MSF Qualification Scheme for International Pharmaceutical Supply

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1. Scope:

- The MSF qualification scheme is concerned with the pharmaceutical quality assessment for drugs. The assessment of medical devices, diagnostic test, vaccines and nutritional products are not covered in this procedure.

- This procedure is applicable to products for international supply, i.e. products supplied through the MSF procurement centres.

- This qualification procedure is not applicable for local purchase, i.e. purchase of drugs within the project countries. For quality assurance principles and assessment of drugs for local purchase refer to the guideline for local pharmaceutical market assessment.

2. Definition:

Qualification is an "essential part of quality assurance. It verifies that the product meets at least the norms and standards set by international organizations. " (WHO Prequalification Project)

3. Objectives:

- To assess the acceptability of pharmaceutical products for international supply
- To clarify and standardize the decision-making procedures:
  - Between MSF operational sections and the procurement centres
  - Between MSF pharmacists and medical directors

4. Principles

4.1. **The basis**:

- The MSF qualification scheme is not intended to interfere with the WHO prequalification (WHO PQ) initiative, nor to duplicate any existing work (GMP inspections, product evaluations) carried out by a National Drug Regulatory (NDRA) in a highly regulated country (refer to definition page)
  - ➔ Any WHO pre-qualified product will be accepted by MSF

➔ Any product registered in a highly regulated country will be accepted by MSF (refer to definition on page 23)
➔ Any other product should be qualified the qualification process described in this document and accepted by the General Directors and the Medical Directors

- The MSF Qualification Scheme is set up to validate product manufacturer couples for the use in MSF projects. However, the MSF validation is not a waiver for national regulations in project countries, and these should be taken into consideration as well.

- This qualification process is conducted through a formal procedure and is formalized through the signature of a Decision Statement by the International Coordination and the Section Pharmacists.

- The characteristics of the qualified product are summarized in a "Product Specification Sheet" (PSS) which is signed by the manufacturer as a commitment to supply MSF a product according to the agreed specifications.

4.2. Responsibilities:

- MSF – General Directors:
  - MSF qualified drugs are often imported in countries where they are not registered by the concerned NDRA. In these cases MSF represented by its General Directors takes the full responsibility
  - Endorse quality assurance policy for medicines of MSF and delegate its implementation to the Medical Directors and the Pharmacist Network

- Medical Directors:
  - Delegate product evaluation to pharmacist under the supervision of the International Pharmacist Coordinator
  - Accept or reject products based on a medical risk-benefit evaluations on the available product information where indicated

- International Pharmacist Coordination[1]:
  - Ensures the correct implementation of the current qualification scheme

[1] Coordination is defined as International Pharmacist Coordinator and the Deputy Pharmacist Coordinator

- Performs the final review of product dossiers and give approval
- Presents product dossiers for decision-making to medical directors where applicable
- Keeps updated information on approved product – manufacturer pair at coordination level

➢ Pharmacists in charge of a product dossier:
- Responsible for collecting the relevant product information from the manufacturer and evaluating against the criteria outlined in the qualification scheme
- Inform the manufacturer of any decisions regarding their products

➢ Responsible Pharmacists of Procurement centres:
- Maintain an updated database of validated product/ manufacturer pairs as reference for procurement

➢ Section pharmacists:
- Ensure that the MSF QA system is functioning according to this procedure by means of an annual audit

4.3. MSF Qualification Tools

- MSF Questionnaires
  - Manufacturer Information File
  - Interagency Product Questionnaire[2]
- MSF Variation Application Form
- Declaration of Equivalence[3]
- Rating table
- Sample Assessment Summary Sheets (SASS)
- Product Assessment Summary Sheet (PASS)
- Product Specification Sheet (PSS)
- Decision Statement (DS)

4.4. Modalities:

- Pharmacists in the procurement centres, the Access Campaign (CAME) or the International Coordination are the key actors for the quality investigations, the technical visits and the compilation and evaluation of

[2] Jointly developed product by the Interagency Group: MSF, UNICEF, ICRC, WHO Prequalification, WHO Procurement, Global Fund, Union for TB and Lung Disease

[3] Declaration of manufacturer that a product provided to MSF is essentially the same than this manufacturer's product with a marketing authorisation in a highly regulated country

the product dossiers. However, any MSF Headquarter (HQ) pharmacist[4] may be involved product assessments (preparation and review of product dossiers).

- Quality Assurance for pharmaceuticals is a backbone of a pharmacists work; all HQ pharmacists have the training and skills required for product evaluations.
- The decision to audit/visit a manufacturing site is the responsibility of the International Coordinator
- External Experts are consulted where necessary. The contracting of an expert is the responsibility of the International Pharmacist Coordinator
- The evaluation of a product dossier is performed against the rating criteria and includes 3 pharmacists:
    - ➔ 1st Pharmacist: initial compilation and assessment of product dossiers
    - ➔ 2nd Pharmacist: independent review of product dossier
    - ➔ International Pharmacists Coordination: Independent final review and approval. This responsibility is delegated to the International Pharmacists Coordination by the section pharmacist[5]
- In case of difficulty or non-consensus, the International Pharmacists Coordinator (IPC) must be involved in the decision
- The characteristics of the qualified product are summarized in a PSS which is signed by the manufacturer. The manufacturer is asked to commit to supply MSF with products in compliance with the specifications laid down in the PSS.
- The IPC informs the procurement centres about the product validation and provides the relevant information for the procurement centers to update their database of purchasable products.
- Section pharmacists endorse this qualification together with the International Pharmacists Coordination by signing a Decision Statement.
- A yearly audit is performed by the section pharmacists (on a sample of 10% of dossiers approved per year) to review the compliance of dossier evaluation with respect to the standards set in the MSF qualification scheme.

