EU Pharma Legislation Reform: Balancing Marketing Authorization, Environmental Risk Assessment, and IP Protection for Enhanced Innovation and Green Transition

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Abstract

This paper examines the proposed reform of European pharmaceutical legislation, with particular focus on the regulation of marketing authorization and pre-authorization environmental risk assessment, as well as the issue of industrial property rights and the proposed relaxation of patent protection. This focus serves to highlight some critical issues related to the role of investments in supporting drug research and production and might be useful for analysing the public-private relationship in the production and commercialization of pharmaceuticals, especially regarding the related impact on attracting private capital for research, innovation, and the green transition of the sector.

Keywords

EU Pharma Legislation, Marketing Authorization, Environmental Risk Assessment, IP Protection, R&D, Green Transition.

I. Context

In recent years, the sustainability of the pharmaceutical industry has attracted increasing attention from consumers, policymakers, and organizations. Since 2016,[1] numerous scientific papers have been published, showing that the presence of biologically active pharmaceutical substances in the environment, particularly detected through water studies, is now a fact.[2] The situation is a growing concern because some of these substances have shown direct and indirect effects on flora and fauna,

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[1] M. Milanesi et al, 'Pharmaceutical Industry Riding the Wave of Sustainability: Review and Opportunities for Future Research' *Journal of Cleaner Production*, 261 (2020).

[2] R.K. Singh et al, 'Strategic Issues in Pharmaceutical Supply Chains: A Review' *International Journal of Pharmaceutical and Healthcare Market*, 10, 234-257 (2016); B.M.K. Manda et al, 'Innovative Membrane Filtration System for Micropollutant Removal from Drinking Water – Prospective Environmental LCA and Its Integration in Business Decisions' *Journal of Cleaner Production*, 72, 153-166 (2014).

and therefore inevitably, on humans.[3] European institutions, seriously disturbed by the situation reported by scientists, have taken these studies into consideration and decided that studying solutions to the environmental impact of drugs during their production, use, and disposal is something for the EU to approach seriously and in an integrated manner.[4] Internationally, both the United Nations 2030 Agenda, particularly Sustainable Development Goal no 6, and the World Health Organization (WHO) stipulate commitments to act to counter the growing presence of drugs in the environment and to combat antimicrobial resistance.[5] The European Green Deal[6] also supports the adoption of measures to address pollution caused by new or particularly harmful sources, such as pharmaceuticals.

Drugs are not industrial products like any others,[7] but 'special' products, characterized primarily by their dual nature as instruments for protecting health, the supreme interest of individuals and the community, and at the same time, as potential objects of economic transactions. Their regulation, which sits at the intersection of different interests,[8] must

[3] W. Kong et al, 'Case Study on Environmental Safety and Sustainability of Pharmaceutical Production Based on Life Cycle Assessment of Enrofloxacin' *Journal of Environmental Chemical Engineering*, 9, 4 (2021); B. Blair et al, 'US News Media Coverage of Pharmaceutical Pollution in the Aquatic Environment: A Content Analysis of the Problems and Solutions Presented by Actors' *Environmental Management*, 60, 314-322 (2017).

[4] European Commission, 'European Union Strategic Approach to Pharmaceuticals in the Environment' (Communication) COM(2019) 128 final, available at https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:52019DC0128&from=ES.

[5] Antimicrobial resistance (AMR) refers to the ability of microorganisms to withstand antimicrobial treatments. The overuse or misuse of antibiotics has been linked to the emergence and spread of microorganisms which are resistant to them, rendering treatment ineffective and posing a serious risk to public health. Residues of medicinal products are widely found in groundwaters and surface waters, including coastal waters and soils, and several publications show that antibiotic residues can contribute to AMR. 'Antimicrobial Resistance' *World Health Organization*, available at https://www.who.int/health-topics/antimicrobial-resistance.

[6] European Commission, 'The European Green Deal' (Communication) COM(2019) 640 final, para 2.1.8.

[7] F. Caroccia, 'La responsabilità per danno da prodotto farmaceutico' *Annali della Facoltà Giuridica dell'Università di Camerino*, 2 (2013).

[8] In the Italian legal landscape, evidence of the aforementioned dichotomy can be found in the very law that established the National Health System, legge 23 December 1978 no 833, Art 29, which states: 'The production and distribution of drugs must be regulated according to criteria consistent with the objectives of the national health service, the social function of the drug, and the predominant public purpose of production'. The provision, in fact, first refers to the objectives of the health system, namely the protection of health as a fundamental right of the individual and an interest of the community (Art 1 of the same law), and secondly it mentions the 'social function' of the drug, an explicit reference to Art 42 of the Constitution and the social function of property that justifies its limitation.

therefore attempt to strike a difficult balance between the protection of health[9] and the protection of economic initiative[10] and competition in the pharmaceutical sector.[11] Secondly, drugs are inherently 'dangerous': compliance with protocols and rules designed to reduce risk during the manufacturing phase ensures that the drug manufacturer can obtain certification of suitability and marketing authorization, establishing a presumption of conformity and safety.

