 2007. Making drugs available at affordable prices; how universities technology transfer offices can help developing countries. J. of Intellectual property law and