

price **re-evaluations** (in order to decrease work load, a focus on a limited number of medicines, e.g. those with high budget impact, could be laid) and referencing to actual prices paid, thus considering possible **discounts**, rebates and similar financial arrangements (as a minimum considering published statutory manufacturer discounts granted to public payers).

The study investigated the policy options of EPR and DP. Further pricing policies, and also reimbursement mechanisms closely linked to pricing (such as value-based pricing, HTA, economic evaluations, managed-entry agreements) were not the scope of this study. While this study argues for a non-mutually exclusive approach of EPR and DP, EU Member States might consider introducing **combinations of further policies** and mechanisms beyond the scope of this report. For instance, the Priority Medicines Report 2004 proposed a methodology to combine cost-effectiveness analysis with a measure of national wealth. It is recommended to initiate further research whose scope is not limited to the two pricing policies of EPR and DP, but allows for consideration of further pricing mechanisms and alternative collaborative approaches, as called for by the Council conclusions on innovation for the benefit of patients as of December 2014. This would involve aiming to provide an answer that will be accepted by Member States and stakeholders of what constitutes a 'fair' price. Both EPR and DP have the limitation of defining the starting price. This highlights the importance of HTA and pharmaco-economic evaluations, and more cooperation in this field among Member States is highly appreciated. However, debates about a 'fair' price for all parties would move beyond (pricing) policies but would also require exploring new ways of financing medicines. Further research on these issues would be required, likely followed up by pilots (similar to the work around the Transparent Value Framework). In this context, debates might no longer be restricted to the issue of pricing (and reimbursement) of single medicines, but finding solutions for funding (and thus ensuring access to) treatments. More evidence base for these discussions will be needed, including knowledge about the components of the costs for research.

Such discussions should be based on evidence (technical work done by researchers) supplemented by inputs of stakeholders. These debates should involve further stakeholders in addition to pricing / reimbursement authorities and industry. In particular, citizens and patients should not be forgotten. The stakeholder review meeting related to this report with representatives from the EC, Member States and associations / interest groups offered a platform for dialogue among the participants. It is recommended considering similar fora for the future in which stakeholders can openly discuss without being bound to an institutional mandate. Such dialogue could allow 'thinking out of the box', beyond pricing policies and beyond the European Union.

Note: Current challenges, in particular the emergence of high-priced medicines, have shown the urgent need for improving existing pricing mechanisms and developing alternative, possibly cooperative, approaches, as expressed in policy papers quoted earlier in this report. In this context, the authors were asked 1) to work out proposals for improving EPR and 2) to develop a possible outline for a DP scheme in Europe. In doing so, in accordance with the specifications of this study, the authors suggested policy recommendations based on existing (though in some fields somewhat limited) evidence and on their own simulations. However, they do not take a relative preference for either EPR or DP schemes at EU-level, but rather present a juxtaposition of technical, economic and legal considerations for both broad policy avenues.

7 References

- [1] Carone G, Schwierz C, Xavier A. Cost-containment policies in public pharmaceutical spending in the EU. Brussels: European Commission, Directorate-General for Economics and Financial Affairs, 2012.
- [2] Kaplan W, Wirtz VJ, Mantel-Teeuwisse A, Stolk P, Duthey B, Laing R. Priority Medicines for Europe and the World 2013 Update; Geneva: World Health Organization (WHO); 2013.
- [3] World Health Organization (WHO). Access to new medicines in Europe: technical review of policy initiatives and opportunities for collaboration and research. Geneva: World Health Organization (WHO), 2015.
- [4] Babar ZUD, Atif M. Differential pricing of pharmaceuticals: a bibliometric review of the literature. *Journal of Pharmaceutical Health Services Research*. 2014;5(3): 149–56.
- [5] Lorenzoni L, Belloni A, Sassi F. Health-care expenditure and health policy in the USA versus other high-spending OECD countries. *The Lancet*. 2014;384(9937): 83–92.
- [6] Karanikolos M, Mladovsky P, Cylus J, Thomson S, Basu S, Stuckler D, et al. Financial crisis, austerity, and health in Europe. *The Lancet*. 2013;381(9874): 1323–31.
- [7] Kentikelenis A, Karanikolos M, Papanicolas I, Basu S, McKee M, Stuckler D. Health effects of financial crisis: omens of a Greek tragedy. *The Lancet*. 2011;378(9801): 1457–8.
- [8] Leopold C, Mantel-Teeuwisse AK, Vogler S, Valkova S, de Joncheere K, Leufkens HG, et al. Effect of the economic recession on pharmaceutical policy and medicine sales in eight European countries. *Bulletin of the World Health Organization*. 2014;92(9): 630–40D.
- [9] Leopold C, Zhang F, Mantel-Teeuwisse AK, Vogler S, Valkova S, Ross-Degnan D, et al. Impact of pharmaceutical policy interventions on utilization of antipsychotic medicines in Finland and Portugal in times of economic recession: interrupted time series analyses. *International Journal for Equity in Health (JEH)*. 2014;13(1): 53.
- [10] Simou E, Koutsogeorgou E. Effects of the economic crisis on health and healthcare in Greece in the literature from 2009 to 2013: a systematic review. *Health policy*. 2014;115(2): 111–9.
- [11] Stuckler D, Basu S, Suhrcke M, Coutts A, McKee M. Effects of the 2008 recession on health: a first look at European data. *The Lancet*. 2011;378(9786): 124–5.
- [12] OECD. Health Data. Paris: OECD, 2015.
- [13] Karikios D, Schofield D, Salkeld G, Mann K, Trotman J, Stockler M. Rising cost of anticancer drugs in Australia. *Internal medicine journal*. 2014;44(5): 458–63.
- [14] Kelly R, Smith T. Delivering maximum clinical benefit at an affordable price: engaging stakeholders in cancer care. *The lancet oncology*. 2014;15(3): e112–e8.
- [15] European Health Forum Gastein. Key Outcomes of the EHFG 2015: Securing Health in Europe – Balancing Priorities, sharing responsibilities (available under

http://www.ehfg.org/fileadmin/ehfg/Programm/2015/EHFG_Gastein_Health_Outcomes_2015.pdf. 2015.

- [16] Vogler S, Zimmermann N, Babar ZUD. Abstracts from the 3rd International PPRI Conference 2015: Pharmaceutical Pricing and Reimbursement Policies: Challenges Beyond the Financial Crisis. *Journal of Pharmaceutical Policy and Practice*. 2015;8.
- [17] Vogler S, Kilpatrick K, Babar ZUD. Analysis of Medicine Prices in New Zealand and 16 European Countries. *Value in Health*. 2015;18(4): 484–492.
- [18] Vogler S, Vitry A, Babar Z–U–D. Cancer drugs in 16 European countries, Australia, and New Zealand: a cross–country price comparison study. *The lancet oncology*. 2015 (published online first: 3 December 2015).
- [19] Europe Economics. *External Reference Pricing*. London: Europe Economics, 2013.
- [20] Konijn P. Pharmaceutical products–comparative price levels in 33 European countries in 2005. *Statistics in focus: Economy and finance*. 2007;45: 1977–0316.
- [21] Leopold C, Mantel–Teeuwisse AK, Seyfang L, Vogler S, de Joncheere K, Laing RO, et al. Impact of External Price Referencing on Medicine Prices–A Price Comparison Among 14 European Countries. *Southern Med Review*. 2012;5(1).
- [22] Leopold C, Mantel–Teeuwisse AK, Vogler S, de Joncheere K, Laing RO, Leufkens HGM. Is Europe still heading to a common price level for on–patent medicines? An exploratory study among 15 Western European countries. *Health policy*. 2013;112: 209–16.
- [23] Vogler S. How large are the differences between originator and generic prices? Analysis of five molecules in 16 European countries. *Farmeconomia Health economics and therapeutic pathways*. 2012;13 (Suppl 3): 29–41.
- [24] European Communities. *High Level Pharmaceutical Forum 2005–2008. Conclusions and Recommendations*. European Commission, Directorate–General Health & Consumers and Enterprise and Industry. 2008.
- [25] WHO Collaborating Centre for Pharmaceutical Pricing and Reimbursement Policies. *Glossary of pharmaceutical terms*. Update 2013. Vienna 2013.
- [26] Council Directive 89/105/EEC of 21 December 1988 relating to the transparency of measures regulating the pricing of medicinal products for human use and their inclusion in the scope of national health insurance systems.
- [27] Vogler S, Martikainen JE. *Pharmaceutical Pricing in Europe. Pharmaceutical Prices in the 21st Century*: Springer; 2015. p. 343–70.
- [28] Espin J, Rovira J, de Labry AO. Working paper 1: External price referencing – review series on pharmaceutical pricing policies and interventions. Geneva: World Health Organization and Health Action International, 2011.
- [29] Leopold C, Vogler S, Mantel–Teeuwisse AK, de Joncheere K, Leufkens HG, Laing R. Differences in external price referencing in Europe–A descriptive overview. *Health policy*. 2012;104(1): 50–60.

- [30] Bouvy J, Vogler S. Background Paper 8.3 Pricing and Reimbursement Policies: Impacts on Innovation. In: Organization WH, Ed. Priority Medicines for Europe and the World "A Public Health Approach to Innovation" Update on 2004 Background Paper. 2013.
- [31] World Health Organization. WHO Guideline on Country Pharmaceutical Pricing Policies. Geneva, 2013.
- [32] Brekke KR, Dalen DM, Strøm S. Should pharmaceutical costs be curbed?; 2012.
- [33] Håkonsen H, Horn AM, Toverud E-L. Price control as a strategy for pharmaceutical cost containment—What has been achieved in Norway in the period 1994–2004? *Health policy*. 2009;90(2): 277–85.
- [34] Merkur S, Mossialos E. A pricing policy towards the sourcing of cheaper drugs in Cyprus. *Health policy*. 2007;81(2): 368–75.
- [35] Paris V, Belloni A. Value in Pharmaceutical Pricing. OECD Health Working Papers, No. 63. Paris: OECD Publishing, 2013.
- [36] Rovira J. Can EU citizens afford their medicines? The financial crisis and access to medicines in Europe. Presentation. High Level Meeting. 2013.
- [37] EFPIA. Improving Patient Access to Innovative Medicines. The Framework in which Differentiated Pricing May Offer a Solution. European Federation of Pharmaceutical Industries and Associations (EFPIA). Brussels, 2014.
- [38] Yadav P. Differential pricing of pharmaceuticals: Review of current knowledge, new findings and ideas for action. A study conducted for the UK Department for International Development (DFID). Zaragoza: MIT Zaragoza International Logistics Program, 2010.
- [39] Simoens S. Sustainable Provision of Generic Medicines in Europe. Leuven, Netherlands: KU Leuven 2013.
- [40] Vogler S. The impact of pharmaceutical pricing and reimbursement policies on generics uptake: implementation of policy options on generics in 29 European countries—an overview. *Generics and Biosimilars Initiative (GaBI) Journal*. 2012;1(2): 93–100.
- [41] European Commission. Communication from the Commission: On effective, accessible and resilient health systems. Brussels: European Commission; 2014.
- [42] European Commission. Council conclusions on the "Reflection process on modern, responsive and sustainable health systems". Employment, Social Policy, Health and Consumers Affairs. Council meeting. Brussels, 10 December 2013.
- [43] European Commission. Council conclusions on the economic crisis and healthcare. Brussels; 2014.
- [44] European Commission. Council conclusions on innovation for the benefit of patients. Brussels, 2014.

- [45] Toumi M, Rémuzat C, Vataire A-L, Urbinati D. External reference pricing of medicinal products: simulation-based considerations for cross-country coordination. Final Report. European Commission, 2014.
- [46] Vogler S, Zimmermann N, Habimana K. Study of the policy mix for the reimbursement of medicinal products. Proposal for a best practice-based approach based on stakeholder assessment. Gesundheit Österreich Forschungs- und Planungs GmbH and Sogeti (commissioned by the European Commission). 2014.
- [47] Gambardella A, Orsenigo L, Pammolli F, Lacetera N, Magazzini L, Mariani M, et al. Global competitiveness in pharmaceuticals, a European perspective. Report prepared for the Directorate General Enterprise of the European Commission. 2000.
- [48] European Commission. High Level Group on innovation and provision of medicines—recommendations for action. Brussels, 2002.
- [49] European Commission. Communication from the Commission to the Council, the European Parliament, the Economic and Social Committee and the Committee of the Regions – A Stronger European-based Pharmaceutical Industry for the Benefit of the Patient – A Call for Action Brussels; 2003.
- [50] European Commission. Better access to medicines for patients in Europe. Brussels; 18 April 2013.
- [51] European Commission DG Enterprise. Call for Proposals – DG ENTR NO ENT GWP 2008 1.2.7.4. Pricing and Reimbursement of medicinal products in EU. Available from: http://www.ueonline.it/networking/uploadorig/27133_orig.pdf. 2008.
- [52] Kanavos P, Nicod E, Espin J. Short- and Long-Term Effects of Value-Based Pricing versus External Price Referencing. 2010.
- [53] European Commission Enterprise and Industry Directorate-General. Development of a database on pricing of medicinal products in the EU. Call for proposal. ACTION ENT/IMA/1.1.10.3.8. Brussels 2009.
- [54] European Parliament. European Parliament legislative resolution of 6 February 2013 on the proposal for a directive of the European Parliament and of the Council relating to the transparency of measures regulating the prices of medicinal products for human use and their inclusion in the scope of public health insurance systems. Brussels; 2013.
- [55] Sion J-L, Kolowca M. Joint Procurement of medical countermeasures: Workshop Joint Procurement for pandemic vaccines. Luxembourg; 2015.
- [56] European Commission. Pharmaceutical Industry: A strategic sector for the European Economy. Brussels: European Commission; 2014.
- [57] Eichler HG, Baird LG, Barker R, Bloechl-Daum B, Børlum-Kristensen F, Brown J, et al. From adaptive licensing to adaptive pathways: Delivering a flexible life-span approach to bring new drugs to patients. *Clinical Pharmacology & Therapeutics*. 2015;97(3): 234-46.
- [58] European Medicines Agency. Adaptive pathways: a future approach to bring new medicines to patients?: European Medicines Agency (EMA); 2014.

- [59] European Commission. Safe and Timely Access to Medicines for Patients (STAMP); Presentation for the EC Expert group; Available under (http://ec.europa.eu/health/technology_assessment/docs/ev_20150323_co08_en.pdf). 2015.
- [60] Record from the 1st STAMP Commission Expert Group meeting, (2015).
- [61] Pan American Health Organization (PAHO). Access to High-Cost medicines in the Americas: Situation, Challenges and Perspective. Technical Series No. 1. Essential Medicines, Access and Innovation. Washington, D.C.: Pan American Health Organization, 2010.
- [62] Kaplan W, Laing R. Priority Medicines for Europe and the World; Geneve: World Health Organization, Essential Drugs and Medicines Policy.; 2004.
- [63] Henry D, Lang D, Hill S. Background Paper 8.2 Approach to the Valuation and Pricing of Future Medicines. In: Priority Medicines for Europe and the World "A Public Health Approach to Innovation", Ed. World Health Organization (WHO), 2004.
- [64] OECD. Pharmaceutical Pricing Policies in a Global Market. Paris: OECD, 2008.
- [65] Kaplan W, Laing R. Priority Medicines for Europe and the World. Geneva: World Health Organization (WHO); 2004. p. 134.
- [66] European Commission. Joint Report on Health Systems. European Economy, Occasional Papers 74. Brussels: European Commission; 2010.
- [67] Toumi M, Rémuzat C. EU Pharmaceutical expenditure forecast. Paris: Creativ_Ceutical, 2012.
- [68] Vogler S, Schneider P. Vergütung der Arzneimitteldistribution in den europäischen Ländern. Vienna: Gesundheit Österreich Forschung und Planung GmbH (GÖ FP), 2015 (unpublished).
- [69] Riesenhuber K. Europäische Methodenlehre: Handbuch für Ausbildung und Praxis: Walter de Gruyter GmbH & Co KG; 2014.
- [70] Gestel R, Micklitz HW. Why Methods Matter in European Legal Scholarship. European Law Journal. 2014;20(3): 292–316.
- [71] Hervey T, Cryer R, Sokhi-Bulley B, Bohm A. Research methodologies in EU and international law: Bloomsbury Publishing; 2011.
- [72] Ognyanova D, Zentner A, Busse R. Pharmaceutical reform 2010 in Germany. Eurohealth. 2011;17(1): 11–3.
- [73] GKV Spitzenverband. Rahmenvereinbarung nach §130b Abs. 9 SGB V zwischen dem GKV Spitzenverband und der Verbänden der pharmazeutischen Unternehmer. 2012.
- [74] Filko M, Szilagyiova P. The Slovak experience in the international price benchmarking for prescription drugs. Value in Health. 2009;12 (7): A229–A30.
- [75] Windmeijer F, De Laat E, Douven R, Mot E. Pharmaceutical promotion and GP prescription behaviour. Health economics. 2006;15(1): 5–18.

- [76] Stargardt T, Schreyögg J. Impact of Cross-Reference Pricing on Pharmaceutical Prices. *Applied Health Economics and Health Policy*. 2006;5(4): 235–47.
- [77] Rosian I, Habl C, Vogler S. *Pharmaceuticals Market Control in Nine European Countries*. Vienna: Österreichisches Bundesinstitut für Gesundheitswesen (ÖBIG), 1998.
- [78] Gandjour A. Reference pricing and price negotiations for innovative new drugs : viable policies in the long term? *Pharmacoeconomics*. 2013;31(1): 11–4.
- [79] Danzon PM. Price Discrimination for Pharmaceuticals: Welfare Effects in the US and the EU. *International Journal of the Economics of Business*. 1997;4(3): 301–21.
- [80] Danzon PM, Epstein AJ. Effects of regulation on drug launch and pricing in interdependent markets. *Advances in Health Economics & Health Services Research*. 2012;23: 35–71.
- [81] Danzon PM, Towse A. Differential pricing for pharmaceuticals: reconciling access, R&D and patents. *International Journal of Health Care Finance & Economics*. 2003;3(3): 183–205.
- [82] Kyle MK. Pharmaceutical price controls and entry strategies. *The Review of Economics and Statistics*. 2007;89(1): 88–99.
- [83] De Weerd E, Simoens S, Hombroeckx L, Casteels M, Huys I. Causes of drug shortages in the legal pharmaceutical framework. *Regulatory Toxicology and Pharmacology*. 2015;71(2): 251–8.
- [84] PGEU. *PGEU Statement on Medicine Shortages in European Community Pharmacies*. 2013.
- [85] Italian Antitrust Authority. *Decision of the case between Aspen Pharma Trading Limited vs Altroconsumo*. Rome: Italian Antitrust Authority; 2014.
- [86] Gray A, Manasse Jr HR. Shortages of medicines: a complex global challenge. *Bulletin of the World Health Organization*. 2012;90(3).
- [87] Vogler S, Zimmermann N, Habl C, Piessnegger J, Bucsecs A. Discounts and rebates granted to public payers for medicines in European countries. *Southern Med Review*. 2012;5(1): 38–46.
- [88] Robertson J, Walkom EJ, Henry DA. Transparency in pricing arrangements for medicines listed on the Australian Pharmaceutical Benefits Scheme. *Australian health review*. 2009;33(2): 192–9.
- [89] Kanavos P, Vondoros S, Irwin R, Nicod E, Casson M. *Differences in costs of and access to pharmaceutical products in the EU*. Brussels: European Parliament, 2011.
- [90] Brekke KR, Holmås TH, Straume OR. Are Pharmaceuticals Still Inexpensive in Norway? A Comparison of Prescription Drug Prices in Ten European Countries. *SNF Report No. 08/10*. 2010.
- [91] Cambridge Pharma Consultancy. *Pricing & Reimbursement Review 2003*. Cambridge, 2003.
- [92] European Commission. *European Competitiveness Report. Economic Reforms and Competitiveness*. Brussels; 2006.

- [93] Kanavos PG, Vandoros S. Determinants of branded prescription medicine prices in OECD countries. *Health Economics Policy and Law*. 2011;6(3): 337.
- [94] Kanavos P, Costa-Font J. Pharmaceutical Parallel Trade in Europe: Stakeholder and Competition Effects. *Economic Policy*. 2005(44): 751.
- [95] Kyle MK, Allsbrook JS, Schulman KA. Does Reimportation Reduce Price Differences for Prescription Drugs? Lessons from the European Union. *Health Services Research*. 2008;43(4): 1308–24.
- [96] Cabiedes Miragaya L. Nuevas perspectivas sobre el precio de los medicamentos: El caso español. *Estudios de Economía Aplicada*. 2013;31(2): 397–415.
- [97] Franken M, Nilsson F, Sandmann F, de Boer A, Koopmanschap M. Unravelling drug reimbursement outcomes: a comparative study of the role of pharmacoeconomic evidence in Dutch and Swedish reimbursement decision making. *Pharmacoeconomics*. 2013;31(9): 781–97.
- [98] Iskrov G, Miteva-Katrandzhieva T, Stefanov R. Challenges to orphan drugs access in Eastern Europe: the case of Bulgaria. *Health policy*. 2012;108(1): 10–8.
- [99] Iskrov GG, Raycheva RD, Stefanov RS. Insight into reimbursement decision-making criteria in Bulgaria: implications for orphan drugs. *Folia Medica (Plovdiv)*. 2013;55(3–4): 80–6.
- [100] Lopert R, Ruiz F, Chalkidou K. Applying rapid 'de-facto' HTA in resource-limited settings: experience from Romania. *Health policy*. 2013;112(3): 202–8.
- [101] Danzon P, Towse A, Mestre-Ferrandiz J. Value-based differential pricing: efficient prices for drugs in a global context. *Health economics*. 2015;24(3): 294–301.
- [102] Danzon PM. The economics of parallel trade. *Pharmacoeconomics*. 1998;13(3): 293–304.
- [103] Kalo Z, Annemans L, Garrison LP. Differential pricing of new pharmaceuticals in lower income European countries. *Expert Review of Pharmacoeconomics & Outcomes Research*. 2013;13(6): 735–41.
- [104] Perez-Casas C, Herranz E, Ford N. Pricing of drugs and donations: options for sustainable equity pricing. *Tropical Medicine & International Health*. 2001;6(11): 960–4.
- [105] Kindermans JM, Matthys F. Introductory note: The access to essential medicines campaign. *Tropical Medicine & International Health*. 2001;6(11): 955–6.
- [106] Eurostat. Eurostat Health Database <http://ec.europa.eu/eurostat/web/health/health-care/data/database>. 2015.
- [107] Moon S, Jambert E, Childs M, von Schoen-Angerer T. A win-win solution?: A critical analysis of tiered pricing to improve access to medicines in developing countries. [Online] *Globalization and Health*. 2011;7: 39.
- [108] Plahte J. Tiered pricing of vaccines: a win-win-win situation, not a subsidy. *The Lancet infectious diseases*. 2005;5(1): 58–63.
- [109] Ramsey FP. A Contribution to the Theory of Taxation. *The Economic Journal*. 1927: 47–61.

- [110] T'Hoën E, Moon S. Pills and pocketbooks. Equity pricing of essential medicines. 2001: 4–5.
- [111] Mossialos E, Dukes G. Affordably priced new drugs for poor populations: Approaches for a global solution. *International Journal of Risk & Safety in Medicine*. 2001;14(1): 1–29.
- [112] Grace C. *Equitable Pricing of Newer Essential Medicines for Developing Countries: Evidence of the Potential of Different Mechanisms*. London: London Business School. 2003: 1–70.
- [113] Shepherd WG. Ramsey pricing: Its uses and limits. *Utilities Policy*. 1992;2(4): 296–8.
- [114] Towse A, Pistollato M, Mestre–Ferrandiz J, Khan Z, Kaura S, Garrison L. European Union Pharmaceutical Markets: A Case for Differential Pricing? *International Journal of the Economics of Business*. 2015;22(2): 263–75.
- [115] Sun H, 孙赫. Differential pricing strategy in improving access to medicine in developing countries: The University of Hong Kong (Pokfulam, Hong Kong); 2012.
- [116] Lang D, Hill S. *Differential Pricing of Pharmaceuticals: What about the rest of the world*. University of Newcastle, Australia; 2004.
- [117] World Health Organization, World Trade Organization. Differential Pricing and the Financing of Essential Drugs. In: Granville B, Ed. *The economics of essential medicines*: London: Royal Institute of Economic Affairs, International Economics Programme; distributed by the Brookings Institution, Washington, D.C.; 2002. p. 209–31.
- [118] Cameron A, Ewen M, Ross–Degnan D, Ball D, Laing R. Medicine prices, availability, and affordability in 36 developing and middle–income countries: a secondary analysis. *The Lancet*. 2009;373(9659): 240–9.
- [119] Mackay B. *Summary Report of Industry Government Forum on Access to Medicines*. Centre DHR. London, 2009.
- [120] Waning B, Kaplan W, King AC, Lawrence DA, Leufkens HG, Fox MP. Global strategies to reduce the price of antiretroviral medicines: evidence from transactional databases. *Bulletin of the World Health Organization*. 2009;87(7): 520–8.
- [121] Balasegaram M. Is tiered pricing the way for vaccines? *Lancet*. 2014;384(9946): 852.
- [122] Hammer PJ. Differential Pricing of Essential AIDS Drugs: Markets, Politics and Public Health. *Journal of International Economic Law*. 2002;5(4): 883–912.
- [123] Light DW, Warburton R. Demythologizing the high costs of pharmaceutical research. *BioSocieties*. 2011;6(1): 34–50.
- [124] DiMasi JA, Hansen RW, Grabowski HG. The price of innovation: new estimates of drug development costs. *Journal of health economics*. 2003;22(2): 151–85.
- [125] Kantarjian HM, Fojo T, Mathisen M, Zwelling LA. Cancer drugs in the United States: Justum Pretium—the just price. *Journal of Clinical Oncology*. 2013;31(28): 3600–4.
- [126] Berkley S. Improving access to vaccines through tiered pricing. *Lancet*. 2014;383(9936): 2265–7.

- [127] Children's Vaccine Initiative (CVI). Report of the Sixth Meeting of the Management Advisory Committee (MAC). London, 1994.
- [128] Kyle M. Strategic responses to parallel trade. *The BE Journal of Economic Analysis & Policy*. 2011;11(2).
- [129] European Commission. Report from the Commission Annual Report (2010–2011) on the application of Council Regulation (EC) No 953/2003 of 26 May 2003 to avoid trade diversion into the European Union of certain key medicines. 2012.
- [130] Lopert R, Lang DL, Hill SR, Henry DA. Differential pricing of drugs: a role for cost-effectiveness analysis? *Lancet*. 2002;359(9323): 2105–7.
- [131] Ball D. Working paper 3: Regulation of mark-ups in the pharmaceutical supply chain – review series on pharmaceutical pricing policies and interventions. Geneva: World Health Organization and Health Action International, 2011.
- [132] Creese A. Sales Taxes on Medicines. Working Paper 5, WHO/HAI Project on Medicine Prices and Availability, 2011.
- [133] Otero Garcia-Castrillon C. El acceso a los medicamentos: Las patentes y el Acuerdo sobre los Derechos de Propiedad Intelectual Relacionados con el Comercio. *Informacion Comercial Espanola Revista de Economia*. 2003(804): 197–217.
- [134] World Trade Organisation (WTO). Agreement on Trade-Related Aspects of Intellectual Property Rights. Signed in Marrakesh, Morocco on 15 April 1994; 1994.
- [135] Global Health Progress. Novo Nordisk: Differential Pricing on Insulin. Available from: <http://www.globalhealthprogress.org/programs/novo-nordisk-differential-pricing-insulin>. 2015.
- [136] Kaul I. New Ways of Financing the Millennium Development Goals. Prepared for a Seminar Co-Organized by Agence Française de Développement (Afd), Institut du Développement Durable et des Relations Internationales (Iddri) and UNDP, 22 January 2004. Paris; 2004.
- [137] Kanavos P, Costa-i-Font J, Merkur S, Gemmill M. The economic impact of pharmaceutical parallel trade in European Union member states: A stakeholder analysis: London School of Economics and Political Science London; 2004.
- [138] West P, Mahon J, Consortium YHE. Benefits to payers and patients from parallel trade: York Health Economics Consortium; 2003.
- [139] Ganslandt M, Maskus KE. Parallel imports and the pricing of pharmaceutical products: evidence from the European Union. *Journal of health economics*. 2004;23(5): 1035–57.
- [140] Forrester IS, Dawes A. Parallel Trade in Prescription Medicines in the European Union: The Age of Reason? *Yearbook of Antitrust and Regulatory Studies*. 2008;1(1): 9.
- [141] European Commission. Council Regulation (EC) No 953/2003 of 26 May 2003 to avoid trade diversion into the European Union of certain key medicines. *Official Journal of the European Union*. 2003.

14.2	Common Agricultural Policy (CAP)	A81
14.2.1	Practice	A81
14.2.2	Costs	A82
14.2.3	Benefits	A82
14.2.4	Limitations	A83
15	Annex 15: Stakeholder review	A84
15.1	Methodology	A84
15.2	Results	A86
15.2.1	Participation	A86
15.2.2	Written stakeholder review	A88
15.2.3	Stakeholder Review Meeting	A90
15.2.4	Follow-up on the stakeholder review	A91
16	Annex 16: Peer review	A92
16.1	List of peer reviewers	A92
16.2	Outcome of the peer review.....	A93
17	Annex 17: References of the Annex	A94

List of figures

Figure A1:	Graphical illustration of the selection process for literature related to EPR	A8
Figure A2:	Graphical illustration of the selection literature related to DP	A9
Figure A3:	Coversheet of the survey	A18
Figure A4:	Example of the questionnaire without pre-filled information	A19
Figure A5:	Differences (in percent) between ex-factory price in the highest and lowest price country, 2013.....	A39
Figure A6:	Proportion (in percent) of medicines for which a country has the lowest/highest price among the sample	A40
Figure A7:	Average percentage above minimum price, by country	A41
Figure A8:	Average percentage difference to mean price, by country	A41
Figure A9:	Percentage above minimum pharmaceutical price and GDP per capita (in PPP)	A42
Figure A10:	Percentage from mean medicine price and GDP per capita (in PPP)	A42
Figure A11:	Escitalopram: 2015 List prices compared to Base Scenario Model Results	A44
Figure A12:	Imatinib: 2015 List prices compared to Base Scenario Model Results	A44

1 Annex 1: Literature review – Methodological specifications

1.1 Search strategy

1.1.1 Overview of the search strategy

A systematic structured literature review was conducted to identify and characterise the use of external price referencing (EPR), to describe its impacts on the prices of pharmaceuticals and to discuss the possible cross-country coordination issues in the EU Member states and in the other countries cited in the scope of the project.

