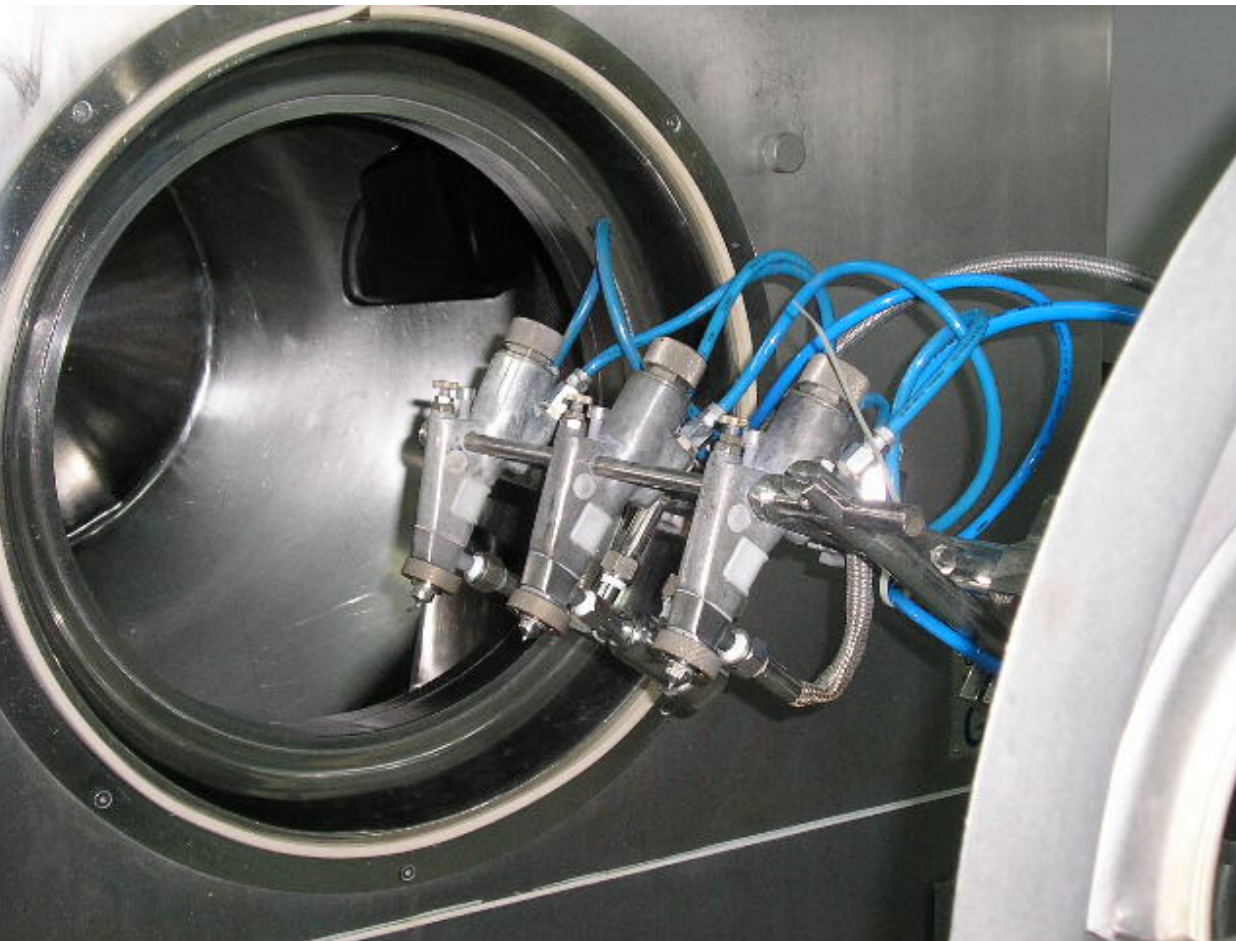


Basic Principles of GMP



Transfer Of Technology Part 1

Annex 7. TRS 961, 2011



Transfer of Technology

- Introduction
- Organization and management
- Premises and equipment
- Quality control: analytical method transfer
- Production: Processing, packaging and cleaning
 - Qualification and validation
- Documentation



Transfer of Technology

- Guideline – provides guidance – in addition to GMP
- Product may be transferred during:
 - Development
 - Scale up
 - Commercial batches - Site transfer (various possibilities)
- TOT defined as “a **logical procedure** that **controls** the **transfer** of any process together with its **documentation** and **professional expertise** between development and manufacture or between manufacturing sites”.

