

Bolar Exemption: Status Quo and Outlook in Light of the Italian Supreme Court's Decision of July 5, 2024

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On July 5, 2024, the Italian Supreme Court, Corte Suprema Di Cassazione, issued an important ruling for the pharmaceutical sector (BeckRS 2024, 19758).

For the first time in over a decade, a supreme national court ruled on the application of the Bolar exception, which allows generic and biosimilar manufacturers to conduct the clinical trials required for marketing authorizations under pharmaceutical law even before the patent expires. The Corte Suprema Di Cassazione ruled that contract manufacturers who are not directly involved in the approval process can also invoke this exemption, but only under strict conditions. This decision is a milestone and the first of its kind to interpret the European Bolar provisions.

I. History and issues surrounding the Bolar exemption

1The so-called Roche-Bolar rule (Bolar Exemption for short; named after the case Roche Products, Inc. Appellant, v. Bolar Pharmaceutical Co., Inc., Appellee, 733 F.2d 858, Fed. Cir. 1984.) allows drug manufacturers to conduct (clinical) studies and trials required for drug approvals during the term of a third party's patent/supplementary protection certificate (SPC). This is intended to enable a more rapid market entry of the reference drug immediately after the expiry of the property right (so-called "Day-1-Entry") and to counteract the otherwise imminent de facto extension of the property right. Without the Bolar Exemption, generic drug manufacturers would only be allowed to conduct the studies required for the approval of the generic drug in accordance with Section 24b AMG after the term of protection has expired.

Not least in response to the introduction of a Bolar exception in the US in 1984 (Art. 271 lit. e 35 USC), the EU introduced the Bolar provision in Art. 10 VI of Directive 2001/83/EC through Directive 2004/27/EC amending Directive 2001/83/EC. This created a balance at European level between patent protection and the interest of generic manufacturers in entering the market immediately after the patent expires. As a result, the EU Member States have implemented the Bolar exception into their national legal systems.

However, there are numerous uncertainties and discrepancies in the interpretation. These result in particular from the general wording of Article 10 VI of Directive 2001/83/EC (Community Code on Medicinal Products for Human Use). The wording leaves open which specific actions are excluded from the protection right and whether the

exception applies only to European marketing authorizations or also to marketing authorizations in non-European countries. It is also unclear which companies benefit from this exception, in particular whether third-party suppliers of active pharmaceutical ingredients (APIs) also benefit. However, there is agreement that the Bolar rule does not apply to commercial activities that are not related to drug approval procedures.

II. Italian court proceedings

1. Facts

4The legal dispute before the Corte Suprema Di Cassazione (hereinafter: Italian Supreme Court) concerned the infringement of Boehringer Ingelheim's patent EP 4 18 716 ("EP 716") by Sicor and its parent company Teva. The patent relates to the active ingredient "tiotropium bromide," a muscarinic receptor antagonist marketed by Boehringer Ingelheim under the brand name "Spiriva." The drug is used as a long-acting bronchodilator for the treatment of asthma. After EP 716 expired in 2010 and the associated SPC 849 expired in 2016, the legal dispute primarily concerned damages (see Mathieu Klos, Italian Supreme Court rules on Bolar exemption in Boehringer Ingelheim dispute, July 23, 2024, JUVE Patent, <https://beck-link.de/xx4 mm> accessed on September 23, 2024).

2. Italian legal situation

5Against this background, it is advantageous to first take a look at the Italian legal situation regarding the Bolar provision. The Italian Industrial Property Code (Codice della Proprietà Industriale Italiano = CPI) regulates the Bolar exception in Art. 68 I lit. b CPI. This stipulates that the exclusive rights arising from a patent do not apply to studies and trials aimed at obtaining approval for the marketing of a medicinal product, even abroad.

a medicinal product, including abroad. In addition, the resulting practical
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3. Lower courts

6Back in 2018, the Regional Court of Milan (Tribunale di Milano, decision of July 24, 2018 - No. 8273) ruled that Sicor infringed Boehringer Ingelheim's patent (see para. 4) and could not invoke the Bolar exception in this specific case. The decisive factor in determining patent infringement was the question of whether the Bolar exception also applies to third-party suppliers and contract manufacturers who produce for generic drug manufacturers but are not themselves involved in the approval process. The court

While it affirmed the applicability of the Bolar exemption to third-party providers in principle, it limited it, as the exemption only applies if the activities are closely linked to the preparation for market authorization. Third-party providers must prove that they acted at the request of a generic drug manufacturer and that the active ingredient is only used for authorization. (cf. Balestrieri/Stefanini/Ellena, Bolar exemption, UPCA and Pharma Package: what to expect? An Italian perspective, April 29, 2024, <https://beck-link.de/r625y> [accessed on September 23, 2024])

7In 2021, the Court of Appeal (Corte d'Appello di Milano, decision of June 8, 2021 - No. 1785) in Milan upheld the first-instance decision. Sicor then appealed to the Supreme Court in Rome.