A systematic structured literature search on EPR was conducted to evaluate the use of EPR and its impacts on the prices of pharmaceuticals. The search strategy followed Toumi M, Rémuzat C, Vataire A-L and Urbinati D [1] since the tender specifications required the literature review on EPR to be incremental to that study. The scope of the search was external price referencing (not internal price referencing) for medicines (except vaccines) in the 28 Member states of the European Union (EU), Norway, Switzerland, Turkey and Iceland. As an incremental literature search to EPR, the period was restricted to the period from December 2012 till January 2015. In contrast to, the systematic literature search on differential pricing (DP) was not restricted to any country, and it covered the period from January 1997 till January 2015. In both searches, studies in English, German, French Spanish and Italian language were considered.

In order to conduct an adequate incremental systematic literature review the same international databases were searched:

- Medline® (searched on the OVID website)
- EMBASE® (searched on the OVID website)
- EconLit

Additionally, a thorough hand search was conducted including a systematically search on the internet, the reference lists of the identified studies and on websites of the international organisations e.g. EU, World Health Organization (WHO), Organisation for economic co-operation and development (OECD), and networks for relevant literature. The literature review as completed by a search in Gesundheit Österreich Forschungs- und Planungs GmbH (GÖ FP) internal information and reports, when relevant.

Screening and selection of the abstracts and full texts was based on criteria defined ex-ante, which are depicted in Table A1 and Table A2. The selection of the studies was subdivided into the first selection of publications and the second selection of full texts, both of which are described below.

1.1.2 Results of the search strategy

The incremental literature search for EPR retrieved 867 records in Embase, 847 in Medline and 71 records in EconLit, adding up to a total of 1,785. 670 duplicates were removed, leaving a total of 1,115 titles and abstracts that were reviewed. Out of the 1,115 abstracts that were reviewed, 66 were included and 1,049 were excluded. Of the 66 papers ordered for full paper review, 2 papers were not available. 35 papers were included for the data extraction, and 29 papers were excluded. The hand search in Google Scholar and other databases retrieved 10 publications which were included, yielding 45 publications for EPR. Search strategy results are summarised in Figure A1.

The literature search for DP retrieved 449 records in Embase, 138 records in Medline and 214 records in EconLit, adding up to a total of 801. 149 duplicates were removed, leaving a total of 652 titles and abstracts that were reviewed. Out of the 652 abstracts that were reviewed, 59 were included and 593 were excluded. Of the 59 papers ordered for full paper review, 1 paper was not available. 49 papers were included for the data extraction, and 9 papers were excluded. The hand search in Google Scholar and other databases retrieved 7 publications which were included, yielding 56 publications for EPR. Search strategy results are summarised in Figure A2.

1.2 Selection criteria

Table A1 and Table A2 specify the selection criteria applied in the literature review for EPR and DP.

Table A1: Selection criteria (abstracts and full texts) for EPR

Exclusion criteria
Formal criteria
E1 Papers published before 01/12/2012
E2 Duplicates
E3 Study is not published in a language listed in the inclusion criteria
E4 Countries which are not listed in the inclusion criteria
Contextual criteria
E5 Internal Reference Pricing
E6 Devices/Services
E7 Vaccines
E8 Studies related to Diagnostic/Epidemiology/Treatment
E9 Not related to pharmaceutical pricing/Study is not relevant for EPR
E10 Subject of the study is related to alcohol/drinking
E11 Subject of the study is related to tobacco/cigarettes/smoking
E12 Subject of the study is related to food/nutrition
E13 Subject of the study is related to environment/nature
E14 Theoretical/Formal modelling
E15 Subject of the study is related to illegal/illicit drugs
Inclusion criteria
I1 All Pharmaceutical products
I2 External Reference Pricing
I3 28 Member states of the EU
I4 Switzerland, Turkey, Norway, Switzerland
I5 Papers in the following languages: English, Italian, French, Spanish, German
I6 Papers published from December 2012 to current

Source: Authors

Table A2: Selection criteria (abstracts and full texts) for DP

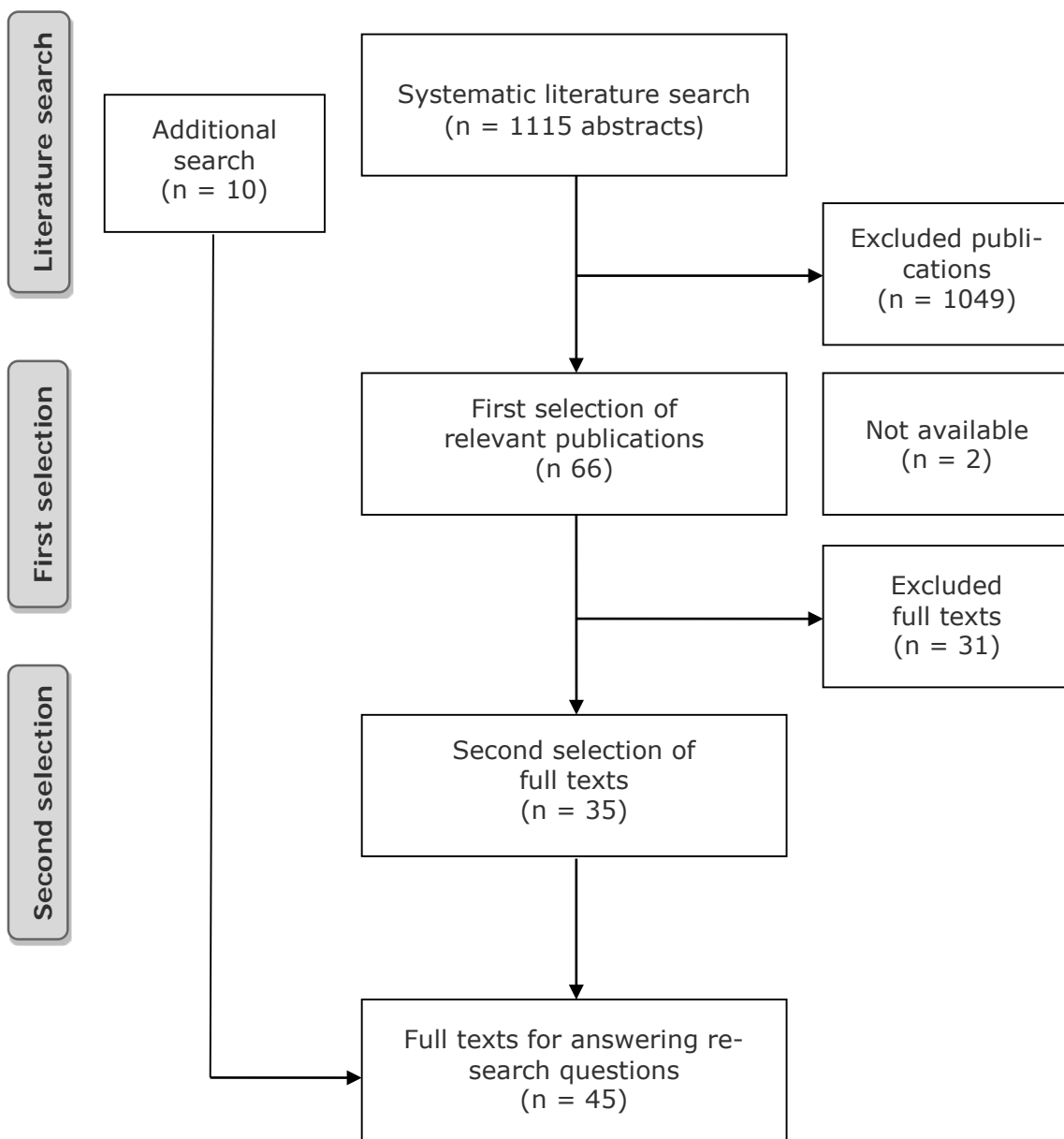
Exclusion criteria	
Formal criteria	
E1	Papers published before 01/01/1997
E2	Duplicates
E3	Study is not published in a language listed in the inclusion criteria
E4	Abstract is not based on a study / Newspaper article / Newsletter / Press release / Poster
Contextual criteria	
E5	Internal Reference Pricing
E6	External Reference Pricing
E7	Devices/Services
E8	Studies related to epidemiology/diagnostic/treatment of diseases
E9	Study is not relevant for DP
E10	Subject of the study is related to alcohol/drinking
E11	Subject of the study is related to cigarettes/tobacco/smoking
E12	Subject of the study is related to food/nutrition
E13	Subject of the study is related to Environment/Nature
E14	Subject of the study is related to illegal/illicit drugs
Inclusion criteria	
I1	All Pharmaceutical products
I2	All countries with relevant experience in DP
I3	Papers in the following languages: English, Italian, French, Spanish, German
I4	Papers published from January 1997 to current

Source: Authors

1.3 Selection process

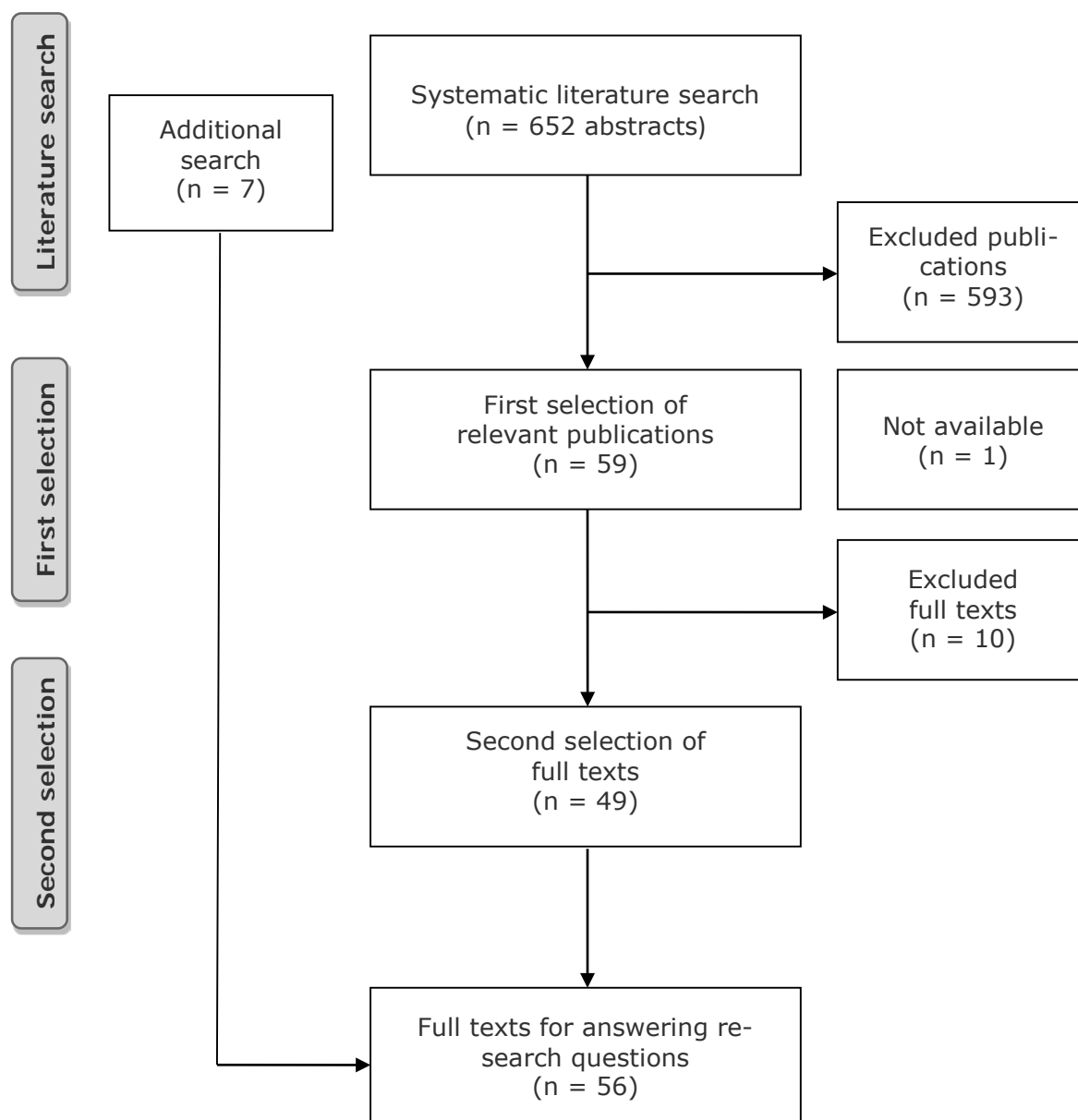
Figure A1 and Figure A2 illustrate the selection processes for literature related to EPR and DP.

Figure A1: Graphical illustration of the selection process for literature related to EPR



Source: Illustration by authors

Figure A2: Graphical illustration of the selection literature related to DP



Source: Illustration by authors

1.4 Analysis of literature

When reading the full texts, relevant information was collected and documented in a literature matrix.

For all references, it was reported:

- Reference (Authors, Title, Journal/source, date of publication)
- Language of the full article/report
- Abstract
- Countries to which the pricing policy was applied to
- Year of reference
- The policy mentioned in the article (EPR, DP, other policies)
- Study design

- Further/Background Information

For literature related to EPR, the following information was reported:

- whether an impact assessment and experiences on EPR were available in terms of savings to public budgets, patient access to medicines, reward for innovation or others
- country specific features of EPR (Number of countries in the basket, Countries in the basket, Medicines covered by EPR, price type which is taken into account for EPR, Calculation method, Evaluation, Changes in EPR)
- Suggestion for best practice or improvements
- Further/Background Information

For literature related to DP, the following information was reported:

- whether an impact assessment and experiences on DP were available in terms of savings for public budgets, patient access to medicines, reward for innovation or others
- country specific features of DP (International or national legal framework, purchaser, medicines covered, specific examples of products or companies)
- Hurdles in implementation
- Suggestion for best practice or improvements
- Further/Background Information

2 Annex 2: Literature review – Included references

- Anonymous (2001): Differential pricing of essential drugs. In: Pan American Journal of Public Health 9/4:275-279
- Babar, Z. U. D.; Atif, M. (2014): Differential pricing of pharmaceuticals: A bibliometric review of the literature. In: Journal of Pharmaceutical Health Services Research 5/3:149-156
- Balasegaram, M. (2014): Is tiered pricing the way for vaccines? In: Lancet 384/9946:852
- Barros, P. P.; Martinez-Giralt, X. (2008): On international cost-sharing of pharmaceutical R&D. In: International Journal of Health Care Finance & Economics 8/4:301-312
- Barton, J. H.; Emanuel, E. J. (2005): The patents-based pharmaceutical development process: rationale, problems, and potential reforms. In: JAMA 294/16:2075-2082
- Berkley, S. (2014): Improving access to vaccines through tiered pricing. In: Lancet 383/9936:2265-2267
- Bloom, D. E. (2000): Something to be done: treating HIV/AIDS. River Path Associates. In: Science 288/5474:2171-2173
- Brick, A.; Gorecki, P. K.; Nolan, A. (2013): Usage of generics in Ireland: Recent trends and policy developments. In: Journal of Generic Medicines 10/2:72-85
- Calmy, A.; Hirschel, B. (2003): Antiretroviral drugs in developing countries: Myth or reality?. [French]. In: Medecine et Hygiene 61/2431:725-730
- Children's Vaccine Initiative (CVI) (1994): Report of the Sixth Meeting of the Management Advisory Committee (MAC), London
- Class, J. N. (2012): Emerging markets and differential pricing policies: A question of global health? In: Journal of Commercial Biotechnology 18/4:40-43
- Cockburn, I; Lanjouw, J. O.; Schankerman, M. (2014): Patents and the Global Diffusion of New Drugs. Centre for Economic Performance, LSE, CEP Discussion Papers
- Costa-Font, J.; McGuire, A.; Varol, N. (2014): Price regulation and relative delays in generic drug adoption. In: Journal of Health Economics 38/1-9
- Costa-i-Font, J.; Font Vilalta, M. (2005): Por un sistema de precios diferenciales de los medicamentos. (Medicines: Differential Prices and Globalization. With English summary.). In: Comercio Exterior 55/5:418-424
- Daems, R.; Maes, E.; Glaetzer, C. (2013): Equity in pharmaceutical pricing and reimbursement: Crossing the income divide in Asia Pacific. In: Value in Health Regional Issues 2/1:160-166
- Danzon, P.; Towse, A.; Mestre-Ferrandiz, J. (2015): Value-based differential pricing: efficient prices for drugs in a global context. In: Health Economics 24/3:294-301
- Danzon, P. M. (1998): The economics of parallel trade. In: Pharmacoeconomics 13/3:293-304

- Danzon, P. M.; Towse, A. (2003): Differential pricing for pharmaceuticals: reconciling access, R&D and patents. In: *International Journal of Health Care Finance & Economics* 3/3:183-205
- Danzon, P. M.; Epstein, A. J. (2012): Effects of regulation on drug launch and pricing in interdependent markets. In: *Advances in Health Economics & Health Services Research* 23/35-71
- Danzon, P. M. (1997): Price Discrimination for Pharmaceuticals: Welfare Effects in the US and the EU. In: *International Journal of the Economics of Business* 4/3:301-321
- Darrow, J. J. (2011): Recent developments in health law. Essential medicines: why international price discrimination may increasingly be the wrong solution to a global drug problem. In: *Journal of Law, Medicine & Ethics* 39/2:291-296
- Davies, J. E.; Neidle, S.; Taylor, D. G. (2012): Developing and paying for medicines for orphan indications in oncology: utilitarian regulation vs equitable care? In: *British Journal of Cancer* 106/1:14-17
- Degrassat-Theas, A.; Paubel, P.; Parent de Curzon, O.; Le Pen, C.; Sinagre, M. (2013): Temporary authorization for use: does the French patient access programme for unlicensed medicines impact market access after formal licensing? In: *Pharmacoeconomics* 31/4:335-343
- Ding, M.; Eliashberg, J.; Stremersch, S. eds (2014): *Innovation and Marketing in the Pharmaceutical Industry: Emerging Practices, Research, and Policies*. International Series in Quantitative Marketing. New York and Heidelberg: Springer,
- Dranitsaris, G.; Truter, I.; Lubbe, M. (2011): The development of a value-based pricing index for new drugs in metastatic colorectal cancer. In: *Journal of Clinical Oncology* 1
- Dubois, P.; Lasio, L. (2014): *Identifying Industry Margins with Unobserved Price Constraints: Structural Estimation on Pharmaceuticals*. C.E.P.R. Discussion Papers, CEPR Discussion Papers: 9881
- Dunne, S.; Shannon, B.; Dunne, C.; Cullen, W. (2013): A review of the differences and similarities between generic drugs and their originator counterparts, including economic benefits associated with usage of generic medicines, using Ireland as a case study. In: *BMC Pharmacology & Toxicology* 14/1
- Espin, J.; Rovira, J.; de Labry, A. O. (2011): Working paper 1: External price referencing – review series on pharmaceutical pricing policies and interventions. World Health Organization and Health Action International, Geneva
- Filko, M.; Szilagyiova, P. (2009): The Slovak experience in the international price benchmarking for prescription drugs. In: *Value in Health* 12 (7)/A229-A230
- Formosa, T.; Adami, M. Z. (2012): Reference pricing for pharmaceuticals: A policy perspective. In: *Journal of EuroMed Pharmacy* 2:4-6
- Fraeyman, J.; Van Hal, G.; Godman, B.; Beutels, P. (2013): The potential influence of various initiatives to improve rational prescribing for proton pump inhibitors and statins in Belgium. In: *Expert Review of Pharmacoeconomics & Outcomes Research* 13/1:141-151

- Franken, M.; Nilsson, F.; Sandmann, F.; de Boer, A.; Koopmanschap, M. (2013): Unravelling drug reimbursement outcomes: a comparative study of the role of pharmacoeconomic evidence in Dutch and Swedish reimbursement decision making. In: *Pharmacoeconomics* 31/9:781-797
- Gandjour, A. (2013): Reference pricing and price negotiations for innovative new drugs : viable policies in the long term? In: *Pharmacoeconomics* 31/1:11-14
- Gandjour, A.; Gafni, A.; Schlander, M. (2014): Determining the price for pharmaceuticals in Germany: comparing a shortcut for IQWiG's efficiency frontier method with the price set by the manufacturer for ticagrelor. In: *Expert Review of Pharmacoeconomics & Outcomes Research* 14/1:123-129
- Glynn, D. (2000): Reimbursement for new health technologies. Breakthrough pharmaceuticals as a 20th century challenge. In: *Pharmacoeconomics* 18 Suppl 1/59-67
- Grace, C. (2003): Equitable Pricing of Newer Essential Medicines for Developing Countries: Evidence of the Potential of Different Mechanisms. In: London: London Business School 1-70
- Granville, B. ed (2002): *The economics of essential medicines*. London
- Royal Institute of Economic Affairs, International Economics Programme; distributed by the Brookings Institution, Washington, D.C.,
- Hammer, P. J. (2002): Differential Pricing of Essential AIDS Drugs: Markets, Politics and Public Health. In: *Journal of International Economic Law* 5/4:883-912
- Hawkes, N. (2013): The government's drug pricing policy is falling apart messily. In: *BMJ* 346/f3634
- Henry, D.; Lexchin, J. (2002): The pharmaceutical industry as a medicines provider. In: *Lancet* 360/9345:1590-1595
- Henry, D.; Lang, D.; Hill, S. (2004): Background Paper 8.2 Approach to the Valuation and Pricing of Future Medicines. In: *Priority Medicines for Europe and the World "A Public Health Approach to Innovation"*. Ed. by World Health Organization
- Henschke, C.; Sundmacher, L.; Busse, R. (2013): Structural changes in the German pharmaceutical market: price setting mechanisms based on the early benefit evaluation. In: *Health Policy* 109/3:263-269
- Horn, H.; Nink, K.; McGauran, N.; Wieseler, B. (2014): Early benefit assessment of new drugs in Germany - results from 2011 to 2012. In: *Health Policy* 116/2-3:147-153
- Inotai, A.; Pekli, M.; Jona, G.; Nagy, O.; Remak, E.; Kalo, Z. (2012): Attempt to increase the transparency of fourth hurdle implementation in Central-Eastern European middle income countries: publication of the critical appraisal methodology. In: *BMC Health Services Research* 12/332
- Iskrov, G.; Miteva-Katrandzhieva, T.; Stefanov, R. (2012): Challenges to orphan drugs access in Eastern Europe: the case of Bulgaria. In: *Health Policy* 108/1:10-18
- Iskrov, G. G.; Raycheva, R. D.; Stefanov, R. S. (2013): Insight into reimbursement decision-making criteria in Bulgaria: implications for orphan drugs. In: *Folia Medica (Plovdiv)* 55/3-4:80-86

- Jack, B.; Lanjouw, J. (2003): Financing Pharmaceutical Innovation: When Should Poor Countries Contribute? Georgetown University, Department of Economics, Working Papers
- Jack, W.; Lanjouw, J. O. (2005): Financing Pharmaceutical Innovation: How Much Should Poor Countries Contribute? In: World Bank Economic Review 19/1:45-67
- Kaier, K. (2013): The impact of pricing and patent expiration on demand for pharmaceuticals: an examination of the use of broad-spectrum antimicrobials. In: Health Economics, Policy, & Law 8/1:7-20
- Kaiser, U.; Mendez, S. J.; Ronde, T.; Ullrich, H. (2014): Regulation of pharmaceutical prices: evidence from a reference price reform in Denmark. In: Journal of Health Economics 36/174-187
- Kalo, Z.; Annemans, L.; Garrison, L. P. (2013): Differential pricing of new pharmaceuticals in lower income European countries. In: Expert Review of Pharmacoeconomics & Outcomes Research 13/6:735-741
- Kanavos, P.; Costa-Font, J. (2005): Pharmaceutical Parallel Trade in Europe: Stakeholder and Competition Effects. In: Economic Policy 44:751
- Kanavos, P.; Nicod, E.; Espin, J. (2010): Short-and Long-Term Effects of Value-Based Pricing vs. External Price Referencing
- Kolasa, K. (2014): Are pricing and reimbursement decision-making criteria aligned with public preferences regarding allocation principles in the Polish healthcare sector? In: Expert Review of Pharmacoeconomics & Outcomes Research 14/5:751-762
- Kontoghiorghe, C. N.; Andreou, N.; Constantinou, K.; Kontoghiorghes, G. J. (2014): World health dilemmas: Orphan and rare diseases, orphan drugs and orphan patients. In: World Journal of Methodology 4/3:163-188
- Kremer, M. (2002): Pharmaceuticals and the Developing World. In: Journal of Economic Perspectives 16/4:67-90
- Lang, D.; Hill, S. (2004): Differential Pricing of Pharmaceuticals: What about the rest of the world.
- Leopold, C.; Mantel-Teeuwisse, A. K.; Seyfang, L.; Vogler, S.; de Joncheere, K.; Laing, R. O.; Leufkens, H. (2012a): Impact of external price referencing on medicine prices - a price comparison among 14 European countries. In: Southern Med Review 5/2:34-41
- Leopold, C.; Vogler, S.; Mantel-Teeuwisse, A. K.; de Joncheere, K.; Leufkens, H. G. M.; Laing, R. (2012b): Differences in external price referencing in Europe-A descriptive overview. In: Health Policy 104/1:50-60
- Leopold, C.; Mantel-Teeuwisse, A. K.; Vogler, S.; de Joncheere, K.; Laing, R. O.; Leufkens, H. G. (2013): Is Europe still heading to a common price level for on-patent medicines? An exploratory study among 15 Western European countries. In: Health Policy 112/3:209-216
- Leopold, C.; Mantel-Teeuwisse, A. K.; Vogler, S.; Valkova, S.; de Joncheere, K.; Leufkens, H. G. M.; Wagner, A. K.; Ross-Degnan, D.; Laing, R. (2014): Effect of the economic recession on pharmaceutical policy and medicine sales in eight European countries. In: Bulletin of the World Health Organization 92/9:630-640


- Lichtenberg, F. R. (2010): Pharmaceutical Price Discrimination and Social Welfare. In: *Capitalism and Society* 5/1:
- Lopert, R.; Lang, D. L.; Hill, S. R.; Henry, D. A. (2002): Differential pricing of drugs: a role for cost-effectiveness analysis? In: *Lancet* 359/9323:2105-2107
- Lopert, R.; Ruiz, F.; Chalkidou, K. (2013): Applying rapid 'de-facto' HTA in resource-limited settings: experience from Romania. In: *Health Policy* 112/3:202-208
- Lopez-Casasnovas, G.; Puig, J. (2000): Review of the Literature on Reference Pricing. Department of Economics and Business, Universitat Pompeu Fabra, Economics Working Papers
- Madhi, S. A.; Levine, O. S.; Hajjeh, R.; Mansoor, O. D.; Cherian, T. (2008): Vaccines to prevent pneumonia and improve child survival. In: *Bulletin of the World Health Organization* 86/5:365-372
- Mateev, N. D.; Manova, M. M.; Petrova, G. I. (2013): Analysis of the changes in pricing regulation on leading analgesics medicines prices and utilization in Bulgaria. In: *International Journal of Pharmaceutical Sciences and Research* 4/1:231-236
- Milstien, J. B.; Batson, A. (1998): Accelerating availability of new vaccines: The role of the international community. In: *Drug Information Journal* 32/1:175-182
- Miraldo, M. (2009): Reference Pricing and Firms' Pricing Strategies. In: *Journal of Health Economics* 28/1:176-197
- Moatti, J. P.; Ventelou, B. (2009): Economie de la sante dans les pays en developpement des paradigmes en mutation. (Health Economics in Developing Countries: The Changing Paradigms. With English summary.). In: *Revue Economique* 60/2:241-256
- Moon, S.; Jambert, E.; Childs, M.; von Schoen-Angerer, T. (2011): A win-win solution?: A critical analysis of tiered pricing to improve access to medicines in developing countries. In: *Global Health* 7/39
- Mossialos, E.; Dukes, G. (2001): Affordably priced new drugs for poor populations: Approaches for a global solution. In: *International Journal of Risk & Safety in Medicine* 14/1:1-29
- Mrazek, M. F. (2002): Pharmaceutical Pricing in the Developing Worlds: Issues of Access to Medicines. In: *Expert Review of Pharmacoeconomics and Outcomes Research* 2/1:43-50
- Otero Garcia-Castrillon, C. (2003): El acceso a los medicamentos: Las patentes y el Acuerdo sobre los Derechos de Propiedad Intelectual Relacionados con el Comercio. (Access To Drugs: Patents and the Agreements on Trade-Related Aspects of Intellectual Property Rights. With English summary.). In: *Informacion Comercial Espanola Revista de Economia* 804:197-217
- Parker-Lue, S.; Santoro, M.; Koski, G. (2015): The ethics and economics of pharmaceutical pricing. In: *Annual Review of Pharmacology & Toxicology* 55/191-206
- Pascual, F. (2014): Intellectual property rights, market competition and access to affordable antiretrovirals. In: *Antiviral Therapy* 19 Suppl 3/57-67
- Perez-Casas, C.; Herranz, E.; Ford, N. (2001): Pricing of drugs and donations: options for sustainable equity pricing. In: *Tropical Medicine & International Health* 6/11:960-964

- Plahte, J. (2005): Tiered pricing of vaccines: a win-win-win situation, not a subsidy. In: *The Lancet Infectious Diseases* 5/1:58-63
- Ridley, D. B.; Schulman, K. A. (2004): Differential pricing of pharmaceuticals in the internet age. In: *Journal of Ambulatory Care Management* 27/3:210-214
- Ridley, D. B. (2005): Price Differentiation and Transparency in the Global Pharmaceutical Marketplace. In: *Pharmacoeconomics* 23/7:651-658
- Satyanarayana, K. (2008): Towards equitable health care: drug prices, and beyond. In: *Indian Journal of Medical Research* 127/4:301-304
- Scherer, F. M.; Watal, Jayashree (2002): Post-TRIPS Options for Access to Patented Medicines in Developing Nations. In: *Journal of International Economic Law* 5/4:913-939
- Scherer, F. M. (2007): *Essential Drugs*. Harvard University, John F. Kennedy School of Government, Working Paper Series
- Scherer, F. M. (2013): *Patents, Monopoly Power, and the Pricing of Pharmaceuticals in Low-Income Nations*. Harvard University, John F. Kennedy School of Government, Working Paper Series
- Schmidt, F.; Egler, M.; Geursen, R. G. (2002): Ramsey pricing as an explanation and justification for price differences in the European pharmaceutical market. [German]. In: *Pharmazeutische Industrie* 64/6:513-519
- Schweitzer, S. O.; Comanor, W. S. (2011): Prices of pharmaceuticals in poor countries are much lower than in wealthy countries. In: *Health Affairs* 30/8:1553-1561
- Siskou, O. R. N.; Kaitelidou, C. D.; Litsa, S. P.; Georgiadou, S. G.; Alexopoulou, A. H.; Paterakis, G. P.; Argyri, P. S.; Liaropoulos, L. L. (2014): Investigating the Economic Impacts of New Public Pharmaceutical Policies in Greece: Focusing on Price Reductions and Cost-Sharing Rates. In: *Value in Health Regional Issues* 4/107-114
- Srivastava, D.; McGuire, A. (2014): Analysis of prices paid by low-income countries - how price sensitive is government demand for medicines? In: *BMC Public Health* 14/767
- Stargardt, T.; Schreyogg, J. (2006): Impact of Cross-Reference Pricing on Pharmaceutical Prices: Manufacturers' Pricing Strategies and Price Regulation. In: *Applied Health Economics and Health Policy* 5/4:235-247
- Stephene, J. (2011): Vaccines as a global imperative-a business perspective. In: *Health Affairs* 30/6:1042-1048
- T'Hoën, E; Moon, S (2001): Pills and pocketbooks. In: *Equity pricing of essential medicines* 4-5
- Tekiner, H. (2014): Pharmacy in Turkey: past, present, and future. In: *Pharmazie* 69/6:477-480
- Tetteh, E. K. (2009): Implementing differential pricing for essential medicines via country-specific bilateral negotiated discounts. In: *Applied Health Economics & Health Policy* 7/2:71-89
- Thomas, A. (2002): The WHO and Drug Pricing: A Proposal for Differentiated Drug Pricing for Developing Countries. In: *New Economy* 9/2:91-95


- van de Ven, N.; Fortunak, J.; Simmons, B.; Ford, N.; Cooke, G.; Khoo, S.; Hill, A. (2014): Minimum target prices for production of direct acting antivirals and associated diagnostics to combat Hepatitis C Virus. In: *Hepatology*
- Vitezic, D.; Madjarevic, T.; Gantumur, M.; Buble, T.; Vitezic, M.; Kovacevic, M.; Mrcic-Pelcic, J.; Sestan, B. (2012): Drug usage by outpatients in Croatia during an 8-year period: Influence of changes in pricing policy. In: *International Journal of Clinical Pharmacology & Therapeutics* 50/7:483-489
- Vogler, S.; Habimana, K. (2014): Pharmaceutical pricing policies in European Countries. Commissioned by Change to Win, Vienna
- Waning, B.; Kaplan, W.; King, A. C.; Lawrence, D. A.; Leufkens, H. G.; Fox, M. P. (2009): Global strategies to reduce the price of antiretroviral medicines: evidence from transactional databases. In: *Bulletin of the World Health Organization* 87/7:520-528
- World Health Organization; World Trade, Organization (2002): Differential Pricing and the Financing of Essential Drugs. In: *The economics of essential medicines*. Ed. Granville, Brigitte. London: Royal Institute of Economic Affairs, International Economics Programme; distributed by the Brookings Institution, Washington, D.C.: 209-231
- World Health Organization (2013): WHO Guideline on Country Pharmaceutical Pricing Policies, Geneva
- Yadav, P. (2010): Differential pricing of pharmaceuticals: Review of current knowledge, new findings and ideas for action. Accident; analysis and prevention. Ed. DFID, A study conducted for the UK Department for International Development. MIT Zaragoza International Logistics Program, Zaragoza

3 Annex 3: EPR survey with competent authorities – Questionnaire


Figure A3: Coversheet of the survey




SOGETI



Gesundheit Österreich
Forschungs- und Planungs GmbH



WHO Collaborating Centre
for Pharmaceutical Pricing
and Reimbursement Policies



UMIT
the health & life sciences university

Study on enhanced cross-country coordination in the area of pharmaceutical product pricing

Country Survey

Gesundheit Österreich Forschungs- und Planungsgesellschaft mbH (Austria), together with SOGETI (Luxembourg) and UMIT – Private Universität für Gesundheitswissenschaften, Medizinische Informatik und Technik GmbH (Austria), has been commissioned by the European Commission to undertake a study on enhanced cross-country coordination in the area of pharmaceutical product pricing.