5. Assessment Process

Parts:

[4] MSF Headquarter Pharmacists: International Pharmacist Coordination team, Procurement Centre pharmacists, Access Campaign Pharmacists, Section Pharmacists

[5] Section Pharmacist: Pharmacist in medical department of each section

The qualification process is divided in two parts:

- The manufacturing site assessment
- The product dossier assessment

Assessment Process

1. Collect information on manufacturers and of products that are of potential interest to MSF
2. Schedule a site audit or a technical visit if needed
3. Formally decide the status of the manufacturing site
4. Request product dossier (Interagency Product Questionnaire with relevant annexes) from manufacturer
5. Evaluate the product dossier
6. Formalize the decision
7. Inform the manufacturer of the decision
8. Update the databases in purchase centres and at coordination level

5.1. MSF Qualification references

- WHO Good Manufacturing Practices (Quality Assurance of Pharmaceuticals, WHO, vol 2, second edition + WHO Technical Reports Series, No 902, 908 & 917).
- WHO pharmaceutical products specifications (Quality Assurance of Pharmaceuticals, WHO, vol 1 & 2 + WHO Technical Reports Series, No 823, 863,902, 908, 937, 943)
- WHO guiding principles for assessing the acceptability of pharmaceutical products (Procedure for assessing the acceptability, in principle, of pharmaceutical products for purchase by United Nations Agencies), WHO Technical Series Report 908, 943
- WHO guidelines regarding the assessment of Multisource products (Marketing Authorization of Pharmaceutical Products with special Reference to Multisource (Generic) Products: a Manual for Drug Regulatory Authority, WHO/DPM/RGS/98.5)
- Classification of orally administered drugs on the WHO Model List of Essential Medicines according to the Biopharmaceutical Classification System (BCS), WHO Technical Report Series 937
- The Internationally recognised Pharmacopoeia (EU, BP, USP, Int. Ph.,...)
- MSF specifications for pharmaceutical products

5.2. The manufacturing site assessment

- Any site that has been approved by the WHO Prequalification inspectors or by a PIC/s member or equivalent inspectorate is automatically approved by MSF (Refer to list of accepted countries under point 8 and 9)

    - WHO PQ and PIC/s equivalent inspections are product oriented. The products accepted after such an inspection are automatically approved by MSF
      (qualification routes "W" and "I")
    - The MSF approval of other products (= other than those specifically inspected by WHO PQ and PIC/s equivalent) manufactured on a site inspected by a PIC/s or equivalent inspectorate can only be granted after a satisfactory technical visit of a MSF pharmacist
      (= technical visit => qualification route "P")
- A site approved by UNICEF inspectors or ICRC auditors [6] (considered as PIC/s equivalent audits) can be approved based on the received report (dated less than 3 years) and a technical visit performed by a MSF pharmacist.
  (=> qualification route "P")
- Non PIC/s or WHO PQ or US FDA inspected or UNICEF/ICRC audited facilities are eligible for MSF approval provided they successfully pass an audit conducted by a MSF mandated or recognised expert
    - GMP audits are performed by the expert AND one MSF HQ pharmacist
    - The decision to approve a Non WHO PQ or PIC/s equivalent site is taken by the International Pharmacist Coordinator on the basis of the expert's report
    - Products manufactured in a Non PIC/s or WHO PQ or US FDA facility can be approved through qualification route "G"

Relevant Documentation:

- GMP audit report(s)
- Manufacturer Information File
- Site Master File
- Documents issued by the NDRA, incl. Manufacturing licenses, CPP, GMP certificates, etc.

5.3. The Product Assessment

Key indicators of the quality of a product are given a rating in order to prepare the decision process:

- Countries of registration +National Drug Regulatory Authority reliability in country of origin
- Stability of finished product
- Finished product (F.P.) analytical reference standards
- Active Pharmaceutical Ingredient (API) Quality Assurance (QA)
- Sample (dosage form + packaging + labelling)

[6] Precondition is that auditors used by UNICEF and ICRC fulfill the MSF requirements for GMP experts

- Manufacturing site level of GMP compliance
- Therapeutic equivalence (if needed)

Required Documentation:

- Interagency Product Questionnaire (IAPQ) plus required annexes
- Expert Reports (e.g. Bioequivalence studies evaluations)
- Product sample (including labelling, SPC etc.)