4. Judgment of the Italian Supreme Court

On July 5, 2024 (Corte Suprema Di Cassazione, decision of July 5, 2024 - No. 18372) that Sicor cannot invoke the Italian Bolar exception and that by manufacturing the active ingredient "tiotropium bromide," it infringes the above-mentioned (see para. 4) patent of Boehringer Ingelheim.

a) Key content

9The Supreme Court thus dismissed Sicor's appeal. It ruled that contract manufacturers who are not directly involved in the approval process can also be included in the privilege and may manufacture APIs before the expiry of the property right. However, this only applies if there is a specific request from a generic manufacturer who is carrying out the approval procedure and provided that both parties agree that the manufacture and supply is exclusively for the purpose of obtaining marketing authorization under pharmaceutical law. Accordingly, generic manufacturers who do not have the necessary technological equipment and expertise are free to commission third-party companies to manufacture and supply the active ingredient. This activity is to be considered lawful insofar as it is carried out within the framework of obtaining marketing authorization.

10At the same time, the Supreme Court emphasizes that the Bolar exception cannot be applied per se to manufacturers or sellers of active ingredients, as such an interpretation would contradict the overriding objective of the Bolar exception, which is to strike a balance between economic freedom in a globally significant industry and the necessary protection of patent holders. The activities of the third-party manufacturer are therefore limited to passive manufacturing and delivery in execution of a specific order and may not include any marketing activities of their own (see para. 13).

11The Supreme Court then explains that Sicor and Teva had already begun producing and advertising tiotropium prior to and independently of a specific order from a generic manufacturer, meaning that the requirement for the Bolar exception established by the court was not met in this case.

12According to the Italian court, it is therefore not sufficient that the manufacture of the respective medicinal product or active ingredient is intended solely for the purpose of conducting clinical trials and is declared as such. Rather, it must be demonstrated in each individual case that the manufacture is based on a specific order from a company that is conducting trials to obtain marketing authorization for the medicinal product under pharmaceutical law. The exceptions referred to in Article 68(b) CPI relate exclusively to activities that serve to obtain marketing authorization for a medicinal product. The court emphasizes that this purpose, especially if the activity is carried out on behalf of a third party and not for its own purposes, must be clearly recognizable from the outset. In view of the wording of the Italian provision, manufacturing and distribution activities that do not yet have a specific connection to the implementation of an approval procedure are not privileged.

13Accordingly, in the opinion of the Italian court, (third-party) manufacturers may not advertise the supply of patented active ingredients, even if these are intended exclusively for use in clinical trials and are declared as such. The court points out in this regard that the manufacturer is free to advertise its activities in general. This gives a generic manufacturer interested in a specific active ingredient the opportunity to contact the company to inquire whether it is willing to manufacture this active ingredient on behalf of the generic manufacturer.

b) Effects

14The decision of the Austrian Supreme Court could also influence the future interpretation of the Bolar exception in other European countries. The Bolar regulation was intended to strengthen the competitiveness of the European generic drug industry and reduce drug costs, which it has succeeded in doing, at least in part.

15According to a study ("Resilience of Pharmaceutical Supply Chains," IW Cologne, IW Consult, and the Healthcare Supply Chain Institute on behalf of the vfa, <https://beck-link.de/m2aer> [accessed on September 23, 2024]), 68% of the production sites for active ingredients that the European pharmaceutical industry needs for its own production are located in Asian countries. ("Pharmaceutical industry warns of dependence on the Far East - EU wants to respond with new drug strategy," Handelsblatt.com, May 20, 2022. <https://beck-link.de/mnsp3> [accessed on September 23, 2024]). The situation is particularly critical for drugs such as antibiotics. (Martuscelli, Made in China

pills come with unwanted side effects for the EU, Politico.eu, April 15, 2021. <https://beck-link.de/vc4rk> (accessed September 23, 2024)] The main reason for Asia's dominant role in generic drug production is the significantly lower production costs made possible by low wages and economies of scale due to large domestic markets. Less stringent environmental regulations in these regions also contribute to the international competitiveness of local companies, and local manufacturers benefit from significantly lower patent protection. If the aim is to counteract the further outsourcing of active ingredient and drug production to China and India, it seems advisable to interpret the European Bolar regulations generously. If it can be proven that production is intended solely for the purpose of conducting clinical trials and is declared as such, or if advertising is carried out with such a reference, it seems entirely reasonable to allow this.

III. Previous national decisions in the Astellas vs. Polpharma legal dispute

Polish and German courts had already dealt with this issue in 2012 and 2013. The legal dispute between Polpharma SA and Astellas Pharma Inc. revolved around the manufacture of the active ingredient "solifenacin succinate," which fell under the scope of protection of the Astellas patent. Polpharma had advertised this active ingredient and sold it to generic drug manufacturers, whereupon Astellas sued Polpharma in Poland and Germany for patent infringement. Polpharma defended itself with the Bolar exception.