To adapt pharmaceutical regulations to the objectives of the European Green Deal and the UN 2030 Agenda, the European Union has included regulations that could have an impact on the sustainability of the sector in the proposed reform of 'general pharmaceutical legislation', i.e., the European Parliament and Council Directive 2001/83/EC[12] and Regulation 726/2004/EC.[13] The proposal follows the path traced by the 'Pharmaceutical Strategy for Europe'[14] and is based on three guidelines: first, acquiring more data on the presence and pollution of pharmaceuticals (analyses are conducted for some types of drugs, especially for human use, but not all active ingredients are monitored); second, promoting the development of innovative ecological solutions, such as new delivery systems, products with lower environmental impact, advanced waste recycling, reduction of water use, green production methods, and recyclable packaging; finally, setting up stricter pre-authorization regulations for the Environmental Risk Assessment (ERA) of drugs,[15] which, according to the European Commission, should prompt pharmaceutical companies to evaluate and limit the potential negative effects of pharmaceutical production on the environment and public health.

[9] 'The essential aim of any rules governing the production, distribution and use of medicinal products must be to safeguard public health'. European Parliament and Council Directive 2001/83/EC, Recital no 2.

[10] The legal basis referred to by the European Parliament and Council Directive 2001/83/EC is, in particular, Art 114 TFEU.

[11] A. Cauduro, *L'accesso al farmaco* (Milano: Ledizioni, 2017), 9.

[12] European Parliament and Council Directive 2001/83/EC of 6 November 2001 on the Community code relating to medicinal products for human use [2001] OJ L311/67.

[13] European Parliament and Council Regulation 726/2004/EC of 31 March 2004 laying down Union procedures for the authorisation and supervision of medicinal products for human use and establishing a European Medicines Agency [2004] OJ L136/1.

[14] European Commission, 'Pharmaceutical Strategy for Europe' (Communication) COM(2020) 761 final, available at https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:52020DC0761&from=EN.

[15] D. Gildemeister et al, 'Improving the Regulatory Environmental Risk Assessment of Human Pharmaceuticals: Required Changes in the New Legislation' *Regulatory Toxicology and Pharmacology*, 142 (2023); C.T.A. Moermond et al, 'Proposal for Regulatory Risk Mitigation Measures for Human Pharmaceutical Residues in the Environment' *Regulatory Toxicology and Pharmacology*, 143 (2023).

II. Environmental Risk Assessment (ERA): Present European Regulation and New Directive Updates on the Impact for Drug Authorization

The environmental risk assessment of drugs is a systematic process aimed at determining the potential negative impact a drug might have on the environment. This process is essential to ensure that drugs do not cause significant harm to ecosystems or public health when they enter the environment, whether during production, use, or disposal. Currently, this is provided for by the European Parliament and Council Directive 2001/83/EC, as amended, in Art 8, para 3, letter ca. It requires that the application for marketing authorization for a new drug is accompanied by a series of information and documents, including an 'Evaluation of the potential environmental risks posed by the medicinal product. This impact shall be assessed and, on a case-by-case basis, specific arrangements to limit it shall be envisaged'.

The proposal[16] to revise the current regulatory texts defines ERA as 'the evaluation of the risks to the environment, or risks to public health, posed by the release of the medicinal product in the environment from the use and disposal of the medicinal product and the identification of risk prevention, limitation and mitigation measures'. It also specifies that 'for medicinal products with an antimicrobial mode of action, the environmental risk assessment also encompasses an evaluation of the risk for antimicrobial resistance selection in the environment due to the manufacturing, use and disposal of that medicinal product'.

This assessment is conducted through a multi-stage process that starts but potentially never ends. This is because it involves a step-by-step approach, which may be affected by requests from Competent Authorities and ongoing advancements in technical, scientific, and regulatory fields, necessitating new risk assessments and updated evidence of environmental impact. Under the current regulations,[17] environmental risk assessment is mandatory[18] for all marketing authorization applications (MAA) for a medicinal product for human use (HMP). It must

[16] European Commission, 'Proposal for a Directive of the European Parliament and of the Council on the Union code relating to medicinal products for human use, and repealing Directive 2001/83/EC and Directive 2009/35/EC' COM(2023) 192 final, available at https://eur-lex.europa.eu/legal-content/EN/TXT/HTML/?uri=CELEX:52023PC0192.

[17] Currently applicable legislative acts that are expected to be affected by the revision are: European Parliament and Council Directive 2001/83/CE on the Community code relating to medicinal products for human use; European Parliament and Council Regulation 726/2004/EC laying down Union procedures for the authorisation and supervision of medicinal products for human use and establishing a European Medicines Agency.