MSF Qualification Scheme

Rating Table

	REGISTRAT. / MANUFACT.	STABILITY	F.P. ANAL. REFERENCE	API QA	SAMPLE / PACK. / LAB.	MFG SITE GMP	
6	REG in an Highly Regulated Country MANUF: PIC/S or eq. country	Satisfactory Type 4	PHARMACOPOEIA BP/USP/Int.Ph. + Additional tests	CEP AVAILABLE	Fully compliant With MSF specifications TRILING. LABEL	SATISFACTORY GMP AUDIT (product oriented) Report received	THERAPEUTIC EQUIVALENCE
5	REG in an Highly Regulated Country MANUF: Non PIC/S or eq. country	Satisfactory Type 2+	PHARMACOPOEIA BP/USP/Int.Ph.	DMF AVAILABLE + GMP	Compliant With MSF specifications BILING. LABEL	SATISFACTORY GMP AUDIT (product oriented)	
4	Not REG in an Highly Regulated Country MANUF : PIC/S or eq. country	Satisfactory Type 2	IN HOUSE EQUIVALENT METHODS	TF AVAILABLE + GMP	Compliant With MSF specifications ENGLISH ONLY	SATISFACTORY GMP AUDIT (not product oriented)	
3	REG: country of origin (non HRC) MANUF: Non PIC/s or eq. country	Temporarly Acceptable	IN HOUSE	PRODUCER IDENTIFIED +	MINOR DEVIATIONS	CORRECTIONS COMMITMENT RECEIVED	
2	REG : any other country MANUF: Non PIC/s or eq. country	UNSATISFACTORY STABILITY STUDIES	IN HOUSE < BP/USP/Int.Ph.	PRODUCER IDENTIFIED	MAJOR DEVIATIONS	CORRECTIONS + NEW AUDIT NEEDED	
1	NOT REGISTERED. in any country MANUF: Non PIC/S or eq. country	NO STABILITY STUDIES AVAILABLE	ANALYTICAL METHODS NOT AVAILABLE	PRODUCER NOT IDENTIFIED	CRITICAL DEFICIENCIES	DEFICIENCIES TOO NUMEROUS TO HOPE RAPID CORRECTIONS	

REGISTRATIONS /country of origin **NDRA RATING**

Rating applies to:

•**the expected reliability in the product data assessment made by the competent authority** responsible for issuing the marketing license, combined with

•**the expected reliability in the national GMP inspections** (performed by the **N**ational **D**rug **R**egulatory **A**uthority) of the country of manufacture.

6	**REGISTERED in a Higly Regulated Country (= HRC) MANUF: PIC/S or eq. country**	Product registered in a Highly Regulated Country and manufactured in a country member of the PIC/S or equivalent Important note : the product is purchased directly from the manufacturer with possible MSF specifications. *Example: Ritonavir oral solution Abbott (Norvir®)*
5	**REGISTERED in A HRC** **MANUF: Non PIC/S or eq. country**	Product registered in Highly Regulated Country, and manufactured in a non PIC/S (or equivalent) country) Important note : the product is purchased directly from the manufacturer with possible MSF specifications. *Example: Ciprofloxacine 500 mg tablets Ranbaxy*
4	**NOT REGISTERED In a HRC country** **MANUF : PIC/S or eq. country**	Product not registered in a Highly Regulated Country, but manufactured in PIC/S (or equivalent) country *Example: Acetylsalicylic acid tablets Creat*
3	**REGISTERED in the Country of origin (non HRC) MANUF: Non PIC/s or eq. country**	Product registered on its domestic market but not registered in a Highly Regulated Country, and manufactured in a non PIC/S. (or equivalent) country *Example: Efavirenz tablets Ranbaxy*
2	**REGISTERED In any other country** **MANUF: Non PIC/s or eq. country**	Product, registered in at least one country but not in a Highly Regulated Country nor in its country of origin, and manufactured in a non PIC/s (or equivalent) country. *Example: Itraconazole capsules Ranbaxy*
1	**NOT REGISTERED in any country** **MANUF: Non PIC/S or eq. country**	Product not registered in any country, and manufactured in a non PIC/s (or equivalent) country.

See Highly regulated countries and PIC/S or equivalent countries definitions at the end of the document page 44 and 45

STABILITY RATING

Rating applies to the stability studies performed on the product in the proposed marketing packaging.

