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A Qualified Person (QP) in the pharmaceutical industry is responsible for ensuring compliance with pharmaceutical legislation in the areas of production, testing and release of medicinal products. He or she is responsible for complete documentation in compliance with the applicable legal requirements. He or she is also personally liable for this. The qualifications that a qualified person must demonstrate are described in Directive 2001/83/EC, Article 49. Which stumbling blocks, problems or difficult situations can a QP be confronted with in the course of his/her work? What business management requirements can be made of them? What to do in situations where making decisions becomes a tightrope walk?

Where in the organisation is the QP located?

A QP performs a wide range of tasks across the entire pharmaceutical quality assurance system. Ideally, he or she should be integrated into the organisation in such a way that he or she can make completely free decisions. In larger companies, the QP is usually under the management of the quality management in an autonomous function. It can also be located at the same level as quality assurance or be identical to the head of quality control. As an external QP, who is active in consulting for companies, he or she is usually directly subordinate to the plant management. These are often medium-sized or small companies. Increasingly, companies are creating quality units, in which the QP is also located. In most cases, the management is directly responsible for these units. Classically, there is a separation into two decision strands: one area that makes personnel decisions and one area that is responsible for decisions concerning pharmaceutical law. This is where the QP would be located.

What about the points "personal liability" and "insurance of a QP"?

There is actually no good and satisfactory answer to this question. Companies usually have a Directors & Officers insurance (D&O insurance), which covers executives, for example, in case of wrong decisions. However, this insurance does not apply to the QP. One participant reported on a solution in his own company, in which the QP is also insured via a public liability insurance and is also mentioned by name. One expert reported that the discussion in a workshop of the QP Association showed that it is usually sufficient to refer to the company's notified QPs. However, this requires a permanent position within a company. In this case, the policy does not have to be changed for each QP notification. A QP should always find out exactly which variant is used in the company and how it is insured in this system. It is of course important that all aspects of civil law are covered.

However, an external QP must insure himself/herself in the form of "liability insurance in the context of scientific and expert activities". A "quality agreement" between the external QP and the company should precisely describe who will be liable for what in the event of a claim.

How often does it happen that a QP is held liable under private law?

"Very, very rarely" was the unanimous opinion within the group of participants and among the experts. Only one case of contaminated blood products with HIV was mentioned, which had already occurred decades ago. At the time, however, there was also criminal energy behind it. The blood products were diluted to such an extent that the HIV pathogens were below the detection limit. One participant also recalled an incident involving blood products in Austria, where the QP had to face a prison sentence.

How should a QP react if he or she has to carry out a market release without access to the documents of the marketing authorisation (MA) or cannot assess the topicality of these documents? How do you make sure that you always get the latest documents?

As an example, a case is reported in which a contract manufacturer had released a product in the "wrong country presentation" because he had no direct access to the MA documents. The argumentation that the responsibility lies with the contract manufacturer due to the contractual regulations was not accepted by the authority. The authority clearly demanded direct access by the QP to the documents, as otherwise the QP could not fulfil his/her function. If the QP nevertheless approves the documents, this could be a reason for the authorities to suspend the manufacturing authorisation.

In global companies it is usually the case that the MA documents are available in a database. During the approval process, „Site Compliance" ensures that the specifications and the manufacturing

process match. Nevertheless, it is very difficult - despite a strict change control procedure - to harmonise the contents of all documents (e.g. normative Russian documents or Japanese application forms were mentioned). It is therefore essential to include in the quality agreement a statement that the client is obliged to inform immediately about any change. One participant reported that despite access to the MA documents, it can nevertheless happen that the client is not in possession of all necessary information and therefore cannot pass it on. From the point of view of the authority, it is understandable that not everything can be checked in terms of content due to different languages. In this case, however, it should at least be possible to check the versioning or the date of issue. Nevertheless, the unanimous opinion of the participants was that in reality it is difficult to systematically track all changes.

What is the attitude of authorities towards external QPs?

External QPs are not excluded by law. Inspectors will have the relevant contract presented to them. It must be precisely defined how often the external QP is on site, or how much time he or she spends on the company. In addition, the question will have to be answered for which other companies the QP is still working for (client list) and how much time is invested there. Travel times and attendance times will also be taken into account, for example. The question "Is there enough time for all these activities?" must be clearly clarified and can also lead to the rejection of an external QP if this is obviously not the case. The QP and his/her qualification for the task performed must be recognised by the authority. Significant changes in the scope of tasks of an external QP or in the environment of the company must be reported to the authority.

