Technology Transfer or Knowledge Transfer?

Russ Somma, Ph.D.
SommaTech,LLC
Affiliate of IPS
Somerset ,New Jersey

Somma Tech
Ideas that speed pharma products to market

Technology Transfer or Knowledge Transfer?

Let's set a time frame for our discussion.

- ***Assume the last ten years!***

Rationale for this timing is based upon several points.

- ***Retrospective gained from several prior presentations.***
- ***Globalization and corporate initiatives undertaken.***
- ***Somebody opened an information highway!***
- ***Evolution of the expectations from a scale-up group!***

Somma Tech
Ideas that speed pharma products to market

Technology Transfer or Knowledge Transfer?

We can no longer think of "tech transfer" in the traditional sense.

- The literature refers to technology transfer as a business strategy for enhancing R&D and commercialization.
  - ***The transfer dimension has been refined.***
- Our role has traditionally been generating information for products and processes.
  - ***How we generate and manage this information must be refined to create a knowledge store.***

Somma Tech
Ideas that speed pharma products to market

Technology Transfer or Knowledge Transfer?

What has not changed is that technology transfer must deliver a product and process which are validated.

The objectives for validation are:

- ***Demonstrate control over the process and finished product.***
- ***Ensure compliance to internal and external requirements.***
- ***Generate a knowledge base for the product as well as accommodate any further business needs.***

Technology Transfer or Knowledge Transfer?

Technology = Knowledge = Continuous Improvement

This relationship is implicit when we consider:

- ***Process introduction is the start toward business efficiency.***
- ***Validation is just one segment of this continuum.***
- ***Well planned technology/knowledge transfer accelerates corporate learning.***

Technology Transfer or Knowledge Transfer?

Knowledge may be categorized into several areas which we need to manage during tech transfer.

- **Incremental knowledge** is a result of ongoing activities and grows with each transfer project.
- **Tacit knowledge or "sticky knowledge"** can not be communicated in a formal, systematic or codified language. "Commonly referred to as a feel for the process".
- **Explicit knowledge** may be set down in procedures and easily codified.

Technology Transfer or Knowledge Transfer?

A goal in tech transfer is to enhance the explicit knowledge base and minimize the tacit aspects.

- This may be overcome using teams representing all the stake holders (production, development, engineering).
- Assigning staff to facilities which are the target transfer sites for process introduction.
- The sharing of experiences is considered superior to “handbook” type policies. Issues are surfaced readily.

This is easier said than done with various products/processes!

Technology Transfer or Knowledge Transfer?

Explicit knowledge is cost effective and transferable.

- It produces a well defined set of core technologies.
- It speeds development and process introduction.
- We deal with explicit knowledge daily. It is the basis of our work (robust formulations, meaningful specifications).

Technology Transfer or Knowledge Transfer?

Incremental knowledge is the impetus for rethinking business processes and is intrinsic in continuous improvement. We learn as we go and share the experience.

- It improves the quality of “handbooks”.
- It moves the collective knowledge base forward.
- It provides information which reduces uncertainty.
- Reducing uncertainty accelerates process transfer.

Technology Transfer or Knowledge Transfer?

Technology Transfer or Knowledge Transfer?

Technology = Knowledge = Continuous Improvement

So what is at the heart of continuous improvement and what aspect links this in our transfer relationship?

- Learning is more accurately organizational learning.
- Knowledge transfer is the basis for this effort.
- Learning occurs during transfer within teams, across teams and from the market.
- Market learning is gained from what we gather from our competitors (industry news, regulatory citations).

SommaTech
Ideas that speed pharma products to market

Technology Transfer or Knowledge Transfer?

Technology Transfer or Knowledge Transfer?

Organizational learning may be facilitated by various traditional means such as handbooks. Information Technology tools such as Groupware are available to supplement these methods.

- ***Lotus Notes for New Product Development***, permits information transfer among many teams using common drives for critical databases.
- ***Starfire*** is customized to accommodate manufacturing process transfer and provides a means to evaluate scale-up risk.

Technology Transfer or Knowledge Transfer?

Streamline technology transfer by minimizing process complexity. Establish the same process technology at all manufacturing sites.

- Establish a common technology agreement between the launch sites (production) and the development area.
- Integrate it into the transfer strategy.
  - Permits accelerated process introduction.
  - Phase III supplies may be sourced.
- Provides an enhancement of core capabilities.

