Transparency, freedom of information legislation and confidentiality in the EU

Carla Schoonderbeek and John Lisman
NautaDutilh NV

Transparency can be divided into:

- **Active transparency.** This is the most important aspect, and concerns the active publication of information by competent authorities. Companies and private persons can request information under freedom of information (FOI) legislation. In relation to this request the competent authorities must, as a minimum requirement, provide information that falls within the category of active transparency (see below, Development of active transparency).

- **Passive transparency.** If the competent authorities do not provide the information stakeholders want, passive transparency rules become relevant (see below, Passive transparency).

The following issues are particularly relevant in relation to both active and passive transparency:

- What constitutes commercially confidential data.
- The applicable legal system on confidentiality in cases that are covered by both:
  - EC pharmaceutical legislation;
  - EC or national freedom of information legislation.
- How differences between European Medicines Agency (EMEA) and EU member states’ policies and procedures should be handled.

The EMEA has recently published policy documents on transparency and other regulatory agencies have followed their lead. However, many issues remain unresolved.

This chapter analyses the effect of the 2004 pharmaceutical review (as laid down in Directive 2004/27/EC amending Directive 2001/83/EC on the Community code relating to medicinal products for human use (Code for Human Medicines Second Amendment Directive) and Regulation (EC) No.726/2004 on the authorisation and supervision of medicinal products and establishing a European Medicines Agency (EMEA Regulation)), relevant legislation and guidelines in the context of four main areas:

- The development of active transparency.
- Passive transparency.
- Confidentiality in relation to what constitutes confidential information.

**DEVELOPMENT OF ACTIVE TRANSPARENCY**

One of the most unexpected changes under the 2001 pharmaceutical review was the introduction of the concept of transparency in relation to marketing authorisation procedures. The aims of the transparency provisions were to improve the:

- Credibility of competent authorities.
- Dissemination of knowledge about authorised medicinal products to healthcare professionals and patients.

Many of the new provisions (see box, Transparency in pharmaceutical legislation) amend authorisation procedures in which the competent authorities took ‘black box’ (that is, non-transparent) decisions. The following requirements, which have changed the competent authorities’ *modus operandi* in relation to marketing authorisation procedures, constitute active transparency:

- Disclosure of identity and conflicts of interest of decision makers.
- Disclosure of agendas and records of meetings.
- Disclosure of voting results and minority views.
- Publication of public assessment reports (PARs).

**Decision-making procedures of the competent authorities**

**Identity of the members of the decision-making bodies and possible conflicts of interest.** The pharmaceutical review introduced a number of specific transparency provisions, aimed at establishing more credibility and trust in the authorisation procedures and the authorities’ role in the procedures.

Members of decision-making bodies cannot have financial interests in pharmaceutical companies or other interests that could conflict with their responsibilities (*Article 126b, Directive 2001/83/EC on the Community code relating to medicinal products for human use (Code for Human Medicines Directive)). These members must make annual declarations of interest and involvement in the development and marketing of medicinal products.

There are comparable disclosure provisions in relation to the EMEA (*Article 63(1) and (2), EMEA Regulation*). These provisions allow assessment by interested parties and the general public of the authorities’:

- Level of impartiality.
- Appropriateness in relation to their composition.
For example, all members of the EMEA scientific committees are posted on the EMEA website with their declaration of interests. Some member states’ competent authorities replicate this approach. These disclosures do not lead to any practical or technical problems.

Agendas of meetings. Agendas and records of meetings of the national competent authorities must be made accessible to the public (Article 126b, Code for Human Medicines Directive). Often, the applicant itself must disclose the lodging of an application under the stock market rules. However, applicants generally do not like to disclose (or have disclosed) the exact status of their application, because the details are considered to be of a commercially confidential nature. This applies to innovators in the pharmaceutical industry and the generic companies.

This concern has lead to extensive discussions on both the:
- Timing of the agenda’s publication.
- The agenda’s level of detail.

These discussions led to a common agreement between national competent authorities and the EMEA within the informal group of the Heads of Medicines Agencies (HMA) (www.hma.eu) (Recommendation on Transparency, 20 November 2009). The Recommendation on Transparency states that it does not make sense to publish an agenda long after a meeting has taken place. Competent authorities therefore decided that publication of agendas should take place before, or at least very close to, the date the meeting takes place.

To comply with confidentiality rules the competent authorities decided that, in the public agendas of competent authorities’ meetings, a medicinal product will only be referred to by mentioning its therapeutic class (that is, the agenda refers to the second level of the WHO Anatomical Therapeutic Chemical (ATC) Classification System, which is used for the classification of medicinal products.). This means that the only information about the medicine under discussion available to the public is its class.

