

Setbacks in Regulatory Data Protection Confront Innovative Drug Developers in the Russian Federation

The International Lawyer



Bruce McDonald

Partner, Smith, Gambrell & Russell, LLP
202-263-4362
bmcDonald@sgrlaw.com



Vladislav Ugrumov

Partner, Gowling WLG
+7 495-787-2073
vladislav.ugrumov@gowlingwlg.com



Denis Kolesnikov

Associate, Gowling WLG
+7 495-787-2070 Ext. 159
denis.kolesnikov@gowlingwlg.com

Setbacks in Regulatory Data Protection Confront Innovative Drug Developers in the Russian Federation

BRUCE McDONALD,* VLADISLAV UGRYUMOV**
AND DENIS KOLESNIKOV***

A December 2015 court decision by the Intellectual Property Court (IPC) of the Russian Federation, affirmed by the Russian Supreme Court on May 26, 2016, has introduced significant legal uncertainty for innovative drug developers in the Russian Federation.¹ In *Novartis AG v. BioIntegrator*, the IPC limited the scope of regulatory protection for investigative data filed in support of an application for marketing approval of a new drug, holding that such protection is limited to undisclosed data, and does not include data that was filed by the developer in support of its application and published in medical journals.² The IPC holding significantly curtailed the ability of drug developers to prohibit the manufacturers of a generic or biosimilar copy of the innovative drug from using their data to support its own competing application. In October 2016, the Russian Ministry of Health proposed amendments to the Law on Circulation of Medicines that would codify the ruling,³ and in January 2018, the Government of the Russian Federation released a comprehensive “Roadmap for Competition in Healthcare” that will accelerate such initiatives.⁴

* Partner, Smith, Gambrell & Russell, LLP, 1055 Thomas Jefferson St., N.W., Suite 400, Washington, D.C. 20007, tel. (202) 263-4362, bmcdonald@sgrlaw.com. The authors of this Article received partial research funding from the Pharmaceutical Research and Manufacturers of America, which represents the innovative biopharmaceutical industry. The views expressed in this Article are solely those of the authors.

** Partner, Gowling WLG, 11 Gogolevsky Boulevard, Moscow, 119019 Russia, tel. +7 495 787 2073, vladislav.ugryumov@gowlingwlg.com.

*** Associate, Gowling WLG, 11 Gogolevsky Boulevard, Moscow, 119019 Russia, tel. + 7 495 787 2073.

1. See Lisa L. Mueller, *Current State of Data Protection and Exclusivity in Russia*, THE NATIONAL LAW REVIEW (Dec. 30, 2015), <https://www.natlawreview.com/article/current-state-data-protection-and-exclusivity-russia>.

2. *Id.*

3. Anna McDonald, *Changes in the Regulatory Control of the Pharmaceutical Market – Q1 2016 Review*, LEXOLOGY (May 11, 2016), <https://www.lexology.com/library/detail.aspx?g=809cb41f-401c-4e26-912a-835ba6540ed8>.

4. Government of the Russian Federation, *Roadmap for Development of Competition in Healthcare*, January 12, 2018, No. 9-r, <http://static.government.ru/media/files/vyoWQD6EZYQkBaQKfKFKAPZqqgtmcHDH.pdf> (last accessed 02/14/2018).

This Article examines the statutory protection of data submitted by drug developers to obtain regulatory approval in the United States and the European Union, the protection afforded under the Agreement of the World Trade Organization on Trade-Related Aspects of Intellectual Property (TRIPS),⁵ and explains why the *Novartis* decision is in conflict with TRIPS and damaging to the prospects of innovation in the Russian pharmaceutical market.

I. Vulnerability of Innovative Drug Developers to Curtailment of the Patent Term

All of the developed countries and most of the developing countries in the world regulate the approval and registration of pharmaceutical products and have statutory requirements to ensure the quality, safety, and effectiveness of medicines.⁶ Of these, the majority provide innovative drug developers with a statutory period of exclusive rights to the use of the data that they submit to the government in support of such registration.⁷

The reason for protecting such data for a limited period of time is that the development of innovative medicines is exceptionally lengthy, expensive, and risky.⁸ A developer seeking approval of a new drug must begin with an investigational new drug application,⁹ including detailed data and reports of all animal and non-clinical testing performed on the drug.¹⁰ Physicians, pharmacologists, chemists, microbiologists, and statisticians must review all laboratory testing, including pharmacology and toxicology reports.¹¹ Only after the government has seen and approved these reports can clinical trials

5. Agreement on Trade-Related Aspects of Intellectual Property Rights, Apr. 15, 1994, Marrakesh Agreement Establishing the World Trade Organization, Annex 1C, 1869 U.N.T.S. 299.