[18] Art 8, para 3 of the European Parliament and Council Directive 2001/83/EC.

be conducted in accordance with specific EMA guidelines, last revised in 2024,[19] with the aim of 'protecting aquatic and terrestrial ecosystems including surface water, groundwater, soil, species at risk of secondary poisoning, and the risk for microbial processes in sewage treatment plants', and it is taken into account in the benefit/risk evaluation of these products. However, in any case, environmental impact is not currently a criterion for rejecting a marketing authorization.

With the proposed issuance of the new 'pharmaceutical package', stemming from the Pharmaceutical Strategy for Europe (Pharma Strategy),[20] which is already at an advanced stage, it is instead envisaged to strengthen the role of environmental risk assessment as a criterion for the marketing authorization of drugs. In particular, Art 15 of the draft Regulation,[21] titled 'Refusal of a centralised marketing authorisation', states:

> '1. The marketing authorisation shall be refused if, after verification of the particulars and documentation submitted in accordance with Article 6, the view is taken that: [...] (d) the environmental risk assessment is incomplete or not sufficiently substantiated by the applicant or if the risks identified in the environmental risk assessment have not been sufficiently addressed by the risk mitigation measures proposed by the applicant in accordance with Article 22, paragraph 3, of the [revised Directive 2001/83/EC]; [...] 2. The refusal of a Union marketing authorisation constitutes a prohibition to market the medicinal product concerned throughout the Union'.

Art 87 of the proposed Directive, on the other hand, prescribes that, even after granting marketing authorization, the competent authority of the Member State may impose on the holder of the same the obligation to carry out a study for environmental risk assessment post-authorization.

[19] Environmental risk assessment of medicinal products for human use – Scientific guideline, Current version – effective from 1 September 2024, available at https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-environmental-risk-assessment-medicinal-products-human-use-revision-1_en.pdf.

[20] European Commission, 'Pharmaceutical Strategy for Europe' COM(2020) 761 final, available at https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:52020DC0761.

Report available at https://health.ec.europa.eu/system/files/2021-02/pharma-strategy_report_en_0.pdf.

[21] European Commission, 'Proposal for a Regulation of the European Parliament and of the Council laying down Union procedures for the authorisation and supervision of medicinal products for human use and establishing rules governing the European Medicines Agency, amending Regulation (EC) No 1394/2007 and Regulation (EU) No 536/2014 and repealing Regulation (EC) No 726/2004, Regulation (EC) No 141/2000 and Regulation (EC) No 1901/2006' COM(2023) 193 final.

Moreover, it requires the collection of monitoring data or information on use if there are concerns about risks to the environment or public health, including antimicrobial resistance, due to an authorized medicinal product or a related active substance. The aforementioned provisions respond to the declared need for greater and more intense interaction between European pharmaceutical regulation and environmental regulation. This in order to balance on the one hand the need to protect the right to health, by ensuring the quality, safety, and efficacy of medicines and the possibility of accessing the best treatments, and, on the other hand, the protection of the environment, always ensuring that 'measures to address risks do not compromise access to safe and effective pharmaceutical treatments for human and animal patients'.[22]

III. Balance and Interference Between ERA Regulations for Drug Marketing Authorizations, IP Protection, and Innovation Support

1. Twin Transition in the Pharmaceutical Sector

It is interesting to note that in all the proposed amendments to pharmaceutical legislation under analysis, there is a close connection between environmental issues and innovation. It is widely stated that 'EU pharmaceutical legislation can serve as an enabling and linking factor for innovation, access, affordability, and environmental protection'.[23]

More generally, under the lens of the European 'twin transition', in all sectors, the two processes of technological and ecological transition are seen as interconnected and synergistic, as technological advancement can facilitate environmental sustainability and, at the same time, greater sustainability can stimulate innovation. But, especially in the pharmaceutical sector – currently scrutinized for the aforementioned potential environmental issues – advanced technologies and innovative practices can significantly contribute to reducing the environmental impact of the production, marketing, use, and disposal of drugs, while improving operational efficiency and product quality.[24]

[22] European Union Strategic Approach to Pharmaceuticals in the Environment, n 4 above, para 3.

[23] European Commission, 'Proposal for a Directive of the European Parliament and of the Council on the Union code relating to medicinal products for human use, and repealing Directive 2001/83/EC and Directive 2009/35/EC' COM(2023) 192 final.

[24] Many productors are working across their pipeline to foresee and prevent unintended impact of drugs. See, for example, the Novartis report describing the process of integrating ESG targets into business strategies, available at https://www.novartis.com/esg/environmental-sustainability.

In terms of sustainable production, exploration of the following solutions could ensure the sustainability of this high-impact industry: the use of biological organisms and advanced biotechnologies to produce pharmaceutical active ingredients with lower greenhouse gas emissions and less chemical waste compared to traditional methods;[25] the use of 3D printing to reduce waste and optimize material use;[26] the integration of digital technologies in supply chain management; the adoption of circular economy practices for recycling packaging materials and reusing pharmaceutical waste;[27] the use of biodegradable materials and advanced technologies for waste treatment or reduction to safely decompose pharmaceutical compounds and prevent environmental contamination; innovation in production processes;[28] and the use of smart manufacturing systems that integrate sensors and advanced automation.[29] It is for these reasons that the European Union certainly wants to support the development of drugs and manufacturing processes that are inherently less harmful to the environment. To do so, recognizes the importance of supporting research and innovation to develop 'greener'[30] drugs and processes that can more easily degrade into harmless substances in wastewater treatment plants and the environment.