The study will analyse the policy options of 'external price referencing' (EPR) and 'differential pricing' (DP) in terms of technical, economic and legal considerations. **The aim is to gain a better understanding of current EPR policies, their limitations as well as possible benefits through cross-country coordination or introduction of differential pricing.**

The attached Country Survey aims to collect and update information on country-specific features and methodology of the EPR policy (if applicable) in all 28 EU Member Countries as well as Norway, Iceland, Switzerland and Turkey.

In order **to keep your workload to a minimum the survey has been pre-filled** with information gained through continuous research of the consortium, particularly data gathered through the PPRI Network, as well as a survey of a previous EU project ('External reference pricing of medicinal products: simulation-based considerations for cross-country coordination') undertaken by another research institute.

The information provided in this survey will be used to gain a better understanding of EPR policies and their limitations as well as to simulate possible coordination and differential pricing scenarios. Further, the collected insights might be used in other EU commissioned projects in the area of pharmaceutical policies.

It would be highly appreciated if you could check the pre-filled information very carefully and possibly correct, update or elaborate with further detail and clarifications. Please return the filled questionnaire to peter.schneider@goeg.at by **31 March 2015**. Peter Schneider is pleased to be available for responding to technical questions (tel.: +43 51561 116).

In case of concerns or further requests regarding the study please contact the project leaders Lena Lepuschütz (lena.lepuschuetz@goeg.at) and Sabine Vogler (sabine.vogler@goeg.at).

Many thanks for your cooperation.

Figure A4: Example of the questionnaire without pre-filled information

Question:	Data gathered from literature/previous surveys:	Data Validation/Is data accurate? (Yes/No)	Corrections/Updates/Further Comments
Does EPR apply in your country?			
Is EPR used as sole or main systematic criterion or as supportive information when setting the price of a new medicine in your country?			
How many reference countries do you have in the ERP basket used by your country?			
Which are the reference countries in the EPR basket used by your country? Please specify, if there are "first-line" or highly prioritised countries and alternative countries.			
What are the types of products regulated by EPR in your country?			
Which price level is taken into account for reference purposes in your country?			
How is the reference price calculated in your country?			
Is there any weighting applied? (e.g. GDP)			
Methodological Issues/Selection of reference Products:			
a) How do you deal with the fact when there is no price available in a reference country?			
b) If a generic form of a product is available in a reference country, which type of product is selected for reference purposes in your country?			
c) If a product is not reimbursed in a reference country, is the price of the non-reimbursed product used as reference?			
d) When different pack sizes are approved in the reference countries at different prices, which pack size is used as reference in your country?			
How are the exchange rates chosen and taken into account?			
Who provides the price information?			
Is the price provided by the manufacturer validated?			
Does your legal framework provide regular revisions of the EPR-based prices in your country? If so, at what frequency?			
How often do you undertake price monitoring and revisions related to EPR-based prices? When was your last revision? (What was the outcome?)			
Are there mandatory discounts, rebates, or similar financial arrangements granted by pharmaceutical industry to the public payer? If so, please describe			
What have been the most important changes in the EPR methodology/process since 2010? (e.g. change in the basket, change in the calculation?)			

4 Annex 4: EPR survey – List of respondents

Table A3: Responding institutions to the country survey about EPR

Country	Institution
Austria (AT)	Austrian Federal Ministry of Health, Gesundheit Österreich GmbH (GÖG)
Belgium (BE)	National Institute for Health and Disability Insurance
Bulgaria (BG)	National Council on Prices and Reimbursement of Medical Products
Croatia (HR)	Croatian Health Insurance Fund
Cyprus (CY)	Ministry of Health, Department of Pharmaceutical Services
Czech Republic (CZ)	State Institute for Drug Control
Denmark (DK)	Ministry of Health
Estonia (EE)	Ministry of Social Affairs
Finland (FI)	Ministry of Social Affairs and Health
France (FR)	Ministry of Social Affairs, Health and Women's Rights
Germany (DE)	Ministry of Health, Department of Pharmaceutical Product Supply AOK Research Institute
Hungary (HU)	National Health Insurance Fund of Hungary
Greece (EL)	National Organisation for Medicines
Iceland (IS)	Icelandic Medicine Pricing and Reimbursement Committee
Ireland (IE)	Department of Health
Italy (IT)	Italian Medicines Agency
Latvia (LV)	National Health Service, Department of Pharmaceuticals and Medical Devices
Lithuania (LV)	National Health Insurance Fund
Luxembourg (LU)	Ministry of Social Affairs
Malta (MT)	Ministry of Health, Pharmaceutical Affairs
Netherlands (NL)	Ministry of Health, Welfare and Sport
Norway (NO)	Norwegian Medicines Agency
Poland (PL)	Ministry of Health, Department of Drug Policy and Pharmacy
Portugal (PT)	National Authority of Medicines and Health Products
Romania (RO)	Ministry of Health, Pharmaceuticals and Medical Devices Policy Department
Slovakia (SK)	Ministry of Health
Slovenia (SI)	Agency for Medicinal Products and Medical Devices
Spain (ES)	Ministry of Health, Social Services and Equality
Sweden (SE)	Dental and Pharmaceutical Benefits Agency
Switzerland (CH)	Federal Office of Public Health
United Kingdom (UK)	Department of Health
Turkey (TR)	Ministry of Health, Turkish Medicines and Medical Devices Agency

5 Annex 5: Proposal for further information to be included in EPR

Table A4: Proposal for further information to be included in EPR, by suggested order of importance

Information	Description	Relevance
Direct price information		
Information on discounts	An information whether the prices indicated are the official list prices, or discounted prices	Basic information
	Discounted prices are displayed in addition to the official list prices	Would considerably improve the EPR system
	An indication whether the discounts are statutory manufacturer discounts granted to public payers, and/or voluntary commercial discounts	In case that no disclosure of the discount were possible
Medicine price type and setting	Defines whether the price data is indicated as ex-factory price, pharmacy purchasing price, pharmacy retail price net or gross Indication of relevant setting (e.g. hospital price)	Basic information for any price comparison; since otherwise no correct price comparison / EPR would be possible
Data of price data	Indication of the latest price update	Basic information
	Information on historic prices, with information on the different uptake dates	Would be recommended for consideration of inclusion; would allow time series analysis
Exchange rate	Current exchange rate and indication of date/period of exchange rate (daily exchange rate, monthly / quarterly average)	Basic information
	Information on the exchange rates over time (in line with historic data)	Relevant and recommended for consideration of inclusion if information on price developments were included
Market volume data	Information on market volume data of the latest available year	Could be used to improve the EPR system by informing about the volume component, thus the relevance of the medicine in terms of consumption
	Developments of market volume data of the last years	Would allow improved interpretation of the data
Information on underlying pricing procedure and arrangements	Information on whether, or not, the price is based on a public tender, or whether it has been further negotiated Information on discount-like financial arrangements such as various managed-entry agreements Information whether EPR is applied as a main policy and price information is used as a supportive information (An asterisk or footnotes might indicate the existence of public tenders, and financial arrangement)	Information allows interpreting better the price data and indicates the validity of prices
Marketing authorization information	Information on whether, or not, the medicine has been centralised authorised, and if yes, the European Medicines Agency (EMA) number Date of marketing authorization Therapeutic indications	Information improves the interpretation of the price data by indicating whether, or not, these are newly launched medicines

Information	Description	Relevance
Pharmaco-economic data	Information on whether, or not, a pharmaco-economic study or Health Technology Assessment (HTA) report is available	Information improves the interpretation of the price data
Indirect price information		
Mandatory discounts	Information on whether, or not, statutory manufacturer discounts to public payers are in place If yes, information on the legal basis and its design/extent	Information could be used for change in the EPR system (consideration of published statutory discounts)
Economic situation	Indicator such as gross domestic product (GDP), purchasing power parities (PPP)	Would indicate on the ability-to-pay of a country Information required in case of the change of the design of EPR system (factoring in the economic situation)
Pharmaceutical expenditure	Information on total pharmaceutical expenditure, and public pharmaceutical expenditure per capita, in the latest available year	Supportive information allowing improved interpretation of price data
	Development total pharmaceutical expenditure, and public pharmaceutical expenditure per capita, of the last years	Supportive information
Methodology of EPR	Number and list of reference countries	Supportive information allowing improved interpretation of price data
	Methodology of reference price calculation	Supportive information allowing improved interpretation of price data
	Methodology of consideration of exchange rate	Supportive information allowing improved interpretation of price data
	Methodology related to non-availability of data	Supportive information allowing improved interpretation of price data
Price reviews	Information on whether regular price reviews are planned If yes, information on the legal/contractual basis, the frequency of reviews, the scope of medicines and planned further measures (revisions) If yes, information on actual implementation, including latest price review and price implementation	Supportive information allowing improved interpretation of price data
Market size	Information on total pharmaceutical sales per capita, supplemented by information on reimbursement and non-reimbursement market	Supportive information allowing improved interpretation of price data Information required in case of the change of the design of EPR system (factoring in market relevance)
Generic market share	Information on generic market share in volume	Supportive information allowing improved interpretation of price data Information required in case of the change of the design of EPR system (factoring in the relevance of off-patent product)
INN (International non-proprietary name) prescribing	Information, whether or not, INN prescribing is allowed, and whether it is mandatory	Supportive information allowing improved interpretation of price data

Source: The authors

It is not suggested that countries include all listed elements into their formal EPR mechanisms. This is merely a list of important information that countries may consider for improving their EPR system, and for instance in the case of PPP or GDP per capita could formally include into their EPR calculation mechanism if they wanted to account for different countries' economic situation. As building price databases and conducting EPR evaluations is administratively time-consuming, the benefit of any extension of the EPR mechanism by including further information should be weighted with the costs of increased administrative burden.

6 Annex 6: DP survey with experts – Questionnaire

Are you involved / have you been involved in differential pricing? If yes, could you please report (countries, purchaser, medicines, procedure)

DP is often considered as 'second-best' option to allow access to medicines otherwise non-accessible; others judge DP as a subsidy. Which is your position on this?

What do you see as benefits of DP?

Benefits in terms of accessibility, savings for public budget, reward for manufacturer?

What do you see as limitations of DP?

It is often argued in literature that DP must be connected with confidentiality? Do you agree?

It is sometimes argued in literature that DP is not a stand-alone policy. Do you agree? Which further policies (e.g. voluntary/compulsory licensing, tendering, competition) would you recommend?

DP practice has been limited to LMIC (unless confidential discounts in Europe are considered as DP, as many argue). Under the condition that restraints for the implementation of DP in Europe could be overcome, would you see DP as a policy option relevant for European countries? Explain why, whether its yes or no?

Which would you consider as the main prerequisites to be addressed in legal, organisational and technical terms to introduce a DP in Europe?

Any further information to be added?

Ideas for further interview partners?

Contact

For further information please contact:

Sabine Vogler, Peter Schneider
Gesundheit Österreich Forschungs- und Planungs GmbH (Austria)
E-Mail: sabine.vogler@goeg.at, peter.schneider@goeg.at
Phone: +43 1 51561/147 or 116

Medicines	Country/ies	Purchaser	Description	Results/Assessment
Vaccines	Low- and middle-income countries	National governments or public sector programmes	<p>Driven by the Bill and Melinda Gates Foundation, in 2011 the decade of vaccines was launched, with the goal to extend – by 2020 and beyond – the full benefits of immunisation to all people. During this initiative pharmaceutical manufacturers updated their tiered pricing schemes. For instance, one producer of vaccines classified countries into seven tiers according to their GNI ranking. To take account for the willingness to invest, each income tier is divided into price ranges based on four criteria:</p> <ol style="list-style-type: none"> 1. The committed duration of vaccination in the disease area 2. Coverage of the target population which rewards the health benefit of well implemented vaccination programmes 3. Vaccines with broad age recommendations 4. The number of doses to be purchases 	<ul style="list-style-type: none"> ▪ The update of the tier schemes aims to support the 17 countries which are anticipated to graduate from GAVI financing ▪ The revised approach to tiered pricing should provide access to and build sustainable supply of vaccines and result in lower prices ▪ It should be noted that the described pricing procedure is not a broad pricing approach across all vaccines. Each manufacturer has its own specific pricing policy.
Several	India	National governments or public sector programmes	<p>Pharmaceutical manufacturers started to create for basic primary care products such as antibiotics, painkillers and antacids separate brands for low-income markets. The packaging of the products use local language and smaller packet sizes for acute therapy in order to keep out-of-pocket costs low</p>	-
Malaria	Africa	National governments	<p>To address unmet patient needs in the context of neglected diseases, pharmaceutical manufacturers entered a public-private partnership. The aim of the partnership was to jointly develop a safe, rapidly acting fixed-dose combination (FDC) to treat malaria</p>	<ul style="list-style-type: none"> ▪ The result was the creation of the ASAQ approach (Adapted Simple Accessible Quality) ▪ Each partner provided considerable expertise within its own domain: Medicines for neglected diseases (DNDi) initiative did much of the pre-clinical and clinical work with various academic institutions around the world whereas the pharmaceutical manufacturer developed the process required to enable the production on an industrial scale ▪ The financial burden for each partner was reduced

Medicines	Country/ies	Purchaser	Description	Results/Assessment
ARV	LDC	National governments or public sector programmes	In recent years, originator companies have started to grant voluntary licences to generic manufacturers under specific conditions. These may include the requirement that producers meet good manufacturing practices (GMP) as defined by the U.S. Food and Drug Administration or the World Health Organisation, or that products be distributed only in LDCs.	<ul style="list-style-type: none"> ▪ Originator companies either provide these licenses royalty fee, depending on the company, the product and the country. In one case, the Licensee pays a 5% royalty fee on finished products, but is free to establish his own prices for these medicines. Through this license approach ARVs of the originator company reach 95 developing countries ▪ A major challenge for local manufacturers in developing countries is to meet the GMP standards in order to obtain licenses and participate in international tenders
Vaccines	LDC	Global Alliance for Vaccines and Immunisation, GAVI	The global alliance for Vaccines and Immunisation (GAVI) established in 2007 the Vaccine Presentation and Packaging Advisory Group (VPAAG)	<ul style="list-style-type: none"> ▪ The efforts of VPAAG targets packaging to ensure that future vaccine products and delivery technologies are designed with characteristics consistent with developing country needs (e.g. fixed dose combinations) and also allow market segmentation. VPAAG has developed a generic preferred product profile as a reference document for vaccines in developments for use in low- and middle-income markets.
ARV	LDC	National governments or public sector programmes	The proportion of patients on triple combination therapy has increased from one-third to nearly two-thirds in Africa. However, the	<ul style="list-style-type: none"> ▪ No single model of price discrimination will be effective for all diseases (HIV, malaria, TB), since the clinical needs, economic incentives and epidemiology of each illness are substantially different ▪ Differential pricing is not necessarily a panacea for all pricing issues. For 15 of 18 differentially priced medicines, prices were higher than for generics. ▪ An Indian pharmaceutical company has repeatedly offered 5% royalty to any brand name pharmaceutical company that would grant a voluntary license to sell patented ARVs in the developing world

Study on enhanced cross-country coordination in the area of pharmaceutical product pricing / Annex

Medicines	Country/ies	Purchaser	Description	Results/Assessment
Malaria	African, Western Pacific and South-East Asian countries	National Governments or public sector programmes	Pharmaceutical manufacturers offer the same antimalarial at two different prices. The brand name is available at a normal price, while the same medicine, under a different name, is available at a preferential price for the needy	<ul style="list-style-type: none"> Under this scheme the access to medicines has increased and in one case a company was able to distribute more than 10 million artemisinin-based combinations therapies.
Leishmaniasis	Worldwide	National governments or public sector programmes	In 2006, a 5 year public-private-partnership was signed, in which the pharmaceutical manufacturer agreed to contribute to 25% of the complete donation for combating leishmaniasis	<ul style="list-style-type: none"> The Pharmaceutical Manufacturer distributed medicines by using a tiered pricing policy among a large number of patients worldwide.
Diabetes	India	National governments or public sector programmes	A pharmaceutical manufacturer has agreed on launching medicines against Diabetes in India. All these medicines will be priced lower than the price of the medicine in the originator's country.	<ul style="list-style-type: none"> Differential pricing is considered by pharmaceutical manufacturers as a measure to increase market sales in emerging markets.
Tuberculosis	LDC	National governments or public sector programmes	Several pharmaceutical companies have signed in 2001 an arrangement to supply six classes of second-line anti TB medicines (variously under-patent, in non-patent monopoly and having generic status)	<ul style="list-style-type: none"> The products are sold at a price that is as low as 5% of what some countries are currently paying for individual medicine Provisions have been included to prevent backflow of these DP pharmaceuticals into high-price markets
Insulin	49 LDC	National governments	Since 2001, a pharmaceutical manufacturer has offered public health systems in 49 LDC human insulin at prices which do not exceed 20% of the average price in Europe, Japan, and North America	<ul style="list-style-type: none"> In 2009, 36 countries used the pricing scheme to buy insulin at or below the threshold price. There are 13 LDC countries which did not use the scheme; the pharmaceutical manufacturer reported that some countries did not respond to the offer, either because there are no private wholesaler or partners, with which to work or because wars or political unrest have made it impossible to do business.

Source: Authors' compilation based on literature review [2-7]

Table A7: Arguments against and in favour of DP reported in literature

Objection against DP	Argument in favour
DP will impair the economic well-being of the innovative industry and its ability to attract capital.	Substantial price reductions through DP will lead to an increase unit sales. As a consequence, manufacturing facilities would run more efficiently and will be subject to economies of scale i.e. reducing costs of production. Vaccines are regularly quoted as a good example, since this market is mainly driven by the volume effect. For the vaccine industry DP has been a profitable pricing strategy and furthermore created the basis for future expansion.
Low-price medicines will 'leak' into high-price markets, undermining earnings there. This 'pharmaceutical leakage' is a non-neglectable phenomenon and often reported in public medicine programmes.	Experience with existing agreements suggest that it is possible to overcome the problem of backflow through a number of complementary mechanisms <ul style="list-style-type: none"> ▪ Obligations imposed in supply contracts ▪ Differential labelling, nomenclature or trademarking of DP products ▪ Legislation to prevent parallel imports from countries with DP ▪ Policies in importing countries to control the flow of DP products
Introducing 'affordable' prices in developing countries, industrialised countries will take these prices as a starting point for their own national reference price systems.	It would be unrealistic if countries where prices had been lowered to serve a poor population (e.g. low- and middle income countries in Africa and Southern America), were to add to the reference list in one or more high-income countries. In order to avoid this risk, a global agreement on DP is needed, subscribed to by all countries rather than relying on ad hoc arrangements.
Industry has already shown that it can handle this problem without public intervention.	Many pharmaceutical companies have not been involved in DP, and those initiatives which apply DP tackle only a fraction of the immense global health problems. The participation of major manufacturers has only happened when there was extreme pressure from external sources.
There is little point in supplying advanced medicines if the mechanisms to deliver them to patients, to prescribe them responsibly and to supervise treatment are lacking; affordable prices are only one part of the 'access to medicines'-puzzle.	The lack of therapeutic skills is indeed a problem with regard to the use of some medicines, but it is not an obstacle in the treatment of other diseases (e.g. tuberculosis, malaria) where simple and practical solutions can be found.
Developing countries do not mobilise resources efficiently; with due effort they could pay more for medicines.	Inefficiency problems with respect to tax collection or excessive spending in questionable fields exist in developing countries, but these issues need to be tackled separately. It is also a questionable argument to suggest that the existence of such problems obviates or even reduces the need to tackle problems related to the access to medicine.
Some medicines are just too expensive in production to be sold at prices affordable to poor people	Pharmaceutical Manufacturers do not disclose the costs of producing pharmaceuticals, but there is plenty of evidence that the mere costs of production are extremely low. In many cases – even for complex molecules – prices fall if the medicine is produced at a large scale. If there are exceptions that justify a public subsidy in order to render them affordable, this needs to be documented
If the industry cuts prices to a bare minimum, they will then be raised again by taxes, import duties and wholesale and retail profits.	This has been observed in practice for contraceptives and vaccines involved in DP. The main question which needs to be settled in this context is whether differentially priced medicines should be restricted to the public or non-profit sectors. On the one hand it ensures better control over the supply and excludes excessive margins, but on the other hand the public sector plays a limited role in the countries where DP is applied

Objection against DP	Argument in favour
Current prices are necessary in order to fund research and development.	Since firms are reluctant to disclose information about their cost structure, it is difficult to assess the size of the fraction of expenditures that pharmaceutical companies devote to research and development (R&D). Creative innovative research represent only one of the elements determining cost and it can be assumed, that it has been superseded by expenditure on marketing and promotion as the main cost driver.
Some important offers of discounted prices or donations made by companies to developing countries have not been taken up.	It has occasionally been the case, but the documentation suggests that the rejection is related to the supply of inappropriate pharmaceuticals. The donation of pharmaceuticals intended to secure tax relief in the exporting country and did not take into account the need of the recipient country.
Differential pricing is illegal.	No documented basis whatsoever can be identified for this objection. In the context of the United States (US) Anti-Trust Law, the law aims to protect the public by preventing collusion between manufacturers on price maintenance. Concerning this goal it coincides with DP which tries to achieve price reductions to the public benefit.
Differential pricing is impossible where a medicine is only likely to be used in a disease occurring exclusively in poor populations.	This objection against DP is justified, as it is a severe limitation of DP to deal with heterogeneous income groups within a country.
Differential pricing by multinationals will adversely affect the generic industry and discourage manufacturing in developing countries.	The bulk of the generic manufacturing industry has related to older but valuable medicines on which patents have expired. Many of these will continue to be essential medicines and DP policies such as voluntary or compulsory licensing will provide the industry with new fields of production.

Source: Mossialos E and Dukes G [8]

9 Annex 9: Euripid survey – Questionnaire

Which would you consider as the benefits and strengths of Euripid?

Which were prerequisites for building up Euripid? Which would you consider as prerequisites for building an effective medicine price database in Europe? What would you do differently if you would build a price database in Europe?

Which would you consider as limitations (weaknesses) of Euripid / of any central medicine price database?

Which further information or classification in Euripid would be helpful?

Which do you consider as opportunities of Euripid, and which as threats?

Any further information / comments that you would like to share with us?

10 Annex 10: Simulations – Model inputs

Table A8: Model inputs for EPR simulations

Country	Is EPR the main criterion?	Regular re-evaluations (in months)	Min. available reference prices required	Calculation methodology	Type of price used	Approx. WS mark-up ¹	Purchasing power parities ²	GDP per capita (in PPS) ³	GDP per capita, PPP (in US\$) ⁴
Austria	Yes	No reevaluation	14	Average	Ex-factory price	9.10%	1.11761	128	45.081
Belgium	No	No reevaluation	1	Average	Ex-factory price	8.50%	1.1259	119	41.573
Bulgaria	Yes	6	1	Minimum	Ex-factory price	9.09%	0.930239	45	15.732
Croatia	Yes	12	2	Average	Pharmacy purchasing price	8.50%	4.81181	61	21.351
Cyprus	Yes	12	1	Average	Pharmacy purchasing price	14.00%	0.892329	89	31.198
Czech Republic	Yes	36	3	Average of 3 lowest	Ex-factory price	4.10%	17.739	82	29.018
Denmark	No EPR	No reevaluation	NA	NA	NA	6.30%	10.1622	124	43.782
Estonia	Yes	12	1	Minimum	Ex-factory price	5.90%	0.72914	73	25.823
Finland	No	60	1	Average	Pharmacy purchasing price	3.00%	1.23362	113	39.869
France	No	60	1	Average	Ex-factory price	4.30%	1.13105	107	37.592

¹ Information taken from Vogler S and Schneider P [9]

² Source: Eurostat Databank; 2013, EU28=1

³ Source: Eurostat Databank; 2013, EU28=100

⁴ World Bank, in PPP (current international US\$), 2013

Country	Is EPR the main criterion?	Regular re-evaluations (in months)	Min. available reference prices required	Calculation methodology	Type of price used	Approx. WS mark-up ¹	Purchasing power parities ²	GDP per capita (in pps) ³	GDP per capita, PPP (in US\$) ⁴
Germany	No ⁵	No reevaluation	1	Average	Ex-factory price	5.90%	1.05124	122	43.887
Greece ⁶	Yes	3	3	Average of 3 lowest	Ex-factory price	4.20%	0.83617	73	25.667
Hungary	Yes	No reevaluation	3	Minimum	Ex-factory price	5.10%	171.,208	66	23.336
Iceland	Yes	24	3	Average	Pharmacy purchasing price	4.30%	183.028	119	42.035
Ireland	Yes	36	1	Average	Ex-factory price	8.00%	1.1021	130	45.677
Italy	No	24	1	Minimum	Ex-factory price	9.10%	1.00888	99	35.075
Latvia	No	24	1	Third lowest price	Ex-factory price	3.30%	0.679363	64	22.534
Lithuania	Yes	12	1	Average	Ex-factory price	8.50%	0.608666	73	25.715
Luxembourg	Yes	12	1	Minimum	Ex-factory price	8.50%	1.21234	257	91.048
Malta	Yes	18	3	Average	Pharmacy purchasing price	0.00%	0.779959	86	29.127
Norway	Yes	12	1	Average of 3 lowest	Pharmacy purchasing price	6.00%	12.1889	186	65.640
Poland	No	24	1	Average	Ex-factory price	6.80%	2.41243	67	23.994
Portugal	Yes	12	1	Average	Ex-factory price	9.30%	0.779828	79	27.509
Romania	Yes	60	1	Minimum	Ex-factory price	12.00%	2.20446	55	18.972
Slovakia	Yes	6	1	Average of 3 lowest	Ex-factory price	13.00%	0.679476	75	26.497

⁵ EPR is not applied in practice. For the simulations, the legal situation related to EPR in Germany was considered.

⁶ Please note that in the case of Greece, due to late receipt of the survey questionnaire, the presented model still presents the old basket including 22 instead of 27 reference countries.

Country	Is EPR the main criterion?	Regular re-evaluations (in months)	Min. available reference prices required	Calculation methodology	Type of price used	Approx. WS mark-up ¹	Purchasing power parities ²	GDP per capita (in PPS) ³	GDP per capita (in US\$) ⁴
Slovenia	Yes	6	1	Minimum	Ex-factory price	6.00%	0.805192	82	28.859
Spain	No	12	1	Minimum	Ex-factory price	5.26%	0.90063	94	33.092
Sweden	No EPR	No reevaluation	NA	NA	NA	3.60%	11.6638	127	44.646
Switzerland	Yes	36	1	Average	Ex-factory price	8.00%	1.82671	163	56.940
The Netherlands	Yes	6	2	Average	Pharmacy purchasing price	10.60%	1.09748	131	46.162
UK	No EPR	No reevaluation	NA	NA	NA	12.50%	0.925106	109	38.255

approx. = approximate, EPR = external price referencing, GDP = gross domestic product, NA = not available, PPP = purchasing power parities, PPS = purchasing power standards, WS = wholesale

Source: Authors' compilation based on country survey with competent authorities

11 Annex 11: Simulations – Additional results

This section aims to provide an overview of real price data, i.e. how price levels compare between countries and relate to countries' economic situation, to complement the different scenarios under EPR and DP methodologies. A short version of the results is available in the main body of this study (cf. chapter 4.2.3).