1.1 – 1.2



Transfer of Technology

- Transfer includes:
 - Documentation and ability
 - Knowledge and experience
- Systematic process
- Documented plan
 - in a quality system
- Development, Production and QC
- SU and RU

1.2 – 1.5



Transfer of Technology

Successful transfer needs:

- Project plan covering quality aspects – based on quality risk management
- SU and RU to have similar capabilities, facilities and equipment
- Technical gap analysis is done
 - technical risk assessment and potential regulatory gaps
 - effective process and product knowledge transfer
- Trained staff

1.6



Transfer of Technology

- Problems communicated from RU to SU
- Continuing knowledge management
- Legal and economic implications
 - intellectual property rights, royalties, pricing, conflict of interest and confidentiality
- Transparent process
- Success: Documented evidence that the RU routinely reproduces the transferred product, process or method against a predefined set of specifications as agreed with SU

1.7 – 1.12



Transfer of Technology

Scope: Covers production and quality control

- All dosage forms - adjusted case-by-case basis (e.g. by using risk management principles). Technical agreement to be in place
 - Particularly close control to sterile products, and metered dose aerosols
- Production
 - active pharmaceutical ingredients (APIs),
 - manufacturing and packaging of bulk materials,
 - manufacturing and packaging of finished pharmaceutical products (FPPs)
 - analytical testing

2.1 – 2.2



Transfer of Technology

Covers:

- Transfer of development and production (processing, packaging and cleaning)
- Transfer of analytical methods for quality assurance and quality control
- Skills assessment and training
- Organization and management of the transfer
- Assessment of premises and equipment
- Documentation; and qualification and validation

2.4



Transfer of Technology

Organization and management

- Takes place between an SU and an RU
- (Another party may be involved coordinating / approving)
- Formal agreement
 - responsibilities before, during and after transfer
- Project management plan
 - identifies and controls all the necessary activities

4.1 – 4.4



Transfer of Technology

Transfer protocol to include:

- Objective and scope
- Key personnel and their responsibilities
- A parallel comparison of materials, methods and equipment
- Transfer stages
- Identification of critical control points
- Experimental design and acceptance criteria for analytical methods

4.5



Transfer of Technology

Transfer protocol to include: (2)

- Information on trial production batches, qualification batches and process validation;
- Change control and deviations encountered;
- Assessment of end-product;
- Arrangements for keeping retention samples
- Conclusion and approval

4.5



Transfer of Technology

SU should provide:

- Validation documentation from SU (normally an established process)
- Criteria and information on hazards and critical steps associated with the product, process or method to be transferred, to serve as a basis for a quality risk management (QRM) exercise at the RU

4.6 – 4.7



Transfer of Technology

SU to assess

- the suitability preparedness of the RU before transfer
 - Premises
 - Equipment
 - Support services (e.g. purchasing and inventory control mechanisms, quality control (QC) procedures, documentation, computer validation, site validation, equipment qualification, water for pharmaceutical production and waste management)

4.8



Transfer of Technology

SU and the RU should jointly verify

- Prepare and execute the transfer protocols and reports
 - Checklist and or flow diagram showing the sequence of steps
- IQ and OQ for manufacturing and packaging equipment and analytical equipment
- Room qualification - manufacture and packaging
 - Joint training programmes and training assessment
 - Change control

4.9 – 4.13,
5.4



Transfer of Technology

Project team

- Relevant disciplines from both the SU and RU sites
- Qualifications and experience
- Defined key responsibilities

4.14 – 4.15



Transfer of Technology

Premises



Transfer of Technology

Premises

- Layout, construction and finishing of buildings and services (HVAC water, power, compressed air) - impact on the product, process or method to be transferred of SU
- Risks of processes (e.g. reactions, exposure limits, fire and explosion risks) and emergency planning (e.g. in case of gas or dust release, spillage, fire)
- Operator exposure (e.g. atmospheric containment of pharmaceutical dust)
- Waste streams and provisions for re-use, recycling and or disposal

7.1 – 7.2



Transfer of Technology

Equipment



Transfer of Technology

Equipment

- SU provide a list of equipment, makes and models
- Production including filling, packing and control
- Qualification and validation documentation
 - drawings;
 - manuals;
 - maintenance logs;
 - calibration logs; and
 - procedures (e.g. regarding equipment set-up, operation, cleaning, maintenance, calibration and storage)

7.3



Transfer of Technology

Equipment

- The RU should review the information provided by the SU together with its own inventory list
- Include qualification status (IQ, OQ, PQ) of all equipment and systems
- Perform a side-by-side comparison of equipment at the two sites in terms of their functionality, makes, models and qualification status.