2. Influence of Patents on Innovation

The inclusion of environmental risk assessment among the requirements for marketing authorization, following the consultation procedure held, was judged by some governments[31] and numerous stakeholders as disproportionate to the already high environmental standards in the pharmaceutical industry[32] and to the objectives of innovation development to benefit the marketing of green drugs. Major doubts have arisen because the environmental risk assessment regulations

[25] D. Etit et al, 'Can Biotechnology Lead the Way Toward a Sustainable Pharmaceutical Industry?' 87 *Current Opinion in Biotechnology* (2024).

[26] M. Elbadawi et al, 'Energy Consumption and Carbon Footprint of 3D Printing in Pharmaceutical Manufacture' 639 *International Journal of Pharmaceutics* (2023).

[27] L. Schenck et al, 'A Commentary on Co-Processed API as a Promising Approach to Improve Sustainability for the Pharmaceutical Industry' 113(2) *Journal of Pharmaceutical Sciences*, 306-313 (2024).

[28] Y. Chen et al, 'Optimization of Key Energy and Performance Metrics for Drug Product Manufacturing' 631 *International Journal of Pharmaceutics* (2023).

[29] F. Destro et al, 'Advanced Methodologies for Model-based Optimization and Control of Pharmaceutical Processes' 45 *Current Opinion in Chemical Engineering* (2024).

[30] K. Kümmerer, 'Increased Handling and Use Measures at the Source and Better Biodegradable Pharmaceuticals Are Necessary in the Long Run for the New Paradigm Called "Sustainable Pharmacy"' 35 *Pharmaceuticals in the Environment, Annual Review of Environment and Resources*, 57-75 (2010).

[31] The Italian government, for example.

[32] Among them are trade associations and also the American Chamber of Commerce.

in the proposed amendments are accompanied by intellectual property protection rules that provide for the modification of the regulatory data protection (RDP) rule to allow biosimilar and generic products to enter the market earlier.[33] Another concern relates to the reduction of the market exclusivity period for companies that do not make their drugs available in all EU markets.[34]

It is well known that the launch of drugs and medical devices on the market is the result of a long-term and highly uncertain process. The research and development investments required to reach this phase are substantial and are recovered through sales only over the long term.[35] Moreover, only a small percentage of products successfully pass the initial stages of experimentation and approval and the average cost of R&D for a new treatment in the pharmaceutical industry has been estimated to be between $780 million and $2.8 billion.[36] Therefore, the study and development of some drugs are not initially incentivized, at least from an economic standpoint.[37]

Consideration of the positive influence of patents on innovation and competition in the pharmaceutical industry is not unanimous; indeed, some studies question it.[38] However, the concern about the reduction in data protection and market exclusivity periods in this specific case is determined by the concurrent need to make costly efforts to obtain a complete risk assessment of drugs before they can be authorized for marketing. Consequently, pharmaceutical companies will need to invest more resources and time to conduct thorough environmental studies, which could result in a significant increase in drug development costs and extend the time to bring them to market and remunerate the effort made through commercialization, without being rewarded by a reasonable

[33] In particular, the predefined RDP period could be reduced from eight to six years. See Art 81, Proposal for a Directive, n 16 above.

[34] A reduction of two years from the ten years during which companies can sell their drugs without competition from generic rivals, adding years of 'additional protection' only if a drug is made available in all EU Member States. If a company does not make its drug available across the entire bloc, generic competitors will be able to do so. Pharmaceutical companies will also be strongly incentivized to sit at the negotiating table on prices to reach a timely agreement in each of the EU Member States.

[35] M.K. Kyle, 'Incentives for Pharmaceutical Innovation: What's Working, What's Lacking' 84 *International Journal of Industrial Organization* (2022).

[36] J.A. DiMasi et al, 'Innovation in the Pharmaceutical Industry: New Estimates of R&D Costs' 47 *Journal of Health Economics*, 20-33 (2016).

[37] E. Zuddas, 'Prime riflessioni sulla proposta di riforma della legislazione farmaceutica dell'Unione europea e il tema dei farmaci orfani' *Corti supreme e salute*, 3, 777-778 (2023).

[38] G. Dosi et al, 'Do Patents Really Foster Innovation in the Pharmaceutical Sector? Results from an Evolutionary, Agent-Based Model' 212 *Journal of Economic Behavior and Organization*, 564-589 (2023).

period of exclusive rights and data protection. All this could delay access to essential drugs, particularly for urgent conditions such as cancer, jeopardizing patient care and timely access to treatments.[39]

At the same time, the reduced protection provided by the modification of pharmaceutical industrial property rules could lead to a contraction of private investment in pharmaceutical research and development, determined by the lower profitability of the investment itself[40]. This also in consideration of the contrast to monopolies and dominant positions imposed by European competition protection rules, which might not adequately guarantee the invested capital in the pharmaceutical sector that requires large amounts of capital for R&D.