Previous comparisons among countries in Europe have shown, for instance, that prices in Germany, Switzerland, Denmark and Belgium tend to be at the higher side, whereas prices in Spain, Italy and France tended to be relatively lower (e.g. [10-12]). However, the literature on price comparisons is scarce, limited by data availability and reliability issues. One limitation faced by almost all such analyses is the reliance on official list prices, which might differ from actual prices paid by social insurances through confidential discount or rebate arrangements.

The analysis is based on 30 high-cost medicines, half from the inpatient, half from the outpatient sector.⁷ Prices are collected for 2013 and available for 16 European countries: Austria (AT), Belgium (BE), Denmark (DK), Finland (FI), France (FR), Germany (DE), Greece (EL), Hungary (HU), Ireland (IE), Italy (IT), Netherlands (NL), Portugal (PT), Slovakia (SK), Spain (ES), Sweden (SE) and the UK (UK). The analysis is based on unit prices, i.e. per unit of intake such as tablet or vial, and the data is sourced from the Pharma Price Information service (PPI) run by Gesundheit Österreich Forschungs- und Planungs GmbH (GÖ FP) [13].

The medicines were chosen on the basis of which constituted particularly large costs for public payers. The sample thus includes some high priced medicines (for 20 percent of chosen pharmaceuticals the median price per unit was above EUR 1,000), as well as some medicines which had large budget impacts due to the quantity prescribed (27% of all median had a median price below EUR 10).⁸

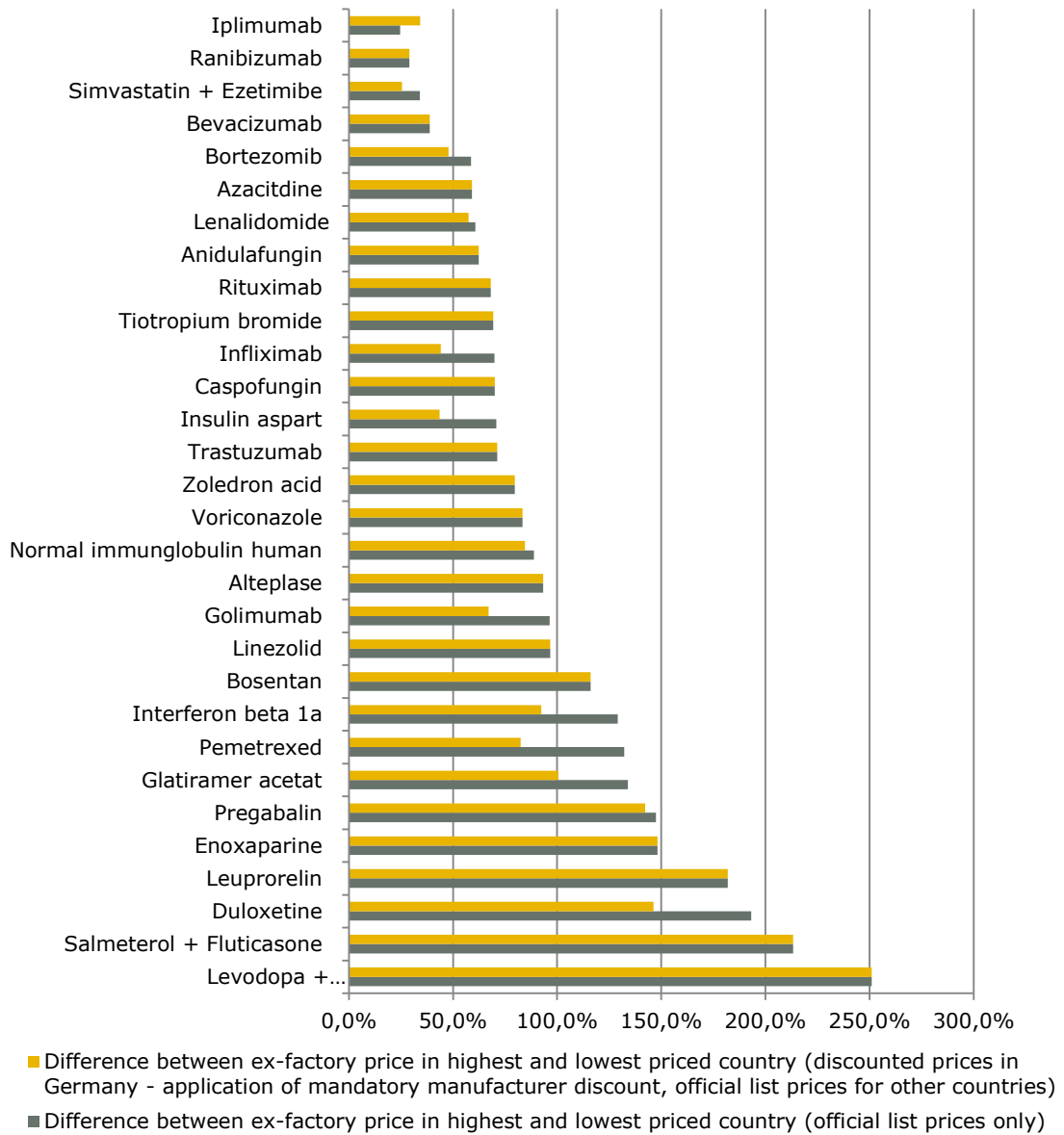
The data analysis uses official ex-factory prices (list prices) of the 16 European countries, and, additionally for Germany, the ex-factory price reduced by the mandatory statutory discount is used. For the other countries no discounted prices are considered, even though they may be reduced by law or rebates, discounts, clawbacks or Managed Entry Agreements which are agreed upon in confidential negotiations.

Prices vary widely between countries, with ex-factory prices in the highest-priced country being between 24.6 percent and 251.1 percent higher than in the lowest-priced country for the relevant medicine (see Figure A5).

⁷ The 30 high-cost medicines were chosen based on information from the Main Association of Austrian Social Insurance Institutions (out-patient sector) and the Viennese hospital association (in-patient sector) about these medicines that accounted for highest expenditure in their budget in 2012.

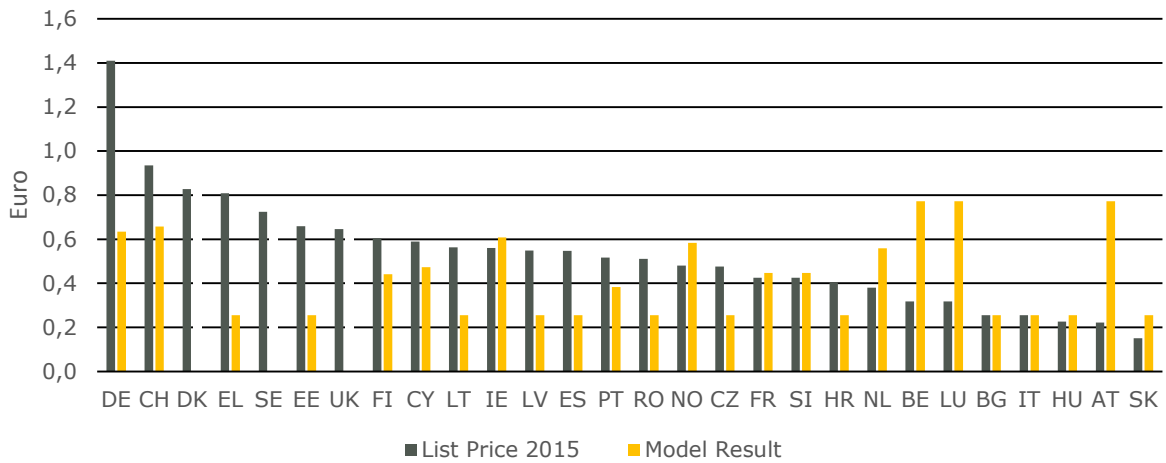
⁸ Price data of generics were excluded from this study. The exchange rates used to calculate Euro prices are the rates provided by the Austrian National Bank for March 2013.

Figure A5: Differences (in percent) between ex-factory price in the highest and lowest price country, 2013



Source: Data provided by Pharma Price Information (PPI) of Austrian Public Health Institute [13]

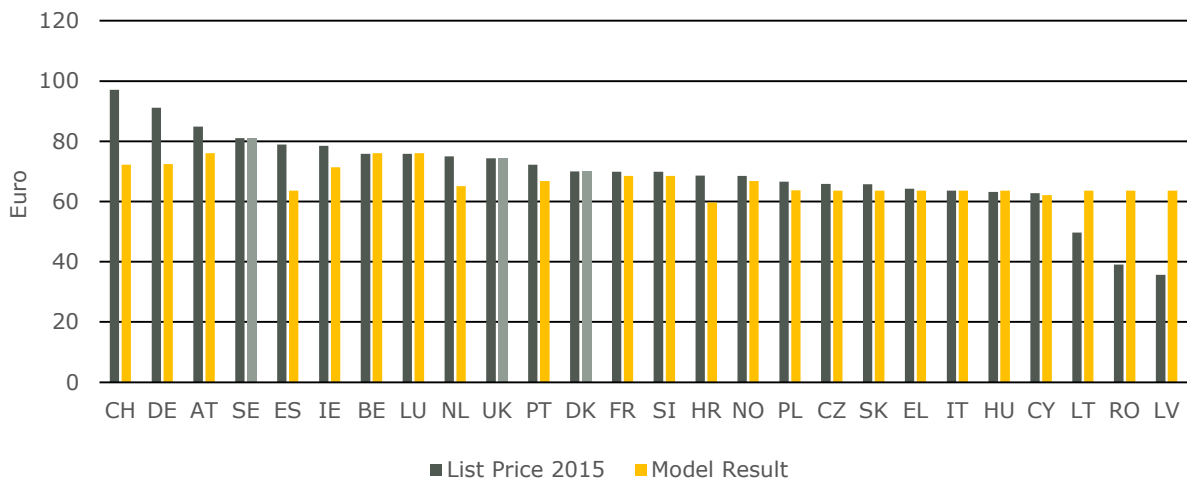
Figure A11: Escitalopram: 2015 List prices compared to Base Scenario Model Results



Source: Pharma Price Information (PPI) service of the Austrian Public Health Institute, authors' calculations

Figure A12 compares current prices of Imatinib with results from the model when actual prices for Germany and Italy are used as launch prices. Here, model prices differ less to the collected pricing data. They differ most for countries with very high or very low prices. Since the model only considers price changes due to EPR, and EPR signifies methodologies such as average or minimum of observed prices in other countries, the model prices never really go above the highest launch price, or below the lowest launch price, with some slight exceptions due to exchange rate fluctuations. Thus, the model results differ most for those countries with actual prices below Italy's where the model results in higher prices on the level of Italian prices.

Figure A12: Imatinib: 2015 List prices compared to Base Scenario Model Results



Source: Pharma Price Information (PPI) service of the Austrian Public Health Institute, authors' calculations

These comparisons illustrate the working of the model when using real rather than fictitious prices and show that model results differ from real prices, however in the directions expected due to the simplifying assumptions made by the model.

12 Annex 12: Price impacting factors

In the following, price studies are analysed with regard to their findings in general and in particular to possible factors.

Table A9: Price studies on possible price impacting factors

Author(s)	KONIJN, Paul
Title	Pharmaceutical products – comparative price levels in 33 European countries
Journal	Economy and Finance
Research question	To construct Purchasing Power Parities by using prices for pharmaceuticals
Country/Countries included	33 European countries (Austria, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Iceland, Italy, Latvia, Lithuania, Luxembourg, Macedonia, Malta, the Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, Switzerland, Turkey, United Kingdom)
Reference year(s)	November 2005
Products	181 different medicines; For each country a list of best-selling medicines has been compiled and products from the top of the list have been selected; the selected product contained on-patent (75%) and off-patent (25%) pharmaceuticals
At what price level	Not clearly specified; It is mentioned that the prices collected should represent the full market price of a product (independent of what is paid out-of-pocket or covered by social security schemes); The author mentions that prices were collected by visiting pharmacies, implying that the pharmacy retail price was used;
Methodology	With the obtained prices for the 181 medicines, purchasing power parities have been calculated
Results	Countries can be divided into six groups: The top groups (IS & CH) have significantly higher price levels, being 60 to 87% higher than the EU25 average. In the second group of most expensive countries price levels are between 15 and 30% higher than the EU 25 average (DK, DE, IE, IT, NO). The third group has price levels between 0% and 15% higher than the EU average (BE, CY, LU, MT, NL, AT, FI). The fourth group has price levels between 0% and 15% lower than the EU25 average (FR, PT, SI, SE, UK). A large group (mainly new EU member states) has price levels between 68 and 80% of the EU25 average (BG, CZ, EE, EL, ES, LV, LT, HU, PL, RO, SK, HR, TR). The lowest price levels are found in the Former Yugoslav Republic of Macedonia at 58% of the EU25 average.
Limitations	The level of uncertainty associated with the underlying price and other data, and the methods used for compiling PPPs and PLIs imply that strict ranking of countries is not advisable
Sponsors	None
Conclusions of the study	Prices for original medicines (those that are or have been covered by a patent) are less dispersed than those of generics
Comments (own)	<p>The author does not adequately address the methodologically challenges when comparing pharmaceuticals. He simply states that pharmaceuticals are relatively easy to compare, since they can be identified among other things by active substance. He provides no description which prices are compared and how differences in packaging or strength are taken into account.</p> <p>If the author had used the pharmacy retail price he should explain how to deal with (1) different VAT rates, (2) the fact that in some countries it is not possible to calculate a pharmacy retail price (UK) and (3) some top-selling products are sometimes only administered in hospitals;</p> <p>No further description on the products and if availability in all countries was a requirement</p>

Source: Konijn P [15]

Author(s)	LEOPOLD, Christine; MANTEL-TEEUWISSE, Aukje Katja; SEYFANG, Leonhard; VOGLER, Sabine; DE JONCHEERE, Kees; LAING, Richard Ogilvie; LEUFKENS, Hubert
Title	Impact of External Price Referencing on Medicine Prices – A price Comparison Among 14 European Countries
Journal	Southern Med Review
Research question	To examine the impact of external price referencing (EPR) on on-patent medicine prices, adjusting for other factors that may affect price levels such as sales volume, exchange rates, gross domestic product (GDP) per capita, total pharmaceutical expenditure (TPE), and size of the pharmaceutical industry
Country/Countries included	14 European countries (Austria, Belgium, Denmark, Germany, Greece, Finland, France, Italy, the Netherlands, Norway, Portugal, Spain, Sweden, Slovakia)
Reference year(s)	2007 & 2008
Products	14 on-patent medicines in the out-patient sectors (hospital-exclusive products were excluded)
At what price level	Ex-factory prices in EUR (For price comparisons, the prices were analysed in prices per units)
Methodology	The unit ex-factory prices in Euro of all products, all countries and of both years were adjusted to a fixed exchange rates were converted to scaled ranks. For the regression analysis the scaled ranks per country and product were weighted. Each country had the same sum of weights. Within a country the weights were proportional to its sales volume in the year.
Results	On average EPR as a pricing policy leads to lower prices. However, the large variation in price levels among countries using EPR confirmed that the price level is not only driven by EPR. The unadjusted linear regression model confirms that applying EPR in a country is associated with a lower scaled weighted rank. This interaction persisted after inclusion of total pharmaceutical expenditure per capita and GDP per capita.
Limitations	The dummy variable EPR implies homogeneity which does not exist: EPR is very differently applied in the countries in terms of the country basket, frequency of price updated and the price calculation method; Another confounding factor is that EPR is only one of many pharmaceuticals price regulation policies
Sponsors	None
Conclusions of the study	Prices for patented products were generally lower in the countries which applied external reference pricing. Possible explanations could be found through an association of the scaled ranks with the pharmaceutical industry size and scaled weighted ranks. However, it needs to be acknowledged that huge price difference could be found between countries which apply external price referencing
Comments (own)	<ul style="list-style-type: none"> ▪ The authors state that the main criterion for choosing the products was the patent status of each medicine; Nothing is mentioned about the relevance of these medicines; ▪ No explanation for choosing the countries is provided ▪ Countries are ranked due to the prices of medicines; by using ordinary least squares (OLS) regression it is only possible to make statements about the qualitative effect of EPR (i.e. positive or negative) but not about the quantitative effect (i.e. size) → a logit regression would have been interesting to examine the probability of yielding a better rank when EPR is in place. ▪ The best predictor for TPE per capita is GDP per capita; the inclusion of both might not be necessary, since also the p-value for GDP per capita was low → a comparison of (adjusted) R², Schwarz-Bayesian Criterion (SBC) or Akaike information criterion (AIC) would have been interesting.

Source: Leopold C, Mantel-Teeuwisse AK, Seyfang L, *et al.* [16]

Author(s)	BREKKE, Kurt Richard; TOR, Helge Holmas; ODD, Rune Straume
Title	Are Pharmaceuticals Still Inexpensive in Norway
Journal	Report of the Institute for Research in Economics and Business Administration (SNF)
Research question	To compare prices of pharmaceuticals in Norway and nine Western European countries which constitute the basket of countries that form the basis for setting maximum prices for prescription medicines in Norway. To study the change in price levels and price indices over the three last three years To compare pharmacy margins across ten countries
Country/Countries included	10 European countries (Norway Austria, Belgium, Denmark, Finland, Germany, Ireland, the Netherlands, Sweden, UK)
Reference year(s)	2007 & 2008
Products	300 top-selling (prescription bound) active substances (include on-patent and off-patent)
At what price level	Pharmacy purchasing price & pharmacy retail price
Methodology	Using the sales data, the authors compute volume-weighted average prices for each active substance; When constructing price indices for other countries they have been assigned Norwegian consumption weights to reflect a representative pattern of consumption in the benchmark country; In this way, it can be ascertained what a typical Norwegian pharmaceutical basket would cost in the various reference countries;
Results	UK, Norway and Sweden are the three cheapest countries in the reference group of then Western European countries, whereas Ireland Belgium and (usually) Germany are the three most expensive countries. This ranking is also fairly consistent across submarkets as the patent and generic market segments;
Limitations	Disadvantages are essentially related to a lack of representativity: <ol style="list-style-type: none"> 1.) Picking only the best-selling pack for each substance, implies that we throw away information about all other packs for this substance 2.) Top-selling pack in Norway may not be among the top-selling ones in the reference countries
Sponsors	None
Conclusions of the study	UK, Norway and Sweden consistently have the lowest pharmacy retail prices of prescription medicines whereas Ireland, Belgium and Germany have the highest prices. Comparing price indices from 2007 to 2009 revealed that there are large changes in the price indices from 2008 to 2009. All countries become more expensive than Norway, but this is mainly driven by exchange rate fluctuation.
Comments (own)	<ul style="list-style-type: none"> ▪ What does volume-weighted mean for an on-patent active ingredient? ▪ When constructing average prices for active ingredients, how are different strengths taken into account: e.g. Rosuvastatin 20 mg and 40 mg? Instead of IMS standard units DDD/ATC per package should have been used for regression ▪ The authors focused on pharmacy retail price without value added tax (VAT) but they did not discuss the comparability of this price level in other countries (e.g. UK). ▪ The authors did not explain if top-selling active ingredients are only administered in the out-patient sector. ▪ The two additional variables in the regression analysis should have been explained more in detail

Source: Brekke KR, Holmås TH and Straume OR [12]

Author(s)	LEOPOLD, Christine; MANTEL-TEEUWISSE, Aukje Katja; VOGLER, Sabine; DE JONCHEERE, Kees; LAING, Richard Ogilvie; LEUFKENS, Hubert
Title	Is Europe still heading to a common price level for on-patent medicines? An exploratory study among 15 Western European Countries
Journal	Health Policy
Research question	To explore whether ex-factory prices of on-patented medicines in Western European countries have converged over a recent period of time
Country/Countries included	15 Western European countries (Austria , Belgium, Denmark, Finland, France, Germany, Greece, Ireland, Italy, Netherlands, Norway, Portugal, Spain, Sweden, Switzerland)
Reference year(s)	2007, 2008, 2010, 2011, 2012
Products	Ten on-patent products according to (1) Patent status (2) ATC groups (3) reimbursement (4) Marketing authorisation holder (MAH) and (5) price segment
At what price level	Ex-factory price in EURO For price comparisons, prices were analysed in prices per daily defined dosis (DDD)
Methodology	To analyse the price variance between countries for each product the range as well as the average of the unit ex-factory price in Euro per DDD indexed to 2007 was calculated each year. To test for price convergence, a score per country was calculated, which is expressed as the percentage deviation of the average price of all countries in each year:
Results	<ul style="list-style-type: none"> ▪ The prices between countries and selected products varied to a great extent. Germany, Denmark and Finland were the countries with the highest prices. Greece was the country with the lowest prices followed by Italy, Spain and France. The price range was relatively small and constant over the years for some products whereas others experienced larger and increasing range. ▪ From 2007 to 2008 price divergence decreased, but from 2008 to 2012, the price divergence is only driven by two country: Germany (27 % higher prices) and Greece (32% lower prices) ▪ The prices of medicines decreases between 2007 and 2012 for all but one product
Limitations	<ul style="list-style-type: none"> ▪ Disregard of discounts/rebates: the unit ex-factory price is listed in national price lists disregards official (statutory) as well as commercial (voluntary) discounts/rebates. This is an issue of transparency as price convergence might have taken place but was hidden as discounts and rebate dynamics are not transparent. ▪ Unavailability of volume data: due to limited financial resource volume data could not be acquired. ▪ Sample size: Due to the small sample size it is a study with an explorative character, and conclusions should be considered tentatively. ▪ Currency fluctuations: Over the period exchange rates fluctuated extremely over time;
Sponsors	None
Conclusions of the study	Differences in medicine prices across countries and over time are confirmed. Instead of the expected price convergences a price divergence can be observed, driven by price changes in only two of the 15 countries. All other European countries remained stable around the country average.
Comments (own)	<ul style="list-style-type: none"> ▪ Relevance of pharmaceutical industry is acknowledged and should be taken into account for further price analysis (e.g. employees in pharmaceutical industry per 100,000) ▪ Volume data are mainly used for the construction of price index

Source: Leopold C, Mantel-Teeuwisse AK, Vogler S, *et al.* [17]

Author(s)	KANAVOS, Panos; VANDOROS, Sotiris
Title	Determinants of branded prescription medicine prices in OECD countries
Journal	Health Economics, policy and law
Research question	To investigate the determinants of the prices of branded prescription medicines across different regulatory settings and health care systems, taking into account their launch date, patent status, market dynamics and the regulatory context by which they diffuse.
Country/Countries included	15 OECD countries (USA, Japan, France, Germany, Italy, Spain, UK, Australia, Mexico, Austria, Portugal, Sweden, Greece, Slovakia, Belgium)
Reference year(s)	2004 and 2007
Products	50 leading originator branded prescription-only products (off-patent/on-patent)
At what price level	Ex-factory prices in EUR (For price comparisons, prices were analysed in prices per DDD)
Methodology	With the collected prices the authors built an econometric model and applied panel data analysis; explaining variables were (1) the number of years since the product's launch in a local market plus its square (2) if generics are available (3) country dummies for UK, USA and MEX (4) exchange rate movements (5) dummy variables for HTAs, IRP and ERP and (6) therapeutic class
Results	<ul style="list-style-type: none"> ▪ Newer classes of prescription medicines are more expensive ▪ The influence of generics is not significant ▪ Country variables are all positive and significant
Limitations	<ul style="list-style-type: none"> ▪ No available data on advertising, for example in the form of expenditure in detailing, to test its impact on prices, although a recent systematic review has shown that advertising influences prescribed volume The inclusion of the US dummy captures any unexplained heterogeneity surrounding direct to consumer advertising as this is the only country in the sample where it is allowed. ▪ Disregard of in-patient sector: it may be the case that outliers may exist in terms of products that are sold in in-patient settings, which are highly specialised. ▪ It is not possible to account for any hidden rebates given from manufacturer to health insurers
Sponsors	None
Conclusions of the study	Ex-factory prices for branded originator prescription medicines between United states and other countries, particularly key European markets, are significant, but these are not the prices that health insurers pay. By contrast, public price differences have been exaggerated and are not as high as originally thought. Differences between USA and Europe are greatest for off-patent originator brands and significantly lower for in-patent originator brands. Product age has a significant effect on originator brand prices in all settings. Price convergence is observed across countries for never compared with older originator brands and could be partly attributed to the extensive use of external price referencing.
Comments (own)	<ul style="list-style-type: none"> ▪ Price comparisons have been conducted at ex-factory price level and pharmacy retail price level, but they did not discuss the comparability of pharmacy retail prices ▪ The inclusions of age square implies an U-shaped relationship probably related to the 'generic paradox' it could have been interesting to calculate at which age the vertex is; ▪ All country dummies for the other countries should have included and then tested if they could have been omitted

Source: Kanavos PG and Vandoros S [11]

Author(s)	VOGLER, Sabine; KILPATRICK, Kate; BABAR, Zaheer-Ud-Din
Title	Analysis of Medicine prices in New Zealand and 16 European Countries
Journal	Value in Health
Research question	To compare prices of medicines, both originators and generics, in New Zealand and 16 European countries
Country/Countries included	New Zealand, Austria, Belgium, Denmark, Germany, Greece, Finland, France, Italy, Ireland, Netherlands, Norway, Portugal, Spain, Sweden, Switzerland, UK
Reference year(s)	June 2012
Products	14 medicines according to (1) equal balance of medicines of different indications (2) different price segments (3) different patent expiry status and (4) different reimbursement status (On-Patent/Off-Patent medicines in In-patient/Out-patient sector)
At what price level	Ex-Factory prices in EUR (For price comparisons, prices were analysed in prices per Unit)
Methodology	After collecting price data on prices per Unit they were order and the range between highest and lowest price was divided into quartiles. Then the remaining prices of the other countries where assigned to each quintile
Results	<ul style="list-style-type: none"> ▪ High variation in medicine prices; for most of the selected medicines, the price of the product in the highest price country was at least twice the price of the medicine in the country with the lowest price. For a few medicines, particularly generics, cross-country price differences amounted up to 1,000% ▪ Among European countries, Greece and Portugal, and also but to a lesser extent Spain United Kingdom, and The Netherlands frequently ranked in the lowest quartile, and have displayed the lowest price in some cases. Countries ranking at the higher end were Switzerland, Germany, Denmark and Sweden.
Limitations	<ul style="list-style-type: none"> ▪ The study is based on single medicines, and therefore the findings can only provide an indication for the price level of medicines in a country ▪ The basket of medicines is not very large but includes a range of medicines addressing different indications. The rather small size of the basket resulted from limited data availability and comparability between European countries and New Zealand, ▪ The price survey is based on official list prices. Due to discounts and rebates in different forms granted by the industry to public payers, the actual prices are likely to be different (i.e. lower). Because these discounts and rebates are mostly confidential and not disclosed, they were not included in the price data
Sponsors	None
Conclusions of the report	Medicine prices varied considerably between European countries and New Zealand. Within the European countries, Greece, Portugal, the United Kingdom and Spain had prices at the lower end, whereas prices in Switzerland, Germany, Denmark, and Sweden were at the upper end. These difference are likely attributable to underlying national pricing and reimbursement policies, which are affected by public health and industry-related policy goals as well as by the economic situation of the country. The study confirmed that countries that were strongly hit by the global financial crisis took several cost-containment measures related to medicine prices such as price cuts.
Comments (own)	<ul style="list-style-type: none"> ▪ Description how the quartiles are constructed is missing ▪ The article provides a good overview about differences in price levels in the examined countries, However, analysis of influences on these differentials is rather descriptive than quantitative (underpinned by an econometric analysis)

Source: Vogler S, Kilpatrick K and Babar ZUD [10]

Author(s)	DANZON, Patricia; FURUKAWA, Michael
Title	Prices and Availability of Pharmaceuticals: Evidence from Nine Countries
Journal	Health Affairs
Research question	To provide a more representative comparison of medicine prices and to examine how relative medicine prices have changed
Country/Countries included	USA, Canada, Chile, France, Germany, Italy, Japan, Mexico, UK
Reference year(s)	1999
Products	249 molecules; selected on leading active ingredients by US unit (dose) sales volume (On-Patent medicines, Off-Patent medicines/Generics, OTCs)
At what price level	(net) Ex-Factory prices in EUR (For price comparisons, prices were analysed in prices per IMS Standard Units) ¹³
Methodology	For each active ingredient a price is calculated through a volume-weighted average price per dose over all presentations in that molecule-indication in that country.
Results	<ul style="list-style-type: none"> ▪ Adjustment for off-invoice discounts reduces US prices by roughly 8 percent overall; the discount adjustment differs slightly across countries depending on the product mix ▪ Prices in Japan are highest followed by US Prices. in Canada prices are the lowest; ▪ When comparisons are restricted to identical presentations this yields upwards-biased estimates of US prices.
Limitations	<ul style="list-style-type: none"> ▪ The data show use of the sample compounds only, not differences in total per capita medicine consumption ▪ The sample selection focused on leading US products and products recently launched in the US, and therefore could appear biased toward launches in the US ▪ The comparison of total units obscures differences in formulations, which are discussed elsewhere
Sponsors	None
Conclusions of the study	<p>When Adjusting for US manufacturer discounts, Japan's prices are higher than US prices. Exchange rate fluctuations contribute to the finding of lower Canadian prices and higher UK prices in 1999 than in 1992. The findings suggest that US-foreign price differentials are roughly in line with income and smaller for medicines than for other medical services.</p> <p>The tendency for US policy-makers to compare US prices to Mexican prices and the threat of importation plausibly makes manufacturers reluctant to offer prices in Mexico that are more in line with that country's average per capita income;</p> <p>The relatively unregulated, more competitive market structure of the US market seems to result in relatively high prices for on-patent originator products and relatively high use of new products, but also strong generic competition, high generic shares and low generic prices.</p>
Comments (own)	<ul style="list-style-type: none"> ▪ The studies aims to make a price comparison between countries at discounted/net prices, but the size of the discounts base on an estimation; For all countries the same discount rate is assumed → sensitivity analysis would have been necessary. ▪ IMS Standard Units do not take into account if the same pharmaceutical form (i.e. tablet) has the same strength; Price per ATC/DDD would have been better

Source: Danzon PM and Furukawa MF [18]

¹³ https://www.imshealth.com/deployedfiles/imshealth/Global/Content/StaticFile/IMS_Therapy_Prognosis_Sample_Report.pdf

Author(s)	DANZON, Patricia; FURUKAWA, Michael
Title	International Prices and Availability of Pharmaceuticals in 2005
Journal	Health Affairs
Research question	To compare pharmaceutical spending, availability, use and prices of pharmaceuticals in 12 countries
Country/Countries included	USA, Canada, France, Germany, Italy, Spain, UK, Japan, Australia, Brazil, Chile, Mexico
Reference year(s)	2005
Products	All prescription medicines and Over-the-counter (OTC) of single-molecule products in the out-patient sector
At what price level	Ex-factory prices & Pharmacy (gross) retail prices
Methodology	Two price indexes were constructed: (1) an index that compared prices for all products that match on active ingredient and indication, regardless of formulation, strength, brand or prescription status (2) an index that compared prices only for products that match on molecule, indication, strength and formulation; All price indexes are weighted by US volume weights and converted into US dollars.
Results	<ul style="list-style-type: none"> ▪ Index (1) showed that most countries' prices are 20-40 percent lower than US prices. Index (2) is similar, generally differing less than five percentage points; Mexican ▪ Foreign public prices are only 10-30 percent lower than the US prices, compared to 20-40 percent lower for foreign manufacturer prices. Distribution margins absorb a larger share of total pharmaceutical spending in several regulated markets. ▪ Comparisons using PPPs rather than exchange rates, because with exchange rates medicine prices are probably biased downwards poorer countries ▪ Manufacturer's prices should be normalised by average income (GDP per capita) as a rough measure for affordability
Limitations	Authors did not report explicitly limitations.
Sponsors	None
Conclusions of the study	<p>Price comparisons with USA are biased upward, because it ignores the US tendency to use more new, expensive products.</p> <p>The higher overall per capita volume in other countries compared to the US is solely attributable to the use of older products</p> <p>The foreign U.S. medicine price differential is smaller at public prices, than at manufacturer prices, because distribution margins are generally higher abroad</p> <p>Price differentials remain roughly in line with differences in per capita income. This suggest that greater affordability of medicines in these countries will require review of their regulatory structure and lack of price competition among generics, in addition to strategies to prevent any concern of originator manufacturers over US price referencing of medicine importation that may contribute to higher prices.</p>
Comments (own)	<ul style="list-style-type: none"> ▪ Exclusion of combination medicines disregards medicines with a considerable proportion of sales (e.g. Eviplera, Altriplera, Harvoni, Symbicort, Truvada) ▪ The authors analysed ex-factory prices and pharmacy retail price with VAT but they did not discuss the comparability of the latter price level in other countries (e.g. UK).