The EMEA Regulation does not contain similar provisions.

Records of meetings. Records of the competent authorities’ meetings must be made accessible (Article 126b, Code for Human Medicines Directive). Two types of topic are discussed in meetings of the competent authorities’ scientific and decision-making bodies (which raises further disclosure issues in relation to timing and level of detail):

- General issues such as ‘household’ matters and scientific guidelines. Publication of the minutes of discussions on general issues does not usually raise problems in relation to commercial confidentiality. However, members of the scientific and decision-making bodies may not want disclose their specific opinion. This is because they will discuss the same issues afterwards in a European forum (such as the Committee for Medicinal Products for Human Use (CHMP)). Disclosing the opinion of participants in a European forum before it takes place could jeopardise the negotiations. Additionally, the credibility of the outcome of the European discussion may be damaged if the public became aware of prior individual national viewpoints. Therefore, it is not desirable to disclose the arguments and outcome of meetings in relation to these general issues.

- Individual medicinal products. The competent authorities widely discussed timing and level of detail in relation to disclosures about individual medicinal products. In relation to timing, consensus was reached that the outcome of a procedure should not be made public before it has been concluded. This means that records of discussions within competent authorities about an individual medicinal product must only be disclosed as soon as the decision on the application becomes definitive (and not before). Therefore, both:
  - records of the meetings must be divided into sections for each medicinal product;
  - each part can be disclosed at the time the marketing authorisation is granted or a variation adopted.

Additionally, the HMA Recommendation on Transparency comments on level of detail. For active transparency, the authorities conclude that decisions on the balance between transparency and commercial confidentiality must be

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based on the EU freedom of information legislation. Article 126b of the Code for Human Medicines Directive explicitly stipulates that the minutes of meetings must be made accessible. However, the HMA’s view is that once the decision has been taken and the procedure deemed concluded, the public can be granted access to the minutes in compliance with the protection of confidential information (that is, personal data or commercially confidential information).

The EMEA Regulation does not contain similar provisions relating to the records of the meetings, so disclosure is not required.

Voting results and minority views. All competent authorities’ decisions must include (Article 126b, Code for Human Medicines Directive):

- Reasons for the decision.
- The minority views that have been defended.
- The outcome of the vote, where decisions are not unanimous.

Members of scientific committees and decision-making bodies are reluctant to disclose names and opinions on specific issues during specific applications, as many feel that they cannot speak openly if their private opinions are disclosed afterwards. This constitutes a barrier to complete transparency. EU regulatory discussions have not led to a consensus on the issue.

Similarly to the national competent authorities, the EMEA must disclose minority views (Article 61(7), EMEA Regulation).

Assessment reports

European public assessment report (EPAR). Regulation (EEC) No. 2309/93 on the authorisation and supervision of medicinal products and establishing a European Agency for the Evaluation of Medicinal Products (old EMEA Regulation) introduced the concept of the EPAR for medicinal products authorised through the centralised procedure. Since the centralised procedure became operational, the concept of the EPAR has evolved gradually and is now clear and generally accepted by industry.

The EMEA must immediately publish, after deleting any information of a commercially confidential nature, an EPAR, including both (Article 13(3), EMEA Regulation):

- The CHMP’s assessment report on the relevant medicinal product for human use.
- The reasons for its opinion in favour of granting authorisation.

The CHMP’s assessment report is the basis for the EPAR. Commercially confidential information is deleted and the resulting document is presented for approval.

There is an EMEA guidance document to clarify commercial confidentiality (see below, EMEA guidance document).

National public assessment report (PAR). On a national level, in 2004 the PAR (similar to the EPAR) was introduced under the Code for Human Medicines Directive. Whenever a marketing authorisation is granted, an assessment report must be published after deletion of commercially confidential data (Article 21(3), Code for Human Medicines Directive). Most marketing authorisation applications use the mutual recognition procedure or the decentralised procedure, so that the actual assessment is performed in only one member state (the reference member state (RMS)). To avoid the need to translate documents into the many EU languages, the Co-ordination Group for Mutual Recognition and Decentralised Procedures – Human (CMD(h)) decided that all assessment reports must be drafted in English by the RMS. If national legislation requires the RMS to also publish the PAR in its own language, it is the RMS’s own responsibility to do so.

To streamline and harmonise the production of PARs for all authorised medicinal products, the CMD(h) decided to follow the principles the EMEA laid down.

Updates of assessment reports. Assessment reports, including PARs, require continuous updating (whenever new information becomes available which is of importance for the evaluation of the quality, safety or efficacy of the medicinal product concerned (Article 21(4), Code for Human Medicines Directive)).

