DRAFT WORKING DOCUMENT FOR COMMENTS:

WHO guidelines on the transfer of technology in pharmaceutical manufacturing

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**WHO guidelines on the transfer of technology in pharmaceutical manufacturing**

<table>
<thead>
<tr>
<th>Description of Activity</th>
<th>Date</th>
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<tbody>
<tr>
<td>Following a recommendation by the WHO Local Production &amp; Assistance Unit, the Fifty-fifth Expert Committee on Specifications for Pharmaceutical Preparations (ECSPP) recommended that the WHO Secretariat enquire if the <strong>WHO guidelines on the transfer of technology in pharmaceutical manufacturing</strong> should be updated in order to support inspections for COVID-19 therapeutics.</td>
<td>October 2020</td>
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<tr>
<td>Preparation of first draft working document.</td>
<td>November 2020</td>
</tr>
<tr>
<td>Mailing of working document to the Expert Advisory Panel on the International Pharmacopoeia and Pharmaceutical Preparations (EAP) inviting comments and posting of the working document on the WHO website for public consultation</td>
<td>December 2020</td>
</tr>
<tr>
<td>Consolidation of comments received and review of feedback.</td>
<td>February 2021</td>
</tr>
<tr>
<td>Preparation of working document for discussion.</td>
<td>February-March 2021</td>
</tr>
<tr>
<td>Discussion of the feedback received on the working document in a virtual meeting with an expert working group</td>
<td>February-March 2021</td>
</tr>
<tr>
<td>Preparation of working document for next round of public consultation.</td>
<td>April 2021</td>
</tr>
<tr>
<td>Mailing of revised working document inviting comments, including to the EAP, and posting of the working document on the WHO website for a second round of public consultation.</td>
<td>April 2021</td>
</tr>
<tr>
<td>Consolidation of comments received and review of feedback.</td>
<td>June – July 2021</td>
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<tr>
<td>Preparation of working document for discussion.</td>
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<tr>
<td>Discussion of the feedback received on the working document in a virtual meeting with an expert working group</td>
<td>August 2021</td>
</tr>
<tr>
<td>Presentation to the Fifty-sixth meeting of the ECSPP.</td>
<td>October 2021</td>
</tr>
<tr>
<td>Any other follow-up action as required.</td>
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</tr>
</tbody>
</table>
WHO guidelines on the transfer of technology in pharmaceutical manufacturing

Background

During the Fifty-fifth World Health Organization (WHO) Expert Committee on Specifications for Pharmaceutical Preparations (ECSPP) meeting, Expert Committee members were updated on the annual consultation of Good Practices for Health Products and Inspection which took place in July 2020 in a series of virtual meetings due to the COVID-19 pandemic. During these virtual meetings, a group of experts made a series of proposals for future activities, one of which was how to determine whether or not the WHO guidelines on the transfer of technology in pharmaceutical manufacturing (1) should also be updated. This original document was published in 2011. Numerous regulatory changes have been made since then. Transfer of technology is considered an integral part of the product life cycle management and is subject to regulatory expectations. This includes a risk-based and science-based process and method design (such as a quality by design approach), achieving a “state of control” and data governance. The original document thus requires updating, not least to support the consistent supply of therapies for critical needs, including public health emergencies.

The Expert Committee asked the WHO Secretariat to explore this proposal.
78 8. Premises
79 9. Equipment and instruments
80 10. Qualification and validation
81 11. Product life cycle and project management principles
82 12. Phases of a technology transfer project
83  Phase I: Project initiation
84  Phase II: Project planning
85  Phase III: Project execution
86  Phase IV: Project review and closeout
87
88 References
89 Further reading
90 Abbreviations
91 Appendix 1. Example of documentation commonly required for the transfer of technology
92
1. **Introduction**

1.1. Technology transfer is a logical procedure that controls the transfer of any process, together with its documentation and professional expertise. Technology transfers may involve development, manufacturing and testing sites.

1.2. The transfer of production and control procedures of pharmaceutical products from one site to another may take place before or after obtaining regulatory marketing authorization. Product transfer may therefore occur during development, during clinical trials, or for full-scale commercialization and commercial batch manufacturing. The level of rigor applied in the technology transfer should be commensurate with the respective product life cycle phase.

1.3. A technology transfer, particularly one between different companies, has legal and economic implications which may include intellectual property rights, royalties, pricing, conflicts of interest and confidentiality agreements. Such matters should therefore be addressed before and during the planning and execution of the transfer.

1.4. A technology transfer requires a planned approach by trained, knowledgeable personnel working within a quality system, with appropriate documentation, data and information covering all aspects of development, production and quality control (QC), as applicable, and considering the stage of the product life cycle.

1.5. A technology transfer takes place between a sending unit (SU) and a receiving unit (RU). In some cases, it may be advantageous to establish a separate unit to manage the project.