Source: Danzon PM and Furukawa MF [19]

13 Annex 13: Legal analysis – Detailed results

The following legal analysis aims at investigating whether and which legal constraints exist in EU law that would prevent the introduction of a EU-wide coordinated Differential Pricing (DP) scheme and whether or which legal changes would be necessary in order to allow such a EU-wide policy.

Whereas there is usually free pricing for medicines not funded by public payer, pricing of medicines eligible for reimbursement are usually regulated by national competent authorities. In reality, different income levels of member states (MS), national policies for pricing and value assessment, varying national approaches to regulating wholesale and retail distribution as well as different taxation of pharmaceuticals influence a pharmaceutical companies' pricing strategies¹⁴.

Pricing policies and laws for the marketing of medicines lie in the national **competence of the 28 EU Member States (MS)** and MS have implemented different pricing strategies and systems. The EU does not have the power to define common market pricing mechanisms, and so pricing is a national issue between national competent authorities.

In this whole process, the **bargaining powers which MS have towards industry differ to a high extent**, partially leading to different result that include, e.g. **volume controls, indirect price, profit controls** and recently Managed Entry Agreements (MEA).¹⁵ As Hervey & McHale (2004) state, the reasons for one or the other approach depend more or less on the necessity of a MS to support its pharmaceutical industry.¹⁶ Similar, the Advocate General argued in his opinion in *GlaxoSmithKline (GSK II)*¹⁷: *'the level at which the selling price or the amount of reimbursement of a given medicinal product is fixed reflects the relative strength of both, the public authorities of the rele-*

¹⁴ For an overview see Directorate-General for Internal Policies (2011), Report requested by the European Parliament's Committee on Environment, Public Health and Food Safety, Executive Summary: Differences in Costs and Access to Pharmaceutical Products in the EU, available at europarl.europa.eu/document/activities/cont/201201/20120130ATT36575/20120130ATT36575EN.pdf (accessed: 3.4.2015): Table 1 at p. 37: Pharmaceutical regulation in Europe (overview) and Impact of MS regulation on differences in pharmaceutical prices and access to medicine, key findings at p. 32.

¹⁵ In its 2008 Communication, the Commission stated in this context, that *'[...]stakeholders continue to raise concerns with regard to the market fragmentation linked to disparities in national pricing and reimbursement schemes, unnecessary regulatory burdens caused by divergences in the implementation of Community legislation, and a lack of commercial interest in national markets which are economically less attractive.'*, Communication to the European Parliament, the Council, the European Economic and Social Committee and the Committee of the Regions regarding Safe, Innovative and Accessible Medicines, towards a Renewed Vision for the Pharmaceutical Sector, COM(2008) 666 final, 10.12.2008, p. 5.

¹⁶ Hervey & McHale (2004), at 321: *'Where a state is concerned also to support its internal pharmaceutical industry, and to promote its research and development and export capacity, the former two methods [remark: profit controls laid down by administrative action or as a result of negotiations between the national government and the pharmaceutical industry] are favoured (for instance, Germany, UK). Where there is less of a concern for the home grown pharmaceutical sector, stricter profit or price controls are more likely to be used (for instance, Belgium, Spain, Portugal, Greece). This division goes some way to explaining the division between 'high price' Member States such as Germany, and 'lower price' Member States such as Belgium.'* For examples of price differences see Directorate-General for Internal Policies (2011), pp. 23 ff.

¹⁷ Joined Cases C-468/06 to C-478/06, *Sot. Léos Kai Sia EE (and Others) v. GlaxoSmithKline AVEE* [2008] ECR I-7137, point 63.

vant Member State and the pharmaceutical companies at the time of the price negotiations for that product.' Recent studies show that **current pricing policies of MS do not lead to relatively lower prices for countries with lower GDP per capita.**¹⁸

When it comes to regulation of **competition and competition policy**, there would thus be many reasons for differentiating the pharmaceutical sector from other markets since health, including medicines, is public good. But even though pricing mechanisms depend to a high extent on MS' pricing and reimbursement policies and in fact there does not exist a regular market for pharmaceuticals¹⁹, the pharmaceutical market has to respect EU rules resulting from the **four freedoms**, including free movement of goods and the pharmaceutical market is – to a certain extent – subject to subsequent **EU competition rules**. Especially in the field of generics and non-prescription medicines, the Commission relies on competition rules for a functioning market. But also the prescription pharmaceutical market, mostly under universal coverage of MS health systems, is subject to free market rules. One of the consequences of this fundamental Treaty principle of free movement of goods and Commission competition policy is the advancement of parallel trade. Albeit the European Court of Justice (ECJ) in the meantime slightly starts to demand a policy change in this context.²⁰

This leads to a rather complicated system with **market influencing factors** resulting from market and competition rules **at EU level** and in the (legislative) power of the EU on the one hand and different **pricing policies in the power of Member States** on the other hand.

In this context it is also important to keep in mind that the EU's pharmaceutical sector policy is in line with its internal market policy and therefore the Commission strongly monitors its **policy impact on pharmaceutical investments and R&D developments**. The Commission already is highly alerted since pharmaceutical R&D activities declined in the EU in comparison to US activities, leading to the question of whether different pricing policies lead to budgetary shortfalls in the pharmaceutical industry and to reduced R&D investments in Europe.²¹

13.1 Division of powers (EU – MS) and the healthcare sector

From a legal perspective, limitations in EU law that can prevent the implementation of a DP scheme coordinated among EU Member States would have its origin in the impact of fundamental Treaty principles (i.e. free movement of goods and its impact: parallel

¹⁸ Carone G, Schwierz C, Xavier A, Cost-containment policies in public pharmaceutical spending in the EU, Economic Papers 461, September 2012, Graph 1, p. 16, available at http://ec.europa.eu/economy_finance/publications/economic_paper/2012/pdf/ecp_461_en.pdf

¹⁹ See e.g. Schulz-Weidner W, Felix F, Die Bedeutung des europäischen Wettbewerbsrechtes für die österreichische Sozialversicherung (Teil I), *SozSi* 2001, 435, at doc view print p. 20: '*Schließlich sprechen aus ökonomischer Sicht ernsthafte Erwägungen für die Annahme, dass durch ein koordiniertes Vorgehen die Voraussetzungen für einen effektiven Wettbewerb überhaupt erst geschaffen werden. Wettbewerb setzt auf der Nachfrageseite voraus, dass der Akteur äußerstenfalls auf das gewünschte Gut verzichten kann, wenn dieser Verzicht auch mit wirtschaftlichen Risiken verbunden sein mag. Mit anderen Worten: 'Risiko' bedingt wenigstens die rechtliche Freiheit, auf ein bestimmtes Produkt verzichten zu können. Im Bereich medizinischer Versorgung ist ein solcher Verzicht seitens der Kassen wegen des Sachleistungsprinzips und des gesetzlichen Sicherstellungsauftrags jedoch schon aus Rechtsgründen nicht möglich, ganz abgesehen davon, dass er im Interesse der Pflichtversicherten auch aus sozialpolitischen Gründen nicht akzeptabel wäre.*'

²⁰ See Legal Analysis, Chapter on Parallel Trade (intra-brand competition).

²¹ See COM(2008) 666 final, supra note 14.

trade) and in areas or categories of missing or non-existing **EU competence**. The following legal analysis therefore first illustrates fundamental principles in this context before specifically analysing limitations on the one hand and areas of competence or possibilities of shaping pharmaceutical pricing policies at EU level on the other hand.

According to Art. 3a 1. Treaty on the European Union (**TEU**)²², the EU can only perform legislative power within the limits of the competences explicitly conferred to the EU (**principle of conferred powers**): '*[C]ompetences not conferred upon the Union in the Treaties remain with the Member States*'. As stated for instance by the German constitutional court, this principle is not only implemented in EU law, but also in German constitutional law, since the European Union is a Union of 28 sovereign states.²³

Further relevant principles defining EU's legislative powers are the principle of subsidiarity and proportionality. According to the **principle of subsidiarity**, '*the Union shall act only in so far as the objectives of the proposed action cannot be sufficiently achieved by the Member States, either at central level or at regional and local level, but can rather, by reason of the scale or effects of the proposed action, be better achieved at Union level*' (**Art. 5 3. TEU**). According to the **principle of proportionality**, '*the content and form of Union action shall not exceed what is necessary to achieve the objectives of the Treaties*'. (**Art. 5.4. TEU**).

As stated by the Protocol (No. 2) on the Application of the principles of subsidiarity and proportionality²⁴ this means that each institution, respectively the **European Commission, is advised to find 'qualitative and, wherever possible, quantitative indicators' to conclude that a specific objective can be better achieved at Union level. Draft legislative acts take account of the need for any burden, whether financial or administrative, falling upon the Union, national governments, regional or local authorities, economic operators and citizens, to be minimised and commensurate with the objective achieved**' (Art. 5). Besides and in order to implement a process to supervise compliance with these principles, the protocol defines that EU institutions shall forward draft legislative acts to national parliaments (Art. 4). The protocol further defines this process and states that '*[w]here reasoned opinions on a draft legislative act's non-compliance with the principle of subsidiarity represent at least one third of all the votes allocated to the national Parliaments [...] the draft must be reviewed.*' After review, the respective EU institution may then '*decide to maintain, amend or withdraw the draft, [whereby] [r]easons must be given for this decision.*' (Art. 7.2).

²² Consolidated Version of The Treaty on European Union (TEU), OJ C155/13, 9.5.2008.

²³ Lock T, Comments on the German Constitutional Court's Decision on the Lisbon Treaty, Why the European Union is Not a State, Some Critical Remarks, *European Constitutional Law Review*, 5: 407-420, 2009, referring to BVerfGE 89, 155, 12 October 1993 (187-188), at p. 410.

²⁴ Consolidated versions of the Treaty on European Union and the Treaty on the Functioning of the European Union - Consolidated version of the Treaty on the Functioning of the European Union - Protocols - Annexes - Declarations annexed to the Final Act of the Intergovernmental Conference which adopted the Treaty of Lisbon, signed on 13 December 2007, OJ C 326 , 26/10/2012 P. 0001 – 0390.

The Treaty on the Functioning of the European Union (TFEU)²⁵ defines three different categories and areas of EU competence (Art. 2-6):

- exclusive EU competence (Art. 3)
- EU competence shared with MS (Art. 4)
- EU competence to carry out actions to support, coordinate or supplement the actions of MS (Art. 6).

In the area of **exclusive EU competence**, the **EU can set binding law** and MS are only allowed to set binding law, if the EU explicitly empowers or obliges them to do so. Among other categories, the EU regulates and sets the **rules for competition** within the EU as well as rules ensuring the European customs union.

Pharmaceutical products (medicines) are products in the sense of Art. 28 ff TFEU. Thus, in the healthcare sector, respectively the pharmaceutical market, the EU has the power to influence and set binding law relating to rules for competition.

Shared EU competence means that MS are still allowed to set binding laws, if the EU declined to regulate, did not regulate at all or did only in part regulate a specific task. Among the main areas of shared competence, the most relevant one in the context of pharmaceutical policy is the **internal market** and its principle of free movement of goods (Art. 28 to 37 TFEU). According to Art. 34 and 35 TFEU, quantitative restrictions between MS are prohibited (i.e. restrictions on imports or exports and all measures having equivalent effects). Nevertheless, such restrictions or prohibitions can be justified on the ground of protecting health and life of humans (Art. 36 TFEU). Besides, **social policy, consumer protection and common safety concerns in the field of public health** are of relevance.

In the field of **supporting, coordinating or supplemental actions**, the EU is not allowed to take actions to harmonise the laws of the MS. Above other categories, the **protection and improvement of public health** as well as the coordination of social policies of MS falls within this area.

Besides, in Art. 9 TFEU, it is stated that the EU '*in defining and implementing its policies and activities [...] shall take into account [...] a **high level of [...] protection of human health.***'

Even though the EU in some specific fields of public health related to common safety concerns may introduce a common standard by harmonising laws of MS (**Art. 168 (4) TFEU** in accordance with Art. 4 TFEU – shared competence), **Art. 168 (7) TFEU** explicitly states that '*Union action shall respect the responsibilities of the Member States for the definition of their health policy and for the organisation and delivery of health services and medical care. The responsibilities of the MS shall include the management of health services and medical care and the allocation of the resources assigned to them.*'

Anyhow, even besides internal market or competition rules, MS seem to more and more support increasing efforts at EU level for more coordination in the field of social and health policy, especially on the '**demand side**'²⁶, in the light of **consumer or patient**

²⁵ Consolidated Version of The Treaty on the Functioning of the European Union (TFEU), OJ C326/47, 26.10.2012.

²⁶ As supposed to the 'supply side' – see Sauter W, The impact of EU competition law on national healthcare systems, *TILEC Discussion Paper*; Vol. 2012-032. TILEC, available at pure.uvt.nl/portal/files/1457810/2012_032.pdf (2.4.2015), at

rights. Even though experience shows that negotiations in these fields prove to be highly demanding²⁷ and Commission policy initiatives or even Council initiatives are sometimes (temporarily) rejected by MS, claiming their sovereign rights.

When it comes to health policy, access to healthcare services and consumer or patient rights it is important to understand and stress the **influence of the European Court of Justice (ECJ)** in this context: by increasingly strengthening **patient rights in cross border health care** in the past years (finally leading to Directive 2011/24/EU on the application of patients' rights in cross-border healthcare²⁸), the Court gradually drove MS towards closer cooperation and coordination in this field. Most recently, the ECJ seems to adjust its opinion towards parallel trade by acknowledging its adverse impacts on patients.²⁹

13.2 Primary EU law (internal market), including competition law, interfering with the pharmaceutical (pricing) market

In order to achieve a high level of human health and patient safety with regard to pharmaceuticals, the EU basically strives to promote a **safe and functioning pharmaceutical market** through an innovative and competitive industry.

To achieve a high level of patient **safety**, the EU introduced a **common system of market authorization, supervision and pharmacovigilance**. Through this system common principles for prior testing, supervision and assessing efficacy of new medicines have been implemented. Companies have two possibilities to obtain marked authorization for new medicines: either through (a) a **centralised application** to the European Medicines Agency (EMA)³⁰ or (b) a **decentralised application** covering only one MS with the option of recognition by other MS through the mutual recognition procedure³¹. Use of the centralised procedure is mandatory for *'biotechnology medicines, products containing [new chemical entities] (NCEs), for the treatment of certain disorders and diseases, and is optional for other NCEs and sufficiently innovative products.'*³²

A **functioning pharmaceutical market** aims at providing sufficient supply and affordable prices of pharmaceuticals. To achieve this goal, the EU engages in market and

p.4: *'When interpreting these developments [remark: meaning application of internal market freedoms to healthcare], it is useful to distinguish between demand (services) and supply (establishment) factors.'*

²⁷ E.g. Van de Gronden J, Szyszczak E, Introducing Competition Principles into Health Care through EU Law and Policy: a Case Study of the Netherlands, *Medical Law Review*, 2014, Vol. 22, No. 2, pp. 238-254, at p. 240: *'The Member States' reluctance to allow EU regulation of health care services is seen in the removal of health care from the Services Directive and the tortuous negotiation of the Patients' Rights Directive in 2011.'*

²⁸ Directive 2011/24/EU of the European Parliament and of the Council of 9 March 2011 on the application of patients' rights in cross-border healthcare, OJ L 88/45, 4.4.2011.

²⁹ See Legal Analysis, Chapter on Parallel Trade (intra-brand competition).

³⁰ Introduced through Regulation (EC) No 726/2004 of the European Parliament and the Council of 31 March 2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency, OJ L 136/1 30.4.2004 .

³¹ Directive 2001/83/EC, as revised through Directive 2004/27/EC of the European Parliament and of the Council of 31 March 2004 (amending Directive 2001/83/EC on the Community code relating to medicinal products for human use), OJ L 136/34, 30.4.2004.

³² Hancher L, The EU pharmaceuticals market: parameters and pathways, in Mossialos E, Permanand G, Beaten R and Hervey T (Eds.), *Health Systems Governance in Europe, The Role of European Union Law and Policy*, European Observatory on Health Systems and Policy, Cambridge University Press, New York (2010), pp. 635-682, at p. 646.

competition policy. By pursuing and promoting an innovative and competitive pharmaceutical industry, consumers and patients shall have access to sufficient and high quality pharmaceuticals.

Normally, a functioning and effective competition is the result of free market price building mechanisms and policies. However, in the field of pharmaceuticals where prices are regulated by each MS, it seems that a functioning competition may only result from **better regulated and coordinated pricing policies**. The power to set binding laws in this field lies with the MS. However, through '**positive**' or '**negative**' **harmonisation efforts**³³ in this area, drawn from primary law in the field of free movement of goods, services and rules on approximation of MS laws as well as competition law, the **EU shapes pricing policies of MS**.

In this context it is important to understand, that EU integrated market and competition law – according to the **principle of primacy of EU law** – takes precedence over national laws of MS, even if these laws systematically have its origin in the social policy area.³⁴ Moreover, competition law has been 'decentralised', meaning that national competition authorities can apply EU antitrust rules to national competition cases with EU dimension.³⁵ Some recent steps taken by national governments after the financial crisis even indicate that '*the interface between competition policy and the healthcare sector is becoming more important.*'³⁶

Internal market law (Art. 28 ff TFEU) generally applies to the pharmaceutical market and trade between MS, prohibiting MS '*quantitative restrictions on imports and exports and all measures having equivalent effect*' (**Art. 34 and 35 TFEU**).³⁷ However, in line with **Art. 36 TFEU**, justifying such restrictions on grounds of health and life protection, the ECJ has given MS some discretion in its rulings, if harmonised law on EU level is missing and in so far as measures by MS are **proportional** and **necessary** to attain the **goal of health and life protection** (e.g.: Case C-400/96 *Harpegnies* [1998] ECR I-5121) or **social security policy** (e.g. the equilibrium of social security systems: Case C-120/95 *Decker* [1998] ECR I-1872 at margin. 39: '*...* it cannot be excluded that the

³³ 'Positive' harmonisation efforts mean regulations and directives, whereas 'negative' harmonisation efforts are efforts finally leading to an adoption of MS laws since laws of MS do not comply e.g. with the principle of free movement of goods or EU competition rules. See also Van de Gronden J, Szyzszak E (2014), supra note 26, at p. 239: '*In the absence of EU legislative competence and the political will on the part of the Member States to regulate health care at the EU level, EU competition law now 'forms a default regulatory framework for the sector'*'.

³⁴ See Hervey T, EU law and national health policies: problem or opportunity, *Health Economics, Policy and Law* (2007), 2: 1-6: at p. 3: '*The free movement and competition rules take precedence over conflicting national rules, of any type, even over conflicting subsequent legislation adopted by national parliaments. [...] This applies even if the aim of the national rules at issue is something other than trade or competition, for instance the protection of social welfare or public health.*' and ECJ case law: *Costa/ENEL* (Case C-6/64 [1964] ECJ 588), *Simmenthal II* (Case C-106/77 [1978] ECR 631), *Internationale Handelsgesellschaft* (Case C-11/70 [1970] ECR 1126).

³⁵ Prosser T, EU competition law and public services, in Mossialos E, Permanand G, Beaten R and Hervey T (Eds.), *Health Systems Governance in Europe, The Role of European Union Law and Policy*, European Observatory on Health Systems and Policy, Cambridge University Press, New York (2010), pp. 315-336 or Sauter W (2012), supra note 25, at p.6, referring to Council Regulation (EC) No 1/2003 of 16 December 2002 on the implementation of the rules of competition laid down in Articles 81 and 82 of the Treaty [now: Art. 101 and 102 TFEU], OJ 2003 L 1/1: '*At national level competition laws in all Member States have converged with EU competition law.*'

³⁶ See Sauter W (2012), supra note 25, referring to developments in Ireland, UK, Bulgaria and the Netherlands at p. 3.

³⁷ E.g.: *Merck & Co. Inc, Primecrown Ltd.*, ao, joined Cases C-267/95 and C-268/95, [1996], I-6371, at margin. 47: '*As to that, although the imposition of price controls is indeed a factor which may, in certain conditions, distort competition between Member States, that circumstance cannot justify a derogation from the principle of free movement of goods.*'

risk of seriously undermining financial balance of the social security system may constitute an overriding reason in the general interest capable of justifying a barrier of that kind [remark: a barrier to the fundamental principle of the free movement of goods] in line with Art. 36 TFEU. This so called '**Social Solidarity Exemption**' is based on the ECJ *Duphar* case, in which the Court stated: '*it must be recognised that Community law does not detract from the powers of Member States to organise their social security systems and to adopt, in particular, provisions intended to govern the consumption of pharmaceutical preparations in order to promote the financial stability of their health-care insurance schemes*'.³⁸

The TFEU sets **rules for undertakings on competition in Art. 101 ff** and its subsequent secondary legislation. Competition rules **aim at equal rank** at providing **efficient competition and market structures** as well as **consumer welfare**.³⁹

The rules are applicable for both, **public and private health care services**. Since *Höfner, Elser*⁴⁰ it is clear that EU competition rules are also applicable to the public sector and public sector agencies are **undertakings** in the sense of EU competition rules when engaging in economic activities.⁴¹ However, for **bodies managing health care schemes**, a far more differentiated view has been taken by the ECJ in *AOK*⁴², stating that '*sickness funds fulfil a function, which is exclusively social and entirely non-profit making, [...] [its] operation is founded on a principle of solidarity [...] [and] the state exercises control over the activity.*' Therefore, the court concludes that they '*do not act as undertakings engaging in economic activity*'. In *AG2R*⁴³ the ECJ then made clear that these requirements (**social, non-profit making function, operation founded on the principle of solidarity and state control**) **all** have to be satisfied in order **not to fall** under **EU competition rules** relevant for undertakings. In this field, as Leigh Hancker states, EU institutions have to ' *[...] strike a balance between the objectives of stimulating innovation while securing affordable access through regulation ex ante [...]* '.⁴⁴

³⁸ Case C-238/82 *Duphar* [1984] ECR 523, margin. 16; see also: Sauter W, supra note 25 summarises at p. 5: '*In sum although there is now a strong precedent for EU involvement in the internal market dimension of healthcare the actual effects of the four freedoms have so far been limited. This is the case especially on the supply side, although where constraints are involved they must be justified and rational, regardless of the absence of a common terms.*'

³⁹ Sauter W (2012), supra note 25, referring to *GSK II* (supra note 16), at p. 9: '*Here it overruled the General Court which had claimed that the consumer interest was indeed the highest value of competition law. The ECJ however clarified that market structure and the position of competitors were objectives of equal rank [...]* '.

⁴⁰ Case C-41/90 *Höfner, Elser* [1991] ECR I-2010, see also *Pavlov*: joined Cases C-180/98 to C-184/98 [2000] ECR I-6497.

⁴¹ See ECJ in *Höfner, Elser*, supra note 39, at point 21: '*It must be observed, in the context of competition law, first that the concept of an undertaking encompasses every entity engaged in an economic activity, regardless of the legal status of the entity and the way in which it is financed and, secondly, that employment procurement is an economic activity.*'

⁴² *AOK Bundesverband et al*, joined Cases C-264/01, C-306/01, C-354/01 and C-355/01 [2004] ECR I-2524, points: 35-37 and 64. See also *Poucet and Pistre*, joined Cases C-159/91 and 160/91 [1993] ECR I-637, *FENIN*, Case C-205/03 [2006] ECR I-6295 and *José Garcia and Others*, Case C-238/94 [1996] ECR I-1679 at point 14: '*Finally, as the Court stressed in Joined Cases C-159/91 and C-160/91 Poucet and Pistre v Assurances Générales de France and Others [1993] ECR I-637, paragraph 13, social security schemes such as those in issue in the main proceedings, which are based on the principle of solidarity, require compulsory contributions in order to ensure that the principle of solidarity is applied and that their financial equilibrium is maintained. If Article 2(2) of Directive 92/49/EEC were to be interpreted in the manner contemplated by the national tribunal, the obligation to contribute would be removed and the schemes in question would thus be unable to survive. The Court has also pointed out that Member States retain their powers to organise their social security systems (see Poucet and Pistre, paragraph 6, and Case 238/82 Duphar v Netherlands [1984] ECR 523, paragraph 16).*'

⁴³ *AG2R Prévoyance v Beaudout Père et Fils SARL.*, Case C-437/09 [2011] ECR I-1003.

⁴⁴ Hancker L (2010), supra note 31, at p. 655.

The rationale behind these judgments has been expressed by the Advocate General in the *FENIN* case⁴⁵: *'The **power of the State**, which is exercised in the political sphere, is **subject to democratic control**. A **different control** is imposed on **economic operators** acting on a market: their conduct is governed by competition law. But there is no justification when the State is acting as an economic operator, for relieving its actions of all control.'*⁴⁶

If the public or private player at hand is classified as undertaking, EU competition rules apply, irrespective of the fact that States might interfere through price setting or reimbursement policies.⁴⁷ According to these rules, relevant for undertakings, the following activities are **not allowed** since interference with the internal market results:

- agreements, which may affect trade between MS (Art. 101 TFEU – **prohibition of cartels**)
- any abuse of dominant position (Art. 102 TFEU – **abuse of dominant position** by a monopolist)
- mergers prohibiting free competition (**merger control**).

According to Art. 101 (3) TFEU agreements, which may affect trade between MS might basically be justified, if contributing to improving the production or distribution of goods or promoting technical or economic progress while allowing a **fair share for consumers**.⁴⁸

In the field of competition law and **supply-side or price related practices, prohibition of cartels** and **abuse of dominant position** are the most relevant competition rules. Thus, the following competition law analysis will focus on these two practices and its application by the Commission and the Courts.

Before analysing relevant ECJ case law in the field of market freedom and competition law in the pharmaceutical sector, it is important to distinguish the following two **relevant product markets**. For **inter-brand competition** analysis (i.e. competition between different brands, .e.g. generics markets) the relevant market is defined by pharmaceuticals, whose prescription practice is based on *'fundamentally the same medical grounds [...], for example, in terms of active principle, tolerance, toxicity, and side effects.'*⁴⁹ For **intra-brand competition** (i.e. competition in relation to the same pharmaceutical product or also called **parallel trade**), the relevant product market are *'all medicines which are capable of being subject to parallel trade in a given Member State'*.⁵⁰

⁴⁵ Case C-205/03, *FENIN* [2006] ECR I-6295.

⁴⁶ Prosser T (2010), supra note 34, at p. 324.

⁴⁷ *Merck and Beacham*, joined cases C-267/95 and C-268/95 [1996] ECR I-6371, p. C-6389, point 47: *'As to that, although the imposition of price controls is indeed a factor which may, in certain conditions, distort competition between Member States, that circumstance cannot justify a derogation from the principle of free movement of goods.'*

⁴⁸ See e.g. *GSK II*, supra note 16.

⁴⁹ Liberatore F, Restrictions on Parallel Trade of Pharmaceutical Products and EU Competition Law, Chapter 17 in Cortese B (Ed.), *EU Competition Law. Between Public and Private Enforcement*, Kluwer Law International BV, The Netherlands (2014), pp. 347-356, available at: www.jonesday.com/files/Publication/5a2fa4ac-8fcb-4fdd-ab38-02d252fcb01d/Presentation/PublicationAttachment/e89a2072-71df-4197-bfff-0254e30b42d8/Restrictions%20on%20Parallel%20Trade%20-%20Francesco%20Liberatore.pdf (accessed: 3 April 2015), at p. 350-351, referring to 97/469/EC: Commission Decision of 17 July 1996 in a proceeding pursuant to Council Regulation (EEC) No. 4064/89 (Case No IV/M.737- Ciba-Geigy/Sandoz), 21.

⁵⁰ Liberatore F (2014), supra note 48, at p. 351, referring to Case T-168/01, *GSK*, 159.

There are a number of cases, both at EU and national level, declaring price fixing strategies or the coordination of market shares as being anti-competitive and thus prohibited.⁵¹

However, since on the one hand the above mentioned diversities in MS's pricing approaches exist, and on the other hand EU market rules (free movement of goods) demand for free movement of pharmaceuticals, the phenomenon of **intra-brand competition** (and **parallel trade**) is a highly relevant one for the European market. Thus, the following analysis will focus on this phenomenon and its handling under EU competition law.