6. See generally Litovkina, *Rezhim eksklyuzivnosti issledovatel'nikh dannikh: mezhdunarodnyi opit i rosiiskoe zakonodatel'stvo* [Modes of Exclusivity for Research Data: International Experience and Russian Law] 4 MEDITZINSKOE PRAVO (2011) (Russ.).

7. International Federation of Pharmaceutical Manufacturers & Associations, *Data Exclusivity: Encouraging Development of New Medicines* (2011), https://www.ifpma.org/wp-content/uploads/2016/01/IFPMA_2011_Data_Exclusivity_En_Web.pdf.

8. See Henry Grabowski et al., *Updated Trends in U.S. Brand-Name and Generic Drug Competition*, 19 J. MED. ECON. 836 (2016).

9. *The FDA's Drug Review Process: Ensuring Drugs Are Safe and Effective*, U.S. FOOD & DRUG ADMIN., <https://www.fda.gov/Drugs/ResourcesForYou/Consumers/ucm143534.htm> (last visited Nov. 6, 2014).

10. 21 U.S.C. § 355(b)(1) (2016); *Investigational New Drug (IND) Application*, U.S. FOOD & DRUG ADMIN., <https://www.fda.gov/drugs/developmentapprovalprocess/howdrugsaredevelopedandapproved/approvalapplications/investigationalnewdrugindapplication/default.htm> (last visited Oct. 5, 2017).

11. 21 U.S.C. § 355(n)(3)(b); 21 C.F.R. § 56.107; SUSAN THAUL, CONG. RESEARCH SERV., R41983, *HOW FDA APPROVES DRUGS AND REGULATES THEIR SAFETY AND EFFECTIVENESS* 5 (2012).

THE INTERNATIONAL LAWYER
A TRIANNUAL PUBLICATION OF THE ABA/SECTION OF INTERNATIONAL LAW

2018]

SETBACKS IN REGULATORY DATA PROTECTION 173

begin on humans.¹² Even passing this part of the approval process is extremely difficult, and it is estimated that “for every five thousand active pharmaceutical ingredients screened in the United States, only five will proceed to clinical testing, and only one will eventually be approved.”¹³

After trials on humans begin, the time and costs of drug development escalate.¹⁴ Clinical testing goes through multiple phases, each taking several years.¹⁵ Each phase involves an increased number of human subjects, and only after all phases are completed can a new drug application be submitted to the government for final review.¹⁶ The final review process can take another several years, and the approval of new drugs is often denied at this stage.¹⁷ Even when approval is granted, the developer’s costs continue, as information about safety and efficacy is inevitably incomplete, and some adverse reactions are discovered only after a drug has been marketed for years.¹⁸ Drug manufacturers must report all instances of adverse drug reactions regardless of whether the physician, the manufacturer, or others believe the reaction to be drug-related.¹⁹ The government retains the ability to revoke approval upon new evidence of risks, to request changes in labeling, and to issue a risk evaluation and mitigation strategy “all in the interest of consumer safety.”²⁰ Innovative drug developers, thus, have substantial regulatory costs even after approval.²¹

The regulatory approval process for innovative drugs in the United States is summarized in Table 1.

12. Veronica S. Jae, Comment, *Simplifying FDASLA: The “Fast Track” to Expedited Drug Approval Efficiency*, 66 ADMIN. L. REV. 173, 176 – 77 (2014).

13. *Id.* at 178.

14. *Id.* at 178-79.

15. *Id.*; see also *FDA’s Drug Review Process*, *supra* note 5.

16. Jae, *supra* note 8, at 178; *FDA’s Drug Review Process*, *supra* note 5.

17. David S. Torborg, Comment, *Design Defect Liability and Prescription Drugs: Who’s in Charge?*, 59 OHIO ST. L. J. 633, 662. (1998).