1.6. The technology transfer project should fulfil the following general principles and requirements. There should be:

- a documented project plan covering the relevant aspects of the project;
- a detailed quality risk management plan;
- a comprehensive gap analysis, including due diligence performed covering technical and regulatory aspects;
• similar capabilities between the SU and RU, including but not limited to, facilities and equipment;
• knowledge of the differences in process ability between the SU and RU, including the impact, risk and control strategies to overcome any differences;
• an adequate number of adequately trained personnel with suitable qualifications and experience; and
• effective process and product knowledge management.

1.7. A technology transfer should include relevant documentation, data, information and knowledge from the SU in order to enable the RU to effectively execute the specified process or procedure in, for example, production and QC. A successful transfer of technology should result in documented evidence that the RU can routinely reproduce the transferred product, process or procedure against a predefined set of specifications as agreed between the SU and RU.

1.8. This document should be read in conjunction with other WHO guidelines as referenced below (2-15), as well as other regulatory guidelines which include The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) Q7, Q8, Q9, Q10, Q11 and Q12. This guideline does not intend to replace any of these guidelines.

1.9. This version of the document provides guiding principles reflecting current good practices (GxP) in the transfer of technology and replaces the previous version published by WHO (1).

2. Scope

2.1. This document provides guiding principles on the transfer of technology. The principles apply to investigational products as well as marketed products.

2.2. Throughout development life cycle stages, transfers should be appropriate and proportionate to the phase of the development program to ensure product development knowledge is maintained and processes are appropriately controlled. This guideline should be applied when transferring the technology of manufacturing processes and analytical procedures relating to
active pharmaceutical ingredients (APIs), isolated API intermediates, bulk drug products and finished pharmaceutical products (FPPs).

2.3. The guideline applies to all pharmaceutical dosage forms and may be adapted on a case-by-case basis by using risk management principles. Particular attention should be given to certain complex formulations.

2.4. Although this document focuses on pharmaceutical products, the principles can also be applied to the transfer of production, related processes and controls for other products such as biopharmaceutical products, advanced therapy medicinal products/cellular and gene therapy products, vaccines, medical devices and vector control products.

2.5. Because each transfer project is unique, the provision of a comprehensive set of guidelines specific to a product or process is beyond the scope of this document.

2.6. This document does not provide guidance on any intellectual property, legal, financial or commercial considerations associated with technology transfer projects. These are prerequisites for a successful transfer that need to be defined and controlled prior to the transfer in the course of due diligence. Examples include Health, Safety and Environmental (HSE) Aspects and the availability of a Confidentiality Disclosure Agreement which should be in place prior to the start of the transfer.

2.7. This document addresses the following principal areas:

- organization and management of the transfer;
- transfer of relevant information in production, including but not limited to processing, packaging and analytical procedures;
- documentation, premises, equipment;
- personnel qualification and training;
- quality management and risk management;
- change management and life cycle approach;
- control strategy; and
- qualification and validation.
3. Glossary

The definitions given below apply to the terms used in these guidelines. They have been aligned as much as possible with the terminology in related WHO guidelines and GxP and included in the WHO Quality Assurance of Medicines Terminology Database - List of Terms and related guideline [https://www.who.int/docs/default-source/medicines/norms-and-standards/guidelines/mqa-terminology-sept-2020.pdf?sfvrsn=48461cfc_5], but may have different meanings in other contexts.

acceptance criteria. Measurable terms under which a test result will be considered acceptable.

active pharmaceutical ingredient (API). Any substance or mixture of substances intended to be used in the manufacture of a pharmaceutical dosage form and that, when so used, becomes an active ingredient of that pharmaceutical dosage form. Such substances are intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment or prevention of disease, or to affect the structure and function of the body.

ALCOA+. A commonly used acronym for “attributable, legible, contemporaneous, original and accurate” that puts additional emphasis on the attributes of being complete, consistent, enduring and available – implicit basic ALCOA principles.

bracketing. An experimental design to test the extremes of, for example, dosage strength. The design assumes that the extremes will be representative of all the samples between the extremes.

change control. A formal system by which qualified representatives of appropriate disciplines review proposed or actual changes that might affect a validated status. The intent is to determine the need for action that would ensure that the system is maintained in a validated state.

confirmation testing. An execution of tests that confirm and validate the results obtained by another.

control strategy. A planned set of controls, derived from current product and process understanding that assures process performance and product quality. The controls can include parameters and attributes related to active pharmaceutical ingredient (API) and finished pharmaceutical product (FPP)
materials and components, facility and equipment operating conditions, in-process controls, finished product specifications and the associated methods and frequency of monitoring and control.

corrective action. Any action to be taken when the results of monitoring at a critical control point indicate a loss of control.

critical. Having the potential to impact on product quality or performance in a significant way.

design space. The multidimensional combination and interaction of input variables (e.g. material attributes) and process parameters that have been demonstrated to provide assurance of quality.

drug master file. Detailed information concerning a specific facility, process, packaging material or product submitted to the medicines regulatory authority, intended for incorporation into the application for marketing authorization.

