Responsible Person: requirements

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1. Purpose and scope

The requirements for a Responsible Person (RP) are described in art. 5, 6, 17, 18, 22, 23, 25, 26 and 39 of the Medicinal Products Licensing Ordinance (MPLO). This Technical Interpretation describes the interpretation of these articles by the Swiss inspectorates. It can also be used by companies as a basis for assessing whether an individual fulfils the requirements for applying to Swissmedic to act as a Responsible Person.

2. Basics

- Therapeutic Products Act (TPA; SR 812.21)
- Medicinal Products Licensing Ordinance (MPLO; SR 812.212.1)
- Good manufacturing practices for small quantities (Regeln der Guten Herstellungspraxis für Arzneimittel in kleinen Mengen), Ph. Helv., chapter 21 (explanatory notes)
- Guidance on good manufacturing practice and good distribution practice: Questions and answers | European Medicines Agency (europa.eu)

3. Definitions and abbreviations

EMA	European Medicines Agency
Ph. Helv.	Pharmacopoea Helvetica
RP	English: Responsible Person (*German*: fachtechnisch verantwortliche Person; *French*: Responsable technique; *Italian*: Responsabile tecnico) The RP is a natural person and cannot be a juridical person.
ATMP	Advanced Therapy Medicinal Products
Supplementary sheet	Formular Gesuch Betriebsbewilligung – Zusatzblatt Requête d'autorisation d'exploitation – Annexe Richiesta d'autorizzazione d'esercizio – Allegato

4. Responsibilities of a RP

The holder or applicant of an establishment licence is responsible to have a suitable RP available. The responsibilities of a RP are described in the following MPLO articles:

- Art. 4, 5 and 7 for the manufacturing of medicinal products,
- Art. 13, 15 and 17 for the wholesale distribution, import and export of medicinal products,
- Art. 22 and 23 for the trade in foreign countries with medicinal products,
- Art. 25 and 26 to perform brokerage or agency activities with medicinal products and
- Art. 27 for the collection of blood.

The RP must be able to execute his/her responsibility and understand the Swiss regulatory requirements in order to ensure compliance of the company. The direct supervision of the company by the RP in order to ensure compliance with the legal requirements must be guaranteed at any time.

5. Qualification to be a RP

According to the MPLO, the criteria for assessing whether a person can be designated as a RP are his education, knowledge, experience, trustworthiness and independence (art. 5, 6, 17, 18,

22, 23, 25, 26, 27 and 39 MPLO). Further criteria concern the language and the direct supervision.

5.1 Education and knowledge

The responsible person must have sufficient knowledge of his or her area of responsibility. Knowledge can be acquired by education and training. The education has to be completed successfully, a diploma or degree must be available. For the education, especially higher studies (university or equivalent/higher technical institute) in the area of natural sciences (or if applicable medicine or engineering) are valued. With regard to manufacturing and/or market release of dosage forms, emphasis is placed on pharmaceutical or biological/natural sciences knowledge. With regard to the manufacturing of active substances, emphasis is placed on analytical/chemical or other technical knowledge relevant to the respective production processes (e. g. biotechnological know-how).

For the manufacturing with release of formula medicinal products (see activities listed on the supplementary sheet Medicinal products or TpP/GT/GMO: S.1.10.N) that are exempt from marketing authorisation based on art. 9 par 2 let a to c^{bis} TPA, a pharmacist diploma together with a valid professional licence of the canton concerned is mandatory (see chapter 20.1.2 und 21.1.2 Ph. Helv.). Exceptions are tolerated in case of hospital radiopharmaceutical establishments, since according to art. 4 par. 1, let. j TPA, they are considered equivalent to an hospital pharmacy. In addition, a certificate in radiopharmacy granted by the European Association of Nuclear Medicine is mandatory for the manufacturing of radiopharmaceuticals (MPLO, art. 6, par. 1, let. d).

Furthermore, RPs are obliged to maintain their knowledge in relation to the products, manufacturing processes and pharmaceutical quality system.