7.4



Transfer of Technology

Factors to be compared include:

- minimum and maximum capacity
- material of construction
- critical operating parameters
- critical equipment components (e.g. filters, screens, and temperature/pressure sensors)
- critical quality attribute
- range of intended use

7.5



Transfer of Technology

Equipment

- Consider location of equipment in facility- and building of the RU
- Draw process maps or flow charts of the manufacturing process
- Consider flows of personnel and material.
- What is the impact of including new products on site?
- Any modification of existing equipment that may be needed to be documented in the transfer project plan.

7.6 – 7.8



Transfer of Technology

Quality control:

**Analytical method
transfer**



Transfer of Technology

- Focus also on transfer of analytical methods
- Registered specifications
- Pharmaceutical products, starting materials, packaging components and cleaning (residue) samples
- Above to be known before process validation study samples are tested
 - Process validation samples may be tested at the RU, the SU or a third laboratory

6.1 – 6.2



Transfer of Technology

Protocol defining the steps for transfer of analytical methods and includes:

- Objective, scope and responsibilities of the SU and the RU
- Specifications of materials and methods
- Experimental design and acceptance criteria
- Reference samples (starting materials, intermediates and finished products)
- Documentation (incl. information to be supplied with the results, and report form; deviations; references and approval)

6.3



Transfer of Technology

The SU's responsibilities (transfer of analytical methods):

- Provide method-specific training
- Assist in analysis of QC testing results
- Define all methods to be transferred for testing a given product, starting material or cleaning sample
- Define experimental design, sampling methods and acceptance criteria
- Provide validation reports (incl. proof of robustness)

6.4



Transfer of Technology

The SU's responsibilities (transfer of analytical methods) (2):

- Provide details of the instruments used
- Provide reference samples
- Provide approved procedures used in testing
- Review and approve transfer reports

6.4



Transfer of Technology

The RU's responsibilities:

- Review analytical methods provided by the SU - agree on acceptance criteria – ensure equipment available and qualified
- Has adequately trained and experienced personnel
- Has documentation system available including / addressing
 - receipt and testing of samples
 - specifications and methods
 - reporting, recording and collating data

6.5

...THEN execute protocol, perform validation, prepare report



Transfer of Technology

Training

- Provided and documented
- Compendial monographs (e.g. The International Pharmacopoeia, European Pharmacopoeia, British Pharmacopoeia and United States Pharmacopoeia)
- Method transfers should take care of the variability and sensitivity of the method and the specifications for the quality parameter
- Experimental designs and acceptance criteria developed
- See examples in next slide

6.6 – 6.8



Transfer of Technology

Test	Considerations for transfer	Replication of tests	Set-up	Acceptance criteria : Direct	Acceptance criteria : Statistically Derived
Assay for potency	<ul style="list-style-type: none"> – <i>Non-specific assay should not be used for stability testing.</i> – Bracketing may be appropriate for multiple strengths 	At each site: 2 analysts × 3 lots, in triplicate (= 18 per site)	Different sets of instruments and columns Independent solution preparation	Comparison of mean and variability	Two one sided <i>t</i> -tests with inter site differences δ 2% , 95% Confidence



Transfer of Technology

Test	Considerations for transfer	Replication of tests	Set-up	Acceptance criteria : Direct	Acceptance criteria : Statistically Derived
Content uniformity	If method is equivalent to assay method, separate transfer is not usually required	At each site: 2 analysts, × 1 lot (= 2 per site)	Different sets of instruments and columns Independent solution preparation	Mean at RU within $\pm 3\%$ of mean at SU; comparison of relative st. dev.	Two one sided <i>t</i> -tests with inter site differences $\delta 3\%$, 95% Confidence



Transfer of Technology

Test	Considerations for transfer	Replication of tests	Set-up	Acceptance criteria : Direct	Acceptance criteria : Statistically Derived
Dissolution	Bracketing may be appropriate for multiple Strengths	6 units (12 if not routine at RU, and for extended release products)		Mean at RU within $\pm 5\%$ of mean at SU	Compare Profile (e.g. F2), or Compare data at Q time points as for assay



Transfer of Technology

Examples

Key Task	Document from SU	Transfer document
Cleaning	SOPs and Validation	SOPs Cleaning validation protocol and report

