

Between transparency and secrecy

How does TTIP impact the publication policy of clinical studies in the pharmaceuticals field?

Remi Maier-Rigaud¹

At a glance

Clinical studies provide the foundations for the authorisation of pharmaceuticals. Health systems and ultimately European consumers would profit from publication of reports on clinical trials. The advantages are wide-ranging: it would be easier to double-check studies and assessments of the benefits of pharmaceuticals could be performed on a much broader and more secure data basis, which would be of general public benefit. Following a decision by the European Ombudsman, the European Medicines Agency (EMA) planned to proactively publish the complete data from clinical trials. The EMA once again significantly scaled down its efforts to achieve greater transparency following the commencement of TTIP negotiations in 2013, while the new EU Regulation provides discretionary latitude for declaring data produced in clinical studies to constitute business secrets.

There has been an intensive debate over the possible benefits and disadvantages of the Transatlantic Trade and Investment Partnership (TTIP) ever since negotiations got underway in July 2013. The convergence of standards in the health field is considered to be especially sensitive and has been under particularly critical scrutiny by civil society actors since they became aware of a “wish list” by the pharmaceutical industry.² Under the negotiating mandate of the EU, sectoral provisions are to be agreed upon for “pharmaceuticals and other health industries” with the “objective of reducing costs stemming from regulatory differences in specific sectors, including consideration of approaches relating to regulatory harmonisation, equivalence, or mutual recognition, where appropriate.”³

The EU’s TTIP negotiating position

The official negotiating position of the EU in the pharmaceuticals field⁴ aims at an intensification of already existing regulatory cooperation with the USA. This includes for example mutual recognition of inspections for the purpose of ensuring good manufacturing practice. To the extent that this initiative seeks to eliminate duplication of work, these

savings on resources are welcomed, as long as this does not have a negative impact on the safety of pharmaceuticals. EU harmonisation efforts are also focusing on the authorisation of biosimilars, generic drugs and children's drugs. An agreement on high transatlantic standards, for example in the determination of reference drugs and proof of bioequivalence, would make it possible for the pharmaceutical sector to save on costs while also enabling faster market authorisation of pharmaceutical products in the interest of patients.⁵

The precondition for authorisation of pharmaceutical products for market, however, is that the applicants demonstrate their effectiveness, safety and quality in clinical trials. The question of how to handle this data is thus of key importance when it comes to efforts to bring about regulatory convergence. The negotiating position of the European Commission calls for possibilities to exchange "confidential/trade secret information" between the EU and the US authority in charge of pharmaceutical products, the Food and Drug Administration (FDA). This includes data from applications for authorisation. Avoiding "unnecessary clinical trials/testing replication" could ease the strain on administrative resources and achieve "important costs savings for industry". "Provisions on the exchange of confidential/trade secret information", which could be placed in the pharmaceuticals annex are a precondition for this. Finally, the Commission has expressed its openness to proposals from the pharmaceutical industry: "Innovative approaches from industry could greatly contribute to the realisation of this objective."

The European Medicines Agency's zigzag course: is there already regulatory chill?

The EU's position of establishing special confidentiality provisions for the pharmaceuticals sector in the TTIP negotiations has apparently already had a deterrent effect on regulatory plans ("regulatory chill") in the area of clinical studies. By way of explanation: after a complaint was

filed by Danish researchers, in a 2010 decision the European Ombudsman called upon the European Medicines Agency (EMA) to provide access to clinical study reports, and came to the conclusion that these do not contain any confidential commercial information. The EMA thereupon began planning proactive publication of clinical studies data. Following this move in the direction of far-reaching transparency, the Agency then began backpedalling in 2014 after conducting public consultations. Revised plans then provided for public disclosure of an incomplete version of reports on trials. After this triggered protests, the EMA finally settled on a compromise solution on 2 October 2014: reports on clinical trials that are submitted within the framework of the centralised authorisation procedure beginning 1 January 2015 will be published after the decision on market authorisation is issued. Usage conditions provide exclusively for non-commercial use. If the data is not only to be viewed on screen, but rather used, comprehensive registration of users is to be required according to EMA's new terms of use. Only reports on clinical trials and not raw data are to be made available in the initial stage. Finally, the EMA wants to first carry out consultations in order to determine what form of publication of raw data from clinical trials could be possible. Even if the EMA generally recognises that the results of clinical trials do not constitute confidential information, it allows editing of the results prior to publication. In the annex to its new transparency policy, the EMA identifies the areas of clinical study reports which typically contain confidential information from which competitors could obtain an advantage in the event of publication and which are to be edited and revised accordingly.⁶

The EU Regulation on clinical trials

The new transparency policy of the EMA is only a transitional solution until the new EU Regulation on clinical trials on medicinal products for human use enters into effect on 28 May 2016.⁷ This provides for clinical trials in several member states only requiring one application, on which a

decision has to be made within 60 days after the application is filed. Simplification of this administrative procedure is expected to translate into cost savings for enterprises and a resurgence of clinical studies conducted in the EU. More transparency is also a declared aim: All clinical studies and reports including a version that can be understood by non-specialists are to be registered in an EMA database, become publically accessible no later than one year after the completion of the trials and generally speaking no longer be considered to be confidential business information. The Regulation provides for exceptions to the obligation to publish data on clinical studies, however. Included in these is “protecting commercially confidential information, in particular through taking into account the status of the marketing authorisation for the medicinal product, unless there is an overriding public interest in disclosure” (Art. 81, 4).