This applies even where there is no PAR for a particular medicinal product (for example, where it was authorised before Article 21(3) of the Code for Human Medicines Directive came into force).

Pharmacovigilance

In relation to information about the safety of medicinal products, the EUDRA-Vigilance database was created under Article 57(1)(d) of the EMEA Regulation. All adverse reactions reported in the member states must be immediately added to the database and made publicly available (Article 102, Code for Human Medicines Directive).

Some member states allow the general public access to general overviews on reported adverse drug reactions. From a regulatory point of view there are concerns in relation to the timing of publication of suspected adverse drug reactions; if at a later date the suspected adverse drug reaction is invalidated, the initial reporting could lead to an unnecessary public response. This has occurred several times, for example the oral contraceptives scare. Therefore, regulators take the view that safety information should only be provided to the public after evaluation by the competent authorities.

No information about reported adverse drug reactions is available on the EMEA website.

EMEA transparency initiative

The EMEA is conducting a public consultation on its draft amendment of the transparency policy. The objectives of this review are to:

- Make the EMEA’s daily operations more transparent. This will both:
  - include a re-assessment of the currently applied balance between transparency and protection of commercially confidential information;
  - lead to more proactive disclosure of information about the scientific evaluation of medicines.

This will help to better explain how the EMEA operates and how it reaches its scientific conclusions.
Cross-border

OUTLINE OF THE SOURCES OF PROVISIONS CONCERNING TRANSPARENCY

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- Strengthen the EMEA's interaction with its stakeholders, in particular patients and healthcare professionals. The existing interaction will be further developed with a view to consulting patients and healthcare professionals on the scientific evaluation of medicines at the level of the EMEA's scientific committees.

- Promote a harmonised approach to transparency across the European medicines network. The EMEA will work closely with the medicines regulatory authorities in the EU member states to provide a harmonised approach to transparency, including consistent implementation across the EU.

The actions proposed under the consultation are in the field of stakeholder participation in the activities of the EMEA. The creation of an EMEA register of documents is particularly relevant. This register will contain all documents held by the EMEA and can be used to base an FOI request on.

Current status of active transparency

The implementation of active transparency in the EU is a work in progress and competent authorities have yet to comply with many of their obligations. Authorities struggle with the now limited scope available to keep information about their decision-making processes confidential. Agendas and records of meetings of decision-making committees are therefore scarce. Some member states publish agendas of their meetings, but the information is not very useful. Records of meetings to be made available do not contain much detail, even if they are disclosed after a final decision on an application.

Achieving the right balance between the general interest of transparency and the applicants’ and holders’ interest that the authorities refrain from disclosing commercially confidential information is always on the agenda of national competent authorities and the EMEA.

A complicating factor is that active transparency obligations for the EMEA and national competent authorities differ. The EMEA is developing guidance in relation to the information they must make available to the public, but it is still unclear which information must be disclosed by national authorities and which information remains undisclosed.

PASSIVE TRANSPARENCY

Information that is not actively made accessible (published) by the EMEA or the national competent authorities can be requested on the basis of:

- Regulation (EC) No. 1049/2001 regarding public access to European Parliament, Council and Commission documents (Public Access to EU Documents Regulation). This includes access to EMEA information.

- National FOI legislation. As active transparency is developing slowly, interested parties try to gain access to information by employing FOI legislation. This legislation, however, does not allow regulatory agencies to disclose information that is considered commercially confidential.

FOI legislation. FOI legislation in the EU is relatively harmonised in structure, if not in application. The Public Access to EU Documents Regulation and the national FOI legislation have a similar structure. The objective of this type of legislation is to allow public access to all documents, so generally all documents must be publicly accessible. However, absolute and relative exceptions apply to this general rule (see box, Overview of freedom of information legislation exceptions). Additionally, specific rules apply in relation to:

- Documents submitted by third parties.
- Internal documents.
- Documents which are only partly confidential.

In the context of transparency, the most important exception is where disclosure would undermine the protection of a commercial interest of a natural or legal person, including intellectual property (unless there is an overriding public interest in disclosure). The exact wording of this exception varies between member states and does not always mirror the EMEA Regulation. FOI legislation is relevant where the authorities have not made documents accessible. It can therefore be considered to constitute passive transparency.

Pharmaceutical legislation. In relation to transparency, there are many provisions requiring deletion of commercially confidential information before publication. As this is one of the principles of
EC law, it is implied to apply even if the relevant provision does not explicitly mention it. Pharmaceutical legislation does not provide definitions or guidance in relation to which information must be considered commercially confidential. However, the HMA follows the rules in the EMEA guidance document (see below, EMEA guidance document). This type of guidance document is also relevant in relation to passive transparency. This is because information that should have been actively disclosed by the competent authorities must be disclosed if requested on the basis of FOI legislation.