finished pharmaceutical product (FPP). A product that has undergone all stages of production, including packaging in its final container and labelling. An FPP may contain one or more active pharmaceutical ingredients (APIs). In some cases, it may be in combination with a medical device.

gap analysis. The identification of the critical elements of a process which are available at the sending unit (SU) but are missing from the receiving unit (RU) with the objective to assess which gaps have potential impact on the process or method and to mitigate those gaps, as appropriate.

good manufacturing practices (GMP). That part of quality assurance which ensures that pharmaceutical products are consistently produced and controlled to the quality standards appropriate to their intended use and as required by the marketing authorization.

in-process control (IPC). Checks performed during production in order to monitor and, if necessary, to adjust the process to ensure that the product conforms to its specifications. The control of the environment or equipment may also be regarded as a part of in-process control.
installation qualification (IQ). Documented verification that the installations (such as machines
equipment and instruments, computer system components, measuring devices, utilities and
manufacturing) used in a processor system are appropriately selected and correctly installed, in
accordance with established specifications.

intercompany transfer. A transfer of technology between the sites of different companies.

intracompany transfer. A transfer of technology between sites of the same group of companies.

operational qualification (OQ). Documented verification that the system or subsystem performs as
intended over all anticipated operating ranges.

performance qualification (PQ). Documented verification that the equipment or system performs
consistently and reproducibly within defined specifications and parameters in its normal operating
environment (e.g. in the production environment).

process validation. The collection and evaluation of data, from the process design stage through to
commercial production, which establishes scientific evidence that a process is capable of consistently
delivering the active pharmaceutical ingredient (API) or finished pharmaceutical product (FPP) meeting
its predetermined specifications and quality attributes.

qualification. Documented evidence that premises, systems or equipment are able to achieve the
predetermined specifications when properly installed and/or work correctly and lead to the expected
results.

quality assurance (QA). “Quality assurance” is a wide-ranging concept covering all matters that
individually or collectively influence the quality of a product. It is the totality of the arrangements made
with the objective of ensuring that pharmaceutical products are of the quality required for their
intended use.

quality control (QC). All measures taken, including the setting of specifications, sampling, testing and
analytical clearance, to ensure that starting materials, intermediates, packaging materials and finished
pharmaceutical products (FPP) conform with established specifications for identity, strength, purity and other characteristics.

quality planning. Part of quality management, focused on setting quality objectives and specifying necessary operational processes and related resources to fulfil the quality objectives.

quality policy. A brief statement that describes the organization’s purpose, overall intentions and strategic direction; provides a framework for quality objectives; and includes a commitment to meet applicable requirements.

quality risk management (QRM). A systematic process for the assessment, control, communication and review of risks to the quality of the pharmaceutical product throughout the product’s life cycle.

receiving unit (RU). The involved disciplines at an organization where a designated product, process or method is expected to be transferred.

sending unit (SU). The involved disciplines at an organization from where a designated product, process or method is expected to be transferred.

standard operating procedure (SOP). An authorized written procedure giving instructions for performing operations, not necessarily specific to a given product or material, but of a more general nature (e.g. operation of equipment, maintenance and cleaning, validation, cleaning of premises and environmental control, sampling and inspection). Certain standard operating procedures may be used to supplement product-specific master and batch production documentation.

starting material. Any substance of a defined quality used in the production of a pharmaceutical product, but excluding packaging materials.

transfer of technology. A logical procedure that controls the transfer of any process, together with its documentation and professional expertise. Technology transfers may involve development, manufacture and/or testing sites.
technology transfer report. A documented summary of a specific technology transfer project listing procedures, acceptance criteria, results achieved and conclusions.

validation. Action of proving and documenting that any process, procedure or method actually and consistently leads to the expected results.

validation batches. Those batches produced by the receiving unit (RU) to demonstrate its ability to manufacture the transferred product which complies with its predetermined specifications, or as part of process performance qualification.

validation master plan (VMP). A high-level document that summarizes the manufacturer’s overall philosophy and approach, to be used for establishing performance adequacy. It provides information on the manufacturer’s qualification and validation work programme and defines details of and timelines for the work to be performed, including a statement of the responsibilities of those implementing the plan.

validation protocol (VP). A document describing the activities to be performed during validation, including the acceptance criteria.

validation report (VR). A document in which the records, results and evaluation of validation are documented and summarized. It should also contain a conclusion of the outcome of the validation.

4. Due diligence and gap assessments

4.1. A process of due diligence and gap assessment visits of the SU and RU should be some of the first steps when considering a technology transfer project.

4.2. The suitability and degree of preparedness of the RU should be assessed prior to the start of the transfer. The procedure to be followed, results and conclusion should be documented.

4.3. The assessment should be done by a team of appropriately qualified persons with knowledge and experience in the field of GxP and the activity to be transferred. It is recommended that the quality units of the SU and RU participate in this activity.
4.4. The assessment should further cover capabilities and resources related to personnel, premises, equipment and instruments, utilities, cleaning, QC, documentation, computerized systems, qualification, validation and further HSE-related considerations including waste management.

