ECJ ruling

Guideline practice—learning from Europe

Medical guidelines are being produced worldwide at such a pace that it is difficult to expect that they will actually be implemented in practice. Consider, for example, how far German jurisprudence is prepared to go in recognising guidelines published abroad in determining whether there have been errors in treatment, even gross ones. This reverses the burden of proof to the detriment of the treating party.

One recalls the controversy between the Higher Regional Court of Koblenz in its decision of 25 June 2014 (5 U 792/13) and the Federal Court of Justice in its decision of 16 June 2015 (VI ZR 332/14) which dealt with the question of whether a regular German hospital should have taken into account in January 2006 a medical guideline from Canada that had been published there in February 2005. The Higher Regional Court had answered this question in the affirmative, while the Federal Court of Justice took a somewhat more nuanced view.

If guidelines are held in such high esteem in liability law, it is all the more important that they reflect the standard of care recognised at the time of their adoption in the sense of evidence-based medicine/evidence-based dentistry, and that any bias is excluded as far as reasonably possible.

Anyone who has ever worked on guidelines knows that the most important bias influencing the content of guidelines is human bias.

In a recent decision dated 14 March 2024 (C-291/22 P), the European Court of Justice in Luxembourg (ECJ) has provided some interesting guidance on human bias in the European Medicines Agency's (EMA) review activities. The case pending before the ECJ concerned, among other things, how the EMA should select experts for the authorisation of medicinal products.

The decision concerns the tension between the expertise that is called upon and the control of that expertise—and thus the core area of any guideline.

The case concerned a drug that had been refused marketing authorisation by the European Commission. The refusal was based on an opinion from the EMA's Committee for Medicinal Products for Human Use (CHMP) and an ad-hoc expert group convened by the EMA. The pharmaceutical manufacturer had complained unsuccessfully that individual members of the expert group were not independent and had conflicts of interest. The manufacturer was successful in having this decision overturned by the ECJ.

The ECJ refers to the fundamental right to good administration enshrined in Article 41 of the European Charter of Fundamental Rights. This fundamental right includes the right of every person to have their affairs handled impartially by the institutions, bodies, offices and agencies of the European Union. This requires sufficient guarantees to exclude any legitimate doubt as to possible bias.

With specific reference to the EMA, the ECJ considers that impartiality would

be compromised if a conflict of interest could arise for one of the members of the CHMP as a result of a clash of responsibilities, irrespective of the personal conduct of that member. Such a breach could lead to the illegality of the decision adopted by the Commission at the end of the procedure. Objective impartiality is also compromised if an expert with a conflict of interest is part of the group of experts consulted by the CHMP in the course of the review leading to the EMA's opinion and the Commission's decision on the application for marketing authorisation. The ECJ considers the conflict of interest to be an objective exclusion criterion. It is irrelevant whether the conflict of interest has become known. If it exists, the respective expert cannot be appointed.

How can the EMA identify such a situation? The ECJ requires the EMA to actively investigate conflicts of interest itself, at least as soon as it has received any indications of such conflicts. In this case, the pharmaceutical manufacturer had provided the EMA with this information. Had the EMA followed up, it would have discovered that one of the authorised experts was the principal investigator for a competing product in the European phase 3 clinical trial for the medicinal product in the authorisation procedure. A conflict of interest could hardly be more obvious.

The ECJ requires that the influence of conflicts of interest to be excluded with certainty, not just the non-participation in or non-voting at advisory meetings.

The ECJ's comments on the influence of conflicts of interest (human bias) are equally important and interesting for the development of guidelines (no. 76–77):

"It must be observed, in that regard, that the opinion expressed by the expert group convened by the CHMP has a potentially decisive influence on the EMA's opinion and, through that opinion, on the Commission's decision. Each member of that group may, in some circumstances, have a considerable influence on the discussions and deliberations that take place, on a confidential basis, within that group. Accordingly, participation in the expert group consulted by the CHMP of a person who is in a situation of conflict of interest gives rise to a situation that does not offer sufficient guarantees to exclude any legitimate doubt as to possible bias, within the meaning of the case-law referred to in paragraph 73 of the present judgment.

Therefore [...] a conflict of interest on the part of a member of the expert group consulted by the CHMP substantially vitiates the procedure. The fact that, at the end of its discussions and deliberations, that expert group expresses its opinion collegially does not remove such a defect. That collegiality is not such as to neutralise either the influence that the member in a situation of conflict of interest is in a position to exert within that group or the doubts as to the impartiality of that group which are legitimately based on the fact that that member was able to contribute to the discussions."

According to the ECJ, it is the EMA's responsibility to identify conflicts of interest and draw the appropriate conclusions.

Anyone analysing guidelines, in particular guideline reports and conflict-of-interest statements, should be able to expect that any guideline author will comply with these requirements of the ECJ and will not accept guidelines developed with the involvement of persons with conflicts of interest. This also applies to existing guidelines. If the involvement of persons with a conflict of interest has clearly had an influence, these guidelines must be withdrawn; otherwise, they must be revised in a timely manner. A conflict of interest must result in the person being removed from the guideline group. If this means that the guidelines will not be developed in the same way as before, so be it.

Author

Prof. Dr iur. Thomas Ratajczak
Berlin · Duisburg · Essen ·
Freiburg i.Br. · Köln · Meißen ·
Munich · Sindelfingen

Posener Straße 1
71065 Sindelfingen
Germany

+49 7031 9505-27 (Sybill Ratajczak)
ratajczak@rpmed.de
www.rpmed.de