How does the authority view the part-time employment of QPs?

Part-time work, depending on the scope of the company's requirements, may be possible in individual cases. There is also no blanket solution for several QPs working part-time in one company. The respective situation within the company must always be examined and is therefore an individual case decision. Two experts, both working as QPs in job sharing, reported on their solution: The products for release were each assigned alphabetically to a QP for release, and mutual representation was also recorded in writing.

How different are the employment conditions of a QP in Germany compared to the rest of Europe?

In principle, the EU GMP guidelines apply to all European countries and are transposed into national law in each country. In Germany we find these guidelines "roughly" in the German Drug Law (AMG) and "more detailed" in the Ordinance on the Production of Pharmaceuticals and Active Substances (AMWHV). In this way, country regulations of different kinds can arise. However, the experts are not aware of any country-specific differences.

What does the authority understand by "appropriate involvement" of an external QP?

Reference is made to the requirements for a QP according to the EU GMP guidelines and the AMWHV. Although these are general, he or she must be informed, for example, about market complaints and inspection results and ensure that the processes of validation and qualification have been carried out correctly. For example, he or she must be involved in the authorisation of relevant SOPs or in the release and information paths. It is only through this "integration" that an external QP has any possibility at all to intervene if something does not run according to plan.

There are quite different views on the place where documents are checked - whether from home or on site in the company or even in another country:

A manufacturing authorisation is valid for the manufacturing site listed therein. If the QP carries out the document inspection outside the site, this activity is not "per se“ covered by the authorisation. The authorities sometimes view this differently. The following case is described: A company with headquarters in Germany and an external QP living in Italy wanted to keep the release register in Italy. This was not accepted by an authority on the grounds that the release register and all other documents should physically be in the German site. A documentation of the release in Italy was not accepted. This is also seen as such for other cases of work-from-home, because ultimately the documents must be in the manufacturing site and therefore the release register must also be kept there by the QP. This scenario was confirmed by a participant in the dialogue. He was not allowed to keep the release register in the "home office", but had to relocate this activity to the manufacturing site. However, working in the home office in combination with sufficient presence time in the company to carry out the release, did not pose a problem.

A "QP-Light" - does that exist?

The general rule is, "A QP is a QP." No compromises can be made here, for example, by only being responsible for technical approvals. He or she must also be notified to the authorities and must be trained. Above all, for the QPs who release the final product, who have to verify decisions, a decision maker other than a notified QP makes no sense. In the case of final release, the QP must ensure that the QPs preceding in the decision chain perform their task to the necessary extent. In this case not only the authority would intervene, but also the QP making the release in his own interest. A "QP light" would be neither target-oriented nor satisfactory.

Can QPs also be brought into the company via a form of temporary employment if required?

This is probably to be seen in a similar way to an external QP, at least from the perspective of pharmaceutical law. In principle, however, the same responsibilities apply as for an external QP: it

must be trained and reported to the authorities and cannot simply be transferred from A to B within one day. It is assumed that contracts with a temporary employment agency are not sufficient. After all, the personal responsibility of the QP is at stake. The question therefore arises in general whether QPs exist at all via temporary employment agencies. From the point of view of labour law and insurance, such a constellation would be difficult. The experts are not aware of such cases.

How can a QP deal with pressure from management?

It is noted that the pressure on the QP does not always come only from the management. It also comes from the packaging, the laboratory, from logistics, often from all sides and the QP is right in the middle of it. Although the QP should be free to decide, he or she senses exactly the expectations from his environment. How can you counter this? As a way of dealing with the resulting pressure, it can help to request information, i.e. data, which is helpful for decision-making. On the basis of data, a well-founded decision can then be made which is comprehensible to everyone, since a precise data analysis has been carried out. Such reasoning often leads to a better understanding of the situation by all parties involved. In large companies, for example, the Global QA can also confirm the demands of the QP if the expectations of the environment have not changed. It is important that the QP should make his/her decisions independently of the management. This should also be included in the job description of the QP. While this is a safeguard, it does not take the pressure off a QP. This is where the concept of quality culture comes in. The CEO should be made responsible for ensuring just such a culture.