4.5. The assessment to determine feasibility for technology transfer may include technical, business, quality, regulatory and legal aspects.

5. Organization and management

5.1. All technology transfer activities should be organized and planned.

5.2. There should be formal agreements between the parties involved in the transfer of technology, which specify the responsibilities of each party before, during and after transfer. The agreement should cover, for example, data management, data integrity, documentation and validation.

5.3. All the necessary activities to be executed during the technology transfer project should be identified, organized and documented at the start of the project. Responsibilities across the SU, RU, sponsor and Marketing Authorization Holder (MAH) should be defined in writing.

5.4. Where applicable, the MAH should coordinate the transfer of the necessary documentation related to the technology transfer from the SU to the RU, including the relevant regulatory documents.

5.5. The SU should provide criteria and information on inherent risks, hazards and critical steps associated with the process, product or procedure to be transferred. These may serve as a basis for the risk assessment exercise.

5.6. The technology transfer should be managed by responsible persons from each site (the SU and RU) and any other units with the appropriate technical and quality oversight. A technology transfer team may be appointed with identified and documented responsibilities.
5.7. The team members should have the necessary qualifications and experience to manage the particular aspects of the transfer.

5.8. The SU should make all the necessary information and knowledge with regard to the product, process or procedure available in relevant documents in order to ensure a successful transfer.

5.9. The RU should be able to accommodate the intended production capacity. If possible, it should be established at the outset whether or not the intention is to perform single-batch manufacture, continuous production or campaigns.

5.10. Consideration should be given to the level and depth of detail to be transferred to support production and any further process development and optimization at the RU as intended under the transfer project plan.

5.11. Consideration should be given to the technical expertise, site technology and site capabilities for the RU. Any process robustness issues should be identified upfront by the SU so that plans may be put in place at the RU.

5.12. The SU should assess the suitability and degree of preparedness of the RU before transfer, with regard to premises, equipment and support services (e.g. purchasing and inventory control mechanisms and pharmaceutical quality system - QC procedures, documentation, computer validation, site validation, equipment qualification, water for pharmaceutical production and waste management).

5.13. The SU and the RU should jointly verify that the following, satisfactorily completed, validation protocols are available:

- installation qualification (IQ) and operational qualification (OQ) data for manufacturing and packaging equipment at the RU site and analytical equipment; and
- qualification of the rooms for both manufacture and packaging at the RU site.

5.14. A training programme should be implemented covering various topics, including those specific to the process, product or procedure to be transferred.
5.15. Changes and adaptations made during the course of the project should be done in accordance with a standard procedure. Risk assessment should cover technical, quality, regulatory and other aspects. The project manager should evaluate the impact to the project cost, schedule, and resourcing based on an updated risk assessment.

5.16. The execution of the technology transfer project should be documented in a report which is supported by the relevant data.

5.17. Whenever possible, the SU should send personnel to the RU site at critical phases of the project to assist with the transfer of knowledge.

5.18. Data should meet ALCOA+ principles.

6. Quality management and quality risk management

6.1. The SU and RU should each have an appropriately designed, clearly defined and documented quality system.

6.2. The quality system should be adequately resourced, implemented and maintained.

6.3. The quality system should incorporate GxP which should be applied to the life cycle stages of the products and processes, including technology transfers.

6.4. The quality system should ensure that:

   • responsibilities are clearly specified in writing;
   • operations are clearly defined in writing;
   • there is a system for quality risk management; and
   • arrangements are made for the documented technology transfer.

6.5. Quality risk management should be implemented as a systematic process for the assessment, control, communication and review of risks.
6.6. The system for quality risk management should be described in writing and cover appropriate areas such as, but not limited to, premises, equipment, materials, products, production, processes, QC, qualification, validation and the process of technology transfer.

6.7. The evaluation of the risk should be based on scientific knowledge and experience including that of the process and product.

6.8. The level of effort, formality and documentation of the quality risk management process should be commensurate with the level of risk.

6.9. The procedures and records for quality risk management should be retained.

7. Documentation

7.1. An authorized technology transfer document, for example, a Master Plan (or Technology Transfer Protocol) should list the intended sequential phases and activities of the transfer, where appropriate. The document should include, for example, the following:

- title;
- objective;
- scope;
- name and addresses of the SU and RU;
- key personnel and their responsibilities;
- phases of the project including key activities, deliverables and the associated accountabilities;
- approximate timing of key activities/deliverables including the timing of trial production batches and validation batches;
- reference to other transfer plan documents relevant to the process being transferred;
- reference to qualification/validation master plans relevant to the process being transferred: equipment/facilities/utilities qualification project plan, site-independent/site-dependent process validation master plan(s), method validation master plan;
- reference to gap assessments and risk assessments;
• acceptance criteria for a successful transfer;
• a parallel comparison of premises, equipment, instruments, materials, procedures, and methods for the transfer under consideration.