1. Germany

In 2012, the Regional Court of Düsseldorf (BeckRS 2013, 1711 = GRUR-Prax 2013, 248 [Ludwig]) ruled that Polpharma, a supplier of active ingredients, could only benefit from the Bolar exception if it was directly involved in the studies conducted by its customers. In the appeal proceedings in 2013, the Higher Regional Court of Düsseldorf (GRUR-RR 2014, 100 - Market Access Privilege = GRUR-Prax 2014, 85 [Allekotte]) broadened the interpretation of this exception and held that third-party suppliers of APIs are protected as long as the supply serves a purpose covered by the Bolar exception and the third-party supplier implements sufficient safeguards to ensure that the API is actually only used to the extent privileged. The Higher Regional Court had referred questions on this matter to the ECJ for a preliminary ruling, but the ECJ did not issue a decision because the legal dispute was settled by a compromise. (BeckRS 2014, 80947 - Astellas Pharma/Polpharma]

2. Poland

18At the same time, in 2013, the Polish Supreme Court (Sąd Najwyższy, judgment of October 23, 2013 – IV CSK 92/13) that the Bolar exception does not apply to the activities of third-party suppliers or manufacturers, even if the manufacturing is carried out for a company that acquires the active ingredient or the medicinal product within the scope of and for the purpose of conducting a marketing authorization procedure.

IV. Current relevance of the Bolar exception

19The Italian decision once again underscores the urgency of further discussion on the harmonization and significance of the Bolar rule within the EU. In view of current developments at the European level, it is essential to examine the Bolar rule in the proposed EU pharmaceutical package and in the EPGÜ.

1. EU pharmaceutical package

On April 26, 2023, the EU Commission presented a proposal (COM[2023] 192 final) for reforming pharmaceutical legislation in the EU, among other things to harmonize the Bolar regulations in the EU and facilitate market access for generic drugs. (For details, see Stief/Grabow PharmR 2023, 317) The timing and exact details of when this reform will come into force are still unclear at present.

21Article 85 of the draft directive proposes extending the Bolar exception to studies and investigations necessary for the assessment of health technologies and for pricing and reimbursement issues. In addition, the exception is to apply not only to generics and biosimilars (as is currently the case according to the wording of Article 10 IV of Directive 2001/83/EC), but also to hybrids, biohybrids, and medicinal products. Contractual partners of the applicant who conduct clinical trials under the Bolar exemption are also to be expressly privileged. The proposed Bolar regulation would thus create an expanded scope of application compared to the previous regulations. While contract manufacturers are now explicitly mentioned, it remains unclear under what conditions delivery to third parties is exempt.

2. Unified Patent Court

22The Bolar rule is found in Article 27(d) of the UPC Agreement. According to this provision, the rights conferred by a unitary patent do not extend to "acts authorized under [...] Article 10(6) of Directive 2001/83/EC, with respect to any patent covering the product within the meaning of either of those Directives." Due to the reference to Directive 2001/83/EC, it can be assumed that Article 27(d) EPC only applies to generics and biosimilars, but does not permit the clinical testing of innovative medicinal products or new indications. In addition, unlike most national regulations, the exception provided for in the EPC is geographically limited to obtaining a marketing authorization for the

The EU imposes restrictions, which seems outdated given the increasingly international nature of clinical trials and makes it impossible to conduct clinical trials in the EU for other approvals in other countries. Thus, the previously enacted EPGÜ restricts the Bolar exception more than the new proposal from the EU Commission, which contradicts the Commission's objectives and seems hardly suitable for bringing more clinical trials back to Europe. Like Section 10 III of the German Patent Act (PatG) and Article 66 2-quater of the Italian Intellectual Property Code (CPI), Article 26 III EPGÜ also stipulates that indirect patent infringers cannot invoke the Bolar exception. It remains to be seen how the EPG will interpret this

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V. Conclusion and practical advice

23It is to be welcomed that Italian case law, at least in principle, advocates the application of the Bolar exception to contract manufacturers as well, and in this respect prefers a teleological interpretation rather than one strictly based on the wording. Particularly in view of the supply bottlenecks observed in recent years and the migration of drug manufacturing to China and India, some would certainly have wished for an even more generous interpretation. However, it is understandable that the Italian courts (as ultimately the German and Polish courts before them) are struggling with the wording of the law and only consider the Bolar exception to be applicable to contract manufacturers if a concrete link to the approval procedure of a third, directly privileged company can be proven in individual cases. According to the wording and structure of the relevant legal provisions, it is plausible to only include contract manufacturers under the Bolar exception if the manufacture and supply are specifically and not just abstractly for the marketing authorization of a third party under pharmaceutical law. This makes the Commission's efforts to reform and extend the Bolar exception all the more welcome and overdue, so that European pharmaceutical manufacturing can compete internationally.

24In view of the national regulations currently still in force and the EPGÜ, contract manufacturers are well advised to offer or manufacture patent-protected drugs or active ingredients only in connection with a specific approval procedure. As a rule, suppliers should only deliver small quantities of a product for specific, privileged purposes, such as trials or market approval studies.

. This restriction should be clearly and individually formulated in the supply contract, rather than just appearing in the general terms and conditions. In addition, the supplier should check whether there are any indications that the customer could use the product for purposes other than the specified privileged purpose. In case of uncertainty, precise wording in the contract, quantity restrictions, or the requirement of a declaration of exemption by the customer are advisable. (see in detail Stief/Matschke GRUR 2021, 1241)

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