6	**Satisfactory Type 4**	Satisfactory stability studies (with no significant changes) on 3 representative batches (*) at 30±2°C / 65 or 70 ±5%RH for the claimed shelf life (real time studies) Test conditions for climatic zone IV A or B Accelerated data at 40±2°C / 75±5%RH for 6 months may support extrapolation of shelf -life
5	**Satisfactory Type 2 +**	Satisfactory stability studies (with no significant changes) on 3 representative batches (*) at 25±2°C / 60±5%RH for the claimed shelf life (real time studies). Accelerated data at 40±2°C / 75±5%RH for 6 months may support extrapolation of shelf -life With additional studies done at other conditions (different from Zone IV A or B)
4	**Satisfactory Type 2**	Satisfactory stability studies (with no significant changes) on 3 representative batches (*) at 25±2°C / 60±5%RH for the claimed shelf life (real time studies). Accelerated data at 40±2°C / 75±5%RH for 6 months may support extrapolation of shelf -life
3	**Temporarly acceptable**	Stability studies underway, but data on fewer than 3 batches or insufficient to cover the proposed shelf-life, commitment from manufacturer to continue long term studies and/or to place additional batches on stability studies, Minimum data acceptable = 2 batches at: - 40±2°C / 75±5%RH for 6months (accelerated) + - 25±2°C / 60±5%RH for 1 year.
2	**UNSATISFACTORY STABILITY** STUDIES	Not fully satisfactory stability studies (e.g. temperature or humidity conditions not coherent with Type 2 or not satisfactorily controlled, insufficient number of batches, insufficient time period covered, missing data, data received not signed, different packaging).
1	**NO STABILITY STUDIES AVAILABLE**	Stability data not available.

- **(*) 2 of the 3 batches should be at least pilot scale batches (min 10% of production batches), the third can be smaller (R & D batch)**
- **For accelerated studies, minimum of three time points should be provided (0, 3, 6 months)**
- **For long term studies, minimum of five time points should be provided for the first year (0, 3, 6, 9, 12 months) and then every 6 months**

Extrapolation of shelf life accepted if available long term stability studies and accelerated stability studies do not show significant Change (see ICH guidance)

Note: Stability T° and H conditions for refrigerated products or products in semi-permeable containers should follow ICH/WHO

F.P. ANAL. REF. RATING

Rating applies to the expected quality assurance given by the Finished Product analytical specifications.

6	**PHARMACOPOEIA BP/US/Int. Ph. + Additional tests**	Tests methods and limits are those of a internationally recognized pharmacopoeia (BP, USP or International Pharmacopoeia) **plus** additional test(s) (e.g. dissolution test) or limits more stringent than those of the reference pharmacopoeia.
5	**PHARMACOPOEIA BP/USP/Int.Ph.**	Tests methods and limits are those of a internationally recognized pharmacopoeia (BP, USP or International Pharmacopoeia)
4	**IN HOUSE EQUIVALENT METHODS**	In house methods and limits are equivalent to the existing international pharmacopoeia
3	**IN HOUSE**	There is no international monography available. In house analytical references are following minimum requirements in international pharmacopoeias for the dosage form
2	**IN HOUSE < BP/USP/Int.Ph.**	In House analytical references less stringent than those of internationally recognized pharmacopoeias (BP, USP, Int. Ph).
1	**ANALYTICAL METHODS NOT AVAILABLE**	In House analytical method not available (cfr Product Questionnaire, Question VIII). Manufacturer not willing to provide necessary information (analytical methods) for the tests to be replicated by a control laboratory.

API QA RATING

Rating applies to the expected reliability in the Quality Assurance on the Active Pharmaceutical Ingredient(s) (APIs) used by the finished product manufacturer.

6	**CEP AVAILABLE**	The API used has a Certificate of suitability to the European Pharmacopoeia (CEP) The CEP was assessed by the QA/QC (cfr Product Questionnaire, question VII) A copy of the CEP with its annexes has been provided to MSF.
5	**DMF AVAILABLE + GMP**	The identity of the producer of the API is stated GMP certificate has been provided to MSF (*). The manufacturer of the API has a Drug Master File (DMF) which has been registered in an ICH country
4	**TF AVAILABLE + GMP**	The identity of the producer of the API is stated GMP certificate has been provided to MSF (referring to local* or WHO reference). The manufacturer of the FP can provide a copy of a Technical File (TF) or DMF (without registration in an ICH country)
3	**PRODUCER IDENTIFIED +**	The identity of the producer of the API is stated. GMP certificate has been provided to MSF (referring to local* or WHO reference) or TF
2	**PRODUCER IDENTIFIED**	No CEP, DMF or TF. The identity of the producer of the API is stated.
1	**PRODUCER NOT IDENTIFIED**	The identity of the producer of the API is not known.

(*) In case the API GMP certificates doesn't refer to WHO GMP, eg the indian GMP certificates referring to the Drugs and Cosmetics Rules, 1945.

SAMPLE / PACK. / LAB. Rating

Rating applies to the compliance with the MSF specifications regarding dosage form, packaging and labelling. This rating is established by scrutiny of the sample(s) provided.

6	**Fully compliant with MSF specifications TRILINGUAL LABEL**	All MSF specifications regarding dosage form, packaging and labelling complied with plus trilingual (or more) labelling (including English/French/Spanish). *Example: Ciprofloxacine Ranbaxy*
5	**Compliant with MSF specifications BILINGUAL LABEL**	All MSF specifications regarding dosage form, packaging and labelling complied with, except language Requirements Bilingual English/French labelling. *Example: Lamivudine/Stavudine tablets Ranbaxy*
4	**Compliant with MSF specifications ENGLISH ONLY**	All MSF specifications regarding dosage form, packaging and labelling complied with, excepted language labelling requirements. Labelling in English only
3	**MINOR DEVIATIONS**	Among others: Storage conditions not stated in °C, container not tamper proof…
2	**MAJOR DEVIATIONS**	Among others: Dosage form not complying with what is expected (“unbreakable” tablets instead of “breakable” tablets, non dispersible tablets instead of dispersible tablets), container not light resistant when required by the Pharmacopoeia, no English on labelling and insert,…
1	**CRITICAL DEFICIENCIES.**	Critical defects on dosage form, on labelling or on packaging that can lead to adverse effect for the patient. Among others: no route of administration on a product for injection, error on labelling that can lead to under or over dosage,…

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MFG SITE GMP RATING

Rating applies to the GMP compliance that can be expected from the manufacturer.