Over time, the complex of the examined policies could result in a smaller share of private capital employed in R&D, unless hefty compensation is made through public intervention.[41] European companies could thus suffer competitive disadvantages compared to countries with less stringent regulations. It should be noted that the global pharmaceutical industry is based on the massive presence of US companies,[42] which constitute the largest and most concentrated segment: among the top ten pharmaceutical companies, five are American; their revenue is equal to 60% of the total turnover of the top ten; the total revenue of American pharmaceutical companies is equal to 49.5% of the global turnover. This shows that US companies are rewarded by their strong concentration, allowing both the American industry and the top companies to maintain a dominant position in domestic and external markets.

The European market, on the other hand, accounts for about 29%, and, also due to policies against monopolistic and/or dominant positions,[43] there is significant fragmentation, as evidenced by data from the EFPIA 2022 report. Only one European company[44] is positioned among the top ten in terms of revenue.

[39] Investments in pharmaceutical research and development (R&D) have significantly increased over the past two decades; however, the rate of new drug approvals remains slow: for instance, fewer than 40 new molecules were approved each year between 1984 and 2018. See https://www.aboutpharma.com/aziende/rd-nel-farmaceutico-trasformazione-necessaria-per-restare-al-passo-con-linnovazione/.

[40] F. Gaessler and S. Wagner, 'Patents, Data Exclusivity, and the Development of New Drugs' 140 *The Review of Economics and Statistics*, 571-586 (2022).

[41] Which in Europe must be provided in compliance with the European State Aid Regulations.

[42] K. Dunleavy, 'The Top 20 Pharma Companies by 2022 Revenue' *Fierce Pharma*, Special Report (2023).

[43] Due to regulations protecting free competition among businesses.

[44] Sanofi Aventis.

However, the European pharmaceutical market is highly competitive internally and is characterized by very high levels of research and development expenditure (which increased even more after the Covid pandemic) and a consequently high number of industrial property titles.[45] If the combination of changes to the ERA, in the sense of making submission of an ERA mandatory for marketing authorization, along with the reduction of IP protection, were to negatively impact private investment in R&D, among other things, a paradoxical situation would arise where there would be fewer opportunities to develop greener drugs, as the objective of the same changes.

The debate on the dichotomy between industrial protection/innovation/access to drugs is not unknown to the Italian regulatory, jurisprudential, and doctrinal landscape. Even in 1978, the issue was addressed by a historic ruling of the Italian Constitutional Court[46] declaring the unconstitutionality of the rule[47] that prohibited the patentability of drugs.[48] Re-reading the ruling and its motivations, almost fifty years later, and evaluating the balancing of values and interests, can provide a valuable insight into attempts to give current answers to issues that, although new, have common elements with those of the past.

Among the reasons for the unconstitutionality of the rule, multiple arguments were also made concerning the need to promote scientific research. The Supreme Court noted in its ruling that 'one of the purposes of granting property rights arising from patenting is to incentivize research, covering first and foremost the substantial expenses that its organization and conduct entail'. After emphasizing that research is either financed by public bodies or by private entities, which therefore have an interest in seeing their participation remunerated, the ruling concluded that 'if the patent institute is considered socially useful in very delicate sectors of collective life, there must be reasonable grounds for differentiation to exclude such usefulness in the pharmaceutical sector'. In much more recent times, the Covid-19 pandemic and the rapid development and commercialization of various vaccines have shown how medical-pharmaceutical research and innovation can be strongly incentivized by the granting of exclusive rights obtained through

[45] M. Filippelli, 'Note introduttive', in Id, 'Concorrenza, regolazione e innovazione nel settore farmaceutico' *Concorrenza e mercato*, 28, 3-7 (2021).

[46] Corte costituzionale 20 March 1978 no 20, available at: https://giurcost.org. See the case note by C. Chiola, 'La brevettabilità dei medicamenti: dagli speziali alle multinazionali' *Giurisprudenza costituzionale*, 682 (1978).

[47] Art 14, regio decreto 29 June 1939 no 1127.

[48] R. Pardolesi, 'Sul divieto di brevettazione di farmaci' *Foro italiano (*1978); C. Casonato, 'I farmaci, tra speculazioni e logiche costituzionali' *Rivista AIC*, 4 (2017).

patenting.[49] These results seem to confirm[50] that IP protection stimulates the costly and complex innovative process, which would hardly be realized without the expectation of exclusivity over the results.