13.3 Parallel trade (intra-brand competition)

Parallel trade arises when (parallel) traders, e.g. wholesalers, purchase a specific brand of a pharmaceutical product in one MS in order to sell this brand or product at a higher price in another MS. Thus, parallel trade occurs, if a genuine product originally sold under patent (copyright/trademark) protection is traded (in another country) without control or permission of the original patent holder. Under intellectual property law (IP law) a patent holder has an absolute right to dispose of the patented product. However, due to the so called '**exhaustion doctrine**' this right is restricted to first distribution. After first distribution, the right of the patent holder to control further distribution and trade is exhausted. With regard to the European market, parallel trade is restricted to the European market since the EU practices the so called '**regional exhaustion doctrine**', allowing only parallel trade of goods authorised and licenced within the EU. This practice is in line with international trade and patent agreements (**TRIPS**⁵²) of World Trade Organisation (WTO) since members (especially the US and EU countries) could not agree on the implementation of an 'international exhaustion doctrine'⁵³ within the TRIPS framework.⁵⁴

⁵¹ For an enumeration and analysis of several recent cases see Lear J, Mossialos E and Karl B, EU competition law and health policy in Mossialos E, Permanand G, Beaten R and Hervey T (Eds.), Health Systems Governance in Europe, The Role of European Union Law and Policy, European Observatory on Health Systems and Policy, Cambridge University Press, New York (2010), pp. 337-378, at pp. 350 ff.

⁵² WTO (1994, entering into force January 1995), Agreement on Trade-Related Aspects of Intellectual Property Rights, Annex 1 C to the Agreement Establishing the World Trade Organization. The EU (since 1995) and its MS are all members of the World Trade Organization (WTO).

⁵³ According to the 'international exhaustion doctrine' parallel imports would be legal no matter where the product has been distributed first and the IP holder loses the right to control further distribution after the product has been put on the market by the IP holder or with his consent at any place of the world.

⁵⁴ See Article 6 (Exhaustion) TRIPS: '*For the purposes of dispute settlement under this Agreement, subject to the provisions of Articles 3 and 4 nothing in this Agreement shall be used to address the issue of the exhaustion of intellectual property rights.*' According to analytic index LXXVIII. Relating to the Text of the Declaration of the TRIPS Agreement and Public Health, this legality of national or regional exhaustion has been explicitly confirmed in the public health context 5 d, '*The effect of the provisions in the TRIPS Agreement that are relevant to the exhaustion of intellectual property rights is to leave each Member free to establish its own regime for such exhaustion without challenge, subject to the MFN and national treatment provisions of Articles 3 and 4.*' See also Rai R K, Jagannathan S, Parallel imports and unparallel laws: an examination of the exhaustion doctrine through the lens of pharmaceutical products, *Information & Communications Technology Law*, Vol. 21, No. 1, March 2012, 53-89 and Sarah R. Wasserman Rajec, Free Trade in Patented Goods: International Exhaustion for Patents, 29 *Berkeley Tech. Law Journal* (2014), available at: <http://scholarship.law.berkeley.edu/btlj/vol29/iss1/7>.

In line with fundamental Treaty principles, the **EU Commission's as well as the ECJ's** attitude towards parallel trade and intra-brand competition traditionally was a supportive one⁵⁵. According to the Commission, EU's market freedom and especially free movement of goods shall exactly enable this kind of competition.

For **pharmaceutical companies**, parallel trade and intra-brand competition means, that they possess intellectual property rights and patent protection for several years, but this does not mean exclusivity in resulting price benefits. Others (i.e. wholesalers) can also benefit from pricing advantages resulting from intellectual property right protection.

Pharmaceutical companies in reacting to the phenomenon of parallel trade (intra-brand competition) basically chose **four different strategies** to reduce parallel trade and its negative competitive effects ⁵⁶:

1. **dual pricing** (see below: GlaxoSmithKline I): 'Dual Pricing strategies seek to **reduce** the price differential between geographical markets and, as a result, the **incentive for arbitrage** in the form of parallel trade.'⁵⁷
2. **supply quota restrictions** (see below: GlaxoSmithKline II and Adalat): 'Supply quota systems come in a variety of forms, but usually they involve a **restriction of supplies to wholesalers** commensurate with the latter's requirements in the domestic market, plus a limited margin.'⁵⁸
3. **specific life cycle management** (see below: Astra Zeneca): Life cycle management practices by pharmaceutical companies are usually strategies aiming at delaying generic market entry (e.g. by using excessive procedures before national patent offices and regulatory authorities). If such strategies for instance are combined with a withdrawal of a marketing authorization, they might also be relevant in the context of parallel trade.⁵⁹

⁵⁵ See e.g. European Commission, Communication on parallel imports of proprietary medicinal products for which marketing authorisations have already been granted, COM (2003) 837 final at p. 6: '*Parallel trade is based on the principle of the free movement of goods within the Internal Market (articles 28-30 of the EC Treaty). In the pharmaceutical sector, it benefits from price divergence as Member States set or, by other means, control the price of medicinal products sold within their respective markets. The European Court of Justice has repeatedly confirmed that medicinal products are not exempted from the rules of the Internal Market and has condemned State measures which restrict, without appropriate justification, parallel imports of medicines. The Court has ruled that certain Member State measures restricting parallel imports may be justified on the grounds of protection of industrial and commercial property and the protection of human health and life, according to article 30 of the EC Treaty.*

⁵⁶ Liberatore F, supra note 48 and Gruber J, Wettbewerb in regulierten Märkten: Arzneimittel, *Österreichische Zeitschrift für Kartellrecht (ÖZK)*, 2010, 180.

⁵⁷ Hancher L (2010), supra note 31, at p. 663.

⁵⁸ Hancher L (2010), supra note 31, at p. 663.

⁵⁹ Hancher L (2010), supra note 31, at p. 655 and Liberatore F, supra note 48 at pp 355, 356: '*The Commission's Pharmaceutical Sector Inquiry Report identified a number of product life cycle management strategies that are at risk of violating EU competition law. The use of such strategies to limit parallel trade was assessed under EU competition law in the AstraZeneca case. In the AstraZeneca case, the Commission found that AstraZeneca had abused its dominant position in relation to its blockbuster medicine Losec by selectively deregistering the market authorizations for Lesoc capsules in three Member States; withdrawing Losec capsules from the market; and launching tablets in those same Member States. [...]. It follows from the General Court's reasoning that, when there is no other documented explanation for the withdrawal of a marketing authorization, this may be assumed to have the sole purpose of restricting parallel trade and is therefore abusive.*'

4. **direct distribution systems:** distribution systems without wholesalers in between; this fourth strategy in most cases means a complete and often expansive restructuring of a company's distribution system and thus is the least relevant one.

Regarding the first three strategies, the ECJ issued rulings and further defined its position towards these practices. The first three strategies as well as the ECJ rulings in reaction to these practices shall be further assessed (the structure is inspired by Liberatore F (2014)⁶⁰:

13.3.1 Dual pricing (Art. 101 TFEU) – *GlaxoSmithKline (GSK I, Spain)*⁶¹

In GSK I the Spanish subsidiary – a company without dominant position – entered into agreements with 75 different wholesalers, fixing different prices for the same products: prices were lower for wholesalers selling products exclusively in Spain (a low price country) and higher prices for wholesalers exporting and selling these same products in MS with higher price levels for pharmaceuticals. This strategy by Glaxo SmithKline's subsidiary intended to impede parallel trade.

The Courts' ruling in GSK I can be summarised as follows:

- ➔ Agreements with wholesalers in low-price countries, providing for different prices – depending on whether wholesalers will export some of the products to high-price countries – are **in principle a restriction of competition** by object⁶², and might impede free movement of goods, thus **violate EU competition law**.
- ➔ However, such **agreements might be justified** in individual cases, **if advantages for consumers outweigh its anti-competitive effects, fulfilling the requirements for an exemption under Art. 101 (3) TFEU with regard to the specific features of the pharmaceutical sector**.

According to Hancher L (2010), *'this judgment will have significant repercussions for future Commission policy. In the past, the Commission has always contended that, while it was broadly sympathetic to the claims of the research-based industry that divergent national price and profit regulations that give rise to parallel trade could threaten their capacity for innovation and their global competitiveness, its hands were tied by the jurisprudence of the Courts, which supported parallel trade as an important stimulus to completing the internal pharmaceuticals market.'*⁶³

⁶⁰ See supra note 48.

⁶¹ *GSK I (GlaxoSmithKline Services Unlimited v. Commission ao)*, joined Cases C-501/06 P, C-306/01, C-354/01 and C-513/06 P, C-515/06 P and C-519/06 P [2009] ECR I-0929I.

⁶² With respect to parallel trade, the Court has already held that, in principle, agreements aimed at prohibiting or limiting parallel trade have as their object the prevention of competition (see, to that effect, Case 19/77 *Miller International Schallplatten v Commission* [1978] ECR 131, paragraphs 7 and 18, and Joined Cases 32/78, 36/78 to 82/78 *BMW Belgium and Others v Commission* [1979] ECR 2435, paragraphs 20 to 28 and 31). ⁶⁰ As observed by the Advocate General in point 155 of her Opinion, that principle, according to which an agreement aimed at limiting parallel trade is a 'restriction of competition by object', applies to the pharmaceuticals sector.

⁶³ Hancher L (2010), supra note 31, at p. 664.

13.3.2 Supply quota restrictions

In reacting to the phenomenon of parallel trade, pharmaceutical companies started to supply wholesalers in one MS with only about enough products to cover domestic sales (supply quota restriction). Thus, by implementing supply quota restrictions, **wholesalers in one MS shall not have excess amounts of pharmaceuticals to export in higher price countries** and to engage in parallel trade or export. Such restrictions typically happen in low-price countries such as Spain or Greece and in amount in its effect to an **export ban** to Member States with higher price levels.

For an assessment of such a strategy under EU competition law it matters whether the company restricting supply is in a dominant position. The following case law analysis therefore distinguishes the case *Lélos v. Glaxo-SmithKline (GSK II)*⁶⁴ that deals with a company in a **dominant position** from the case *Adalat*⁶⁵ dealing with a company in a **non-dominant position**.

Supply quota restrictions of a company in a dominant position (Art. 102 TFEU) – *Lélos v. GlaxoSmithKline II (Greece)*⁶⁶

In this case the Greek Appeal Court (*Trimeles Efeteio Athinon*) turned to the ECJ, inquiring *'whether there is an abuse of a dominant position contrary to Art. 82 EC [now: Art. 102 TFEU] if a pharmaceuticals company occupying such a position on the national market for certain medicinal products refuses to meet orders sent to it by wholesalers on account of the fact that those wholesalers are involved in parallel exports of those products to other Member States.'*

The ECJ's key findings in GSK II are basically the following:

- ➔ **Parallel trade does have positive effects** on prices and thus for consumers in **parallel importing states**, which must be considered.⁶⁷
- ➔ *'[I]t should be noted, on one hand, that the control exercised by Member States over selling prices or the reimbursement of medicinal products does not entirely remove the prices of those products from the law of supply and demand.'*⁶⁸
- ➔ *'Where a medicine is protected by a patent which confers a temporary monopoly on its holder, the **price competition which may exist between a producer***

⁶⁴ Judgement of the Court (Grand Chamber) in Joined Cases C-468/06 to C-478/06, *Sot. Lélos kai Sia EE (and Others) v. GlaxoSmithKline AVEE* [2008] ECR I-7139, see also supra note 16.

⁶⁵ Judgement of the Court in Joined Cases C-2/01 P and C-3/01 P, *Bundesverband der Arzneimittel-Imorteur (and Others) v. Bayer AG* [2004] ECR I-64 – *'Adalat'* or *'Adalate'*

⁶⁶ See supra note 16.

⁶⁷ *'[...] [E]ven in Member States where the prices of medicines are subject to State regulation, parallel trade is liable to exert pressure on prices and, consequently to create financial benefits not only for the social health insurance funds, but equally for the patients concerned, [...]. [...] [T]here can be no escape from the prohibition laid down in Article 82 EC for the practices of an undertaking in a dominant position which are aimed at avoiding all parallel exports from a Member State to other Member States, practices which, by partitioning the national markets, neutralise the benefits of effective competition in terms of the supply and the prices that those exports would obtain for final consumers in the other Member States.'*, supra note 16, points 56 and 66.

⁶⁸ Supra note 16, point 61.

*and its distributors, or between parallel traders and national distributors, is, until the expiry of that patent, the only form of competition which can be envisaged*⁶⁹.'

- **Member States' price regulation** in the pharmaceuticals sector 'is one of the factors **liable to create opportunities for parallel trade**'.⁷⁰
- The ECJ explicitly stated that it is aware of the **risk** that competition policy and market rules in combination with national pricing policies might **lead companies not to place its medicines on the market at all in a Member State, where the prices of those products are set at a relatively low level**, thereby jeopardizing consumer interests. Thus, it concluded, 'a company must nevertheless be in a position to take **steps that are reasonable and in proportion to the need to protect its own commercial interests**'.⁷¹
- **Reasonable and Proportionate Measure Test:**
Courts therefore have to assess in every individual case, 'whether the refusal by a pharmaceuticals company to supply wholesalers involved in parallel exports constitutes a **reasonable and proportionate measure** in relation to the threat that those exports represent to its **legitimate commercial interests**, it must be ascertained whether the orders of the wholesalers are out of the ordinary.'⁷²

Following this reasoning, a **dominant company may refuse to supply exporters** (in higher price countries) **out of the ordinary supply** to respond to different pricing areas, caused by MS' deviating policies.

Even though the ECJ **stresses that parallel trade does have a positive effect on consumers (i.e. in parallel importing states)**, and thus principally upheld a positive attitude towards parallel trade as the only remedy for competition in a patented market, **it acknowledged existing legitimate commercial interests of a company** in taking **reasonable and proportionate measures to minimise parallel trade**.

The Court stated that **supply quota restrictions by a dominant company** – even though potentially being abusive – **might be justified if reasonable and proportionate in order to pursue legitimate commercial interests**. By applying this test, national authorities as well as national courts will have to assess **suitability and necessity** of the restriction and **balance harms and efficiencies**. However, the case leaves much uncertainty about how to 'properly assess and enhance competition on innovation in this sector in order to achieve the greatest benefit for the public.'⁷³

⁶⁹ Supra note 16, point 64.

⁷⁰ Supra note 16, point 67.

⁷¹ Supra note 16, points 68 and 69.

⁷² Supra note 16, point 70.

⁷³ Nguyen T, Minssen T, Groussot X, The Rule of Reason under Article 82 EC After Sot Lelos kai Sia, 6 July 2009, electronic copy available at: papers.ssrn.com/sol3/papers.cfm?abstract_id=1431010, at p. 21: 'This uncertainty is inter alia reflected by the fact that both the pharmaceutical industry and the parallel traders have claimed for victory after the ruling.'

Supply quota restrictions in non-dominant position (Art. 101 TFEU – *Adalat*)⁷⁴

Bayer AG – the parent company of subsidiaries in all EU MS – has manufactured and marketed under the trade name '**Adalat**' or '**Adalate**' a range of medicines with the active ingredient nifedipine to treat **cardiovascular disease**.⁷⁵

In most MS, the price of Adalat is directly or indirectly fixed by national health authorities. Between 1989 and 1993 the prices fixed by the Spanish or French health services were, on average, 40 % lower than prices in the UK.

Exploiting these price differences, wholesalers in **Spain** (starting in 1989) and in **France** (starting in 1991) began exporting Adalat to the UK, causing an alleged loss of sales for the UK subsidiary of Bayer (according to Bayer sales in the UK fell by almost half from 1989 to 1993 because of these parallel imports, causing a loss of turnover of 230 Mio DM).

As a result, Bayer started to change its delivery policy and began to **cease fulfilling all the increasingly large orders placed by wholesalers in Spain and France**.

The Commission thus started an administrative investigation procedure, finally leading to the decision that **Bayer Spain and Bayer France infringed Art. 85 (1) EC** [now: Art. 101 (1) TFEU], by imposing an export ban on Spanish and French wholesalers. The Commission adopted a decision, requiring Bayer to change its policy infringing Art. 81 (1) EC [now: Art. 101 (1) TFEU] and imposed a fine of 3 Mio Ecus on Bayer.

This Commission decision has been challenged and brought before the General Court and the ECJ, finally leading to court rulings, both annulling the Commission's decision.⁷⁶

As Liberatore states: '*[i]t follows from this case law that, provided he does so without abusing a dominant position, and there is no concurrence of wills between [...] [the company] and its wholesalers [implying an agreement in the sense of Art. 101 (1) TFEU], a manufacturer may adopt the supply policy which he considers necessary, even if by the very nature of its aim, for example, to hinder parallel imports, the implementation of that policy may entail restrictions on competition and affect trade between Member States.*'⁷⁷

However, since both, the General Court as well as the ECJ mainly assessed whether there has been an agreement in accordance to Art. 81 EC [now: Art. 101 TFEU], no

⁷⁴ Supra note 64.

⁷⁵ See supra note 64, points 1 to 4.

⁷⁶ Findings of the Court, supra note 64: point 140. '*By these pleas, the appellants are seeking to challenge the assessment by the Court of First Instance that the Commission could not effectively rely on the case-law precedents referred to in order to call into question the analysis which led the Court of First Instance to conclude that in this case acquiescence of the wholesalers in Bayer's new policy was not established (paragraph 159 of the judgment under appeal).*' and point 141. '*In that respect, it is important to note that this case raises the question of the existence of an agreement prohibited by Article 85(1) of the Treaty. The mere concomitant existence of an agreement which is in itself neutral and a measure restricting competition that has been imposed unilaterally does not amount to an agreement prohibited by that provision. Thus, the mere fact that a measure adopted by a manufacturer, which has the object or effect of restricting competition, falls within the context of continuous business relations between the manufacturer and its wholesalers is not sufficient for a finding that such an agreement exists.*'

⁷⁷ Liberatore F (2014), supra note 48, at p. 354.

further information on ECJ's attitude towards parallel trade in general or its effects has been provided.

13.3.3 Product life cycle management (Art. 102 TFEU) – AstraZeneca⁷⁸

Product life cycle strategies are relevant in the context of generic medicines, intending to delay or prevent market authorization of these products and parallel trade. In the *AstraZeneca* case, the Commission imposed a fine of EUR 60 million on AstraZeneca AB and AstraZeneca plc for having abused the patent system and the procedures for marketing pharmaceutical products in order to prevent or delay the arrival of competing generic medicines on the market and to impede parallel trade.⁷⁹

As Liberatore F (2014) states: '*It follows from the General Court's reasoning that, when there is **no other documented explanation for the withdrawal of a marketing authorization, this may be assumed to have the sole purpose of restricting parallel trade and is therefore abusive.** Accordingly, a **dominant company** comes under a positive obligation to ensure that its marketing authorizations are maintained so that it is easier for parallel imports to continue.*'⁸⁰

13.3.4 Reaction in MS' laws to parallel trade (Art. 34 to 36 TFEU)

It would be beyond the scope of this legal analysis to scrutinise all MS's laws related to parallel trade of medicines. However, some legal effects shall be pointed out exemplarily. Basically, it can be observed that **MS (predominantly) affected by parallel exports** increasingly start to issue export bans on medicines within the past years, whereas **MS benefiting from parallel imports** implemented supply strategies promoting the sale of imported medicines from lower-priced countries (e.g. according to § 129 (1) 2. of the German Social Security Act (Sozialgesetzbuch (SGB), (V)), pharmacies are obliged to preferably sell imported medicines, if the prices for these products are at least 15 Euro (or 15 %) below pharmacy retail price). The following overview focuses on recent developments, mainly in countries affected by parallel exports of medicines.

Distinct measures of MS

Allegedly, MS affected by parallel exports have to deal with shortages of certain medicines. ECJ rulings allowing pharmaceutical companies to execute quota restrictions in specific cases and if '*legitimate commercial interests*' justify these restrictions, should also be considered in this context (see GSK II above). In reaction to this problem, MS concerned issued laws, allowing the competent authorities to issue **export bans** on medicines affected.

In December 2013, Member of European Parliament (MEP) Thomas Ulmer officially raised the issue of the **Greek export** ban on certain medicines in reaction to allegedly existing shortages of specific medicines due to parallel exports.⁸¹ Other countries such

⁷⁸ Judgement of the Court (First Chamber), Case C-457/10 P [2012], *AstraZeneca AB, AstraZeneca plc v. European Commission*.

⁷⁹ Commission Decision C(2005) 1757 of 15 June 2005.

⁸⁰ Liberatore F (2014), *supra* note 48, at p 356.

⁸¹ Question for written answer E-013769/13 to the Commission, 4 December 2013, OJ C 263/234, 12.8.2014.

as **Hungary, Bulgaria, Slovakia, the Czech Republic, Romania, Estonia, Poland, Portugal, Spain and Italy** have either already implemented or drafted similar laws.

These laws typically provide for a **mandatory notification** of medicine agencies, if reimbursed medicines are exported or if there is a disruption of supply. The agency then usually has the right to (temporarily) object to exports within a certain time limit, if quantities of the medicine are insufficient to meet demand, could lead to a (temporary) shortage or if the shortage could pose a serious threat to the health and life of patients.

The European Commission officially answered the question raised by Thomas Ulmer by stating that each complaint and information needs to be examined on a case by case basis, examining whether the export ban violates Art. 34-36 TFEU. Regarding Greece, the Commission so far reported on 3 February 2014 that *'the problems with Greece have been resolved in the course of contacts the Commission had with Greece. The Commission examines all complaints it receives and if the problems remain unresolved it could refer a case to the Court of Justice.'*

In **Bulgaria** the export notification/authorisation procedure, criticised by the European Commission for infringement of free movement of goods, has been scrutinised by the Bulgarian **constitutional court**. The Court found that the **grounds on which the competent medicine agency could object to exports violate the Bulgarian constitutional principles of equal treatment of market players and proportionality**. The court basically stated that the lack of specific and quantifiable criteria is disproportionate and not suited to ensure security and sufficiency of local supplies. However, the requirement for notifying medicines agencies about exports has not been revoked.⁸²

In **Italy**, a recent law provides that **essential medicines** must always be available. Besides, the Italian Medicine Agency (AIFA) and the Italian Ministry of Health plan to publish a weekly list of medicines short of supply. However, in the course of drafting the new law it has been criticised that the term 'shortage' is not clear at all. Does it refer only to cases, in which there is no therapeutic alternative? The United Kingdom and France also implemented laws providing for mandatory lists of medicine shortages.

⁸² Melck B, Parallel-export bans: Member states in collision course with EU regulations?, HIS blog, December 11, 2014, referring to legal provisions in **Slovakia, Bulgaria, the Czech Republic, Hungary, Romania, Estonia and Poland** available at: <http://blog.ihs.com/parallel-export-bans%3A-member-states-in-collision-course-with-eu-regulations> (accessed: 1 June 2015), European Federation of Pharmaceutical Industries (Efpia), Policy proposals to minimise medicine supply shortages in Europe, 25 March 2014, referring to specific legal provisions in **Bulgaria, Czech Republic, France, Greece, Hungary, Poland, Portugal, Romania, Slovakia and Spain**, available at: <http://www.efpia.eu/uploads/Modules/Documents/pac-280214-ai6-a2-shortages-position-paper-final.pdf> (accessed: 1 June 2015), Fessenko D, Issaev S, **Bulgarian Constitutional Court** repeals grounds for blocking parallel exports of medicines, February 2015, available at <http://www.kinstellar.com/insights/detail/202/bulgarian-constitutional-court-repeals-grounds-for-blocking-parallel-exports-of-medicines> (accessed: 1 June 2015), PharmDedict, **Bulgaria**: restrictions on the export of medicinal products, available at: <http://pharmdedict.com/bulgaria-restrictions-on-the-export-of-pharmaceutical-products/> (accessed: 1 June 2015), Biro H, Baker & McKenzie, New law introduces supply obligation and export ban on medicines, August 19, 2013, referring to **Hungary**, available at: <http://www.lexology.com/library/detail.aspx?g=d9db6589-f73e-4b34-90a3-22c182bffd4> (accessed: 1 June 2015), Lucchini C, Medicines shortages: an European overview? A clear definition of the terms shortages and a measurable scope of the problem are required to prevent patient's discomforts, Pharma world magazine 4 April 2014, referring to legal provisions in the **United Kingdom, France, Greece, Poland, Spain and Italy**, available at: <http://www.pharmaworldmagazine.com/medicines-shortages-an-european-overview/> (accessed: 1 June 2015), Liptáková J, Chamber of Pharmacists proposes tightening rules on re-export of medicines, Parallel Trade in Drugs plagues **Slovakia**, The Slovak Spectator, 7 October 2013, available at <http://spectator.sme.sk/c/20048436/parallel-trade-in-drugs-plagues-slovakia.html> (accessed 1 June 2015).

With these (temporary) **notification or authorisation laws on exports** of medicines, parallel trade (i.e. parallel export) as alleged primary cause of medicine shortages shall be combated. However, the phenomenon of medicine shortages in European countries needs to be further analysed. Recent studies show that **parallel trade is by far not the sole cause for medicine shortages in Europe**.⁸³ Rather, there are several **predictable and unpredictable** causes for shortages, e.g. unpredictable: manufacturing problems, raw material shortages, non-compliance with regulatory standards, unexpected demand or natural disasters, epidemics, packaging shortages, etc. or predictable: product discontinuation, industry consolidation, rationing / quotas, limited manufacturing capacity, etc.⁸⁴ Besides, causes can be located at the **supply side** (e.g., manufacturing difficulties, unavailability of raw materials, natural disaster, etc.) or at the **demand side** (e.g., unexpected increase in demand, unforeseen shifts in clinical practice, parallel trade etc.)⁸⁵.

The European Association of Hospital Pharmacists (EAHP) published a survey on the medicines shortage problem in Europe in 2014. According to this survey with 600 responses from hospital pharmacists in 34 countries, 86% reported that medicines shortages are a '*current problem in the hospital they work in.*'⁸⁶ In 2012, Gray and Manasse as well as Pauwels et al. identify shortages of medicines as a **complex global challenge**, not only in developing countries, but also in the US, Canada, Australia and European countries.⁸⁷ Besides, Pauwels et al conclude that '**[p]roduction problems seem the leading cause of shortages in European countries [...]**' and that there '**[i]s a strong link between production problems and market attractiveness**'⁸⁸.

The fact that the US, where parallel trade is no issue, is affected by this problem as well, recent studies on causes for medicine shortages in Europe stress that parallel trade cannot be the sole / main cause. **Thus, uncoordinated mandatory notification regimes and export notification/authorisation laws in European countries could be analysed as to whether these measures are well suited and proportionate** for combating this serious health risk and for securing safe supply for patients in Europe.

Recent studies rather indicate that the manifold reasons for medicine shortages call for a joint European policy to combat this **cross-border health threat**⁸⁹: one of the find-

⁸³ Pauwels K, Huys I, Casteels M, Simoens St, Drug shortages in European countries; a trade-off between market attractiveness and cost containment?, *BMC Health Services Research*, 2014, 14:438.

⁸⁴ For a detailed list of reasons for drug shortages according to a study conducted in Europe see Birgli AG, An Evaluation of Medicines Shortages in Europe with a more in-depth review of these in France, Greece, Poland, Spain, and the United Kingdom, July 2013, available at: <http://static.correofarmaceutico.com/docs/2013/10/21/evaluation.pdf>.

⁸⁵ Supra note 82 at p. 1.

⁸⁶ The survey is available at: <http://www.eahp.eu/practice-and-policy/medicines-shortages>.

⁸⁷ Gray A, Manasse H, Shortages of medicines: a complex global challenge, *Bulletin of the World Health Organization*, 2012; 90: 158-158A as well as Pauwels K et al, supra note 82.

⁸⁸ Supra note 82 at p 8.

⁸⁹ For the US, several legislative acts have been passed in order to fight drug shortages. Besides, the FDA developed a Strategic Plan for Preventing and Mitigating Drug Shortages in October 2013 (see <http://www.fda.gov/Drugs/Drug-Safety/DrugShortages/>). FDA in close cooperation with pharmaceutical manufacturers publishes a drug shortage database (<http://www.accessdata.fda.gov/scripts/drugshortages/default.cfm>) and helps to mitigate the underlying causes. According to FDA statistics, progress in fighting drug shortages has been made from 2011 to 2014: see <http://www.fda.gov/Drugs/DrugSafety/DrugShortages/ucm441579.htm> (accessed 1 June 2015).

ings in a recent Study was that '[...] availability problems are not limited to small markets and an effective response to availability problems would need to take into account more than just issues relating to authorisation and **focus on the EU as a whole.**'⁹⁰

The EC Pharmaceutical Committee published a number of legal tools for national authorities in case of shortages, intending to ensure adequate supply (e.g. according to Article 126a of Directive 2001/83 EC: '*In the absence of a marketing authorisation or of a pending application for a medicinal product authorised in another Member State in accordance with this Directive, a Member State may for justified public health reasons authorise the placing on the market of the said medicinal product.*')⁹¹. Besides, the **EMA** publishes a **catalogue on medicine shortages** that affect or are likely to affect more than one European Union (EU) Member State⁹² and published a **reflection paper on medicinal product supply shortages**⁹³. In its reflection paper, the EMA indicates, that the problem of shortages in some cases already represented a **serious health-threat**⁹⁴, comprising of **shortages of essential, life-saving medicines**: '*In some cases defective medicines had to be left on the market to prevent shortages of life saving medicines as there is no available alternative and risks to a possible exposure with the defective product are considered less than those linked to the unavailability of the product.*'

So far, initiatives at EU level seem to be not sufficiently comprehensive enough, and responses to the medicines shortages are predominantly undertaken by competent national authorities that use different approaches (e.g. including differing definitions of 'shortage', etc.).

Parallel trade, MS's patent protection and compulsory licensing in the EU

Under the WTO/TRIPS agreement there exists the option of **compulsory or voluntary licensing**, i.e. breaking the patent holder's right to exclude others, if the **patent holder was given the possibility of voluntary licensing, receives adequate remuneration and does have the right to legal review.**⁹⁵ For 'national emergencies', 'other

⁹⁰ Matrix insight, Study on the Availability of Medicinal Products for Human Use, Specific Request EAHC/2011/Health/01 Lot 1, 21 December 2012, final report available at: http://ehpta.eu/pdf/Matrix_report.pdf at p. 6.

⁹¹ For a comprehensive overview of legal tools, possible remedies and communication see European Commission, Pharmaceutical Committee (PHARM 610), Subject: Shortages of medicinal products due to quality or manufacturing issues, 22 October 2012, available at: http://ec.europa.eu/health/files/committee/69meeting/pharm610_shortages.pdf
http://ec.europa.eu/health/files/committee/69meeting/pharm610_shortages.pdf

⁹² See: http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/document_listing/document_listing_000376.jsp&mid=WC0b01ac05807477a6

⁹³ See EMA, Reflection paper on medicinal product supply shortages caused by manufacturing/Good Manufacturing Practice Compliance problems, 22 November 2012, available at: http://www.ema.europa.eu/docs/en_GB/document_library/Other/2012/11/WC500135113.pdf.