6	**SATISFACTORY GMP AUDIT (product oriented) Report received**	Product manufactured on a production unit , successfully audited by (or for) MSF, or by the WHO pre-qualification project, or by a PICs member (or equivalent NDRA) or UNICEF or ICRC. GMP audit specifically focused on the product. MSF has received a copy of the report.
5	**SATISFACTORY GMP AUDIT (product oriented)**	Product manufactured on a production unit , successfully audited by (or for) MSF, or by the WHO pre-qualification project, or by a PICs member (or equivalent NDRA) or UNICEF or ICRC. GMP audit specifically focused on the product. MSF does not have a copy of the report. *Examples: Fluconazole 200 mg tablets Cipla –Kurkhumb ; All products WHO pre-qualified*
4	**SATISFACTORY GMP AUDIT (not product oriented)**	Product manufactured on a production unit , successfully audited by (or for) MSF, or by the WHO pre-qualification project, or by a PICs inspectorate (or equivalent NDRA) or UNICEF or ICRC. The GMP audit did not specifically focused on the product. *Examples: Azithromycin 250mg caps Cipla-Vikhroli; Efavirenz 600 mg tablets Ranbaxy-Dewas*
3	**CORRECTIONS COMMITMENT RECEIVED**	Manufacturer's commitment to address the deficiencies pointed out during the GMP audit provided to MSF and approved by the GMP expert. *Example: Core-Ahmedabad*
2	**CORRECTIONS + NEW AUDIT NEEDED**	Corrections to the deficiencies pointed out during GMP audit or MSF visit need to be addressed by the manufacturer and to be checked by a (new) GMP audit.
1	**NOT COMPLIANT WITH WHO GMP STANDARDS**	The GMP deficiencies pointed out during the GMP audit or MSF pharmacist's visit are too numerous to hope rapid corrections.

Therapeutic Equivalence

This indicator cannot be rated as:

- No consensus on international standards is available for the time being
- A proof of therapeutic equivalence is not available for the vast majority of multi source generic products
- Several formulations do not require a proof of therapeutic equivalence (IV formulations, oral solutions, simple IM preparations...)
- On the basis of their solubility, permeability and therapeutic risk several molecules can be exonerated of equivalence studies (cfr Biopharmaceutical Classification System = BCS), WHO Technical Report Series 937

This indicator cannot be rated, therefore:

- The need for a proof of therapeutic equivalence is consensually evaluated by the MSF HQ pharmacists
- The decision is taken on a case by case basis.
- This indicator is given a mark that is attached to the product rating
    - (a) = a bio equivalence study has been performed
        - a5) both the report and the Contract Research Organisation (CRO) have been satisfactory assessed by an expert
        - a4) the BE report has been satisfactory assessed by an expert but we have no information on the CRO
        - a3) the CRO is validated by an expert but the BE report has not been assessed
        - a2) the BE report has not been assessed and we do not know anything about the CRO
        - a1) we do not have a copy of the BE report
    - (b) = the equivalence of the product has been tested in vitro
        - b3) the compared dissolution profile report has been assessed by an expert
        - b2) the comparative dissolution profile (CDP) report has not been assessed
        - b1) we do not have a copy of the CDP report
    - (c) = a simple dissolution test has been done
    - (d) = no test is available
    - (e) = not relevant (a proof of therapeutic equivalence is not needed)

Decision Process

Principles

Product with all ratings ≥ 3 → **Product QUALIFIED**
Product status decided by MSF pharmacists group

Product with all ratings ≥3 except one at level 2 → **Product "APPROVED" or "NOT APPROVED"**
Product status decided by MSF pharmacists
but info to Medical Directors

Product with one rating at level 1 or more than one at level 2 → **Product "NOT QUALIFIED"**
by MSF pharmacists
Route M possible if needed (Medical decision)

6. Decision Process

6.1. General Rules:

- Only products rating all criteria > or = 3 can be considered as "Qualified" at the MSF pharmacists level
- The decision to **approve** or **not approve** a product with all ratings ≥3 except one at level 2 can be taken within the pharmacists. The International Pharmacist Coordinator will inform the medical directors on the decision.
- Products with 1 rating at level 1 or more than 1 ratings <3 will be considered as "Not Qualified". The medical directors may accept or reject such products based on their own risk – benefit assessment. Medical director's approvals are considered **temporary approvals.** The decision is documented in the product dossier. The Pharmacist Coordinator is responsible for follow up and feedback to the medical directors.
- The products on which no consensus can be reached within the sections will be considered as "Not Qualified"

6.2. Endorsement of decision

- If the 3 reviewers agree on the ratings and the ratings for all criteria ≥ 3, the IPC can endorse the validation and give the green light for purchasing to the procurement centres
- The IPC is responsible to present at regular intervals all validated product dossiers to the section pharmacists for formal endorsement and signature of the decision statement.
- In all other cases the green light to the procurement centres can only be given after endorsement by the section pharmacists and/or medical directors as applicable.