Technology Transfer or Knowledge Transfer?

Transfer Streamlining

- Combine efforts where possible such as
  - Site Qualification
  - OQ data for the process
  - Use final market image
- Avoid radical process changes, use the SUPAC guides to establish sameness of equipment and process.
- Develop a process using a sub batch concept, for solid dosage forms this reduces validation and supplies a defendable basis for changes in scale.
- Scale-up = increased number of sub batches.

Technology Transfer or Knowledge Transfer?

***Culture of the launch site plays heavily into the way in which we work within the structure. We must establish this upfront*.**

- This is an integral pattern of behavior and thinking.
- “This is the way we do things”.
- Within group companies this is reasonably clear.
- Other affiliations require this to be developed.
- Collaborations must have a two tier approach one is the contractual while the other is a daily working agreement.
- Agreements must be shared with all team members.

Technology Transfer or Knowledge Transfer?

Where will we transfer the product?

While this seems a basic question it actually presents some of the more difficult issues. If we consider the possible scenarios as:

- An existing group company
- Contractor for custom manufacturing aspects
- Collaboration with an established company
- Facilities which are purchased for expansion (avoid purpose built facilities).

Technology Transfer or Knowledge Transfer?

Where will we transfer the product?

We must consider that the area has a supportive infrastructure and this goes beyond a GMP area and QC area!!!

A minimal list includes:

- Water, potable and purified
- Steam, pressure and capacity
- HVAC, environmental and process
- Waste, management, landfill, sewer, solvent emissions
- Permit to operate the business

Technology Transfer or Knowledge Transfer?

Minimal list (continued):

- Labor pool of trained personnel
- Registration with local agencies
- Communication level, language
- Business interruption protection

Technology Transfer or Knowledge Transfer?

Process development should be used as a platform to establish proven acceptable ranges starting early in the development cycle.

Proven acceptable ranges:

- Provide a historical database for the product.
- May start at a broad range during the early stages which are subsequently tightened.
- Require a systematic reporting method which is referenced during pilot scale, scale-up and validation.
- Become a part of the knowledge store for the product,and basis for statistical process control.

Technology Transfer or Knowledge Transfer?

Proven acceptable ranges (continued):

- Establish a chart for all process steps and controllable parameters
- Brief description of the process step and controlled parameter
- The engineering units which are recorded
- The anticipated result for exceeding the proven acceptable range
- Risk evaluation of exceeding the range is it major or minor

Technology Transfer or Knowledge Transfer?

Proven acceptable ranges (continued):

- Establish the operating range to be utilized in the plant for process control
- The proven acceptable range is documented. It may be referenced in the development report, batch records, validation reports and protocols
- Acceptable ranges which are dependent on scale changes may be listed as to be determined (number of spray guns, FBD air volumes)

Technology Transfer or Knowledge Transfer?

FDA instructs investigators to look for a series of product information during PAIs which may be interpreted as a *Knowledge Store*. The title of these data may vary but the information needed may be listed as:

- Drug substance characterization
- Process procedures
- In-process tests
- Finished product specifications
- Dissolution profiles
- Stability

Technology Transfer or Knowledge Transfer?

While it is not required, the completion of technology transfer through validation would appear as the most expedient means to assure rapid market entry.

This appears to suggest it is good business to complete validation prior to a submission!

- This view may not be acceptable to all the players but it seems a logical strategy.
- Our hypothesis is that validation is just one step in the journey to 100% business efficiency (Peak Sales!)

Somma Tech
Ideas that speed pharma products to market

Technology Transfer or Knowledge Transfer?

Establish both a *good scientific* and *common sense* approach to rate each process step as having high, low or no impact on product quality.

This will aid in minimizing the subsequent validation effort (SUPAC equipment terms add clarity).

Critical area checklist:

- Weighing / addition of raw materials (vendors,personnel)
- Pre-blending of materials (volume, bulk density)
- Granulation (speed, rate of addition, time)
- Drying (LOD, time, temperature)

Technology Transfer or Knowledge Transfer?

Critical area checklist (continued):

- Particle size reduction (screen, feed rate, speed)
- Blending / lubrication (time, bulk density, assay)
- Compression (speed, feed rate, force)
- Coating (suspension prep., endpoint, air flow, temperature, spray rate)

This scheme provides for subsequent data review for traits and atypical behavior. Data may be shown graphically to identify process variability within established specifications (process comparability).