The HMA also follows the conditions in the Public Access to EU Documents Regulation.

A very important aspect of passive transparency is that the requesting party can only request documents that he is aware exist. All documents that must be made available under relevant legislation can be requested from the competent authorities (including the EMEA) on the basis of FOI legislation.

See also box, Outline of the sources of provisions concerning transparency.

Current status of passive transparency

To gain information about authorisation procedures, much use is made of FOI legislation. In this area, experience and case law are relatively undeveloped. Many issues relating to the level of transparency to be expected are clarified in the transparency provisions in pharmaceutical legislation.

The national competent authorities clarify issues relating to whether specific data are commercially confidential. However, the standards for transparency are set by pharmaceutical legislation, the EMEA and the HMA.

In practice, decisions about the disclosure of information must be made on a case-by-case basis, emphasising the practical effect disclosure would have in relation to commercial issues. The EMEA principles are not always appropriate because they mainly relate to EPARs. National FOI requests can and do go beyond the information included in EPARs. In this respect, an important development will be the new register of EMEA documents that can be used to base a FOI request on. It is expected that this register will be available at the end of 2009.

COMMERCIALLY CONFIDENTIAL INFORMATION

Which information is commercially confidential?

Whether information is deemed to be commercially confidential depends on the circumstances and the disclosing authority. However, all information relating to a medicinal product’s manufacturing and to details of starting materials (for example, sources and specification) should be considered commercially confidential. Information about the side effects and efficacy of a medicinal product could have a negative effect on a pharmaceutical company’s trade and stock value.

EMEA guidance document

The EC standard for decisions about the commercially confidential nature of information held by regulatory authorities is the EMEA guidance document called Principles to be applied for the deletion of commercially confidential information for the disclosure of EMEA documents (EMEA/45422/2006). This guidance document focuses on commercially confidential information in the EPAR (see above, Development of active transparency: Assessment reports - European Public Assessment Report (EPAR)) and has also been adopted by the HMA. It requires the division of information to be deleted into two categories:

- **Confidential intellectual property, know-how and trade secrets.** This includes formulas, programmes, process or information contained or embodied in a product, unpublished aspects of trade marks, patents and so on.
- **Commercial confidence.** This includes companies’ structures and development plans.

OVERVIEW OF FREEDOM OF INFORMATION LEGISLATION EXCEPTIONS

**Absolute exceptions**

There are absolute exceptions to access where disclosure would undermine the protection of:

- The public interest in relation to any of the following:
  - public security;
  - defence and military matters;
  - international relations;
  - financial, monetary or economic policy.
- Privacy and the integrity of the individual.

**Relative exceptions**

The following relative exceptions apply to access:

- Where disclosure would undermine the protection of any of the following:
  - the commercial interests of a natural or legal person, including intellectual property;
  - court proceedings and legal advice;
  - the purpose of inspections, investigations and audits.
- Access to an internal document will be refused if disclosure of the document would seriously undermine the decision-making process.

These relative exceptions only apply where there is no overriding public interest in disclosure.

**Third party documents**

In relation to third party documents, the third party must be consulted to assess whether an exception applies (unless it is clear that the document must or must not be disclosed).

**Partial disclosure**

If only parts of the requested document are covered by any of the exceptions, the remaining parts must be disclosed.
There are different considerations depending on the type of information:

- **Information relating to the pharmaceutical development.**
  As a rule, this is considered to be confidential, unless a specific reason for disclosure exists.

- **Preclinical and clinical data in the file (including opinions of the CHMP).** Only data that could be used to identify company strategies and plans are considered to be prima facie commercially confidential.

- **Information obtained through inspections.** This is not considered confidential unless the information relates to new facilities or procedures which are still confidential.

The EMEA Regulation contains no specific guidelines for pharmacovigilance.

One of the main weaknesses of this document is its limited scope: it only considers EPARs. In practice, many other documents (for example, detailed reports on adverse drug reactions or documents related to scientific advice provided by the EMEA or the national competent authorities) must be assessed in relation to commercial confidentiality.

**BATTLE OF RULES**

As already discussed, the Code for Human Medicines Directive and FOI legislation are based on the principle that all information is made accessible, except for that which is commercially confidential (that is, information the disclosure of which would undermine commercial interests of a natural or legal person (Public Access to EU Documents Regulation)). The 'battle of rules' concept concerns who takes the decision as to which information should be labelled commercially confidential.