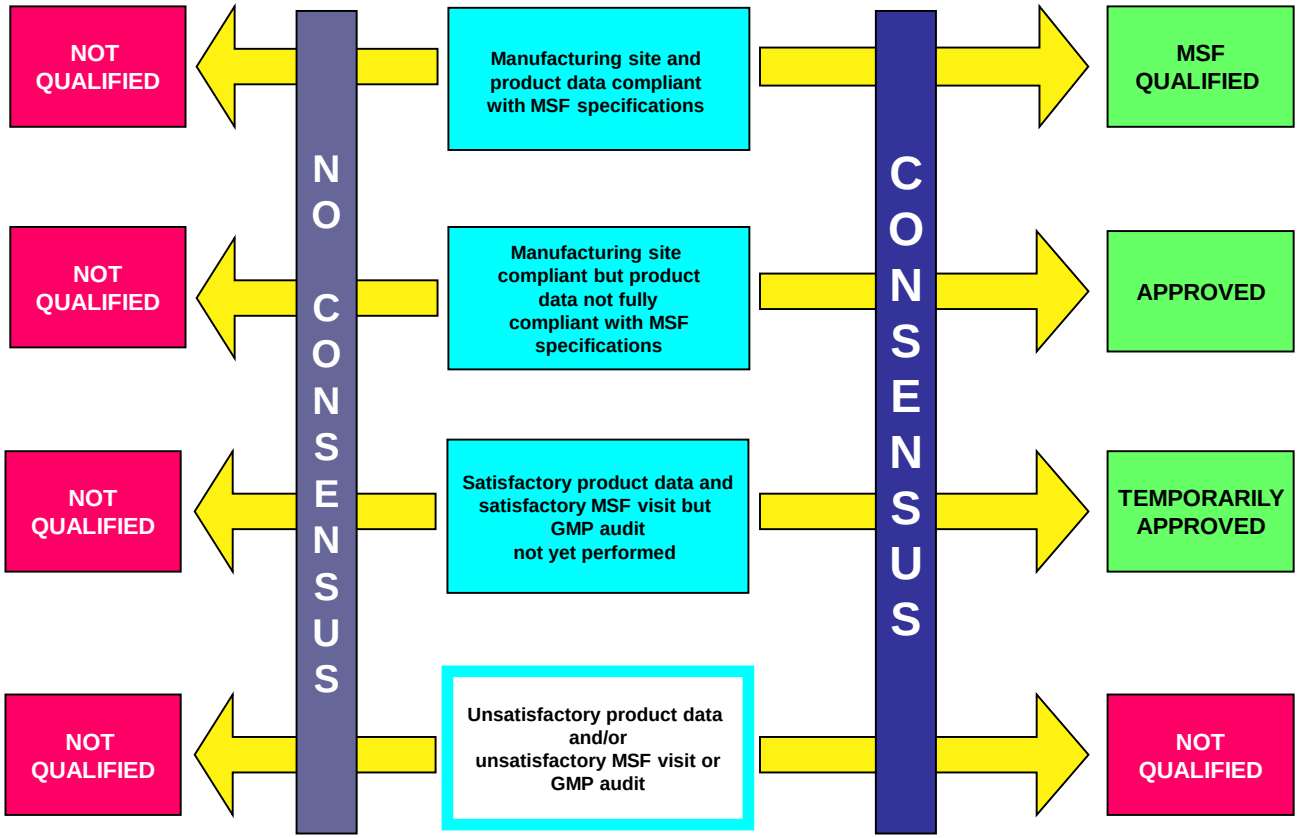
6.3. Exceptions to General Rules:

- A product can be "temporarily approved" by the pharmacists without a GMP audit
    - When the evaluation of the product dossier is successful
    - AND when a technical visit has been conducted on the manufacturing site with a positive outcome
    - A GMP audit is required for a final approval within the next 6 months

- A product that is "not qualified" or "temporarily approved" can be purchased in exceptional conditions (route M)
    - The need for such a product must be balanced with the weaknesses of the dossier
    - The benefit/risk evaluation is done by the medical directors