18. Bruce N. Kuhlik & Richard F. Kingham, *The Adverse Effects of Standardless Punitive Damage Awards on Pharmaceutical Development and Availability*, 45 FOOD DRUG COSM. L. J. 693, 696 (1990).

19. 21 C.F.R. § 312.80(a), (c) (2015) (explaining that applicants must report an “adverse drug experience,” and that an adverse drug experience is “[a]ny adverse event . . . whether or not considered drug related.”).

20. Jae, *supra* note 8, at 179.

21. *Id.* (citing 21 U.S.C. § 255(e), (o)(3)(A) (2016)); SUSAN THAUL, HOW FDA APPROVES DRUGS AND REGULATES THEIR SAFETY AND EFFECTIVENESS 8 (2012).

Table 1²²

New Drug Development Process

Phase	Description
Preclinical Investigations	Laboratory analysis; animal testing
Clinical Evaluation Phase 1	Human trials beginning with examination of pharmacologic actions and safe dosage range; how the drug is absorbed, distributed, metabolized, and excreted; and its duration of action
Clinical Evaluation Phase 2	Controlled studies in volunteers to assess the effectiveness of a drug. Simultaneous animal and human studies can continue to examine further the safety of the drug.
Clinical Evaluation Phase 3	Testing using a greater number of volunteer patients. The drug is administered by practicing physicians to those suffering from the condition the drug is intended to treat. These studies must confirm earlier efficacy studies and determine low-incidence adverse reactions.
Clinical Evaluation Phase 4	Studies conducted after approval by the Food and Drug Administration (FDA), during general use of the drug by medical practitioners. Also referred to as post-marketing studies.

In light of these requirements, the average time between the first identification of a new chemical compound and the marketing of the final product is ten to fifteen years,²³ and the average period of protection for an innovative drug following the receipt of marketing approval is only twelve to thirteen years.²⁴ As a result, the twenty-year patent term provided by international treaty is insufficient to recoup the investment in development without a stat-

22. See generally Gail A. Van Norman, *Drugs, Devices, and the FDA: Part 2*, 1 JACC: BASIC TO TRANSLATIONAL SCIENCE 277 (2016).

23. Pharmaceutical Research and Manufacturers of America, *Drug Discovery and Development: Understanding the R&D Process* (2007), http://cmidd.northwestern.edu/files/2015/10/Drug_RD_Brochure-12e7vs6.pdf; Henry Grabowski, *Follow-On Biologics: Data Exclusivity and the Balance Between Innovation and Competition*, 7 NATURE REV. DRUG DISCOVERY 479, 481 (2008).

24. See Henry Grabowski et al., *Visited Trends in U.S. Brand-Name and Generic Drug Competition*, 19 J. MED. ECON. 836 (2016). For drugs experiencing initial generic entry in 2013 – 2014, the average market exclusivity period was 12.5 years for drugs involving new molecular entities with sales greater than \$250 million (in 2008 dollars) in the year prior to generic entry, and 13.6 years overall. See *id.* See also Henry G. Grabowski & John M. Vernon, *Effective Patent Life in Pharmaceuticals*, 19 INT'L J. TECH. MGMT. 98, 116 (2000); Aaron S. Kesselheim & Jonathan J. Darrow, *Hatch-Waxman Turns 30: Do We Need a Re-Designed Approach for the Modern Era?*, 15 YALE J. OF HEALTH POL'Y, L., AND ETHICS, 293, 308 (2015), <http://digitalcommons.law.yale.edu/yjhple/vol15/iss2/2>.

tory extension of the patent term to account for a portion of the time consumed in the regulatory approval process.