Note: A list with examples of documents commonly required in technology transfer is presented in Appendix 1.

7.2. Standard operating procedures (SOPs) should be followed, describing actions to be taken during the technology transfer process.

7.3. Records should be maintained for the activities performed during the technology transfer process (e.g. a technology transfer report). The report content should reflect the protocol and SOPs that were followed. The report should summarize the scope of the transfer, the critical parameters as obtained in the SU and RU, and the final conclusions of the transfer. Changes, deviations, investigations and relevant appropriate actions taken should be recorded. The SU should provide all the relevant supportive documents with data, results and other relevant information to facilitate a successful transfer of technology and also comparison of data.

8. Premises

8.1. The RU should have appropriate premises with the layout, construction and finishing suitable for the intended operations. Utilities such as heating, ventilation and air conditioning, as well as gas and water systems, should have sufficient capacity and should be appropriate for the intended process, product or procedure to be transferred.

8.2. The SU should provide the RU with information on relevant health, safety and environmental issues, including:
• inherent risks of the manufacturing processes (e.g. reactive chemical hazards, exposure limits, fire and explosion risks);
• health and safety requirements to minimize operator exposure (e.g. atmospheric containment of pharmaceutical dust);
emergency planning considerations (e.g. in case of gas or dust release, spillage, fire and firewater run-off); and

• identification of waste streams and provisions for re-use, recycling and/or disposal, including antimicrobial substances.

9. Equipment and instruments

9.1. The SU should provide a list (or similar document) of equipment and instruments involved in the production, filling, packing and QC testing. It should include the makes and models of the relevant equipment and instruments, including those of single-use, to ensure evaluation of similar principles of operation.

9.2. A review and a side-by-side comparison of equipment, instruments, as well as process steps and parameters of the SU and RU should be carried out in terms of their working principle, capacity, make and models to ensure that they are capable of appropriately performing the required processes and methods.

9.3. The facility- and building-specific location of all equipment at the RU should be considered at the time of drawing up process maps or flow charts of the manufacturing process to be transferred, including flow of personnel, flow and intermediate storage of materials.

9.4. Where the review and comparison identify any gaps or differences, the appropriate action should be taken. This may include the adaptation of existing equipment or acquisition of new equipment. Any modification or adaptation of existing equipment to become capable of reproducing the process being transferred should be documented.

9.5. Production volumes and batch sizes at the SU and RU should be compared. Where batch sizes are different, the impact should be assessed as part of risk assessment and the appropriate action planned and taken. Other factors relating to equipment to be reviewed may include:

• minimum and maximum capacity;
• material of construction of contact surfaces;
• critical operating parameters;
• components (e.g. filters, screens, and temperature/pressure sensors); and
• range of intended use.

9.6. The impact of the potential product to be transferred, on existing products manufactured on
site (and vice versa), should be assessed.

10. Qualification and validation

10.1. The extent of qualification and validation to be performed should be determined on the basis
of risk management principles, taking into account the product’s life cycle phase.

10.2. Equipment and instruments should be qualified and calibrated before using them to support
the technology transfer activities.

10.3. Process validation should be done according to guidelines as published in current WHO

10.4. Production processes and analytical procedures should be appropriately transferred to the RU
following documented procedures. Where validation data exist, these should be included in
the transfer.

10.5. For cleaning procedures, development and validation should be done in accordance with the
guidelines as published in current WHO Technical Report Series (6). Points to consider when
using HBEL in cleaning validation (14) should be taken into account in establishing cleaning
procedures, cleanability studies and setting acceptance limits.

10.6. Analytical procedures should be validated or verified according to the guidelines as published

10.7. Qualification and validation procedures, protocols, data and results should be appropriately
recorded. The documents should be retained as defined in procedures.
11. Life cycle approach

11.1. The relevant stage of the life cycle of the facility, equipment, instrument, utility, product, process or procedure to be transferred should be taken into consideration when the transfer is planned and executed. This also applies to the control strategy and process validation.

11.2. The responsible entities should monitor the progress of the project at each applicable stage of the life cycle aspect of the transfer to ensure a successful completion of the transfer.

12. Phases of a technology transfer project

12.1. The technology transfer project plan may be divided into different phases. These may include, for example:

- Phase I: Project initiation;
- Phase II: Project planning;
- Phase III: Project transfer execution; and
- Phase IV: Project review and closeout.

Phase I: Project initiation

12.2. During the initiation phase of the project, a unit should normally identify the need for the technology transfer. This may be because of lack of capacity, transfer from development to commercial site or transfer from one company to another.

12.3. The units should establish initial discussion and identify whether or not there is any interest for such a project (See also section on due diligence above.)

12.4. The RU should be able to accommodate the intended activity.

12.5. The RU should have the necessary technical expertise, technology and capability.
12.6. A sufficient level and depth of detail to support the activity, and any further development and optimization at the RU, should be transferred.