5.2 Experience

Depending on the type of activities performed by the company and education/knowledge of the RP, the required experience ranges from a minimum of one year up to four years. In any case, the RP must have the technical know-how of the processes he/she will be responsible for. The level of professional knowledge and additional experience required also depends on the type of medicinal product (MPLO, art. 6, art. 18, par. 1, and 2 let. a, art. 23 par. 5 and art. 26 par. 5). Persons who are responsible for an area with specific risks or other peculiarities must, in addition, have acquired at least 1 year of experience in an environment that has addressed the risk or peculiarity in question (e. g. sterile medicinal products, ATMPs, biotechnological medicinal products, blood products etc). The experience expected includes primarily the following points:

- GMP experience is required for the manufacturing, import and/or wholesale including market release of medicinal products and/or licences with the module for the issuing of manufacturing orders activities (see activities listed on the supplementary sheet Medicinal products or TpP/GT/GMO: S.2.6, S.4.6 and/or S.5.3).
- GDP experience is required for the import and/or wholesale with or without market release activities, as well as export, brokerage- and/or agent activities and/or trade in foreign countries.
- For manufacturing, import and wholesale of blood and blood components including market release: knowledge and experience of blood collection for transfusion, haematology or blood transfusion.

Brokerage, agents and trade in foreign countries-activities do not count as GDP experience for the assumption of a function as a responsible person in a company with import, export and/or wholesale activities.

This experience can be acquired:

- by activities where the individual is in charge of, or partially responsible for, the manufacturing of medicinal products or ATMP (GMP), or the wholesale of medicinal products (GDP);
- by involvement in quality assurance work within a company/institution that manufactures medicinal products or transplant products.

5.3 Trustworthiness

Swissmedic considers RPs to be untrustworthy if they have infringed the Therapeutic Products Act, the Federal Act on Narcotics and Psychotropic Substances or any subsidiary ordinance, or if they have committed other relevant infringements to other related legislation (e. g. drug counterfeiting, illegal trading, drug-trafficking). The infringements must have been the subject of a legal judgement or confirmed in form of a legal valid decision or directive.

If criminal proceedings are pending against the RP for infringing the Therapeutic Products Act or the Federal Act on Narcotics and Psychotropic Substances Swissmedic may suspend the assessment of an application or suspend a licence.

5.4 Independence

In order to guarantee that decisions regarding quality are taken independently, the RP must not be a member of production or be subordinate to the head of production. Whether an exception can be granted for a given company (i. e. for a very small company) is examined on a case-by-case basis.

Furthermore, art. 5 par. 6, art. 17 par. 6, art. 23 par. 6 and art. 26 par. 6 of the MPLO state that the RP may not sit on one of the facilities' supervisory committees and must decide on the release or rejection of batches independently of the executive board (= Geschäftsleitung / direction/direzione). Therefore, a CEO of a company or someone having a similar function (i. e. a member of the very restricted company's management) cannot be appointed as RP. A dual role as RP and as chairman of the supervisory committee or principal shareholder is not acceptable. However, a dual role as a member of the management and as a RP is basically acceptable. Under certain circumstances it is easier to enforce quality-relevant decisions towards the executive board when the RP is part of the management. Whether an exception can be accepted for a given company (i. e. for a very small company) is examined by Swissmedic on a case-by-case basis.

The company must be able to provide written rules stating the responsibilities of the RP within the company (including those of deputies) and the RP's authority to issue directives and to take decisions.

5.5 Language

The RP must be proficient enough in at least one of the Swiss national languages in order to be able to read, understand and interpret laws, ordinances, etc. without intermediaries. The RP must also be able to interact within the company, with the staff and the local authorities in such

a way as to comply with all the requirements laid down in the MPLO. The RP should therefore speak one of the official local languages of the canton where the inspection takes place and where the licensed site is located.

5.6 Direct supervision

The direct supervision of a facility by a RP is understood as the supervision of at least all the critical steps/operations with regard to the company's processes.
The RP is responsible for the direct supervision of the company and is expected to be regularly present at the facilities where the activities take place in order to overview the organisation and all activities to ensure compliance with the legal requirements at any time.

In this context, a purposeful operative organization means that the RP carries out his/her direct supervision on the site(s) where the authorised activities according to the establishment licence are being performed by the company's personnel (including the RP) and that the RP has sufficient decision power to take any action which is necessary to ensure compliance with legal requirements. The direct supervision of a company is considered to be to some extent independent of the number of batches or products which are manufactured, distributed and/or traded. It is therefore assumed that a regular, minimal presence is necessary even if very few medicinal product related activities take place. It is also expected that the RP will be present during an inspection and demonstrates, at this point, that he/she has sufficient knowledge regarding to the company's processes to assume overall responsibility. Recurrent compliance issues may be regarded as the result of insufficient RP supervision.