The need for regulatory data protection has increased over the last decade with surging investment in pharmaceutical research and development. By 2003, the cost to develop and win marketing approval for a new drug was \$802 million.²⁵ By 2014, that number reached an astonishing \$2.6 billion, including marketing, capital costs, research and development, and recovery of losses from unsuccessful drugs.²⁶

II. Expedited Approval of Generics and Biosimilars

Many countries, including Russia and the United States, have expedited registration procedures to avoid the duplication of efforts by the producer of a generic or biosimilar drug containing the same active ingredient as the originally registered “reference” drug.²⁷ To obtain approval for the marketing of a generic or biosimilar drug, it is unnecessary to submit the results of preclinical investigations and clinical testing as a means of demonstrating its efficacy and safety, and it is sufficient, instead, to rely on data establishing the pharmacology of the drug and its “bioequivalence” to the original or “reference” drug.²⁸

The cost of obtaining marketing approval for a generic drug can be a thousand times less than the cost incurred by the developer of the reference drug. In contrast to the average \$2.6 billion investment in research, development, and regulatory approval of the innovative drug, the generic copy of the drug can be manufactured with an investment of only two to three million dollars in reverse engineering and marketing approval.²⁹

25. See Christopher P. Adams & Van V. Brantner, *Estimating the Cost of New Drug Development: Is It Really \$802 Million?*, 25 HEALTH AFF. 420 (2006), <http://content.healthaffairs.org/content/25/2/420.long>; Joseph A. DiMasi et al., *The Price of Innovation: New Estimates of Drug Development Costs*, 22 J. HEALTH ECON. 151, 180 (2003).

26. Jerry Avorn, *The \$2.6 Billion Pill—Methodologic and Policy Considerations*, 372 NEW ENG. J. MED. 1877, 1878 (2015); Joseph A. DiMasi et al., *Innovation in the Pharmaceutical Industry: New Estimates of R&D Costs*, 47 J. HEALTH ECON. 20, 27 (2016) (estimating that pre-approval R&D costs average \$2.6 billion per drug); *Cost to Develop and Win Marketing Approval for a New Drug is \$2.6 Billion*, TUFTS CTR. FOR STUDY OF DRUG DEV. (Nov. 18, 2014), http://csdd.tufts.edu/news/complete_story/pr_tufts_csdd_2014_cost_study.

27. In the United States, a generic drug manufacturer can obtain expedited approval by showing “bioequivalence” to a reference-listed drug that has already been approved by the FDA, that is, that the generic drug contains the same active ingredients, employs the same route of administration, presents the same dosage form, and exhibits the same strength as its brand name counterpart. See generally 21 U.S.C. § 355(j)(2)(A)(i) – (iii) (2016). The generic drug must be identical to its branded equivalent in “active ingredients, safety, and efficacy.” *PLIVA, Inc. v. Mensing*, 564 U.S. 604, 612 n.1 (2011). A generic drug application must also show that “the labeling proposed for the new drug is the same as the labeling approved for the listed drug.” § 355(j)(2)(A)(v).

28. See generally § 355(j)(2)(A)(i) – (iii), (v).

29. Adi Gillat, *Compulsory Licensing to Regulated Licensing: Effects on the Conflict Between Innovation and Access in the Pharmaceutical Industry*, 58 FOOD DRUG L. J. 711, 725 (2003).

THE INTERNATIONAL LAWYER
A TRIANNUAL PUBLICATION OF THE ABA/SECTION OF INTERNATIONAL LAW

176 THE INTERNATIONAL LAWYER

[VOL. 51, NO. 2

Consequently, producers of generics can push the original drug developer out of the market within several months following expiration of the patent.³⁰ An investigation of six drugs for which the period of exclusivity expired between 2009–2013 demonstrated that, within three months of such expiration, generics occupied 60 percent of the respective markets.³¹

The expedited registration of generic and biosimilar drugs is statutorily permitted only after a temporary period of regulatory data protection or “data exclusivity,” *i.e.*, the period of time during which the developer of the original drug has the exclusive right to commercial use of the data from his own investigations that he filed in his application for regulatory marketing approval.³²

Regulatory data protection provides the incentive for innovative drug researchers and developers to invest in the cost of preclinical investigations, clinical trials, and the production of data necessary for regulatory approval.³³ In the absence of government intervention in the form of data and marketing exclusivity, generic drug producers would be able to immediately reap the rewards of the investigations conducted by innovative drug developers. By “referencing” the data from innovative drug investigations without incurring expenses of producing that data, generic drug producers can offer a lower price and will push the innovative drug developer out of the market without a period of data exclusivity.