**Centralised procedure.** For medicinal products authorised through the centralised procedure, the EMEA decides what is commercially confidential on the basis of pharmaceutical legislation and EC FOI legislation. If a stakeholder does not agree with the EMEA's decision, this can be litigated before the Court of First Instance at the European Court of Justice (ECJ).

**National decisions.** It is more complicated where a medicinal product is authorised through mutual recognition or a decentralised procedure. In principle, a concerned member state (CMS) must decide on the level of detail to be disclosed to the applicant. The national administrative courts can review these decisions. Authorities and national courts experience the following difficulties when making decisions:

- That they must apply national legislation to the decision, even where the procedure during which the information was received was of a European nature.

- That every decision taken on a national level affects national decisions and court rulings in all other member states, because any information disclosed in any member state is also available to anyone in the EC.

Where an FOI request relates to documents drafted for grant or maintenance of a marketing authorisation, good practice indicates that competent authorities should interpret relative exceptions to access in their national FOI legislation in a manner consistent with the Code for Human Medicines Directive (which is intended to harmonise all aspects of national law relating to the grant of marketing authorisations). This obligation relates to both:


- Any domestic provision that may contradict, or constitute a variation of, the results contemplated under the Code for Human Medicines Directive (for example, the national FOI acts).

Therefore, an exception relating to commercial confidentiality in national FOI legislation must be interpreted and applied in line with Article 21(4) of the Code for Human Medicines Directive. This provides that the competent authority must delete any information of a commercially confidential nature before publishing its PAR. Article 21(4) must be interpreted in light of both the:

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**CASE STUDY**

For the ADHD medicinal product, Strattera, new pharmacovigilance data have been gathered over the years. The UK Medicines and Healthcare products Regulatory Agency (MHRA) has acted as reference member state (RMS) for Strattera and is therefore responsible for the assessment report. Because Strattera was authorised before the obligation to publish a public assessment report (PAR) entered into force, no PAR was drafted for this product.

An interest group seeks information about the safety of Strattera and therefore requests the information contained in the (updated) assessment report under freedom of information (FOI) legislation in:

- The UK.
- Some other member states.
- The Netherlands (as concerned member state (CMS)).

The following occurs:

- The MHRA provides the assessment report after deletion of all information it considers commercially confidential. The main issue is the level of detail of safety information about the medicinal product.

- The Netherlands Medicines Evaluation Board refers the applicant to the MHRA.

- The Netherlands administrative court must make a ruling on whether either:
  - the PAR as disclosed by MHRA complies with Dutch FOI legislation;
  - other decisions must be made.

A battle of rules occurs. Directive 2001/83/EC on the Community code relating to medicinal products for human use (Code for Human Medicines Directive) leads to a harmonised PAR, which should be appropriate in all CMSs. However, this battles with the national FOI legislation and national courts (before which FOI legislation is invoked), which act on their own national rules.
General principles of EC law on the protection of confidential information and business secrets, as developed by the ECJ.

Overall goal of the Code for Human Medicines Directive (that is, to harmonise all aspects of the grant of market authorisation for medicinal products). It therefore appears that the assessment should be made by the RMS and the CMS authorities should not attempt to predict or contradict the RMS’s decision. National authorities and courts must adhere to the EC PAR and EC decisions relating to which data can be disclosed.

See also box, Case study.

Current position in relation to confidentiality decisions

The national courts are often required to take decisions about disclosure of regulatory information, often referring to national FOI legislation. It is questionable whether these national FOI rules are appropriate for taking transparency decisions, because regulatory processes and rules on transparency are available in EC legislation. Therefore, as the rules for transparency and disclosure are found under EC harmonising legislation, it appears that national decision-making powers in this field are exhausted. The practical consequence of this is that, under the decentralised or mutual recognition procedures, final decisions on transparency should remain with the RMS and its national courts. CMSs and their courts should comply with decisions made in the RMS. However, this principle is not a legal certainty as it has not yet been reviewed by the ECJ.

The EMEA’s consultation procedure on future transparency

Transparency has been a topical issue since the 2001 pharmaceutical review and remains so. Neither the EMEA (together with the Commission) nor the national competent authorities have drafted or agree on concrete rules relating to the timing and level of detail of disclosed information on the procedures and medicinal products in the EC. The EMEA is undertaking a consultation procedure in relation to improving transparency. It is hoped that the adoption of a renewed EMEA transparency policy will lead to a harmonised approach for national competent authorities as well. In the meantime, competent authorities’ transparency related decisions are vulnerable for stakeholders who do not agree with either the disclosure of (detailed) information or with authorities refusing to disclose requested information.

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