**Phase II: Project planning**

12.7. The SU and RU should jointly establish a team that will coordinate activities and execute the technology transfer exercise. Where the technology transfer involves a site that has limited manufacturing experience or the process being transferred is complex, the SU should consider providing extensive training and on-site support before the project execution phase begins.

12.8. The team should perform a risk assessment based on the available data, information and knowledge of the premises, materials, products, procedures and other related information.

12.9. The team should prepare the technology transfer document such as the project plan.

12.10. The team should develop a control strategy which includes, for example:
- risks;
- raw, starting and packaging material attributes;
- analytical procedures in QC;
- critical quality attributes (CQAs), critical process parameters (CPPs) and in-process controls; and
- acceptance criteria and limits.

12.11. The specifications and critical material attributes of the starting materials (APIs and excipients) to be used at the RU should be consistent with those materials used at the SU.

12.12. The SU should provide the RU with the open part of the Drug Master File (DMF), API Master File (APIMF), or equivalent information, as well as any relevant additional information on the API of importance for the manufacture of the pharmaceutical product.

12.13. The specifications of excipients should be made available by the SU for transfer to the RU site.
12.14. Product, process and procedure knowledge should be an essential part of the transfer process from SU to RU.

12.15. The critical quality attributes, critical process parameters, material attributes, control strategy and any other impacting elements on the quality of the product should be available. (See also ICH guidelines.)

12.16. The SU should provide the product information including its qualitative and quantitative composition, physical description, method of manufacture, in-process controls, control method and specifications, packaging components and configurations, and any safety and handling considerations to the RU.

12.17. The SU should provide any information on the history of process development which may be required to enable the RU to perform any further development and/or process optimization after successful transfer.

12.18. The SU should provide to the RU information on any health, safety and environmental issues associated with the manufacturing processes to be transferred and the implications thereof (e.g. need for gowning or protective clothing).

12.19. The SU should provide to the RU information on current processing and testing, including but not limited to:

- a detailed description of facility requirements and equipment;
- information on starting materials, applicable Material Safety Data Sheet (MSDS) where required, storage and distribution requirements for raw materials and finished products;
- description of manufacturing steps (narrative and process maps or flow charts, and/or master batch records), including the qualification of in-processing hold times and conditions, the order and method of raw material addition and bulk transfers between processing steps;
- description of analytical procedures;
- identification and justification of control strategy (e.g. identification of critical performance aspects for specific dosage forms, identification of process control points,
product quality attributes and qualification of critical processing parameter ranges,
sampling plans, statistical process control (SPC) charts);

• design space, in cases where this has been defined;
• validation information (e.g. validation plans and reports);
• annual product quality reviews;
• stability information;
• an authorized set of protocols and work instructions for manufacturing; and
• environmental conditions or any special requirement needed for the facility or
equipment depending on the nature of the product to be transferred.

12.20. Information on packaging to be transferred from the SU to the RU should include specifications
for a suitable container and closure system, as well as any relevant additional information on
design, packing, processing or labelling requirements and tamper-evident and anti-counterfeiting measures.

12.21. For QC testing of packaging components, specifications should be provided including drawings,
artwork and material.

Phase III: Project transfer execution

12.22. The team should execute the project in accordance with the procedures and agreed plan.

Production (example: finished pharmaceutical product)

12.23. During the transfer process, the RU should identify any differences in facilities, systems and
capabilities and discuss these with the SU. The SU should cooperate with the RU to understand
the potential impact and satisfactorily address this in order to assure equivalent product
quality. Based on the information received from the SU, the RU should consider its own
capability to manufacture and pack the product to the required standards and should develop
the relevant site operating procedures and documentation before the start of routine
production.

12.24. The RU should address the following tasks:
• comparison and assessment of suitability and qualification of facility and equipment;
• description of manufacturing process and flow of personnel and of materials at the RU (narrative and or process maps or flow charts);
• determination of critical steps in manufacture, including hold times, endpoints, sampling points and sampling techniques;
• writing and approval of a training plan, SOPs for all production operations (e.g. dispensing, granulation or blending or solution preparation, tablet compression, tablet coating, encapsulation, liquid filling, primary and secondary packaging and in-process QC), packaging, cleaning, testing and storage;
• evaluation of stability information, with generation of site-specific stability data if required; and
• compliance with regulatory requirements for any changes made (e.g. in terms of batch size).

12.25. The transfer of packaging operations should follow the same procedural principles as those of the product processing.

12.26. RU should determine the need for qualification and validation for the packaging process.

Quality control: analytical procedure transfer

12.27. Analytical procedures used to test pharmaceutical products, starting materials, packaging components and cleaning (residue) samples, if applicable, should be implemented at the testing laboratory before the testing of samples for process validation studies is performed by the RU. The transfer of the analytical procedure may be accomplished by several approaches such as confirmation testing, comparability testing between SU and RU results, co-validation between laboratories, or through a “paper-based knowledge” transfer. The strategy chosen should be risk-based and scientifically justifiable.