⁹⁴ For a definition of 'serious cross-border health threat' see Art. 3 Decision No 1082/2013/EU of the European Parliament and of the Council of 22 October 2013 on serious cross-border threats to health and repealing Decision No 2119/98/EC, OJ L 293/5 5.11.2013.

⁹⁵ The TRIPS Agreement lists a number of conditions for issuing compulsory licenses, in Article 31. In particular: normally the person or company applying for a license has to have **tried to negotiate** a voluntary license with the patent holder on reasonable commercial terms. Only if that fails or if there is an **emergency** (e.g. anti-competitive practices, other national emergencies) a compulsory license can be issued. Even if a compulsory license (e.g. without agreement of the patent holder) has been issued, the **patent owner has to receive payment**. The TRIPS Agreement says '*the right holder shall be paid adequate remuneration in the circumstances of each case, taking into account the economic value of the authorization*', but it does not define '*adequate remuneration*' or '*economic value*', leaving this decision to the competent authorities

circumstances of extreme urgency', 'public non-commercial use' (or 'government use') or anti-competitive practices, there is no need to try first for a voluntary licence. The EU and its MS **voluntarily** declared that they would not use this system for imports (i.e. from non-EU countries).

In line with these international provisions, the EU and its Member States use **compulsory licensing measures in order to fight violations of market or competition rules** - thereby giving competition rules and free movement of goods privilege over intellectual property protection. In a human rights sense, this attitude also favours public interest and equal access to scarce medicines to comprehensive protection of intellectual property rights. In Case C-7/97 Oscar Bronner GmbH&Co. KG v. Mediaprint Zeitungs-und Zeitschriftenverlag GmbH&Co. KG, the Advocate General Jacobs stated that a compulsory license *can be granted 'in terms of competition policy only in cases in which the dominant undertaking has a genuine stranglehold on the related market'*.⁹⁶

Thereby, EU free market rules: Art. 29, 34, 35 and 36 as well as EU competition rules: Art. 101 and 102 would set the scope for compulsory licensing measures, for EU MS' authorities aiming at achieving and promoting access to medicines for all. Consequently, any compulsory licensing measure will be scrutinised under EU free market and competition rules. As Tudor (2012) summarises after analysing recent ECJ case law, any **compulsory licensing decision** must

- **not interfere with free movement of goods** within the EU, even if MS's authorities have filed the decision; however,
 - in case of **voluntary placement** (final outcome is an agreement between companies), the patent right holder and producer may not block any re-entry of that good (produced in another EU MS) and **parallel trade** within the EU may not be inhibited;
 - in case of **involuntary**, compulsory licensing (compulsory licensing is the decision of public authorities), parallel import of that good from a competitor may be blocked (unless there is an economic link between the patentee and the compulsory licensee);
- a dominant position alone does not justify any compulsory licensing;

of the country concerned. Besides, a compulsory license under the TRIPS agreement **can never be an exclusive** one. Thus, the patent owner still has the same rights (e.g. the patent-holder can continue to produce), but is in competition with the holder of the compulsory license. Over all, any compulsory licensing should be **subject to legal review** in the country. – see https://www.wto.org/english/tratop_e/trips_e/public_health_fa_q_e.htm.

⁹⁶ Tudor J, Compulsory Licensing in the European Union, *Geo. Mason J. Int'L Com. Law*, Vol 4:2, 2012, pp 222-258, at p. 225: 'There is significant contention, however, that there is a growing divide between the United States and the European Union on how to handle competition matters (i.e., 'antitrust' in the United States). In regard to this division, the United States is more likely to defend intellectual property rights than the European Union which is more likely to protect competition interests. For example, the European Union is more likely to consider the interests of potential licensors (e.g., intellectual property holders) and licensees in contrast to United States courts. In addition, the showing of a dominant position – the equivalent to the concept of market power in the United States – has a lower threshold in Europe than in the United States. Thus, it is easier to show a competition rules/antitrust violation in Europe. Therefore, the European Union is more likely to grant a compulsory license than the United States courts. Since 1988, this trend in the European Union has become more significant.'; in the context of human rights see also id. at p. 227.

- **only if a company in a dominant position abuses this position**, compulsory licensing might be justified (e.g. if any abuse leads to a violation of public interests, i.e. access to medicines or any risk to public health).⁹⁷

However, since these basic principles only result from EU case law and only specific fields are explicitly regulated (e.g. Directive 98/44/EC on the legal protection of biotechnological inventions⁹⁸), there is no harmonised regulatory EU-approach so far.

13.4 Secondary EU law interfering with the pharmaceutical (pricing) market: Transparency Directive⁹⁹

In some fields the EU has implemented certain common standards. In order to authorise safe, effective and high quality medicines, the **EU issued common rules for marketing authorisation** of pharmaceuticals. Thus, rules to obtain marketing authorisation are harmonised for the European market. However, as already pointed out, there are no common, coordinated price building mechanisms in the EU and in this sense there is no coordinated European internal market for pharmaceuticals. According to **Art. 168 (7) TFEU, the Member States are responsible for organising their healthcare systems**, including mechanisms for reimbursement and pricing decisions. *For instance, Member States usually evaluate the cost-effectiveness of authorised medicines, or their relative efficacy as well as the short- and long-term effectiveness compared to other products in the same therapeutic class, in order to determine their price, funding and utilisation in the framework of their health insurance system.*¹⁰⁰

Even after obtaining marketing authorisation according to European legislation, Member States can further regulate whether and how a medicine can finally be put on the market. Since **such practices lead to a distortion of the internal market and competition**, these **measures need to fulfil certain basic conditions of procedural transparency** according to primary EU law (Art. 114 TFEU), providing the legal basis for approximation of MS' laws. Thus, based on Art. 114 TFEU as well as settled ECJ case law relating to procedural conditions, the Council Transparency Directive has entered into force in 1989¹⁰¹. It is the attempt to move towards a **better coordinated and genuine single market in the field of pharmaceuticals through secondary legislation at EU level**. The manner in which national policies operate as well as criteria on which they are based in this sector shall be better aligned.

The directive provides for national authorities to **operate within specific time limits** (from 90 to 180 days)¹⁰² and to publish **price lists** as well as a list of pharmaceuticals

⁹⁷ Supra note 95, pp. 255-257; For an overview of recent European Union Compulsory Licenses see KEI, Research Note: Recent European Union Compulsory Licenses, March 1, 2014, available at keionline.org/sites/default/files/Annex_B_European_Union_Compulsory_Licenses_1Mar2014_8_5x11_0.pdf (accessed: November 16, 2015).

⁹⁸ Directive 98/44/EC of the European Parliament and of the Council of 6 July 1998 on the legal protection of biotechnological inventions, OJ L 213/13, 30.7.1998, Article 12.

⁹⁹ Council Directive of 21 December 1989 relating to the transparency of measures regulating the pricing of medicinal products for human use and their inclusion in the scope of national health insurance systems, 89/105/EEC, OJ L 40/8, 11.2.89.

¹⁰⁰ See Proposal for a Directive of the European Parliament and of the Council relating to the transparency of measures regulating the prices of medicinal products for human use and their inclusion in the scope of public health insurance system, COM(2012) 84 final, 2012/0035 (COD), at p. 2.

¹⁰¹ Directive 89/105/EC, supra note 98.

¹⁰² Directive 89/105/EC, supra note 98, Article 3, 1.

with increased prices within this period of time.¹⁰³ Any MS imposing a **price freeze** on all or certain products shall review conditions for this freeze at least once a year.¹⁰⁴ If a MS adopts a system of direct or indirect controls on the profitability of persons responsible for placing medicines on the market, specific information has to be published and the Commission has to be informed.¹⁰⁵ Specific procedural requirements are provided for, if a medicine is covered by the national health insurance system only after the competent authorities have decided to include a product in a **positive** or **negative list**.¹⁰⁶ These procedural requirements imply the availability of a remedy involving effective legal protection and the possibility to **appeal to a judicial body**, not simply an administrative one.¹⁰⁷

Since 1989 the directive has neither been amended nor changed. However, since then, the European **pharmaceutical market has changed significantly** (e.g. in the field of generic medicines or the development of HTA strategies). For this reason and to implement ECJ case law¹⁰⁸, signalling legal uncertainties and reduced transparency of national pricing and reimbursement measures, the Commission issued a proposal for a revised directive in March 2012.¹⁰⁹

The revised proposal basically retained the key principles of the 1989 directive, but additionally

- sought to **clarify the scope of the directive** (no application to measures involving public procurement and voluntary contractual agreements with companies),
- clarified that **time limits** for pricing and reimbursement decisions **include all procedural steps leading to the decision**, including HTA where applicable,
- provided for **shorter time limits** for pricing and reimbursement decisions,
- provided for states' non-interference of **patent** and **safety issues** in the context of pricing and reimbursement decisions and
- for **different instruments to facilitate dialogue** on the implementation of the Directive and to ensure its effective enforcement.¹¹⁰

The revised proposal has been criticised, especially since time limits provided had been too short and allegedly impossible for Member States to implement. Therefore, the Commission issued a revised version in 2013, providing for

- longer time limits for pricing and reimbursement decisions,
- revised remedies procedures and provisions for penalty payments and
- less strict reporting requirements for MS' authorities.¹¹¹

¹⁰³ Directive 89/105/EC, supra note 98, Article 3.

¹⁰⁴ Directive 89/105/EC, supra note 98, Article 4.

¹⁰⁵ Directive 89/105/EC, supra note 98, Article 5.

¹⁰⁶ Directive 89/105/EC, supra note 98, Articles 6 and 7.

¹⁰⁷ Commission v. Austria Case C-352/07 of 2 April 2009 and Hervey T & McHale J (2004), supra note 15, at p. 324.

¹⁰⁸ Including: Case C-424/99 of 27 November 2001, Commission v. Austria, Case C-229/00 of 12 June 2003, Commission v. Finland, Case C-245/03 of 20 January 2005, Merck, Sharp & Dohme, Case C-296/03 of 20 January 2005, GlaxoSmithKline, Case C-317/05 of 26 October 2006, Pohl-Boskamp, Case C-311/07 of 17 July 2008, Commission v. Austria Case C-352/07 of 2 April 2009, Menarini and joined cases C-353/07 to C-356/07, C-365/07 to C-367/07 and C-400/07.

¹⁰⁹ Supra note 99.

¹¹⁰ See Overview of the main legal elements, supra note 98, at p. 6.

¹¹¹ See e.g. Website of the UK Parliament: www.publications.parliament.uk/pa/cm201415/cmselect/cmeuleg/219-xxxii/21910.htm (accessed: 5 May 2015).

Besides, the European Parliament further amended the proposal, providing for further development of the **EURIPID price information database**.¹¹²

Nevertheless, in March 2015, the **Commission withdrew the proposal since a number of MS still opposed the revised version and no agreement has been reached**.¹¹³

For now, it would be premature to outline any way forward. However, the removal of the revised version indicates that **any further coordination approach in the field of pharmaceutical pricing and reimbursement through secondary legislation is difficult to attain**. According to the information provided by the Minister to the UK Parliament, MS still oppose to any further coordination approach, arguing with **missing subsidiarity and proportionality** of such initiatives.¹¹⁴

Since pricing policies are not coordinated within the EU (neither the current version nor the revised and removed version of the Transparency Directive provide for procedural provisions in this context), such practices might have unintended effects, possibly not thoroughly assessed by MS while using EPR: *'While the ERP mechanism may provide useful benchmarks for price negotiations between governments and producers, some stakeholders have voiced concerns about ERP being applied **without taking into consideration the socioeconomic features of each country** and in particular over the fact that reference prices affected by such emergency measures may influence the price level in other MS or in third countries.'*¹¹⁵

13.5 Regulation related to differential pricing

The EC launched regulation related to differential pricing, however to provide a framework for differential pricing between the EU and non-EU countries in the area of external trade.

The **Council Regulation (EC) No 953/2003** of 26 May 2003 to avoid trade diversion into the European Union of certain key medicines (currently under revision: 2014/0165 (COD)) has been introduced to support the principle of tiered pricing between the EU

¹¹² See '(15a) Member States should ensure the public availability of documents and information in an appropriate publication, in accordance with national practice, which could include electronic and online format. They should also ensure that the information delivered is understandable and supplied in a reasonable quantity. The Commission and the Member States should also examine how to continue to co-operate on the functioning of the EURIPID price information database, which provides EU-wide added value in terms of price transparency.', available at <http://www.europarl.europa.eu/sides/get-Doc.do?type=REPORT&reference=A7-2013-0015&language=EN>.

¹¹³ OJ, C 80/08, Volume 58, 7 March 2015; see also: supra note 110: '7.9 The Minister notes the lack of progress made in Council working group discussions since 2013. At the last meeting, in June 2014, he adds: 'A number of Member States continued to raise significant concerns about the amended proposal, particularly relating to issues of subsidiarity and proportionality, and because it was felt to be imposing a one-size-fits-all approach to varied national pricing and reimbursement policies. The UK position had remained more positive than those of most other delegations, although we also had some major concerns that still needed to be addressed, such as about the time limits for decisions on pricing and how these are calculated. 'Whilst progress had been expected with the Italian Presidency of the Council, none of [the] meetings that had been scheduled since June 2014 took place.'

¹¹⁴ Supra note 110.

¹¹⁵ Commission Staff Working Document, Pharmaceutical Industry: A Strategic Sector for the European Economy, SWD(2014) 216 final/2, 1 August 2014, p. 10

MS and low- and middle income countries. This regulation provides for safeguards to prevent leaking of tiered products from low- and middle-income countries outside Europe into the EU: Authorised tiered priced products are marked with a logo. The manufacturer basically has two options to achieve the differential price: a certain percentage of the average ex-factory price charged in high-priced countries (e.g.: 25%) or the direct production costs plus a certain percentage (e.g. 15%). These tiered priced products with logo are then subject to specific trade rules.

Some specific mechanisms of the Council Regulation, even if relevant for the area of external trade, could be another point of reference to provide technical solutions related to the implementation of DP within the EU.

13.6 Conclusions

There are **several constraints** in EU law that prevent the introduction of an EU-wide coordinated DP scheme. Even though the EU strives at realising a free, internal market in the pharmaceutical sector with equal and affordable access to medicines in all MS, the EU does not have the legal power to regulate the market after market authorisation of medicines has been obtained. In accordance with Art. 168 (7) TFEU, MS have the competence to regulate pricing and reimbursement of medicines, which is justified by MS by the specific nature and tradition of their health care systems. This leads to a highly diverse market for pharmaceuticals with split competences and considerable price differences between MS.

Due to this diversity of the EU pharmaceutical market, and patent-exhaustion after first sale, **parallel trade** results, leading – at least short-term – to reduced prices for consumers in importing MS with high price levels, but potentially threaten supply in MS with low price levels for pharmaceuticals. In addition, pharmaceutical companies' or wholesalers' revenues in high-price countries allegedly decrease, possibly leading to higher prices and reduced investments in R&D.

For this reason, **pharmaceutical companies have developed several strategies** in order to diminish effects of parallel trade, i.e. dual pricing strategies, supply quota restrictions and specific life cycle management policies. These strategies have been scrutinised by European Commission and the ECJ and have in some cases been classified as anti-competitive. The ECJ ruled that agreements of pharmaceutical companies with wholesalers in low-price countries providing for different prices– depending on whether wholesalers would export products to high-price countries – violate EU competition law, but might be justified under certain circumstances and if advantages for consumers outweigh its anti-competitive effects.¹¹⁶ Besides, the ECJ ruled that a company in a dominant position may refuse to supply out of ordinary exporters' orders in higher price countries, if these measures are proportionate and reasonable, thereby acknowledging existing legitimate commercial interests of pharmaceutical companies.¹¹⁷ If a company does not abuse a dominant position, a manufacturer may adopt a supply policy, which he considers necessary, even if by the very nature of its aim, the implementation may restrict competition.¹¹⁸ However, the Commission and the ECJ criticised pharmaceutical

¹¹⁶ See *GSK I*, supra note 60.

¹¹⁷ See *GSK II*, supra note 16.

¹¹⁸ See *Adalat*, supra note 64.

companies' strategy to delay market entry of generic products by using different life cycle management strategies.¹¹⁹

These rulings show that the ECJ on the one hand still stresses positive effects of parallel imports, but on the other hand acknowledges legitimate commercial interests of pharmaceutical companies, if **reasonable and proportionate strategies** are applied or if **consumer interests outweigh its anti-competitive effects**. But even though the ECJ provides some guidelines on possibilities for pharmaceutical companies to diminish negative effects of parallel trade, these rulings leave many open questions, e.g. how to apply the reasonability and proportionality test, leading to **legal uncertainty**, e.g. what is specifically meant by a pharmaceutical company's 'legitimate commercial interest', which concrete market conditions in terms of concrete quantifiable criteria have to be fulfilled in order to justify limits in supply and how shall they be determined or how to determine best consumer interests? Thus, **through its competition policy, European Institutions have some possibilities to react to the effects of different MS pricing and reimbursement policies in the field of medicines on undertakings**. However, these measures do not seem to support the healthcare objective of equal and affordable access to patented medicines in all MS.

Consequently, the European Commission built on already **existing legislative opportunities** in order to further advance coordination of MS' pricing and reimbursement policies. However, above described experiences with the delayed and finally removed revision of the Transparency Directive indicated that it is difficult to direct MS' pricing strategies through secondary legislation. Any **legislative coordination initiative** in this field would have to be well argued, based on **'qualitative and, wherever possible, quantitative indicators' to convince MS that this objective can be better achieved at Union level**.¹²⁰

Besides, recent activities of MS, i.e. **(temporary) export bans and authorisation / notification procedures** will have to be scrutinised under Articles 34 to 36. It will be necessary to analyse measures taken by MS in relation to a specific product for necessity (public health and access to medicines) and proportionality (reasonable, quantifiable criteria).

Alternatively, initiatives through the so called '**Open Method of Coordination (OMC)**' sometimes might be more successful than legislative initiatives; specifically in fields traditionally not assigned to the European level by MS. The Lisbon Summit introduces this policy of 'spreading best practice and achieving greater convergence towards the main EU goals. According to the Conclusions, this involves: fixing guidelines (with specific timetables); establishing quantitative and qualitative indicators and benchmarks (against the best in the World); national and regional targets; and periodic monitoring, evaluation and peer review organised as mutual learning processes.¹²¹

¹¹⁹ See *AstraZeneca*, supra note 77.

¹²⁰ See the Protocol (No 2) on the Application of the Principles of Subsidiarity and Proportionality, supra note 23.

¹²¹ European Commission, Joint report on social protection and social inclusion 2007: social inclusion, pensions, healthcare and long-term care', Directorate-General for Employment, Social Affairs and Equal Opportunities (2007), available at ec.europa.eu/social/BlobServlet?docId=2014&langId=en; see also: Greer S, Vanhercke B, The hard politics of soft law; the case of health, in Mossialos E, Permanand G, Beaten R and Hervey T (Eds.), *Health Systems Governance in Europe, The Role of European Union Law and Policy*, European Observatory on Health Systems and Policy, Cambridge University Press, New York (2010), pp. 186-230, at p. 193-197.

Indeed, there are several points of reference for the Commission to provide sound guidance for MS and to promote transparency of pricing and reimbursement measures or to assess necessary (temporary) export bans and authorisation / notification procedures, e.g. **to provide information and qualitative or quantitative data on effects of different price levels within the EU on consumers and patients** (especially in relation to Directive 2011/24/EU on the application of patients' rights in cross-border healthcare), the **Joint Procurement Agreement of medical countermeasures** that provides a legal framework for joint procurement and specific mechanisms of the **EU Regulation (COM(2014) 319 final) related to differential pricing** for external trade that might provide **guidance** for intra-EU use.

14 Annex 14: Examples of EU coordination mechanisms – Detailed information

14.1 EU Emission Trading System

14.1.1 Practice

The EU Emission Trading System (ETS) aims to reduce emissions of man-made greenhouse gases in the EU by putting a limit on the overall emissions of carbon-dioxide in high-emitting sectors. All 28 EU Member States plus Iceland, Norway and Liechtenstein participate in the EU ETS [20]. Emission Trading is based on the idea of Ronald H Coase who stated that negative externalities of the market (emission of greenhouse gases) can be efficiently internalised if the property rights to a common good (clean air) are clearly specified [21]. In the case of emission, all members of the society are entitled to clean fresh air and manufacturers have to release that right through freely traded certificates.

The EU launched ETS in 2005 as the cornerstone of its strategy for cutting emissions of carbon dioxide (CO₂) and other gases at least costs. In contrast to traditional 'command and control' regulation, emissions trading make use of market forces to find the most efficient way of reducing emissions. A market distributes scarce resources according to signals expressed in relative prices. By limiting the overall volume of greenhouse gases that can be emitted each combined with the issue of emission certificates, the EU puts a price on carbon and thereby giving a financial value to each ton of emissions saved. EU ETS incentivises to invest in clean technologies and low-carbon solutions which is strengthened furthermore by allowing companies to buy credits from emission-saving projects around the world [20].

The Emission Trading Directive (2003/87/EC) for establishing the EU ETS was adopted in 2003, and free trade of certificates was put into existence in 2005. Since its introduction, EU ETS has experienced three trading periods. The first trading period took place between 2005 and 2007 and was used for 'learning by doing'. Although the EU has established the world's biggest carbon market the price of first-period allowance fell to close to zero. The main reason was the excessive amount of allowances due to exaggerating emission reports of the Member States. Therefore, in the second trading period between 2008 and 2012, the number of allowances was reduced by 6.5 percent annually. However, this period coincided with the economic downturn after the credit crunch leading to a surplus of unused allowances. The third period started in 2013 and will last until 2020, and it is accompanied by further reforms [20].

The EU ETS covers emission of three different greenhouse gases in certain sectors which constitute 45% of total greenhouse gas emissions from the 28 EU countries. These are carbon dioxide (CO₂) from power plants, a wide range of energy-intensive industry sectors and commercial airlines, Nitrous oxide (N₂O) from production of nitric, adipic, glyoxal and glyoxalic acids and Perfluorocarbons (PFCs) from aluminium production. From 2013 onwards, the cap on emissions from power stations and other fixed installations is reduced by 1.74 percent every year, summing up to a total reduction of 21 percent in 2020 from these sectors compared to the 2005. A separate cap is applied to the aviation sector which is 5 percent below the average annual level of emissions in the years 2004-2006 [20].

Emissions certificates are allocated through two mechanisms: (1) Auctioning; Businesses have to buy their allowances at auctions. (2) Free allocation; businesses receive their allowance for free. Which type of mechanism applies depends on the sector, in

which the business is operating, but in the recent trading period there was a shift towards auctioning and free auctioning should phase out completely by 2027 [20].

14.1.2 Costs

Costs for participating in the EU ETS can be divided into 3 broad categories: (1) Costs of obtaining emission allowances (excluding the price of the allowances) (2) Costs of monitoring, verifying and reporting emissions and (3) costs of managing the portfolio of allocated emission allowances. Most of costs are not proportional to the size of the emission or the size of the allocation, making the EU ETS particularly burdensome for small emitters [22].

In 2005, the Commission conducted a survey among Member States to evaluate the costs for participation in the EU ETS for smaller installations. The survey revealed that most countries do not have much detailed information on the costs of participation. The estimated costs of the EU ETS participation for smaller installations are reported in the table below [23].

Table A10: Costs estimates of EU Emission Trading System

Country	Cost reported
Germany	EUR 12,500.00 to more than EUR 20,000.00 per installation
Denmark	Total recurring costs of at least EUR 4,300.00 – EUR 7,000.00 per installation covering costs of registration with the administration, monitoring, verification etc. Depending on complexity of the installation
Sweden	Total recurring costs of EUR 2,100.00 – 5,000.00 per installation in phase I and EUR 1,400.00 – EUR 2,600.00 per installation in phase II
United Kingdom	Total administrative costs EUR 3,675.00 - EUR 4,415.00

Source: Research by GÖ FP

A range of studies aimed to assess administrative compliance costs under EU ETS. The Emissions Trading Group (ETG) Working Group 5/6 gathered data on (1) staff costs, (2) non-staff costs (3) total indicative costs and (4) one-off costs and estimated the total annual costs per installation in Phase I at GBP 27,000.00 [24]. The National Audit office conducted a survey, in which companies reported total annual costs of GBP 35,000.00, composed of monitoring and reporting (GBP 26,000.00) and average annual verification costs (GBP 9,000.00) [25]. In an impact assessment of the Emission Trading Scheme the European Commission stated that the range of estimated administrative costs for operators range varies between EUR 2,000.00 to EUR 15,000.00 per year, and for authorities between EUR 3,000.00 and EUR 10,000.00 per site and year [26]. King et al. (2010) estimate the average administrative burden of the EU ETS to be around GBP 16,400.00 (including one-off costs and fees). If wider administrative costs are included the average can increase to GBP 21,000.00. In their assessment, the authors found a significant variation from sector to sector. From the operator's perspective, the costs of the extension of the EU ETS in 2008 were estimated at EUR 3.05 Mio. for operational expenditure, EUR 6.727 Mio. for human resources and associated costs, and EUR 1.881 Mio for administrative expenditures other than human resources, summing up to EUR 11.658 Mio. [27].

14.1.3 Benefits

Evaluating emission trading schemes it must be done cautiously because it is important to distinguish between the inherent strengths or weaknesses of emission trading (from theoretical viewpoints) and those contingent matters of performance which are rather related to (1) the particular design of characteristics of the scheme, (2) its fit with the context of application or (3) the intensity by which the pollution abatement is enforced. Every Emission Trading system operates with quite different strengths and weaknesses in different context and its different design [28].

Coverage: The centralised function of the European Commission facilitated the introduction of the coordination mechanisms on a large scale, covering all 28 EU Member States plus Iceland, Norway and Liechtenstein. Under the EU ETS, individual countries are responsible for emissions monitoring, reporting verification and enforcement under the ETC. The European Commission contributed to the success of implementation by approving national budgets, establishing common registry protocols and providing information and technical assistance [29].

Reducing uncertainty: The joint implementation (JI) and the clean development mechanism (CDM) within the EU ETS enable participants in the schemes to undertake emission-saving investments in other countries and credit these savings towards their emission targets. CDM covers projects in countries without an emission target under the Kyoto Protocol i.e. developing nations, whereas JI applies to projects in countries that have agreed on an emission target i.e. other industrialised countries and countries with economies in transition. Efforts in JI and CDM are rewarded with credits known as 'emission reduction units' (ERU) and can be converted 1:1 to emission certificates¹²². The EU ETS creates a stable environment for investors in emerging markets for JI and CDM projects and encourages more investment in such projects and promotes the transfer of environmentally sound technologies.

Compatibility: The EU ETS is compatible with schemes in other countries that have ratified the Kyoto protocol. The market for trading certificates can be readily expanded if countries agree to recognise allowances issued by the other. In a major step towards an international emission trading system, the European Commission and Australia have agreed, that by mid-2018 the schemes from both continents will be fully linked. Negotiations are also under way with Switzerland on linking the EU ETS.

14.1.4 Limitations

The EU ETS was designed as the largest emission trading scheme in the world and the first application of emission trading on a large scale, making it an ambitious and highly challenging policy experiment. Due to the lack of comparable experience in this field, the implementation was sometimes characterised by a learning-by-doing process.

National Allocations Plans vs. central coordinating organisation: The market mechanism distributes goods on signals the participants send and receive. Emission trading schemes are designed markets, where the demand and the supply are dependent on government decisions. Demand is driven by the coverage of the system, whereas supply is determined by the volume of allowance allocation. In order to derive the cap of emissions certificates, every member state was required to develop a national allocation plan

¹²² Excepted are nuclear energy projects, afforestation or reforestation activities and projects involving the destruction of industrial gases.

(NAP). Since countries feared a competitiveness loss of their national industries due to higher production costs and the lack of data at the installation level, the calculation of NAPs lead to substantial over-allocation of emission allowances in the first period. Therefore the EC took a stronger role in the in the second period to provide a higher overall stringency of the allocation caps [29, 30].

Inclusion of Transport: In the beginning, the EU ETS scheme was limited to four emission intensive sectors: (1) energy activities (2) production and processing of ferrous metals (3) mineral industry and (4) other industries [30]. However, the transport sector, which accounts for a large fraction of emissions, was not included. Only in the third trading period, some steps were made in this direction, by including aviation, but not road transport. It was argued that the inclusion of road transport would increase the cost of certificates and the marginal abatement cost, and therefore could have a negative impact on the competitive advantage. Also problems related to limited effectiveness of emission trading for road transport were identified [31].

Emission banking: The actual system does not consider the possibility to 'save' not-consumed allowances and transfer them to later periods. This supplementary regulation is known as emission banking and breaks through the stringency of the EU ETS by offering additional freedom to participants in the system. Seller of certificates would not be required to find purchasers of their licenses within a certain period, if the price of this allowance is relatively low [32]. Emission banking can also contribute to reduce price volatility, which hampers investment decisions of economic agents [30]. In order to prevent excessive storage of emission allowances, demurrage can be applied to older certificates.

Stand-alone policy: In theory, emission trading is a cost-efficient tool to internalise negative market externalities. However, in practice it is not clear how much of the emission reductions are attributable to emission trading. In Europe, due to the economic crisis and the lower economic activity, emissions were reduced substantially [33]. Also for the 1995 introduced 'Clean Air Act' some authors claim that the reduction of Sulfur dioxide (SO₂) emission by electric utilities was unrelated to emission trading but to other factors [34].

14.2 Common Agricultural Policy (CAP)

14.2.1 Practice

The Common Agricultural Policy (CAP) is not one policy but rather a set of policies aimed at raising farm incomes in the EU, which have radically changed over time. The early CAP was established as price floor for many major farm products like grains, dairy products, beef, veal and sugar. The prices held above world prices through a system of import tariffs which changed daily according to world market conditions and direct purchases as the last resort. The goal of the early CAP was to ensure that imports never pushed EU prices below the price floor. Price supports have huge distributional consequences from the producer and consumer perspective. The benefits of price supports mainly go to larger farms, because they produce a lot and – due to economics of scale – tend to produce more efficiently i.e. at lower costs. Since the owners of large farms tend to be rich, the benefits of a price floor are systematically biased in favour of larger and wealthier producers. Furthermore, price floors are paid for by consumers, because they have to pay the higher price for food. As poor families spent a higher fraction of their income on food, prices are more important to their budget and, price floors are therefore a regressive consumption tax [35].

