European Network of Centres for Pharmacoepidemiology and Pharmacovigilance

Response to:

COMMUNICATION FROM THE COMMISSION TO THE EUROPEAN PARLIAMENT, THE COUNCIL, THE ECONOMIC AND SOCIAL COMMITTEE AND THE COMMITTEE OF THE REGIONS

'A comprehensive approach on personal data protection in the European Union'

Submitted by the European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENCePP)

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Why is ENCePP responding?

The European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENCePP) comprises more than 100 centres, networks and data sources across 17 European Countries and aims to further strengthen the post-authorisation monitoring of medicinal products in Europe. ENCePP is an initiative from the European Medicines Agency (EMA), which coordinates and facilitates the Network.

Pharmacepidemiology is the field of public health research that studies effects of medicinal products in large populations, mostly after these products have come to the market. Examples include studies on the risk of myocardial infarction after use of rofecoxib (Vioxx®) or H1N1 vaccination and Guillain-Barré Syndrome or narcolepsy. In order to conduct these studies, data from routine health care on millions of persons, which is accumulated in large insurance or medical record databases, are used. Since the early nineties these databases have become the state of the art resource for postmarketing monitoring of the (adverse) effects of medicinal products.

Whilst ENCePP members agree with the principles in the communication document of the need to protect the rights and freedoms of individuals and the need to achieve an internal market, they respond to this communication to express their concern that secondary use of health data for public health research is not specifically addressed in the current communication. Failing to consider this use in the updated legislation will impact negatively on the ability to conduct studies that assess effects and safety of medicinal products in daily clinical practice.

ENCePP endorses the need for protection of individuals' rights to privacy

ENCePP fully recognises and endorses the need for protection of individuals' right to privacy, the need for harmonisation of legislation in this regard and the need for better enforcement of this legislation across the Member States of the European Union. Safeguarding data confidentiality has been a key area of consideration in public health research; the introduction of Directive 95/46 on the Protection of Individuals with regard to the Processing of Personal Data has lead to careful implementation of a range of measures to ensure protection of data confidentiality whilst allowing free flow of data for the benefit of public health. At present, ENcePP is faced with many differences in interpretation and implementation of the Directive 95/46 on the Protection of Individuals with regard to the Processing of Personal Data across Member States. This does not facilitate free flow, or pooling of data across countries, which is sometimes necessary to address safety issues faster. Better harmonisation across Member States, as suggested in the communication document, would have facilitated some of the public health and drug safety research examples mentioned further on in this response document.

ENCePP wishes to highlight that there are ways to protect the privacy of individuals whilst allowing secondary use of their data – release of data does not necessarily constitute a breach of the right to privacy. ENCePP foresees that data minimisation measures, prohibiting the use of data for purposes other than for which the data were generated originally, and implementing a generalised 'right to be forgotten' will be detrimental for future investigations into public health hazards. Therefore, while noting that provisions are made to ensure the 'right to be forgotten', ENCePP suggests the Commission also considers those situations in which individuals actively express their wish to make their data available for public health research purposes – a 'right *not* to be forgotten', or a 'right to be remembered'. ENCePP suggests that generally the public wants their adverse health experiences to be at least of some benefit to others; the public have a right to expect that mechanisms will be available that allow the use of their (anonymised) data within large databases without their implicit (logistically often impossible) permission for public health benefit – whilst safeguarding, and balanced against their right to, privacy. Respecting such wishes would imply respecting people's right to autonomy as well as individuals' right to have their data used for their (in)direct benefit.

In this response document, examples are provided where such secondary use of data has occurred whilst fully protecting data confidentiality and individuals' right to privacy. The examples illustrate why these data are needed as otherwise we would have been unaware of hazards to public health and important regulatory actions would not have been taken as a result of our being ignorant of the risks. Similarly, the examples illustrate how we ensure beneficial products remain available to the public because secondary use of data helps to refute spurious claims of harm.

Recent examples of secondary use of anonymised health care data for the benefit of public health whilst protecting individuals' right to privacy

In the 2009 H1N1 pandemic, target populations for prioritisation in the vaccination programs were defined based on identification of increases in mortality using routinely collected health care data.[1] ***Safety of the H1N1 vaccines*** was monitored using a combination of spontaneous reports and systematic evaluations of safety. To enable interpretation of the case reports and calculation of observed versus expected rates of adverse, potentially vaccine-related events, the background incidence rates of such adverse events were calculated using routinely collected health care data. An increased risk of Guillain-Barré syndrome (GBS), of the magnitude of that suspected in the USA in 1976, was refuted using such data. GBS is very rare; combining data from sources across EU member states was crucial to enable the evaluation of this potential association. The study was completed within 12 months; this would not have been possible if routine health care data had not been available. Similar studies have been carried out in the USA, again using routinely collected health care data.[2] At present, routinely collected health care data from across Europe are being used for a similar and more rapid assessment of the safety signal

generated in Finland and Sweden of a potential link between H1N1 2009 vaccine exposure and narcolepsy. In addition, the need to study safety of the vaccine in vulnerable groups such as pregnant women and children has been highlighted, including the prerequisite that this has to be done using routinely collected data.[1]

In 2006, data from an epilepsy pregnancy registry suggested ***lamotrigine***, a relatively new antiepileptic medicine, gives an increased risk of orofacial cleft in the offspring if taken during the first ***pregnancy*** trimester.[3] Pregnancy registries have certain limitations when they are used for studying drug safety in pregnancy and the claim of harm has not been confirmed in two more recent studies, which used high-quality data collected in routine clinical practice.[4,5]