12.28. A protocol and Test Transfer Plan defining the steps should be prepared for transfer of analytical procedures. The analytical procedures transfer protocol should include:
• a description of the objective, scope and responsibilities of the SU and the RU;
• a specification of materials and methods;
• the experimental design and acceptance criteria;
• documentation (including information to be supplied with the results, and report forms to be used, if any);
• procedure for the handling of deviations; and
• details of test samples (starting materials, intermediates and finished products).

12.29. The SU's responsibilities for the transfer of analytical procedures typically are to:
• provide method-specific training for analysts and other QC staff, if required;
• assist in analysis of QC testing results;
• define all procedures to be transferred for testing a given product, starting material or cleaning sample;
• define experimental design, sampling methods and acceptance criteria;
• provide any validation reports for procedures under transfer including proof of their robustness;
• provide details of the equipment used, as necessary (part of validation report, if available) and any standard test samples;
• provide approved procedures used in testing; and
• review and approve transfer reports.

12.30. The RU should exercise its responsibility to:
• review analytical procedures provided by the SU, and formally agree on acceptance criteria before execution of the transfer protocol;
• ensure that the necessary equipment for QC is available and qualified at the RU site. The equipment used by the RU during the analytical transfer should meet the appropriate specifications in order to ensure the requirements of the procedure or specification are met;
• ensure that adequately trained and experienced personnel are in place for analytical testing;
• provide a documentation system capable of recording receipt and testing of samples to the required specification using approved test procedures, and of reporting, recording and collating data and designation of status (approved, rejected, quarantine);
• execute the transfer protocol;
12.31. The appropriate training should be provided and all training activities and outcomes should be documented.

12.32. Reference should be made to compendial monographs such as The International Pharmacopoeia, European Pharmacopoeia, British Pharmacopoeia and United States Pharmacopeia, where these are relevant.

12.33. An experimental design should be prepared which includes acceptance criteria for the analytical testing procedures.

12.34. Where products are transferred from one unit to another, the applicable analytical procedures should also be transferred.

12.35. Relevant analytical procedure development and validation documentation should be made available by the SU to the RU, if required.

12.36. The appropriate transfer protocols and procedures should be followed when analytical procedures are transferred.

12.37. The number of analysts involved in the transfer, from both SU and RU, should be defined and justified.

12.38. The parameters to be included in the experimental evaluation of the transfer of the analytical procedure should be defined and justified.

12.39. Acceptance criteria should be set to determine the success of the transfer. Statistical trending of results should be undertaken in order to demonstrate capability of the procedure.
Cleaning

12.40. To minimize the risk of contamination and cross-contamination, adequate cleaning procedures should be followed.

12.41. Cleaning procedures and their validation should normally be site-specific. In order for the RU to define its cleaning strategy, the SU should provide information on cleaning at the SU to minimize cross-contamination due to residues from previous manufacturing steps, operator exposure and environmental impact, including:

- information on cleanability;
- information on solubility of active ingredients, excipients and vehicles;
- minimum therapeutic doses of active ingredients;
- toxicological assessment; and
- existing cleaning procedures.

12.42. Additional applicable information should be provided, such as:

- cleaning validation reports (chemical and microbiological);
- potential degradation products and impurities;
- risks of antimicrobial resistance;
- information on cleaning agents used (efficacy, evidence that they do not interfere with analytical testing for residues of APIs, removal of residual cleaning agents); and
- recovery studies to validate the sampling methodology.

12.43. Before the transfer, the SU should provide information on limits for product residues and the rationale for limit selection.

12.44. Based on the information provided by the SU, cleaning procedures should be designed at the RU, considering relevant characteristics of the residues to be cleaned (e.g. potency, toxicity, solubility), manufacturing equipment design and configuration; and cleaning agent.
Phase IV: Project review and closeout

12.45. The progress and success of the transfer of technology should be monitored and reviewed during and after completion of the project. The review should further ensure that, as appropriate, stability studies are started and continued; post-marketing commitments are monitored; and new material suppliers are integrated into the quality management system.

12.46. Compliance with the procedures and protocols should be verified. Deviations and changes should be documented and investigated where appropriate.

12.47. Where possible, data and results should be subjected to appropriate statistical calculation and evaluation to determine trends, compliance with control limits and capability studies.

12.48. A technology transfer report should be prepared, based on the data and information obtained during the project. The supportive data should be kept and be accessible.

12.49. The report, which should include an assessment of the data and information and a conclusion, should be authorized by the persons responsible in doing so.
References


Further reading

• International conference on harmonisation of technical requirements for registration of 
pharmaceuticals for human use. ICH harmonised tripartite guideline. Pharmaceutical 

• International conference on harmonisation of technical requirements for registration of 
pharmaceuticals for human use. ICH harmonised tripartite guideline. Quality risk 

• International conference on harmonisation of technical requirements for registration of 
pharmaceuticals for human use. ICH harmonised tripartite guideline. Development and 
manufacture of drug substances (chemical entities and biotechnological/biological entities). 