Regulatory data protection, as such, is not a privilege accorded to drug developers, but a period of time during which the regulatory barriers to the marketing of all drugs are borne equally by all applicants.³⁴ During the period of data exclusivity, *each* applicant is required to prove, prior to marketing a molecular compound or its equivalent, that the compound is safe and effective based on a full array of preclinical investigations and clinical trials that have been conducted, financed, or acquired by *that applicant*.³⁵ Data exclusivity is required in order to eliminate the loss of market share by equalizing the position of the first comer and all subsequent applicants for registration of a drug.³⁶ Data exclusivity works to the benefit not only of the innovative drug developer, but also of generic drug manufacturers, who gain the opportunity for an expedited procedure to

30. *Id.* at 717.

31. Murray L. Aitken et al., *The Regulation of Prescription Drug Competition and Market Responses: Patterns in Prices and Sales Following Loss of Exclusivity* 1 (Nat'l Bureau of Econ. Research, Working Paper No. 19487, 2013).

32. See, e.g., European Generic Medicines Ass'n., *Making Medicines Affordable*, (2010), http://www.wipo.int/mwg-internal/de5fs23hu73ds/progress?id=GRid3nCaOhBjBkFPDuztOpj2_ObPgoEYT6iImjqSkBY.

33. *Reducing Data Protection For Biologics Would Slow Medical Progress And Chill R&D Investment In The U.S.*, PHARMACEUTICAL RESEARCH AND MANUFACTURERS OF AMERICA (Oct. 2015) <https://www.phrma.org/fact-sheet/data-exclusivity-for-biologics>.

34. Erika Lietzan, *The Myths of Data Exclusivity*, 20 LEWIS & CLARK L. REV. 91, 110 (2016).

35. *Id.*

36. *Id.* at 107.

register their bioequivalent and biosimilar drugs following the period of exclusivity.

III. Data Exclusivity vs. Marketing Exclusivity

Data exclusivity is to be distinguished from the exclusive right to market a particular drug, or “marketing exclusivity.” *Data exclusivity* refers to the period during which the regulatory authority may not *examine* a subsequent application for approval of a new drug using data from the developer’s original application.³⁷ Data exclusivity does not prevent other applicants from preparing their own data to support a marketing application.³⁸ *Marketing exclusivity* refers to an additional period during which an application for approval of the generic product may be filed and examined, but not *approved*.³⁹ Both forms of exclusivity are distinct from the exclusive rights to a patent, which require the patent holder to independently identify and pursue infringers.

IV. Patent Protection Distinguished

In some cases, the period of data exclusivity coincides with the period of exclusive patent rights.⁴⁰ But, regulatory data protection is a critical supplement, not a substitute, for patent protection. Regulatory data protection augments patent protection on innovative medicines by providing temporary protection for the comprehensive package of information that biopharmaceutical innovators must submit to regulatory authorities to demonstrate the safety and efficacy of a medicine for marketing approval, providing critical incentives for investment in new treatments and cures.⁴¹

Regulatory data protection and patent protection are conceptually different. Whereas a patent affords its holder a legal right to exclude others from use of the invention claimed in the patent for a fixed period (normally twenty years), data exclusivity temporarily prohibits competitors of the innovative drug developer from relying on the test and other data submitted by the innovator to secure marketing approval.⁴² As such, producers of generics and biosimilars are not prohibited from undertaking the procedure

37. Prihodko, *Pravovoy rezhim zasbchity dannykh o rezul'tatakh doklinicheskikh i klinicheskikh issledovaniy lekarstvennykh sredstv v SSHA i YES* [Legal Regime for the Protection of Data on the Results of Preclinical and Clinical Studies of Drugs in the US and the EU], SEKTORY PRAVA (Oct. 11, 2016), <http://xn——7sbbaj7auwnffhk.xn—p1ai/article/21448> (Russ.).

38. *Id.*

39. *Id.*

40. Alexey Zalesov, *Novatory nuzhdayutsya v zasbchite* [Innovators Need Protection], ROSSIYSKAYA GAZETA (Feb. 25, 2016), <https://rg.ru/2016/02/25/otsutstvie-patentov-v-farmaceutike-zatormo-zilo-by-ee-razvitiye.html> (Russ.).

41. Lisa Diependaele et al., *Raising the Barriers to Access to Medicines in the Developing World—The Relentless Push for Data Exclusivity*, 17 DEVELOPING WORLD BIOETHICS 11, 12 (2017).