IV. Compliance of Pharmaceutical Sector Contracts with the Sustainable Development Principles and the Relevance of the DNSH Principle

1. Sustainable Development and Contracts

At this point, the question arises as to whether, in order to promote the ecological transition of the pharmaceutical industry, sector contracts can be shaped by environmental sustainability principles, and if so, how and with what consequences. It is not appropriate here to delve deeply into a civil law examination of whether the principle of sustainable development can have binding force in contractual matters. The issue is debated in Italian doctrine,[51] which is divided in two. Some believe that the principle can have horizontal application, i.e., that it can be effective in relationships between private parties, either directly[52] or indirectly through judgments based on the parameter of 'worthiness'.[53] Others assert that it is a principle that can operate only in the vertical sense, regulating the conduct of Member States and their administrative bodies.[54] While the first opinion

[49] M. Filippelli, n 45 above.

[50] On this point, however, there is no consensus. For an overview of the different positions, see: G. Ghidini, *Profili evolutivi del diritto industriale* (Milano: Giuffrè, 3rd ed, 2015), 82-94; and M. Libertini, 'Tutela a promozione delle creazioni intellettuali e limiti funzionali della proprietà intellettuale' *AIDA*, 299 (2014)

[51] P. Dell'Anno, 'Il ruolo dei principi del diritto ambientale europeo: norma d'azione o di relazione?', in D. Amirante ed, *La forza normativa dei principi (il contributo del diritto ambientale alla teoria generale*) (Padova: CEDAM, 2006), 117; G. D'Amico, 'Problemi (e limiti) dell'applicazione diretta dei principi costituzionali nei rapporti di diritto privato' *Giustizia civile*, 448 (2016).

[52] M. Pennasilico, 'La "sostenibilità ambientale" nella dimensione civil-costituzionale: verso un diritto dello sviluppo "umano ed ecologico"' *Rivista quadrimestrale di diritto dell'ambiente*, 27 (2020).

[53] M. Pennasilico, 'Dal «controllo» alla «conformazione» dei contratti: itinerari della meritevolezza' *Contratti e impresa*, 844 (2020); Id, 'La sostenibilità ambientale nella dimensione civil-costituzionale', n 52 above, 29; P. Perlingieri, '«Controllo» e «conformazione» degli atti di autonomia negoziale' *Rassegna di diritto civile*, 211 (2017); Id, 'Persona, ambiente, sviluppo', in M. Pennasilico ed, *Contratto e ambiente* (Napoli: Edizioni Scientifiche Italiane, 2016), 325; A. Jannarelli, 'Principi ambientali e conformazione dell'autonomia negoziale', ibid 19.

[54] V. Barral, 'Sustainable Development in International Law: Nature and Operation of an Evolutive Legal Norm' 377 *European Journal of International Law* (2012); F. Fracchia, *Introduzione allo studio del diritto dell'ambiente* (Napoli: Editoriale Scientifica, 2013), 118; R. Leonardi, *La tutela dell'interesse ambientale tra procedimenti, dissensi e*

remains uncertain, also due to the semantic indeterminacy that characterizes the principle of 'sustainable development' and therefore the objective difficulty in identifying the exact contours of a binding rule to be applied in private relationships, there is no doubt today about the binding nature of environmental sustainability obligations in public contracting, especially through the application of the DNSH 'Do No Significant Harm' principle.[55]

The principle, as it is used today, was introduced by the European Parliament and Council Regulation 2020/852/EU, also known as the Taxonomy Regulation, which aims to establish a framework to facilitate sustainable investments in the European Union. It stipulates that an economic activity, in order to be financed with European funds, must not cause significant harm to any of the six environmental objectives defined by the Regulation.

Art 12 of the same Regulation 2020/852/EU mentions pollution from pharmaceutical substances, stating that:

> 'An economic activity shall qualify as contributing substantially to the sustainable use and protection of water and marine resources where that activity either contributes substantially to achieving the good status of bodies of water (…) by: (a) protecting the environment from the adverse effects of urban and industrial waste water discharges, including from contaminants of emerging concern such as pharmaceuticals and microplastics, for example by ensuring the adequate collection, treatment and discharge of urban and industrial waste waters'.

In Italy, the binding nature of the DNSH principle in the allocation of public funds and public procurement is now a well-established reality following the long-standing Minimum Environmental Criteria (CAM).[56]

silenzi (Torino: Giappichelli, 2020); C. Irti, 'Gli "appalti verdi" tra pubblico e privato' *Contratto e impresa/Europa*, 204 (2017).

[55] B. Miralles et al, 'The Implementation of the "Do No Significant Harm" Principle in Selected EU Instruments' (Luxembourg: Publications Office of the European Union, 2023).

[56] These are specific measures, approved by the Decree of the Minister of the Environment and Energy Security, aimed at integrating environmental sustainability requirements for various categories of public administration tenders. They fall within the policy tools for 'green public procurement'. The use of Minimum Environmental Criteria (CAM) is referenced by decreto legislativo 31 March 2023 no 36, Art 57, para 2.

More specifically, public contracts[57] financed with PNRR[58] funds are undoubtedly subject to the application of the principle in question, for which Italy has made specific commitments to the European Commission.