• International conference on harmonisation of technical requirements for registration of 
pharmaceuticals for human use. ICH harmonised tripartite guideline. Technical and 
regulatory considerations for pharmaceutical product life cycle management. Q12. Final 


• International Medical Device Regulators Forum. Essential Principles of Safety and 
Performance of Medical Devices and IVD Medical Devices. 31 October 2018 
(http://www.imdrf.org/docs/imdrf/final/technical/imdrf-tech-181031-grrrp-essential-

Abbreviations

ALCOA+ “attributable, legible, contemporaneous, original and accurate”.

API active pharmaceutical ingredient

FPP finished pharmaceutical product

GMP good manufacturing practices

GxP good practices

ICH The International Council for Harmonisation of Technical Requirements for 
Pharmaceuticals for Human use

IPC in-process control

IQ installation qualification

OQ operational qualification
<table>
<thead>
<tr>
<th>No.</th>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>982</td>
<td>PQ</td>
<td>performance qualification</td>
</tr>
<tr>
<td>983</td>
<td>QA</td>
<td>quality assurance</td>
</tr>
<tr>
<td>984</td>
<td>QC</td>
<td>quality control</td>
</tr>
<tr>
<td>985</td>
<td>QRM</td>
<td>quality risk management</td>
</tr>
<tr>
<td>986</td>
<td>RU</td>
<td>receiving unit</td>
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<tr>
<td>987</td>
<td>SOP</td>
<td>standard operating procedure</td>
</tr>
<tr>
<td>988</td>
<td>SU</td>
<td>sending unit</td>
</tr>
<tr>
<td>989</td>
<td>TRS</td>
<td>Technical Report Series</td>
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<tr>
<td>990</td>
<td>VMP</td>
<td>validation master plan</td>
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<tr>
<td>991</td>
<td>VP</td>
<td>validation protocol</td>
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<tr>
<td>992</td>
<td>VR</td>
<td>validation report</td>
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</tbody>
</table>
### Appendix 1

**Example of documentation commonly required for the transfer of technology***

The table below provides an example of documentation commonly required for the transfer of technology.

<table>
<thead>
<tr>
<th>Aspect</th>
<th>Related documentation</th>
</tr>
</thead>
</table>
| Regulatory | Regulatory process description  
Applied regulatory documentation |
| Starting materials (active pharmaceutical ingredients (API) and excipients) | Drug Master File (DMF), API Master File (APIMF),  
Active Substance Master File (ASMF)  
Material Safety Data Sheets  
Product development report  
Storage conditions  
Stability data  
Forced stability data  
Specifications  
Supplier qualification  
References |
| Formulation | Formulation development reports  
Master formula  
Material compatibility/interaction studies  
Specifications for delivery devices |
| Batch manufacturing | Master of executed batch record  
Scale up information  
Risk assessment  
Critical process parameters In-process control specification  
Scale up protocol and report  
Process validation |
| Packaging | Packaging material specification  
Master of executed packaging record  
Validation  
Sampling plan  
Acceptance Quality Level (AQL) for products and defects  
Packaging validation |
| Finished product | Specification |
| Analytical procedures | Analytical test procedures  
Analytical procedure development  
Analytical procedure validation |
<table>
<thead>
<tr>
<th>Category</th>
<th>Documents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standard test procedures</td>
<td></td>
</tr>
<tr>
<td>Instrument specifications</td>
<td></td>
</tr>
<tr>
<td>Quality control</td>
<td>Sampling procedures (e.g. in-process control)</td>
</tr>
<tr>
<td></td>
<td>Stability testing protocol and procedures</td>
</tr>
<tr>
<td></td>
<td>Release test analytical procedure validation</td>
</tr>
<tr>
<td>Equipment and instruments</td>
<td>List of equipment and instruments</td>
</tr>
<tr>
<td></td>
<td>Preventive maintenance information</td>
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<tr>
<td></td>
<td>Overview of qualification</td>
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<tr>
<td>Cleaning</td>
<td>Cleaning validation master plan</td>
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<tr>
<td></td>
<td>Cleaning procedure development and cleanability</td>
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<tr>
<td></td>
<td>Cleaning procedures</td>
</tr>
<tr>
<td></td>
<td>Health Based Exposure Level (Permitted daily exposure) information reports</td>
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<tr>
<td></td>
<td>Analytical procedures validation for cleaning</td>
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<tr>
<td></td>
<td>Cleaning validation reports and recovery study reports</td>
</tr>
<tr>
<td>Other documents</td>
<td>Recalls and complaint reports</td>
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<tr>
<td></td>
<td>Bio-batch information</td>
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<td></td>
<td>Pilot batch information</td>
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<tr>
<td></td>
<td>History of changes and change management</td>
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<tr>
<td></td>
<td>Hold time protocols and reports</td>
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</tbody>
</table>

*Note: These are examples. All the required documents should be identified for the different tasks.*