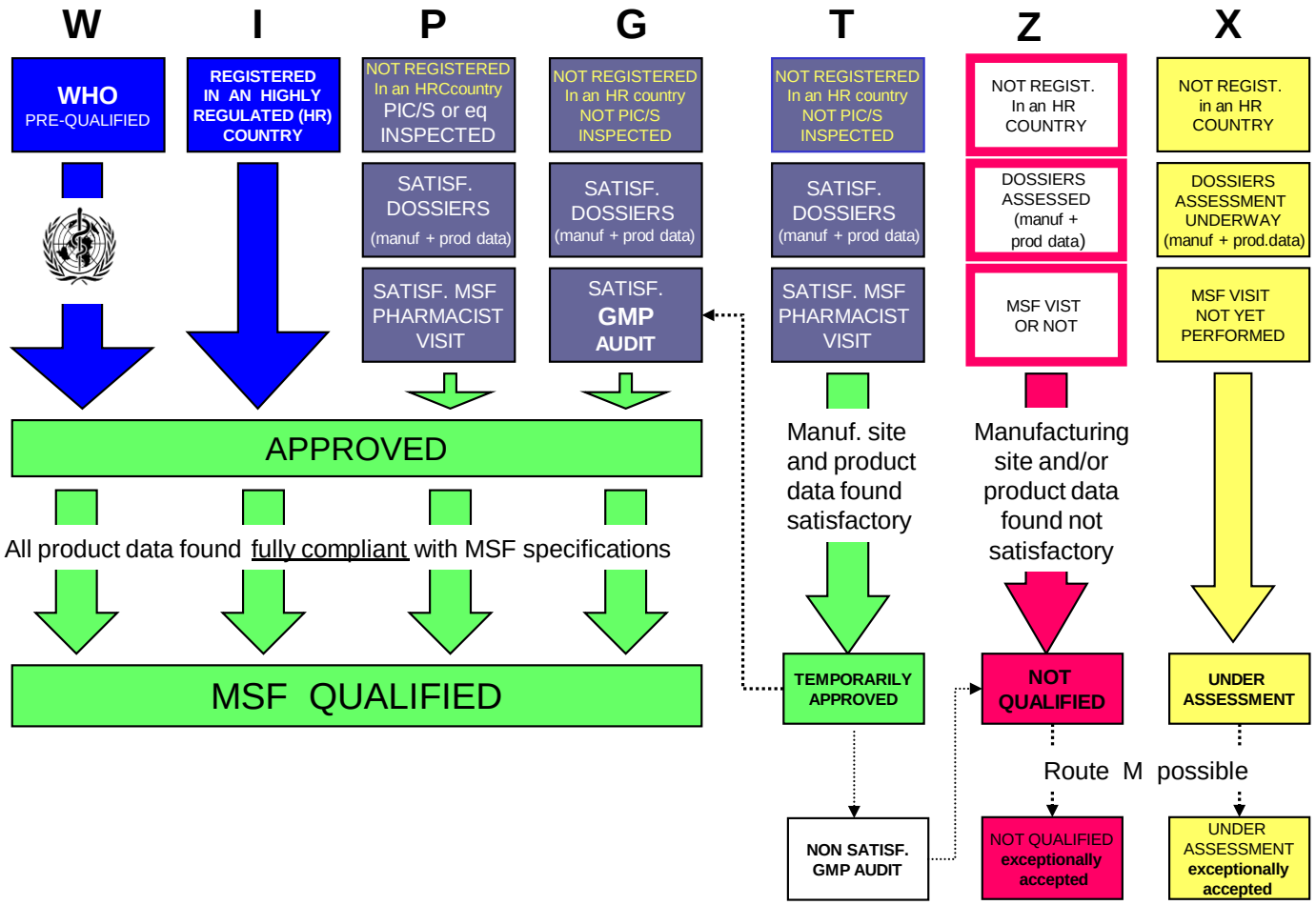
- Medical directors' decisions for exceptional product approvals are summarised and signed by the IMC. The approval document will be filed as part of the product dossier.
- The authorisation for an exceptional purchase must be communicated in writing to the IPC

Pharmacists decision : the options

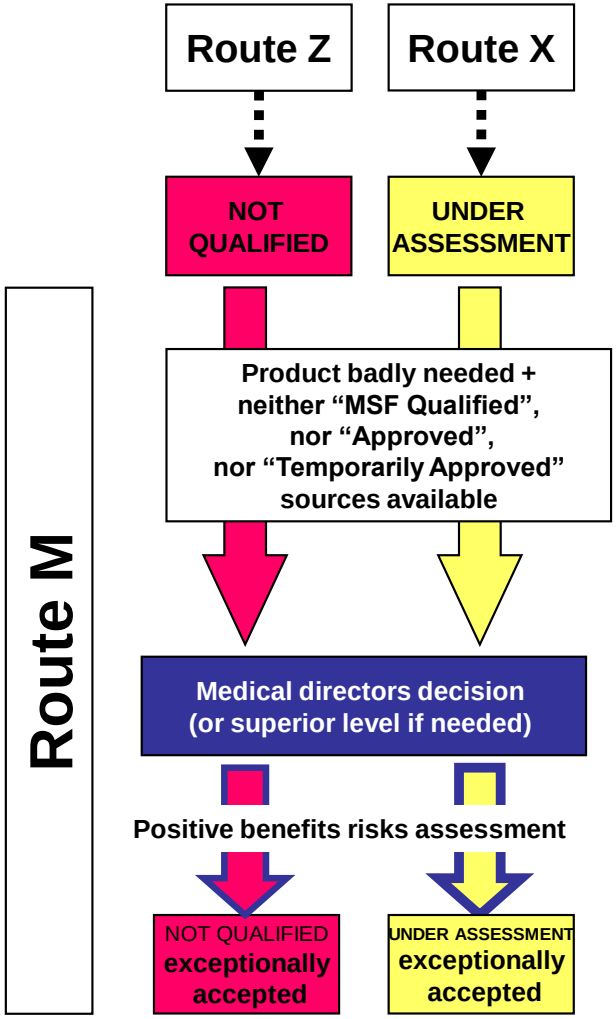


MSF Qualification Scheme

Routes



Routes (cont)