Access to clinical studies data: the key to more evidence-based provision of pharmaceuticals

A transparent approach to handling reports on clinical trials is of considerable importance to health systems.⁸ The possibility of reviewing study results is a fundamental principle promoting scientific progress in the interest of patients:

- First of all, reports on clinical trials contain significantly more information than published academic articles and allow review of the studies that have been carried out by other researchers. There are prominent examples such as the flu medication Tamiflu, for which published studies are contradictory, even though a good deal of money has been spent on the medicine, especially by the public sector.
- Secondly, clinical study reports make possible the execution of metastudies in which unusual results can be explored for which individual studies would offer too small a database.
- Thirdly, reports on clinical trials (including unsuccessful ones) offer insight into study de-

signs, avoidable mistakes and best practices. This allows duplicate work to be avoided and study designs to be improved in the interest of the participating test persons.

- Fourthly, clinical study reports provide the most important data foundation for evidence-based assessment of medical procedures such as evaluation of the benefits of pharmaceuticals. Publication of clinical study reports would contribute significantly to ensuring that health insured persons only pay high prices for new pharmaceuticals if an additional benefit is confirmed by independent, evidence-based research. In a statement issued on the transparency policy of the EMA, the Institute for Quality and Efficiency in Health Care (IQWiG), which is charged with Health Technology Assessment (HTA) in Germany, emphasises that clinical study reports contain twice as much information as published studies. Access to clinical study reports would also have a positive impact on companies that have to demonstrate the advantage of their new medicines over comparative existing therapies within the framework of benefit assessments. Explorative endpoints lying outside the indication applied for in the marketing authorisation procedure such as, for example, quality of life are also of importance to the assessment of benefits.⁹ EMA currently lists especially explorative endpoints as possible confidential information that would be deleted from publically accessible versions of reports.

On the whole, an intensified exchange of information between regulatory authorities is to be welcomed and can contribute to the safety of and access to pharmaceuticals. The question of transparent handling of data from clinical studies must be treated separately from this. Although both the transparency policy of the EMA as well as the new EU Regulation provide more transparency, they continue to offer discretionary latitude to keep pertinent data from clinical trials secret. Given this, it is problematic that the Commission's TTIP negotiating position focuses on the handling of confidential information and

thus apparently a need for confidentiality is assumed in spite of the controversy raging over transparency of clinical study reports. This threatens to prejudice both EMA's transparency policy and interpretation of the EU Regulation.

On the whole, public access to clinical studies data is of much too much importance to safe, innovative and affordable pharmaceutical products to allow this issue to be decided in a trade agreement.

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- 1 The author works as researcher in the fields of social policy and health economics at the Faculty of Economics and Social Science at the University of Cologne.
 - 2 cf. Common Network: The Transatlantic Trade and Investment Partnership (TTIP): A Civil Society Response to the Big Pharma Wish List, Brussels 2014, http://commonsnetwork.eu/wp-content/uploads/2014/03/CivilSocietyResponse_BigPharma_WishList_final.tdf (20.10.2014).
 - 3 Council of the EU: Directives for the negotiation on the Transatlantic Trade and Investment Partnership between the European Union and the United States of America, 11103/13 DCL1, 9.10.2014, Brussels 2013, p. 13.
 - 4 cf. European Commission: The Transatlantic Trade and Investment Partnership (TTIP). Regulatory Issues. EU position on pharmaceutical products, 14.5.2014, Brussels 2014, http://trade.ec.europa.eu/doclib/docs/2014/may/tradoc_152471.pdf (9.1.2015).
 - 5 There is a comprehensive analysis of the negotiating position of the EU in the area of pharmaceutical products in the study by Diels, Jana; Thorun, Christian: Chancen und Risiken der Transatlantischen Handels- und Investitionspartnerschaft (TTIP) für die Verbraucherwohlfahrt, Friedrich-Ebert-Stiftung, WISO Diskurs, Bonn 2014, pp. 26-32.
 - 6 cf. EMA: European Medicines Agency Policy on Publication of Clinical Data for Medicinal Products for Human Use, EMA/240810/2013, 2.10.2014, London 2014.
 - 7 cf. EU 2014: Regulation no. 536/2014 on clinical trials on medicinal products for human use, in: Official Journal of the EU, L. 158, 27 April 2014.
 - 8 cf. Goldacre, Ben: Are Clinical Trial Data Shared Sufficiently Today? No, in: BMJ 347, 2013.
 - 9 cf. Wieseler, Beate; McGauran, Natalie; Kaiser, Thomas: EMA's Transparency Policy: A Placebo Intervention?, in: BMJ 348, 2014, <http://www.bmj.com/content/348/bmj.g3432/44/699175> (20.10.2014).

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