The QP of a contract manufacturer releases a batch and issues a corresponding certificate. The own QP does not agree with this. - How do you clarify a difference of opinion on the release?

The QP who releases a product for the market bears the responsibility and is therefore also responsible for the decision for or against a release. If, for example, the QP releasing a product for market release does not agree with the evaluation of deviations by the contract manufacturer's QP, the whole thing goes back to the contract manufacturer until there is an adequate solution or evaluation.

How does the release of an active substance take place if it cannot be analysed?

In most cases, these are "legacy issues": specifications that were so accepted in earlier times. If the relevant MA states that the active substance does not need to be analysed, then this is accepted by the authorities. If, however, the MA documents state that the active substance must be analysed and this - for whatever reason - cannot be analysed, then the competent authority should be contacted in any case. Under these circumstances, the QP should

not simply issue a release because this has been done for years. The pharmaceutical entrepreneur has made a corresponding declaration for the analysis of the active substance, which he must also comply with.

Is there a Whistle-Blower ID for QPs? (Reference to a reflection paper of the EMA)

There is a six page document from EMA entitled "EMA's handling of information from external sources disclosing alleged improprieties concerning EMA activities related to the authorisation, supervision and maintenance of human and veterinary medicinal products". It mentions a body to which one can turn with questions and information on incorrectness. These enquiries will be treated confidentially. An organisational form is currently being established which could then act accordingly. There is nothing concrete at present, but it is to come.

Conclusion:

- Ideally, a QP should be integrated into the organisation in such a way that he or she can decide completely freely. In larger companies it is usually under the direction of the quality management, but increasingly it is also located in the quality unit, which in turn reports directly to the management.
- A QP should inform himself/herself precisely to what extent and whether he or she is covered by civil law, e.g. through the public liability of the company. An external QP must insure himself/herself in the form of "liability insurance within the scope of scientific and expert activities".
- Direct access of the QP to the MA documents must always be guaranteed.
- The following applies to external QPs: It must be precisely defined how often the external QP is on site, or how much time he or she spends there. In addition, the authorities will surely ask which other companies they work for (client list) and how much time is invested there. The question "Is there enough time for all these activities?" must be clearly clarified.
- Part-time work of a QP depending on the scope of the company's requirements may be possible in individual cases. There is no blanket solution for this. Whether this can be regarded as adequate for a company must be decided in each individual case.
- A QP is considered to be "appropriately involved" if, for example, he or she is informed about deviations or can ensure that the processes of validation and qualification have been carried out correctly. He or she must also be integrated in the authorisation of relevant SOPs or in the release and information channels.

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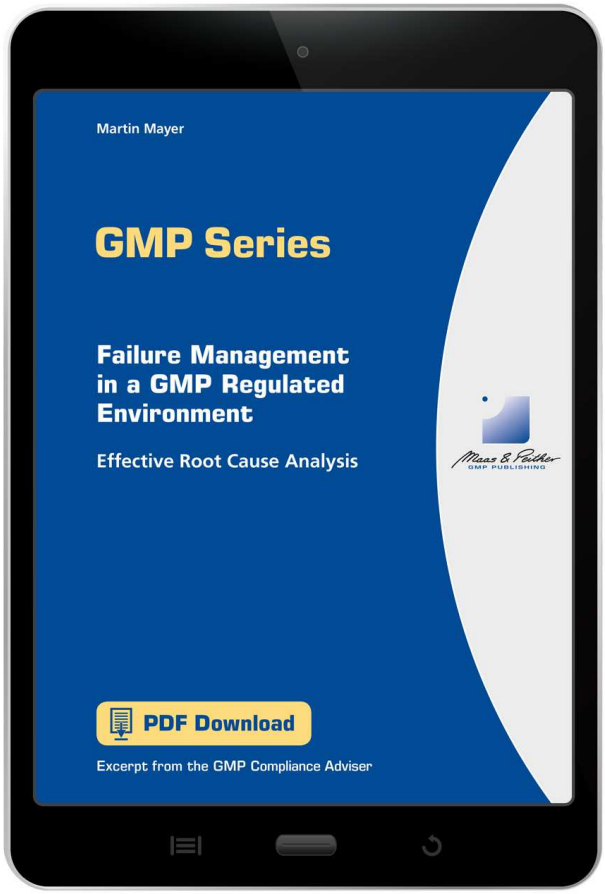

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