5.6.1 Domicile

A direct supervision implies that the RP must live within reasonable distance of the site. As a guidance value the RP should live within two hours travelling time from the site. In case of emergency situations, the RP must be able to reach the site at any time in a timely manner. The RP may reside in a neighbouring country (in a region close to the Swiss border).

5.6.1.1 Remote technical and market release

Remote technical and market release could be accepted under certain circumstances. The technical and market release have to be carried out according to MPLO art. 5, 7, 12, 13, 17 and 18. However, the remote release must take place within the residence of the RP, in Switzerland, where, should the need arise, an inspection could be carried out. Moreover, compliance to the points listed in the EMA publication questions and answers on remote batch certification/confirmation by the qualified person (QP) apply mutatis mutandis.

5.6.2 Presence on site

In accordance with the MPLO, art. 5 par. 7, art. 17 par. 7, art. 23 par. 7 and art. 26 par. 7, it is in principle possible, that the function of the RP can be carried out on a part-time basis or as a specific mandate, as long as the size and type of the facilities permit so.
It is expected that the RP will establish and maintain a current list of critical steps/operations for which his/her presence on site is required, which should be commensurate with the risks related to the processes at the authorised site (art. 5 par. 1 and 7, art. 6 par. 3, art. 17 par. 1 and 7, art. 18 par. 3, art. 23 par. 1, 7 and 8 and art. 26 par. 1, 7 and 8 MPLO). Based on this list, the RP will set his/her minimum hours of presence on site (see also below). This list will also help the establishment licence holder/applicant to fulfil the requirement of having a purposeful operative

organization (art. 3 par. 1 let. d, art. 11 par. 1 let. e, art. 21 par. 1 let. c, art. 24 par. 1 let. c MPLO).

The minimum hours of presence on site of a RP should not be below 10% of a full-time position and should ensure direct supervision of the company as defined above.
The presence of the RP on site at regular intervals is required at all licensed sites, including for example at pharmaceutical warehouses.

The direct supervision of sites without manufacturing activities and without product storage by a RP can be performed with reduced physical presence, provided that he/she has electronic access to all information deemed necessary according to art. 17 and 23 MPLO and is in close contact with the company's personnel.

The RP should physically attend the site to ensure compliance with the quality system and where there are specific issues or cases which cannot be satisfactorily clarified or resolved through electronic means.
In case of poor compliance and/or many deviations during inspections, an intensified presence of the RP on site is expected, thus independently if physical activities with medicinal products take place or not at the company.

It is expected that proof of the actual hours of presence can be provided (e. g. by means of a presence list).

5.6.3 Pensum

Regardless of the physical presence on the site (see above), the pensum of the responsible person must in any case have a duration that is commensurate with the activity of the company. However, the responsible person has tasks and responsibilities that cannot realistically be realised without having an activity corresponding at least to 10% of a full-time job.

In any case, the minimum number of working hours of the RP which are dedicated to his or her function as RP must be specified in an employment contract and/or job description.

5.6.4 Part-time RP

5.6.4.1 Number of mandates

When employing a person as RP on a part-time or mandate basis, it should be considered whether he or she is working for multiple companies. If a part-time RP has other liabilities of any kind (as RP or not) it is expected that the total number of working hours do not exceed 100% of a fulltime position and that the RP does not hold more than five mandates. This information should be available and included in a regular review of the mandate of the RP.

6. Deputies

The MPLO, art. 5 par. 4, art. 17 par. 4, art. 23 par. 3 and art. 26 par. 3, states that a deputy RP must have sufficient qualifications to execute this role. The criteria for assessing the said qualifications are the same as those applying to a RP. The same requirements also apply concerning the domicile of the deputy RP (see chapter 5.6.1). An individual whose application to become a RP has been rejected because of trustworthiness is considered not suitable to act as a deputy RP. The scope of the deputy's activities should be stated in writing in a job or function description. The RP is responsible that his/her deputy possesses the necessary qualifications for

his/her role. The deputy is expected to replace the RP in the event of the latter's absence and has therefore to be experienced and constantly trained in the company's quality system, processes and products. However, the ultimate and overall responsibility for the safety, efficacy and quality of the medicine and for ensuring adherence to the legal obligations and standards lies always with the RP. Swissmedic does not check or approve the deputy responsible person in the context of licence applications.