Technology Transfer or Knowledge Transfer?

Establishing a technology strategy which will qualify change in the context of scale-up / transfer as well as possible post approval changes expedites product development and shortens approval time.

Effort spent in creating an IVIVC relationship early in the development cycle is well placed.

- While not always possible it will yield benefits for formulation and process optimization and the creation of meaningful specifications.
- The data will be specific to the formulation in question which may be considered a downside.

Technology Transfer or Knowledge Transfer?

An IVIVC strategy makes it part of the methods used to guide formulation development. This approach is used by development contractors.

IVIVC Strategy:

- At the product concept phase use a target in vivo profile and base in vitro specifications on an assumed IVIVC. The prototype is tested using various dissolution methods.
- The result will be a comparison of dissolution methodology with biodata allowing an IVIVC to be established.

Technology Transfer or Knowledge Transfer?

IVIVC Strategy (continued):

- During optimization of the formulation / process the IVIVC is defined and predictions from the IVIVC validated.
- During scale-up the dissolution data are used to judge the impact of process changes,as well establishing final specifications for dissolution.
- The database may be utilized during further scale-up and site transfer as well as supporting post approval changes.

Technology Transfer or Knowledge Transfer?

Alternative methods may be used to determine differences resulting from process modifications which build on establishment of meaningful specs.

- The f 2 test while part of SUPAC may be effectively used to measure differences in dissolution profiles resulting process / formulation changes.
- Comparability protocols may also be based upon these data during later stage changes and subsequent justification to regulatory agencies.

Technology Transfer or Knowledge Transfer?
So Where Are We?

- Technology = Knowledge = Continuous Improvement
- Use Incremental Knowledge to Grow
- Minimize tacit knowledge - Maximize explicit knowledge
- Watch our competitors, monitor the market and learn
- Streamline, reduce complexity and combine efforts
- So whose culture is this anyway?
- Know *a lot* about where you are going
- Use a chart to list proven acceptable ranges
- Make validation part of the business strategy
- Leverage your ability to change (IVIVC)
- Pick up those frequent flyer miles!

Somma Tech
Ideas that speed pharma products to market

Technology Transfer or Knowledge Transfer?

References

M. Subramanian, S. R. Rosenthal, Journal of Management Studies, 6, 773(2) (1998)

O. Gasmann, M. Zedtwitz, R&D Management, 3, 147 (1998)

W.B. Werther, E. Berman, Organizational Dynamics, 3, 20 (1994)

A. Rangaswamy, Journal of Marketing Research, 1, 177(8) (1997)

R. Kieffer, L. Torbeck, Pharmaceutical Technology, 6, 66 (1998)

J. Butler, The Pharmaceutical Journal, 1, 31 (1999)

Guide to Inspection of Solid Dosage Forms Pre/Post Approval Issues for Development and Validation, Issued January, 1994

Technology Transfer or Knowledge Transfer?
References (contd)

P. J. von Dochren, R. St. John Forbes and C. D. Shively, Pharm Tech, 6, 139 (1982)

K. D. Popp, Drug Dev. And Ind. Pharm., 13, 2339 (1987)

K. Chapman, R&D to Manufacturing, ERIPT Meeting, 1983

R. Somma, Technology Transfer, The International Experience, EPTM Meeting, 1990

R. Somma, The Research-Production Interface, AAPS Annual Meeting, 1995

- L.Bush, "The End of Process Validation as We Know it?", Pharm. Tech.,p.36, August, 2005
- R.Somma, "Technology Transfer or Knowledge Transfer", Advances in Tableting Technology, April 2005

Technology Transfer or Knowledge Transfer?

References (contd)

- T. Sami**,** "Novartis Using PAT with aid of IVIVC**",** Validation Times**, p.3,** Vol.5, No.6, 2003
- ICH Q8**,** Pharmaceutical Development, Draft 1, No.3, October 25,2005.
- QbD Principles to be Implemented in Future FDA Guidance**,** DIA Dispatch**,** Oct. 28,2005**.**

Technology Transfer or Knowledge Transfer?

Contact Information

Russ Somma,Ph.D.

SommaTech, LLC

3 Executive Drive

Somerset,NJ 08873

732-748-1990 ext. 203

rsomma@ipsdb.com

SommaTech

Ideas that speed pharma products to market