In the first years after its introduction CAP as price floor worked quite well and provided higher and stable prices food. Although these artificial higher prices were paid by consumers, it was not criticised by them, because as the average income in that time rose faster than food prices. However, in this period agriculture witnessed revolutionary advances which boosted yields and created a cascade of unintended consequences as CAP rewarded output. Budget, food disposal and farm income problems as well as 'factory farming' and harming the prospects of developing nations are the most notable references. Breaking the link between the payments and overproduction was considered as solution to that problem and therefore payments were gradually decoupled i.e. the size of the payment was not related to the produced amount [35]. The MacSharry Reform in mid-1992 and the Fischler reform in 2003 brought substantial changes, moving from a production-oriented policy towards single-farm payment, decoupling the production from subsidies [36]. The money was paid directly to the owner of the farmland regardless of whether the owner was a farmer or not. The only requirement was to continue farming.

Today's CAP has two pillars: the first concerns direct payments and the cost of the remaining price supports, and the second pillar is the so-called 'Rural Development'. Council Regulation 1234/2007 established a common organisation of agricultural markets which main framework was also retained for the new CAP Period from 2014 till 2020. However, the new CAP design pursues a more holistic approach with better targeted instruments of the first pillar, complemented by regionally tailor-made and voluntary measures of the second pillar [37]. The common rules regulate the EU internal agricultural markets through market interventions (public intervention or aid for the private storage), special intervention measures (exceptional market supports in crisis), quota schemes (fixed national production quotas for sugar) and aid schemes for several sectors (e.g. programmes promoting the consumption of fruit and milk in schools). For instance, the production of sugar beets (with the EU being the world's leading producer of beet sugar) is regulated via a production quota that is divided between nineteen EU Member States. Farmers receive for quota sugar beets from sugar factories a minimum fixed price whereas out-of-quota sugar beet has to be sold at market prices. A EU reference price for white sugar was fixed, and, if EU market prices fall below 85% of the reference price, private storage aid can be activated [38].

14.2.2 Costs

Evaluating the costs of CAP is a difficult task because there do not exist many publications on that topic. In a study published in 2007, DG AGRI estimated that CAP cause on the producer level Germany 480.37 million Euro total administrative costs. This corresponds to 1,298 Euro average administrative costs per producer/farmer at. When distributing the total administrative costs to acreage, the administrative costs amount to 28 Euro per ha. The relation between total CAP payments and total administrative costs is 9.3%. The most burdensome subject in CAP at producer level is the application for the decoupled payment which constitutes 98.3% of all administrative costs [39]. On the operator's level no data on the costs on running this allocation mechanism is available.

14.2.3 Benefits

Ensuring the safety and quality of food: Due to climate change, oil shortages the availability of quality land and water, some parts of the world experience food shortages. Since its introduction CAP has contributed to ensure food security for European citizens. It also helps to guarantee that Europe's consumers get food that meets quality requirements. For instance, organic farmers and food producers are encouraged to use the EU organic logo where at least 95% of the product's ingredients have been organically

produced and it complies with the rules of an official inspection scheme. This benefit has been regularly recognised by European citizens, which think that agriculture and rural areas are an important matter for the future of the EU [40].

14.2.4 Limitations

Duration of decision finding in political sensitive areas: The evolution of CAP reveals a central problem: a coordination mechanism in a politically sensitive area – as food and nutrition clearly for various reasons clearly is – can take long time and large efforts the larger the group is. The original coordination mechanisms worked well for a low (rather homogenous) number of countries in the beginning, but over time (and several enlargements later) it became a subject for many quarrels among EU members.

Impeding the signal function of prices requires regular adjustments: Experience from the 70's and 80's showed that due to CAP the prices lost its function as signal for relative scarcity. High prices resulted in 'wheat, beef, and butter mountains' which either rotted or sold as animal feed. The policy of exporting the food 'surplus' abroad created a foreign trade problem and had severe consequences on producers in other countries. The evolution of CAP showed that any coordination mechanism needs to be adjusted for transformations which occur within the system and is at best a snapshot of an ongoing adjustment process [35].

Complexity: Although the logic behind CAP claims to be simple i.e. raising farm incomes in the EU, the set of policies with which this aim should be achieved, has become more and more complex. This is reflected in the fact that the average European citizens does little know about agricultural or agricultural policy [41]. A centralised coordination mechanism of the complexity of CAP bears the risk that Europeans citizens alienate from an issue which affects them fundamentally.

15 Annex 15: Stakeholder review

15.1 Methodology

The contractor was asked to perform a stakeholder review for this study as defined under the Call for tender n. EAHC/2013/Health/01 for concluding Multiple Framework Contracts with reopening of competition to support the implementation of the Health Programme (2008-2013) and the Health Programme (2014-2020) for large reports.

The key elements of such a stakeholder review were defined by the EC as follows

- Minimum 20 stakeholders, up to 60 stakeholders to be suggested, to be approved by Chafea/DG SANCO;
- Comments from stakeholders to be collected in writing, to be presented to Chafea/DG SANCO;
- One face-to-face meeting needed with Chafea/DG SANCO;
- The review shall include a stakeholder meeting with minimum of 20 stakeholders in Luxembourg or Brussels;
- Duration: maximum 8 weeks.

Thus, the Tender Specifications asked for two elements of the stakeholder review: a written review, and a stakeholder review meeting.

According to the Tender Specifications of the Study on 'Enhanced cross-country coordination in the area of pharmaceutical product pricing', the stakeholder review shall be 'open to participation of EU-level representatives from patients, public payers and medical industry'.

In the proposal, the contractor proposed the following criteria for a representative selection of stakeholders:

- Extending stakeholder groups beyond the Tender Specifications: Based on the experience of a previous piece of research ('Study of the policy mix for the reimbursement of medicinal products' by Vogler et al. 2014), the contractor proposed to also include the stakeholder groups of consumers, competent authorities for pricing and reimbursement and healthcare professionals such as doctors and pharmacists. Industry should be represented by different industry branches focusing on different types of medicines, e.g., research-based pharmaceutical industry (also considering biotech industry), generics and biosimilar industry, and self-medication industry. Medical devices were not considered as within the scope of the consultation since the study targets only pricing policies for medicines.
- EU-level representativeness: The contractor considered stakeholder representatives from the European associations as primary target for the stakeholder review. They are the key contact points, and should therefore to be addressed for the 'full' stakeholder review (both comments in writing and at the meeting). However, with a view of addressing up to 60 stakeholders (as requested in the Tender Specifications), the European institutions would be not sufficient. Therefore, some representatives from the Member States, but active in the associations, should also be involved in the stakeholder review. The contractor was of the opinion that the decision on whom to nominate should be with the European associations, and thus suggested going through the European associations for their nominations (where applicable).

Based on these considerations, the contractor proposed a differentiated approach for the written review and the stakeholder review meeting: We were convinced that a high number of high-quality stakeholder responses on the draft findings would provide an

added value to the project. However, to allow for a constructive dialogue during the meeting, offering enough time for the representatives of the stakeholder groups to address all relevant topics during the stakeholder meeting, the contractor suggested to limit the number of participants in the meeting to around 20-25 stakeholders, whereas the remaining stakeholders have the possibility to comment in writing. The stakeholder representatives to be invited to the meeting should primarily come from affiliations to the European associations, plus some Member State' representatives from associations and competent authorities for pricing and reimbursement / public payers. Our rationale for proposing this was that the same approach was applied for the Working Groups of the Platform 'Access to Medicines in Europe' under the Process on Corporate Social Responsibility in the Field of Pharmaceuticals.

We also suggested the principle of 'one institution – one voice/representative' so that the consulted stakeholders would be invited to provide their comments in their role as representatives of the institutions they represent. As a result, we suggested accepting one coordinated response per institution (either European association or national stakeholder organisation) in the written stakeholder review.

These principles were presented in the proposal, presented at the kick-off meeting in Brussels on 19 December 2014 and confirmed in a revised inception report accepted by the EC in January 2015.

In line with these principles, the contractor proposed a list of stakeholders to be invited for the stakeholder review meeting. We discussed this list of stakeholders with the EC at the kick-off meeting in Brussels on 19 December 2014. In principle, the list was accepted, and it was expanded thanks to some further suggestions of the EC. The finally agreed list of stakeholders to be invited to the stakeholder review meeting was confirmed through EC's approval of the inception report in January 2015.

For the written review, participants were invited to provide their feed-back in a 'feedback template', divided into 'general comments' and 'specific comments' related to specific parts (sentences / paragraphs) of the draft report.

While it was expected that all participants of the stakeholder review meeting had read and were familiar with the draft report, the meeting was still opened with a presentation of the key findings of the draft report. The presentation of the results was accompanied by a summary of major comments, sometimes contradictory, of the written comments. Following the discussion of the presentation, some specific questions were discussed:

- EPR – A tool for access to medicines and/or cost-containment
 - How can EPR be designed to be improved in order to be able to possibly work as instrument towards increased access to medicines and increased cost containment? (e.g. Improvement in the formulae, in the MS coordination – cf. proposals for cooperation in the study)
- DP – A tool for increasing access to medicines
 - Should a DP scheme be developed in the European Union, and if yes – how? (e.g. how to differentiate prices, limitations, MS coordination)
- Ways forward for the future
 - What is missing?
 - Proposals for (future) research and for policy-making?

The meeting was held under the Chatham House Rules.

15.2 Results

15.2.1 Participation

We sent the draft interim report on 10 August 2015 to a total of 51 institutions, thereof 13 stakeholders (associations / interest groups)¹²³, 32 Member State institutions (pricing authorities), and 6 DP experts (that had been available for interviews). We received written feedback from a total of 23 institutions, thereof 7 stakeholders, 16 Member States institutions from 15 Member states, and 2 DP experts. Written feedback was received between 14 August and 7 September 2015. The lengths of the written comments varied between nearly 50 pages and one paragraph. If shorter comments were provided, stakeholders did not use the feed-back template.

A total of 34 people participated in the stakeholder review meeting held in Brussels on 17 September 2015. In addition of representatives of DG SANTÉ and further Directorate-Generals of the European Commission and permanent representatives of following EU Presidencies, 11 stakeholder representatives and 11 Member State representatives (two of them also represented a stakeholder perspective) attended the meeting. For further information about the participation in the stakeholder review see Table A11.

Table A11: Stakeholder review process

Stakeholder/Member State	Written comments (between 14 August and 7 September)	Participation in the workshop (17 September 2015)
European Social Insurance Platform (ESIP)		✓
Association Internationale de la Mutualité (AIM)	✓	✓
Bureau Européen des Unions de Consommateurs (BEUC) and national associations	✓	✓
Health Action International (HAI)	✓	✓
European Patient Forum (EPF) and national associations		✓
European Public Health Alliance (EPHA)	✓	✓
European Federation of Pharmaceutical Industries and Associations (EFPIA) and national associations	✓	✓
European generic and biosimilar medicines Association (EGA) and national associations	✓	✓
European Association for Bioindustries (EUROPABIO)		
Association Européenne des Spécialités Pharmaceutiques Grand Public (AESGP)		✓

¹²³ The report was shared with associations and interest groups on European level, who were allowed circulating the draft report within the boundaries of their national associations.

Stakeholder/Member State	Written comments (between 14 August and 7 September)	Participation in the workshop (17 September 2015)
European Association of Hospital Pharmacists (EAHP)		✓
Comité permanent des médecins européens (CPME) & n. assoc.	✓	✓
Euripid		✓
Austria		
Belgium		✓
Bulgaria		
Croatia	✓	
Cyprus		
Czech Republic		✓
Denmark		
Estonia		
Finland	✓	
France		✓
Germany	✓	✓
Greece		✓
Hungary	✓	✓
Iceland		
Ireland	✓	
Italy		
Latvia		✓
Lithuania	✓	
Luxemburg		
Malta	✓	✓
The Netherlands		✓
Norway	✓	
Poland		
Portugal		
Romania		
Slovakia	✓	✓
Slovenia	✓	
Spain	✓	✓
Sweden	✓	
Switzerland	✓	
Turkey	✓	
United Kingdom	✓	
DP experts	✓	

Dutch representative also represented ESIP, Hungarian representative also represented EURIPID

15.2.2 Written stakeholder review

Overall, different approaches in commenting the draft reports were observed between comments provided by stakeholders (associations / interest groups as defined above) and those of Member States. Since Member States representatives had already been involved in the survey about their EPR systems, they understood the sharing of the draft report as an opportunity to validate and confirm the information about their country. Comments of stakeholders, overall, were thus not country specific but more general. In some cases, the general comments provided did not necessarily refer to the draft report, but were general statements related to EPR, DP and/or pharmaceutical policies.

Among others, the study aimed to start the discussion about improvements for EPR and exploring alternative pricing possibilities, including DP. This 'pedagogic exercise' was apparently successful since the contractor received several comments, particularly from Member States, that the study helps to increase their understanding about DP. Both stakeholders and Member States expressed their pleasure to see the launch of a critical discussion about limitations of EPR by the EC through the commissioning of this report.

The different parts of the report were addressed in different frequencies. Most comments probably related to the validation of the country-specific information about EPR (usually confirming that this information was correct). For the remaining non-country specific information, considerably more comments referred to the EPR section compared to the DP section. No stakeholder comments related to the legal analysis¹²⁴. One stakeholder critically addressed the methodology of the simulations, proposing to run a dynamic instead of a static model.

General comments related to EPR were as follows:

- Several comments concerned the limitations of EPR that were generally acknowledged by both stakeholders and Member States.
- It was suggested that the non-availability of medicines should be further stressed. One stakeholder recommended considering it in the simulations, in connection with the disclosure of discounts.
- Several comments referred to the role of EPR within the menu of policy options. Stakeholders but also, to a lesser extent, Member States comments stressed that EPR should be not used as a single tool, but also and particularly with other (pricing) policies. Further, it was commented that pricing is only one part of the tools to ensure equitable access to medicines while containing costs.
- One stakeholder addressed the scope of this policy, stating that EPR should not be used for generics.

The most controversial issue related to EPR (but also addressed again in the DP sections) concerned transparency. While one stakeholder stated that elements of price information, in particular discounts, rebates, and managed-entry agreements, should be kept confidential, as this was understood as part of the business, other stakeholders and Member States opted for (full) disclosure of these price reductions.

These controversial approaches were also reflected in more specific comments related to two of the four proposals to improve EPR.

¹²⁴ However, some conclusions resulting from the legal analysis (with regard to the Council Regulation (EC) 953/2013 to trade diversion into the EU of certain key medicines (EU tiered pricing regulation)) were challenged.

The first proposal concerned an extended price database, and this appeared to be the part of the report that attracted most comments. Most comments related quite specifically to the already existing database Euripid. Member States confirmed the usefulness of that database as a supporting tool for doing EPR. Stakeholders who did not have access to the Euripid database raised concern about possible methodological limitations of that database. It was suggested that a price database should not contain price data calculated on average margins (e.g. ex-factory prices based on average wholesale margins). Stakeholders without access to the Euripid database called for a price database open to either all stakeholders or to industry only which was suggested be invited to validate the prices in Euripid. Some stakeholders and Member States addressed again the issue of confidential discounted prices, and called for the inclusion of discounts in a price database.

While there were controversial views between the commenters about confidentiality, the proposal of the study authors to consider at least published mandatory discounts in EPR was only addressed by one commenter representing a stakeholder. This proposal was challenged since mandatory discounts were seen as a temporary measure only¹²⁵.

No explicit written comments were made with regard to regular price monitoring, and only few comments related to a coordinated EPR formulae. Overall, the proposal of weighting prices by the income / wealth of the countries was welcome by several commenters, both stakeholders and Member States representatives.

General comments related to DP were as follows:

- One industry stakeholder challenged the definition for DP that was applied in the study. In line with the Tender Specifications to study a government policy measure, the study elaborated about DP in a format as a coordination measure applied by Member States, and did not consider 'Ramsey pricing' or 'price differentiation'. The stakeholder would have preferred to further include an assessment of current price differentiation by industry through granting confidential discounts to public payers.
- However, the applied definition might apparently not have been clear enough since another stakeholder expressed the concern that differential pricing could run the risk of being first and foremost used as a commercial strategy allowing pharmaceutical industry to maximise their profits.
- Some stakeholders from consumers/patients side confirmed findings of the literature reported in the study that other instruments, in particular generic competition might be more effective, not only related to cost-containment, but also for ensuring long-term access to medicines.
- Some commenters (both stakeholders and Member States) expressed concern about the feasibility of a DP scheme in Europe and doubt whether there might be sufficient political will.
- In this respect, some reflections were made of what would be the most appropriate price to start with in the DP model. One stakeholder challenged the proposal made in the report to design the DP model in a way that higher-income countries would not pay more with DP than without DP.

¹²⁵ The study authors do not agree. There are examples of mandatory discounts in European countries that have been in place for some years (e.g. Italy, Spain).

- It was felt by an industry representative that the issue of parallel trade was not sufficiently explicitly highlighted in the study.
- Concern was addressed that the Member States might be under pressure to reimburse a differentially priced product.

References related to further examples of DP initiatives were made, and it was suggested considering drawing conclusions from literature related to risks and benefits of donations.

Few specific comments were made with regard to the outline that the authors were asked to develop on how a DP scheme in Europe might look like:

- The authors were asked by a commenter (Member State) to elaborate further on the organisational aspects of a DP model in Europe.
- Another commenter (stakeholder) challenged the proposal that orphan medicines might not be a good example for a DP pilot due to their specific character.

Overall comments, not directly linked to EPR or DP, reflected the different views of power between stakeholders and Member States. While a commenter from an international organisation considered Member States in their current role as 'price takers', industry referred to the authorities as 'price setters'. Some commenters raised questions about how to establish a 'fair' EPR and DP scheme ('what is a 'fair price' for all) and about the cost of research (and their funding: 'Do societies have to pay the cost of research'). Further, the study only concerned two of the three objectives as defined in the European processes such as the Pharmaceutical Forum (see Chapter 2 on Background), i.e. access to equitable medicines and cost-containment/financial sustainability. Stakeholders felt that, though acknowledging that this was not the scope of the study, industry perspective in general and the objective of reward for innovation should also be taken into consideration.

15.2.3 Stakeholder review meeting

Some of the issues that had been raised in the written review were also addressed during the stakeholder review meeting. These included:

- The issue of transparency that was debated controversially between stakeholders (in addition, the idea was raised that different levels of transparency with regard to different target groups might be in place).
- The definition of DP (the definition of a government-fledged DP system was challenged).
- The difficulties related to defining a starting price were discussed.
- Limitations of EPR were again highlighted.
- The importance of political will as a prerequisite for starting a new pricing policy such as differential pricing was stressed.
- The scope of EPR (one stakeholder repeated that EPR should not be used for generics).
- Stakeholders asked to elaborate on the industry perspective in general and the objective of reward for innovation.
- It was repeated that prices are not the only component of pharmaceutical policies.
- The importance of other tools and policies was stressed. In particular compulsory licensing and TRIPS flexibilities were mentioned, as well as generic policies, where appropriate. Further, the importance of horizon scanning and HTA was also highlighted.

Since the stakeholder review meeting was designed in a way to allow addressing further issues (beyond the scope of the study), the following topics were debated in the meeting:

- One stakeholder mentioned the importance of managed-entry agreements, and considered them as an appropriate policy option to address current challenges, however limited capacity in countries was identified.
- Clarity on the mandate of the representatives who jointly procure on behalf of authorities was defined as a prerequisite for meaningful negotiations from industry's perspective.
- Increased pressure from the public about new treatments can influence 'technical' assessments.
- Though limitations of EPR and DP were seen, these policies should not be stopped but adjusted in a way that the ideas and elements were changed.
- Stakeholders and Member States representatives stressed the need to have a better understanding about the cost of research.

The following suggestions were made during the stakeholder review meeting:

- Improving the capacity of procurers to negotiate and to become price setters;
- Policy-makers should define what the health care system is willing, and can afford, to pay, and should then communicate this to industry (thus moving from an offer-based to a demand-based system);
- Need for finding new ways of financing;
- Moving away from the focus on medicine prices to a more comprehensive consideration of the treatments;
- Opening up the discussion on parallel trade related to medicines;
- Considering also the impact of pricing policies on the distribution (wholesale and pharmacies);
- Collaboration between countries shall consider discussing further areas of cooperation beyond pricing issues;
- Citizens and consumers should be increasingly involved;
- The EC was asked to support Member States, in disseminating information about upcoming products and technologies, and by helping countries in building capacity related to price negotiations;
- It was suggested to start research and practical pilots on the methodology for defining a 'fair' price;
- An independent review on the cost of research was requested;
- Stakeholders would highly appreciate a continuation of a multi-stakeholder dialogue as it was done in the stakeholder review meeting (the meeting was seen as a step in the right direction for enhancing dialogue and coordination).

15.2.4 Follow-up on the stakeholder review

This stakeholder review report aims to strike a balance between providing information of relevant comments of stakeholders and Member States and ensuring threshold of confidentiality.

The contractor considered all comments provided by the stakeholders and Member States in writing and in the course of the meeting and duly revisited the text of the draft report where considered appropriate.

16 Annex 16: Peer review

16.1 List of peer reviewers

The following tables provides an overview of the peer reviewers contacted in line with the methodology agreed with EC and decided in chapter 3.5.2.

Table A12: List of possible peer reviewers

Name	Institution	Country	Status
Babar, Zaheer-Ud-Din	University of Auckland	New Zealand	Written review received
Brekke, Kurt	Norwegian School of Economics	Norway	Declined to review for time constraints
Busse, Reinhard Panteli, Dimitra	University of Technology Berlin	Germany	Written review received
Danzon, Patricia	University of Pennsylvania	United States	Did not review for time constraints
Docteur, Elizabeth	Elizabeth Docteur Consulting	United States	Written review received
Espin, Jaime	Andalusian School of Public Health	Spain	Written review received
Glynn, Dermot	Europe Economics	United Kingdom	Written review received
Henry, David	University of Toronto	Canada	Declined to review for time constraints
Hollis, Aidan	University of Calgary	Canada	Written review received
Kanavos, Panos	London School of Economics	United Kingdom	Did not review for time constraints
Kyle, Margaret	Toulouse School of Economics	France	Written review received
Laing, Richard	Boston University	USA	Declined to review for time constraints
Morgan, Steve	University of British Columbia	Canada	Written review received
Rovira, Joan	University of Barcelona	Spain	Written review received
Stargardt, Tom	University of Hamburg	Germany	Declined to review for time constraints
Toumi, Mondher	University of Aix-Marseille	France	Did not review for time constraints
Towse, Adrian	Office of Health Economics	United Kingdom	Did not review for time constraints

16.2 Outcome of the peer review

The response of the peer reviewers to the report was very positive. More comments were related to EPR than to DP. Several comments reiterated the limitations of EPR and asked the authors to spell them out more explicitly.

Some comments were made to invite the authors for further specifications and explanations (e.g. related to the definition of DP, to statutory discounts), and comments included practical suggestions related to editing.

Content-wise, it was suggested by a few reviewers to acknowledge and explain how the pharmaceutical industry acts strategically in response to pharmaceutical pricing mechanisms, in particular EPR. The issue of the pharmaceutical research, currently being linked to pricing policies, was addressed by some reviewers, and authors were asked to highlight the characteristics of R&D as a public good, and the role of public funding of biomedical research. Several reviewers regretted that further policies besides EPR and DP were beyond the scope of the study. They would have welcomed a discussion about value-based pricing and HTA in the report. Overall, reviewers were concerned about the premium-priced medicines that challenged the financial sustainability of publicly funded health care systems and urged for developing alternative models to fund innovation. Most peer reviewers acknowledged a need for more transparency (while arguing about the difficulty to achieve a disclosure of discounts), and were rather positive to the implementation of a DP scheme or DP-like features.

17 Annex 17: References of the Annex

- [1] Toumi M, Rémuzat C, Vataire A-L, Urbinati D. External reference pricing of medicinal products: simulation-based considerations for cross-country coordination. Final Report. European Commission, 2014.
- [2] Babar ZUD, Atif M. Differential pricing of pharmaceuticals: a bibliometric review of the literature. *Journal of Pharmaceutical Health Services Research*. 2014;5(3): 149–56.
- [3] Bundesministerium für wirtschaftliche Entwicklung und Zusammenarbeit. Bringing Medicines to Low-Income Markets: A guide to creating inclusive business models for pharmaceutical companies. 2012.
- [4] Glaxo Smith Kline Communications and Government Affairs. GSK Public Policy Position: Tiered Pricing Approaches for Vaccines. 2014.
- [5] Steinbrook R. Thailand and the compulsory licensing of efavirenz. *New England Journal of Medicine*. 2007;356(6): 544.
- [6] Yadav P. Differential pricing of pharmaceuticals: Review of current knowledge, new findings and ideas for action. A study conducted for the UK Department for International Development (DFID). Zaragoza: MIT Zaragoza International Logistics Program, 2010.
- [7] Global Health Progress. Novo Nordisk: Differential Pricing on Insulin. Available from: <http://www.globalhealthprogress.org/programs/novo-nordisk-differential-pricing-insulin>. 2015.
- [8] Mossialos E, Dukas G. Affordably priced new drugs for poor populations: Approaches for a global solution. *International Journal of Risk & Safety in Medicine*. 2001;14(1): 1–29.
- [9] Vogler S, Schneider P. Vergütung der Arzneimitteldistribution in den europäischen Ländern. Vienna: Gesundheit Österreich Forschung und Planung GmbH (GÖ FP), 2015 (unpublished).
- [10] Vogler S, Kilpatrick K, Babar ZUD. Analysis of Medicine Prices in New Zealand and 16 European Countries. *Value in Health*. 2015;18(4): 484–492.
- [11] Kanavos PG, Vondros S. Determinants of branded prescription medicine prices in OECD countries. *Health Economics Policy and Law*. 2011;6(3): 337.
- [12] Brekke KR, Holmås TH, Straume OR. Are Pharmaceuticals Still Inexpensive in Norway? A Comparison of Prescription Drug Prices in Ten European Countries. SNF Report No. 08/10. 2010.
- [13] Gesundheit Österreich GmbH (Austrian Health Institute). Pharma Price Information (PPI) service. Further information available from: www.goeg.at/en/PPI. Vienna.
- [14] Europe Economics. External Reference Pricing. London: Europe Economics, 2013.
- [15] Konijn P. Pharmaceutical products-comparative price levels in 33 European countries in 2005. *Statistics in focus: Economy and finance*. 2007;45: 1977–0316.

- [16] Leopold C, Mantel–Teeuwisse AK, Seyfang L, Vogler S, de Joncheere K, Laing RO, et al. Impact of External Price Referencing on Medicine Prices–A Price Comparison Among 14 European Countries. *Southern Med Review*. 2012;5(1).
- [17] Leopold C, Mantel–Teeuwisse AK, Vogler S, de Joncheere K, Laing RO, Leufkens HGM. Is Europe still heading to a common price level for on–patent medicines? An exploratory study among 15 Western European countries. *Health Policy*. 2013;112: 209–16.
- [18] Danzon PM, Furukawa MF. Prices and availability of pharmaceuticals: evidence from nine countries. *Health Affairs*. 2003: W3–521.
- [19] Danzon PM, Furukawa MF. International prices and availability of pharmaceuticals in 2005. *Health Affairs*. 2008;27(1): 221–33.
- [20] European Commission. The EU Emission Trading System (EU ETS). http://ec.europa.eu/clima/publications/docs/factsheet_ets_en.pdf. Accessed 18. Juni 2015. 2013.
- [21] Coase RH. The Problem of social cost. *JL & econ*. 1960;3: 1.
- [22] Ruokonen J. Developing the EU Emission Trading Scheme: an analysis of key issues for the nordic countries. Commissioned by the Nordic Council of ministers. 2007.
- [23] Graus W, Voogt M. Report under the Project "Review of EU Emission Trading Scheme". Commissioned by European Commission. 2007.
- [24] Emission Trading Group (ETG). Administrative Cost of the Emissions Trading Scheme to Participants. A Working Group 5/6 Study, September 2008. 2008.
- [25] National Audit Office (NAO). European Union Emissions Trading Scheme. 2009.
- [26] European Commission. Impact Assessment of Directive of the European Parliament and of the Council amending Directive 2003/87/EC so as to improve and extend the EU greenhouse gas emission allowance trading system. 2008.
- [27] European Commission. Proposal for a Directive of the European Parliament and of the Council amending Directive 2003/87/EC so as to improve and extend the greenhouse gas emission allowance trading system of the Community. 2008.
- [28] Baldwin R. Regulation lite: the rise of emissions trading. *Law and Financial Markets Review*. 2008;2(3): 262–78.
- [29] Ellerman AD. The EU's Emissions Trading Scheme: A Proto–Type Global System? Harvard Project on International Climate Agreements. 2008.
- [30] Kettner C, Köppl A, Schleicher S. The EU Emission Trading Scheme: Insights from the first trading years with a focus on price volatility. WIFO Working Papers, 2010.
- [31] Desbarats J. An Analysis of the Obstacles to Inclusion of Road Transport Emissions in the European Union's Emissions Trading Scheme. Institute for European Environmental Policy: London, UK. 2009.

- [32] Fritsch M, Wein T, Ewers H-J. Marktversagen und Wirtschaftspolitik: mikroökonomische Grundlagen staatlichen Handelns; Munich: Vahlen; 2005.
- [33] Borkent B, Gilbert A, Klaasen E, Neelis M, Block K. Dynamic Allocation for the EU Emission Trading Scheme. Commissioned by the Dutch Ministry of Infrastructure & Environment and the Dutch Ministry of Economic Affairs. Utrecht: ECOFYS, 2014.
- [34] Ellerman AD, Montero J-P. The declining trend in sulfur dioxide emissions: Implications for allowance prices. *Journal of Environmental Economics and Management*. 1998;36(1): 26-45.
- [35] Baldwin R, Wyplosz C. *The Economics of European Integration*; New York: McGraw-Hill; 2009.
- [36] Swinnen JF. *The perfect storm: The political economy of the Fischler reforms of the common agricultural policy*; Ceps; 2008.
- [37] European Commission. *Overview of Cap Reform 2014-2020. Agricultural Policy Perspectives Brief*. 2013(5).
- [38] European Commission Agricultural and Rural Development. Sugar. http://ec.europa.eu/agriculture/sugar/index_en.htm. Accessed 18 June 2015. 2014.
- [39] European Commission DG AGRI. *Study to assess the administrative burden on farms arising from the CAP-Final report*. Brussels, Directorate-General for Agriculture and Rural Development (DG Agri). 2007.
- [40] Special Eurobarometer. *Europeans, Agriculture and the Common Agricultural Policy*. European Commission. 2008.
- [41] Special Eurobarometer. *Europeans, Agriculture and the common agricultural policy (CAP)*. AGRI ECD. 2014.