In practice, funding decrees and specific technical tender documents explicitly detail the essential elements necessary for compliance with the DNSH principle,[59] and administrative mechanisms that automatically suspend payments and invoke proceedings in the case of non-compliance with the DNSH are sometimes provided. Similarly, in public procurement, administrations guide interventions to ensure conformity by including appropriate references and specific indications in their planning documents, for example through the adoption of exclusion lists and/or selection criteria in project funding notices; they include DNSH requirements in the tender specifications and contracts (and verify them during the selection phase), signed with contractors; they adopt compliant criteria to ensure adequate design and implementation of interventions; and they define the necessary documentation for any controls.

The remedies for non-compliance with these provisions differ depending on the phase of the tender to which they refer. For the public selection phase, the exclusion of competitors who do not meet the required criteria is generally provided for. Numerous court rulings enforce the application of the principle, such as the decision declaring the legitimacy of excluding a competitor from the tender procedure due to the inadmissibility of the technical offer for lack of a document identifying elements for verifying DNSH constraints in a tender for the supply of electric buses.[60]

As for the contract execution phase, non-compliance with the DNSH compliance conditions, ascertained following the monitoring and checks carried out or requested by the contracting authority, in addition to the application of penalties as stipulated in the contract, if provided, typically constitutes grounds for automatic contract termination under Art 1456 of the Civil Code.

[57] The Ragioneria dello Stato, with Circular no 32 of 2021, adopted Guidelines for compliance with the DNSH principle in public tenders, providing operational instructions to Contracting Authorities. The Guidelines were recently updated with Circular no 22 of 14 May 2024.

[58] As provided by Art 18 of the European Parliament and Council Regulation 2021/241/EU.

[59] For example, for all interventions involving the purchase of computers, electrical and electronic equipment, and servers by a public authority, management and operational guidelines are provided, including the requirement that products must have an environmental label according to the UNI EN ISO 14024 classification, or alternatively, a declaration from the manufacturer certifying that the typical energy consumption does not exceed certain predefined limits. This according with the Circular referenced in n 57 above.

[60] Tribunale amministrativo regionale Puglia 4 March 2024 no 263.

2. DNSH Principle in Pharmaceutical Contracts: A Double-edged Sword

With this said, narrowing the field of investigation to the application of the DNSH principle to pharmaceutical sector contracts, the following considerations are relevant: firstly, among the sectors provided for in the technical sheets of the 'Operational Guide for Compliance with the DNSH Principle'[61] – related to each intervention sector (e.g., the construction of new buildings, photovoltaics, cycle paths), which provide the administrations responsible for PNRR measures and the implementing bodies with a summary of operational and regulatory information identifying DNSH constraints and a checklist for verification and control for each intervention sector – the pharmaceutical sector is not included. The activities of interest that might be included could fall under sheet no 26 – 'Enterprise and Research Financing', which do not require belonging to a specific NACE code,[62] but contracts for the supply of medicines would still be excluded.

Beyond this, even hypothetically considering the introduction of specific binding provisions for DNSH compliance in tenders for the purchase of pharmaceuticals,[63] their practical implications would need to be evaluated. From this perspective, the administration's use of early termination instruments in the case of a breach of environmental obligations is not always feasible.[64] Indeed, in the specific case of pharmaceutical supply, it is inappropriate considering the peculiarity of the interests pursued. The supply of medicines to healthcare facilities serves the highest purpose of health protection and the guarantee of the broadest enjoyment of the right to pharmaceutical assistance for all citizens. The termination of contracts with such an objective – even if aimed at environmental protection goals – is not a satisfactory remedy for these interests. It is not always possible to replace the supply of a product with biosimilar or equivalent medicines produced by other suppliers since

[61] Updated with the Circular referenced in n 57 above.

[62] The NACE code (Nomenclature statistique des Activités économiques dans la Communauté Européenne) is a statistical classification code for economic activities, defined by the European Parliament and Council Regulation 1893/2006/EC.

[63] This is undoubtedly a prerogative granted to national legislators who, while respecting supranational regulations, can indeed issue legislative provisions that oblige administrations to pursue environmental interests with their procurement. This has happened, for example, with decreto legislativo 18 April 2016 no 50, which introduced the mandatory application of the Minimum Environmental Criteria (CAM) in Art 34. This provision finds even greater legitimacy after the constitutional amendment of Arts 9 and 41, which increased the importance and strengthened the role of environmental interests.

[64] E. Caruso, 'Public Procurement Between Sustainability Goals and Competitive Purposes: In Search of a New Equilibrium' *P.A. Persona e Amministrazione*, 10, 1, 298 (2022).

drugs of a certain brand, as long as they are covered by market exclusivity or defined as orphan drugs,[65] are considered irreplaceable goods.

