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POINT OF VIEW

Anything new in EU pharmacovigilance?

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New legislative provisions [1, 2] aim at improving *the operation of Union law on the pharmacovigilance of medicinal products for human use*. Published at the end of 2010, they will come into force in the EU by mid-2012

Merging useful information

The Regulation [1] rightly suggests that *the Eudravigilance database should be ...strengthened as the single point of receipt of ...information*. Relying on multinational safety data rather than on information from smaller samples would permit faster recognition of drug toxicity and a more reliable assessment of the impact of the database on drug benefit–risk profiles. The Regulation also establishes that uniform criteria and procedures are to be adopted throughout the EU, with standard format and content for the electronic transmission of reports and information. Since the benefit–risk profile of drugs is affected by the actual conditions of their use, it is also important that *the term 'adverse reaction' .. covers noxious and unintended effects resulting ...also from medication errors and uses outside the terms of the marketing authorisation, including the misuse and abuse*.

Transparency would ensure better pharmacovigilance

Less agreeable is the suggestion that the *database should be fully and permanently accessible to the Member States, the Agency and the Commission, and accessible to an appropriate extent to marketing authorisation holders and the public.* Should it not be fully accessible to everyone—or at least also to health professionals and scientists? Physicians could be urged to spontaneously report events they might have considered unrelated to the drug until they read about other similar sample cases. Alongside spontaneous reporting, proactive pharmacovigilance should be fostered. Independent reviews of data by epidemiologists and medical scientists could help establish the size of a risk based on sparse signals (for instance, more frequent signals and the consequent appearance of the risk in a given subgroup of patients). Therefore, researchers should not only be allowed access, but this group should in fact be encouraged to regularly access the database. The pharmacovigilance authorities should promote, commission and fund independent studies on critical safety issues. Academia should also be involved in the implementation—not very promising to date [3, 4]—of the risk management plan submitted by companies with their marketing authorisation application and of the post-authorisation safety studies demanded by the European Medicine Agency (EMA) for specific medicinal products requiring additional monitoring.

Need for independent evaluation/decision

In place of the proposed safety agency [4] it is deemed *appropriate to create a new scientific committee within the* EMA. This would be acceptable if the proposed Pharmacovigilance Risk Assessment Committee were an independent body. Instead, *for the sake of consistency and continuity of the safety assessments*—says the law—*the final responsibility for issuing an opinion on the risk–benefit assessment of*

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medicinal products.…should remain with the Committee for Medicinal Products for Human Use (CHMP). Since this committee is the one that granted the marketing authorisation, it may unconsciously feel bound to uphold its earlier evaluation and decision. This in spite of the fact that the evaluation that allows drugs onto the market is mostly based on efficacy findings in small groups of patients, while post-marketing assessment of the benefit–risk profile draws on more reliable safety data emerging from much larger populations. The potential conflict of interests can only be avoided by commissioning the two evaluations, as distinct functions in different phases, to two independent bodies [4].

Funding pharmacovigilance

The pharmacovigilance needs adequate funding which, according to the Regulation, should be raised *by empowering the Agency to charge fees to marketing authorisation holders.* The fact that, as for any other EMA activity, the funds collected would be *under the permanent control of the Management Board* and rapporteurs of any assessment procedures would *receive payment through* the EMA, is not sufficient *to guarantee the independence of the Agency.* The financial relationship with industry undermines the EMA's independence in the eyes of the public. The European Commission (EC) should collect the fees from pharmaceutical companies and grant the EMA financial support that is independent of the activities undertaken, the products and the companies involved.

Public health and commercial priorities

One final note on the political context of the new legislation. The impression that the EC keeps treating drugs more as consumer goods than health tools is supported by the wording of the Directive [2]: while recognising that *the fundamental objective of the regulation of medicinal products is to safeguard public health*, it states that...*the existing pharmacovigilance provisions ...should be strengthened and rationalised... in order to prevent or eliminate those obstacles to the free movement of medicinal products* that have been generated by *divergent actions by Member States in relation to safety issues…* The recent removal of the EMA from the control of the Enterprise and Industry Directorate does not per se ensure that, at least when dealing with drugs, the EC will make public health interests prevail over a commercially oriented view. It is hoped that the Health and Consumer Policy Directorate, now responsible, will ensure that—as the Regulation wishes—*the strengthened system of pharmacovigilance does not lead to the premature granting of marketing authorisations.* The legislator's wish may well sound strange, but it is not surprising in the light of the several marketing authorisations that remain "conditional" or "under exceptional circumstances" for so long because of a lack of comprehensive efficacy or safety data. The Health Directorate should see that all the commitments to convert temporary approvals to normal are properly fulfilled in due time so as not to leave products on the market that have an uncertain benefit—risk profile. The reasons for the commitments, the approach for solving them and the results should all be made public in order to make patients, prescribers, and payers aware of the present limitations and be able to make their own appropriate decisions.

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References

1. Regulation (EU) No 1235/2010 of the European Parliament and of the Council of 15 December 2010 amending, as regards pharmacovigilance of medicinal products for human use, Regulation (EC) No 726/2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency, and Regulation (EC) No 1394/2007 on advanced therapy medicinal products. Available at: http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2010:348:0001:0016:EN:PDF
2. Directive 2010/84/EU of the European Parliament and of the Council of 15 December 2010 amending, as regards pharmacovigilance, Directive 2001/83/EC on the Community code relating to medicinal products for human use. Available at: http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2010:348:0074:0099:EN:PDF
3. Frau S, Font Pous M, Luppino MR, Conforti A (2010) Risk management plans: are they a tool for improving drug safety? Eur J Clin Pharmacol 66:785–790. doi:10.1007/s00228-010-0848-8
4. Garattini S, Bertele' V (2010) Rosiglitazone and the need for a new drug safety agency. Br Med J 341:c5506. doi:10.1136/bmj.c5506