Route Z
Route X
NOT QUALIFIED
UNDER ASSESSMENT
Route M
Product badly needed + neither "MSF Qualified", nor "Approved", nor "Temporarily Approved" sources available
Medical directors decision (or superior level if needed)
Positive benefits risks assessment
NOT QUALIFIED exceptionally accepted
UNDER ASSESSMENT exceptionally accepted

7. Monitoring and follow-up

- Information and documentation regarding the qualified products are regularly updated
- Monitoring of product information to be done **every 3 years** based on the previous PSS signed.
- Variations are assessed according to the MSF variation procedure and presented by the pharmacist in charge of the product dossier to the International Coordination for a new decision
- The databases are updated accordingly
- Manufacturing sites are periodically revisited in order to verify the GMP compliance. PIC/s or equivalent sites are monitored by technical visits. MSF audits are followed up with technical visits, but audit to be repeated within **5 years**.
- A sample of batch records of purchased products are consulted at the time of the monitoring visits/audits in order to make sure that products supplied are conform with the "Product Specification Sheet"
- Information on complaints, quality problems, batch recalls are communicated to the IPC and the section pharmacists, registered at Coordination level and taken into account for maintaining or adapting the status of the product

8. "Highly Regulated Countries" definition for MSF

Registration by NDRA in these countries means automatic product approval by MSF through Route I

- ICH participating authorities
  - **US, Japan, Austria, Belgium, Cyprus[7], Denmark, Finland, France, Germany, Greece, Ireland, Italy, Luxembourg, Portugal, Spain, Sweden, The Netherlands, United Kingdom**
  - *Bulgaria,Czech Republic, Estonia, Hungary, Latvia, Lithuania, Malta, Poland, Romania, Slovak Republic, Slovenia :* could be considered as highly regulated countries ONLY for products registered through European centralized procedure or via mutual recognition (with registration in another EU country listed in the first part).
- EU accession countries: approval as highly regulated country on a case by case analysis:
  - Cyprus: accepted for marketing authorizations or renewed marketing authorizations from 1st January 2006
- EEC countries (agreement with EMEA)
  - **Norway, Iceland, Liechstenstein**
- Switzerland
- PIC/S countries non ICH considered as highly regulated:
  - **Australia, Canada**
- **US FDA tentative approval**

9. "PIC/s or equivalent inspectorate" definition for MSF

List of countries of where inspections are considered acceptable for MSF
(i.e. no MSF GMP audit is required, but technical visits if audit was not product specific).

- List of PIC/s countries acceptable for MSF: Australia, Austria, Belgium, Canada, Czech Republic, Cyprus, Denmark, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Liechtenstein, Malaysia, Netherlands, Norway, , Portugal, Slovak Republic, Spain, Sweden, Switzerland, United Kingdom
- PIC/s equivalent: Japan, US, Luxembourg,

[7] For products registered or renewed marketing authorization after 1st January 2006

10. GLOSSARY

- API: Active Pharmaceutical Ingredient
- BCS: Biopharmaceutical Classification System
- BE: Bioequivalence
- BP: British Pharmacopoeia
- CDP: Comparative Dissolution Profile
- CEP: Certificate of suitability with the European Pharmacopoeia
- CPP: Certificate of Pharmaceutical Product
- CRO: Contract Research Organization
- DMF: Drug Master File
- DS : Decision Statement
- EEC: European Economic Community
- EMEA: European Medicines Agency
- EU: European Union
- FP: Finished Product
- GMP: Good Manufacturing Practices
- HQ: Headquarter
- HQ Pharmacists: International Coordination Team, Procurement Centre Pharmacists, Access Campaign Pharmacists
- HRC: Highly Regulated Countries
- IAPQ: Interagency Product Questionnaire
- IC: International Coordination
- Int. Ph: International Pharmacopoeia
- IPC: International Pharmacists Coordinator
- MIF: Manufacturer Information File
- MSF: Médecins Sans Frontières
- NDRA: National Drug Regulatory Authority
- PASS : Product Assessment Summary Sheet
- PIC/S: Pharmaceutical Inspection Convention Scheme
- PSS: Product Specification Sheet
- QA: Quality Assurance
- QC: Quality Control
- SASS : Sample Assessment Summary Sheet
- TF: Technical File
- US FDA: United States Food and Drug Administration
- USP: United States Pharmacopoeia
- WHO: World Health Organization
- WHO PQ: WHO prequalification