Given the above, for the purpose of achieving environmental protection goals against pharmaceutical pollution, the contractual route does not seem to be the most suitable. For similar, albeit not identical, reasons, the implementation of the Corporate Sustainability Due Diligence Directive[66] is also not the most appropriate tool,[67] because the remedy is merely punitive/compensatory.[68]

If the European and national legislator's aim remains to reduce, if not eliminate, the presence of pharmaceutical compounds in the environment, then other instruments should be used to incentivize green production.

V. Conclusion

In the extraordinary complexity and delicacy of the topic of sustainability of the pharmaceutical industry, which intersects with areas of combating climate change, innovation, and IP protection, it is undoubtedly necessary to consider the medium- to long-term impacts of the introduced provisions, and also to evaluate them in relation to other innovations, to avoid effects worse than those that it is intended to prevent. Specifically, excessively rigid environmental assessment (making it mandatory), combined with the restriction of IP protection terms, means risking discouraging private investments in the pharmaceutical sector.

Therefore, it is essential to identify possible regulatory strategies to achieve a balance between the two needs: ensuring greater sustainability and safety in the production and marketing of drugs while not hindering research and development and private investment in innovation.

Innovation policies are traditionally divided into two categories: those that can 'pull' innovation from the private sector by making investments more profitable through increased profits from the developed products, or 'push' innovation by public entities by underwriting the associated costs.[69] Among the 'pull' policies, all strategies of patent restriction or expansion can be included. On the other hand, among the 'push' policies, there are general policies such as R&D tax credits as well as more specific grants or subsidies for specific projects with well-defined objectives.

[65] Orphan drugs are medications intended for the treatment of rare diseases that risk not being produced due to their limited use by a small number of patients, and thus being minimally profitable.

[66] European Parliament and Council Directive 2024/1760/EU.

[67] B. Saavedra Servida, 'Sostenibilità ambientale, autonomia privata e private regulation' *Dialoghi di diritto dell'economia*, 21 (2024).

[68] Arts 25 and 26.

[69] M.K. Kyle, n 35 above.

A good strategy in this regard could be, first of all, to introduce specific incentives for Sustainable Pharmaceutical Research for companies that invest in the research and development[70] of sustainable drugs, also creating special authorization regimes for State Aid.[71] It should be noted that currently, despite the peculiarities of the pharmaceutical sector, aid granted by States to companies does not have a specific regulation in European law but falls mostly within the general framework of aid for research and development.

Among the possibilities, granting tax credits,[72] which, unlike other types of aid (particularly direct subsidies), allow companies to select investment projects without orienting them and, if designed to be independent of the profitability of the research conducted, would be able to incentivize investments characterized by greater uncertainty and more modest expected returns, just as in the case of R&D activities.[73]

As for Environmental Impact Assessment, it could provide for a procedure and requirements that are proportionate and effective for the intended purposes, to avoid overburdening companies with excessive or merely formal requirements that do not add significant value to environmental protection.

A 'Fast-Track' procedure for sustainable innovations could also be considered, i.e., particularly accelerated authorization for products that demonstrate significant environmental benefits (without compromising safety and efficacy), also differentiating ERA requirements based on the product's risk class and reducing burdens for low-impact products.

More specifically, similar to the mechanisms of self-certification,[74] this 'accelerated procedure' could be considered for pharmaceutical products developed with the declared intent of bringing green innovation to the sector, in order to contribute to the sustainability goals of the industry. Simultaneously, a priority review line could be established for these products, thereby reducing the waiting times for authorizations. The implementation of a continuous, ex-post monitoring system could then allow for verification that products authorized through the 'Fast-Track'

[70] For an overview of the topic of tax incentives that can promote innovation, see P. Boria, 'La ricerca e l'innovazione industriale come fattori di una fiscalità agevolata' *Diritto e pratica tributaria*, 5, I, 1869-1911 (2017).

[71] G. Fonderico, 'Aiuti di Stato e industria dei medicinali', in M. Filippelli, n 45 above, 76.

[72] E. Olive et al, 'Do R& D Tax Credits Impact Pharmaceutical Innovation? Evidence from a Synthetic Control Approach' *Research Policy*, 53 (2024).

[73] F. Gastaldi and F. Venturini, 'Gli incentivi fiscali alla Ricerca e Sviluppo in Italia' *Ufficio parlamentare di bilancio. Focus tematico*, 8, (2022).

[74] For example, companies can currently self-certify compliance with the DNSH principle.

procedure continue to maintain the promised environmental benefits without compromising the safety and efficacy of the drug.

Regarding data protection and market exclusivity, if the current levels of data protection are maintained and compensation mechanisms implemented for companies that make their data 'open' for public research purposes, a good balance could be achieved between protecting R&D investment and market access for competing products that can offer lower prices and greater accessibility.

In sum, environmental considerations should be integrated in a way that supports rather than hinders the primary goal of providing safe and effective drugs to patients in need. Special consideration should go particularly to the medium- to long-term effects of these measures so that they do not lead to less environmental sustainability of the pharmaceutical market if it is partially depleted of private investments in R&D for green drugs.