42. *Id.*

THE INTERNATIONAL LAWYER
A TRIANNUAL PUBLICATION OF THE ABA/SECTION OF INTERNATIONAL LAW

178 THE INTERNATIONAL LAWYER

[VOL. 51, NO. 2

for registration of their drugs, *provided that* they submit the results of their own investigations, even though it is ordinarily unfeasible to do so because of the time and expense.⁴³

Patent protection and data exclusivity serve different aims. While patents are necessary to stimulate innovations that meet the criteria of patentability in terms of novelty, inventive step, and industrial application, the primary purpose of data exclusivity is to stimulate the development of innovative drugs for which the active ingredients and compounds have not been previously approved by the government and to invest in investigations that confirm the safety of drugs for use in humans and their effectiveness for the cure of disease.⁴⁴

The data necessary to obtain a pharmaceutical patent is also different from that necessary for marketing approval.⁴⁵ There is substantially no correspondence between the documents and information necessary for marketing approval and that necessary to establish patentability. The purpose of data exclusivity is to stimulate the investigation and production of such additional data as is required for marketing approval but unrelated to obtaining a patent.⁴⁶

Moreover, in instances where a drug is not patentable, data exclusivity is the only means by which the drug developer can recoup its investment.⁴⁷ Many drugs are un-patentable because of the inability to comply with formal requirements, for example, where a prior publication is disclosed that defeats the novelty of the invention. In those instances, only data exclusivity can provide the incentive to market the drug. For example, if the anticancer drug Taxol (paclitaxel) were not protected by data exclusivity, then the developer, Bristol-Myers Squibb, would be unable to recoup its investment in its development, valued at more than \$500 million, and would have no incentive to market the drug.⁴⁸

Considering that the first sale of a drug occurs only ten to fifteen years after the beginning of the patent term, the remaining term of the patent is ordinarily not sufficient for the developer to recoup his investment in development of the drug. Whereas the average period on the market for an innovative drug before generic entry is only 12.5 years from the moment of first sale, even accounting for an extension of the patent term,⁴⁹ the time necessary to recoup an investment in a biologic drug is even longer,

43. *Id.*

44. *Id.* at 16-17.

45. See Gargi Chakrabarti, *Need of Data Exclusivity: Impact on Access to Medicine*, 19 J. OF INTELL. PROP. RTS. 325, 329 (2014).

46. *Id.*

47. *Id.* at 332-333.

48. *Id.* at 333. Erica Lietzan offers numerous examples where the preparation was protected under the data exclusivity regime in the absence of patents. See Erika Lietzan, *The Myths of Data Exclusivity*, 20 LEWIS & CLARK L. REV. 91, 110 (2016).

49. See Henry Grabowski et al., *Visited Trends in U.S. Brand-Name and Generic Drug Competition*, 19 J. MED. ECON. 836 (2016).

averaging from 12.9 to 16.2 years.⁵⁰ In such situations, data exclusivity serves as an essential addition to the patent term, and only by means of patent protection and data exclusivity collectively can developers be afforded the opportunity to recoup their investment in the development, investigation, and marketing of innovative drugs.

V. Regulatory Data Protection in the United States

Until 1984, generic companies in the United States were required to generate their own test data for marketing approval, and pharmaceutical patent holders could treat their own undisclosed clinical trial and other data that they submitted to the Food and Drug Administration (FDA) as trade secrets.⁵¹ The FDA protected the confidentiality of such information and prohibited generic manufacturers from “referencing” such data in order to obtain marketing approval for therapeutically equivalent products.⁵² While generic companies could have performed their own expensive, time-consuming, and duplicative clinical trials, hardly any did so because of the costs and delays, compounded by the ethical issues raised when clinical trials are repeated on human subjects where the outcomes are already known.⁵³

The Hatch–Waxman Act⁵⁴ made it easier to obtain FDA approval of generic drugs by “strik[ing] a balance between ‘two conflicting policy objectives: to induce name-brand pharmaceutical firms to make the investments necessary to research and develop new drug products, while simultaneously enabling competitors to bring cheaper, generic copies of those drugs to market.’”⁵⁵