In 1998, a case series was published in the Lancet suggesting ***MMR vaccine*** increases the risk of autism.[6] Uptake rates of the vaccine dropped following publication of the case series, resulting in outbreaks of measles and mumps. Epidemiological studies were subsequently published that consistently found no evidence of such a link and the uptake rates have increased again.[7,8,9]

Rosiglitazone is an oral antihyperglycaemic agent used in the treatment of type II diabetes. In 2007, a meta-analysis of clinical trials highlighted a potential increase in risk of myocardial infarction of rosiglitazone compared with other products. Many studies followed, including more meta-analyses as well as observational studies using healthcare databases. A retrospective analysis of a cohort of patients prescribed rosiglitazone based on the UK GP database, THIN was undertaken by the EMA in August 2010. It suggested that about 8% of patients take rosiglitazone despite having cardiac contraindications. This 'real-life' use of the drug was taken into account in the September 2010 EMA's Committee for Medicinal Products for Human Use (CHMP) recommendation of the suspension of the marketing of rosiglitazone in the EU.[10,11,12,13]

The examples used above are a selection of many. They include examples of secondary use of data for the benefit of vulnerable groups, for the evaluation of rare but serious and avoidable adverse events, for the benefit of large populations with chronic disease. Some of the examples highlight how data flow across EU Member States is possible and sometimes a prerequisite for answering important public health questions.

In the examples mentioned, routinely collected health care data were used for purposes other than for which the data were originally collected. Privacy of individuals was safeguarded by anonymising data at source, through a clearing house, or at the earliest possible point following record-linkage. At present, ethics committees and institutional review boards play a crucial role when decisions regarding such secondary use of data are made. In addition, various governance bodies are in place with the explicit remit of safeguarding individuals and preventing abuse, as well as allowing use of the data for societal benefit. Despite this, situations remain where differences in interpretation of the 1995 Directive on Data Protection between Member States severely delay or obstruct this type of research.

At present, the remit, responsibilities and authorities of ethics committee responsibilities and governing bodies differ according to the jurisdiction. ENCePP recognises this is important in view of national, local and cultural considerations that may need to be taken into account; equally, it often has implications on study design, conduct or feasibility when implementing public health research across Member States. ENCePP suggests that when harmonisation of legislation is considered, this is an additional aspect to be taken into account. ENCePP endorses the need for control to ensure adequate safeguards of the data. If the conduct of supranational research for public health benefit in the EU is to be successful, it is important to have in place a harmonised, or at least convergent, legislation across the Member States.

Examples of policy documents from the European Union and the United States highlighting the importance of using health care data for the benefit of public health

In December 2008, the Commission made legislative proposals for strengthening pharmacovigilance. The Commission's reasoning was that whilst medicinal products contribute considerably to health, they can, also have adverse effects. Reference was made to an estimated 5% of all hospital admissions being due to adverse drug reactions (ADRs), and ADRs being fifth most common cause of hospital death. It was estimated that 197,000 deaths per year in the EU are caused by ADRs, with a total cost to society of around €79 billion.[14] The resulting legislation, which was published in December 2010, foresees post authorisation safety studies and effectiveness of risk minimisation. [15,16] This will require secondary use of healthcare data.

The Food and Drug Administration (FDA) in the USA has started the Sentinel Initiative in recognition of the need to use innovative methods to monitor FDA-regulated products and to enhance public health safety by secondary use of anonymised health data. In the autumn of 2007, Congress passed the FDA Amendments Act (FDAAA), mandating the FDA to establish an active surveillance system for monitoring drugs that uses electronic data from healthcare information holders. The Sentinel initiative is the FDA's response to that mandate. Its goal is to build and implement a new active surveillance system that will eventually be used to monitor all FDA-regulated products in a total of at least 100 million patients. The FDA has used administrative and insurance claims databases to investigate safety questions about Agency-regulated products, but generally it has only worked with one particular healthcare system at a time (for instance, Medicaid data alone, or data from one Health Maintenance Organisation) to evaluate a given safety issue. The disadvantage hereof is the inability to generalise to the general population and the relatively short duration of follow-up of individuals, which severely limits the ability to evaluate a range of medicine safety questions. The aim now is to create a linked, sustainable system--which FDA calls the Sentinel System--that will draw on existing automated healthcare data from multiple sources to actively monitor the safety of medical products continuously and in real-time.

Establishing a long-term, sustainable system raises many questions of considerable public interest, including issues about governance, privacy, data standards and public availability of results. FDA has fostered a broad public forum to explore the complexities of creating such a system.

Similar initiatives of linking databases and pooling data of up to 50 million subjects to enhance monitoring of safety of medicinal products have been funded by the European Commission through the seventh Framework program (e.g. EU-ADR,[17] SOS,[18] ARITMO,[19] EUROMediCAT[20]), the European Centre for Disease prevention and Control (VAESCO[21]), and the public-private partnership IMI (PROTECT[22]). Given the desirability, as recognised by healthcare professionals as well as the general public, of using healthcare data for societal benefit and given the associated developments to enhance existing systems, ENCePP urges the Commission to consider the impact of the communication and any proposed changes in legislation in the light of our ability to support and improve public health in general, and more specifically, to monitor the safety of medicinal products in Europe.

Conclusion

For reasons outlined in this response document, ENCePP requests that the Commission gives careful consideration to the secondary use of health care data and carries out an assessment of the impact on public health of any proposed changes in data protection legislation and guidance when revising the data protection rules. ENCePP suggests the legislation on the use of personal data, including sensitive (health care, genetic) data, needs to include a section on the use of such data for purposes of supporting and improving public health. There are technological and other means of allowing such use of person-level data whilst protecting individuals' right to privacy.

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