7. Possibilities regarding delegation

A RP has a clearly defined area of work within which he or she is granted unrestricted responsibility and authority to issue directives and take decisions. The RP must have a thorough knowledge of the quality system and have the means, authority and information to be able to take all the decisions foreseen by his/her function in full knowledge of the facts. The delegation of certain tasks from the RP to one or several other persons is nevertheless possible as long as GMP and GDP regulations are respected. The compliant execution of delegated tasks must be ensured via an established QM system (SOP, job description, training, etc.), regular checks must be carried out by the RP (e. g. audit system). Even in case of delegation, the ultimate and overall responsibility for the safety, efficacy and quality of the medicine and for ensuring adherence to the legal obligations and standards lies always with the RP.

However, the direct supervision of the facilities cannot be delegated to others by the RP. Additionally, it is expected that the RP is involved in and approves the final assessment of all critical processes (e. g. PQR, critical deviations, management review, recalls/quality defect notifications, quality agreements, Validation Master Plans) and therefore has direct access to all relevant QMS documents and he/she is also aware of and participates in the approval of relevant SOPs for QMS processes. Furthermore, it is expected that release decisions can only be taken by him/her personally or under her/his direct supervision and responsibility. It is therefore not allowed to delegate them to a person/unit independent of her/him.

8. Absence of the responsible person

A prolonged absence of the responsible person going beyond the normal holiday leave can be accepted in justified situations such as absence due to illness. Nevertheless, it must be clear in every given moment who has the overall responsibility defined in the art. 5, 6, 7, 11, 12, 13,15, 17, 18, 21, 23, 24 und 26 MPLO. An absence of up to four months can be accepted without further action as long as the deputy is operational and acts on behalf of the responsible person (see also art. 5 par. 4, art. 17 par. 4, art. 23 par. 3 and art. 26 par. 3 MPLO). However, in all cases where the deputy can no longer be deemed to be acting on behalf of the responsible person (e. g. termination of the responsible person's contract for whatever reason, definitive departure of the responsible person or absence longer than four months), the deputy responsible person should be able to take over the tasks and the full responsibility of the responsible person. This must be regulated internally in writing (the deputy responsible person must confirm in writing that he/she has taken over the tasks and full responsibility). If this situation lasts or is expected to last longer than 4 months, it is mandatory to submit an application for a change of responsible person to Swissmedic.

In case of maternity leave of the responsible person, an absence of up to 6 months can be accepted if it is planned that she will continue in her function as responsible person after the maternity leave. In this exceptional case the deputy goes on acting on behalf of the responsible person for the whole period with the agreement of the responsible person.

9. Changes to the previous version

- Whole text: checking and corrections of legal references. Editorial improvements
- Chapter 2: listing of the MPLO articles suppressed (redundancy with chapter 1 and 4); addition of reference to Guidance on good manufacturing practices, Good manufacturing practices for small quantities, Ph. Helv., and good distribution practice, Question and answer by the EMA
- Chapter 3: addition of the definition of EMA and Ph. Helv., reference to MPLO deleted
- Chapter 5.1: precisions about required education and knowledges
- Chapter 5.2: precisions about activities were GDP and/or GMP experience are required. The experience with regulatory issues as acceptable criterium has been removed. Precision about the experience required for an area with specific risks. Precision, that brokerage, agents, trade in foreign countries-activities do not count as GDP experience
- Chapter 5.4: Executive board corrected with company's management, board of director corrected with supervisory committee
- Chapter 5.5: precisions about the RP language requirements
- Chapter 5.6: precision about the understanding of what is the direct supervision of a facility
- Chapter 5.6.1: new chapter about remote technical and market release
- Chapter 5.6.2: chapter subject changed from part-time RP (now moved to chapter 5.6.4) to presence on site. Addition of precisions about the expected presence on site of the RPs. Precision of conditions permitting a reduction of physical presence on site. Precision about the cases where an intensified presence on site is expected.
- Chapter 5.6.3: new chapter about pensum of the RPs.
- Chapter 6: precision, that the same requirements apply for the deputy RP as for the RP, inclusive domicile. Deputies RP are not checked by Swissmedic in the context of licence applications
- Chapter 7: precisions about possibilities and conditions for tasks delegation. Precisions about critical processes and release activities
- Chapter 8: precisions regarding the absence of the RP

10. Annexes

- None