The Hatch–Waxman Act was adopted to allow for faster introduction of generic competition in exchange for:

- limited but strictly enforced periods of regulatory data protection;
- increased rights of drug developers to restore patent terms that were shortened by clinical trials and the regulatory approval process (patent term extension); and
- a linkage system conditioning registration of generic equivalents to the absence of valid patent claims.⁵⁶

50. Henry Grabowski et al., *Data Exclusivity for Biologics*, 10 NATURE REVIEWS DRUG DISCOVERY 15, 15 (2011).

51. Brook K. Baker, *Ending Drug Registration Apartheid: Taming Data Exclusivity and Patent/Registration Linkage*, 34 AM. J. L. & MED. 303, 305 (2008).

52. *Id.*

53. *Id.*

54. Drug Price Competition and Patent Term Restoration Act of 1984 (Hatch–Waxman Act), Pub. L. No. 98-417, 98 Stat. 1585 (1984) (codified as amended at 21 U.S.C. § 355 (2017)).

55. *aiiPharma Inc. v. Thompson*, 296 F.3d 227, 230 (4th Cir. 2002) (quoting *Abbott Labs. v. Young*, 920 F.2d 984, 991 (D.C. Cir. 1990) (Edwards, J. dissenting on other grounds)).

56. Rebecca S. Eisenberg, *The Role of the FDA in Innovation Policy*, 13 MICH. TELECOMM. & TECH. L. REV. 345, 357 – 58 (2007). In Russia, there is no patent linkage; in contrast to the United States and other developed countries, innovative drug developers in Russia are not notified of marketing approval applications filed for potentially infringing products and are

THE INTERNATIONAL LAWYER
A TRIANNUAL PUBLICATION OF THE ABA/SECTION OF INTERNATIONAL LAW

180 THE INTERNATIONAL LAWYER

[VOL. 51, NO. 2

Generic companies in the United States gained from the Hatch-Waxman Act because they can now seek regulatory approval for bioequivalent drugs through an abbreviated new drug application procedure that no longer requires the duplication of investigative data and clinical trials.⁵⁷ If the generic producer can show that the generic drug has the same active ingredients and is “bioequivalent” to the original innovative drug and that the generic is manufactured according to Good Manufacturing Practice (GMP), then the generic receives regulatory approval under a quicker process.⁵⁸

In addition to relieving them from the cost of conducting duplicate investigations and clinical trials, the Hatch-Waxman Act allowed generic producers in the United States to file an application for regulatory approval of a generic drug even during the patent term of the original drug under certain conditions.⁵⁹ In addition, the first generic entrant to successfully challenge patent right claims and obtain approval is granted a six-month period of marketing exclusivity against later filed generics.⁶⁰

Innovative drug developers in the United States also gained from the Hatch-Waxman Act, winning two kinds of data exclusivity in addition to the seven-year orphan drug marketing exclusivity they obtained a year earlier.⁶¹ For innovative drugs not previously approved by the FDA, the registrant is granted five years of data exclusivity prohibiting submission of a follow-on application for regulatory approval of a generic equivalent, even if the product is unpatented or off-patent.⁶² “The five-year bar against follow-on applications is shortened to four years if the generic company is claiming patent invalidity or non-infringement.”⁶³

A shorter period of three years was enacted by the Hatch-Waxman Act whenever a new drug application is filed for a new indication for an existing drug, a new formulation or delivery system, or a new combination, if the application is accompanied by at least one new clinical investigation necessary for approval.⁶⁴ “However, unlike five-year data exclusivity, a second applicant can seek tentative approval at the FDA during the period of” three-year “exclusivity, even though final approval” is not “granted until

generally unable to secure provisional enforcement measures. See PHARMACEUTICAL RESEARCH AND MANUFACTURERS OF AMERICA, SPECIAL 301 SUBMISSION 2017 19 (2017), <http://phrma-docs.phrma.org/files/dmfile/PhRMA-2017-Special-301-Submission.pdf>.

57. Brook K. Baker, *Ending Drug Registration Apartheid: Taming Data Exclusivity and Patent/Registration Linkage*, 34 AM. J. L. & MED. 303, 305 (2008).

58. *Id.* at 305–06.

59. *Id.* at 306.

60. *Id.*

61. *Id.* An orphan drug is a pharmaceutical agent that has been developed specifically to treat a rare medical condition, the condition itself being referred to as an orphan disease. See Orphan Drug Act, 21 U.S.C. § 360 (2017).

62. Baker, *supra* note 35, at 306.

63. *Id.*

64. *Id.*

**PUBLISHED IN COOPERATION WITH
SMU DEDMAN SCHOOL OF LAW**

THE INTERNATIONAL LAWYER
A TRIANNUAL PUBLICATION OF THE ABA/SECTION OF INTERNATIONAL LAW

2018]

SETBACKS IN REGULATORY DATA PROTECTION 181

the three-year term has elapsed.”⁶⁵ Moreover, the new exclusivity only attaches to the change and does not alter the exclusivity period of the original product.⁶⁶

Fundamental to the protection of patents in the Hatch-Waxman Act was a new form of “patent linkage” involving the creation of a reference list of patented pharmaceuticals called the “Orange Book.”⁶⁷ Under this system, the producers of registered drugs record their patent claims in the FDA’s Orange Book at such time as the drugs received marketing approval.⁶⁸ If a generic producer subsequently files an application for approval of the generic equivalent, the producer has to certify for each patent: (1) that there are no conflicting patents; (2) that any relevant patents have expired; (3) that registration of the new generic would not become final until expiration of the relevant patents; or (4) that the patent is invalid or would not be infringed.⁶⁹ In the event of invalidity or non-infringement claims, the patent holder is notified and given the opportunity to bring a patent infringement action.⁷⁰ If the suit is filed within forty-five days of the notice, it triggers a thirty-month stay.⁷¹

As a result of Hatch-Waxman, “the percentage of prescription drugs filled by generics soared from 19 percent in 1984 to 74 percent in 2009,” and “[t]oday generics account for 91 percent of all prescriptions filled in the United States.”⁷²

Regulatory data protection (RDP) “is particularly critical for biologic medicines, which may not be adequately protected by patents alone.”⁷³ Made from living organisms, “biologics are so complex that it is possible for others to produce a version—or ‘biosimilar’—of a medicine that may not be covered within the scope of the innovator’s patent.”⁷⁴ The Biologics Price Competition and Innovation Act of 2009 created a pathway for approval of biosimilars, but in turn, determined that the appropriate data protection term for biologics is a period of twelve years.⁷⁵ This number was based on research demonstrating the need for incentives to ensure that “biopharmaceutical innovators and the associated global scientific ecosystem are able to sustainably pursue groundbreaking biomedical research.”⁷⁶

65. *Id.* at 306-307.

66. Drug Price Competition and Patent Term Restoration Act of 1984 (Hatch-Waxman Act), Pub. L. No. 98-417, 98 Stat. 1585 (1984) (codified as amended at 21 U.S.C. § 355 (2017)).

67. Baker, *supra* note 35, at 307.

68. *Id.*

69. *Id.*

70. *Id.*

71. *Id.*

72. *Pharmaceutical Research and Manufacturers of America (Phrma)*, Special 301 Submission 2017 (Feb. 10, 2017) at 21, <https://www.keionline.org/sites/default/files/PhRMA-2017-Special-301-Submission.pdf>.

73. *Id.*

74. *Id.*

75. 42 U.S.C. § 262 (2010).

76. Phrma, *supra* note 37, at 21.

VI. International Practice

Too many trading partners of the United States do not provide regulatory data protection.⁷⁷ “This is contrary to WTO rules, which require parties to protect regulatory test data submitted as a condition of obtaining marketing approval against both disclosure and unfair commercial use.”⁷⁸ Examples include “Algeria, Argentina, Brazil, China, Ecuador, Egypt, India, Turkey and Venezuela.”⁷⁹ “U.S. trade agreements generally require parties to provide RDP for a specified period of time, but some partner countries have not fully honored their commitments.”⁸⁰ “For example, Mexico and Peru provide RDP for small-molecule treatments, but not for biologics.”⁸¹ In Chile, protection is unavailable “for new uses, formulations, compositions[,] or dosage forms.”⁸² “Canada passed legislation in 2014 that gives the Health Minister broad discretion to share undisclosed test data without safeguards to protect against unfair commercial use.”⁸³

VII. European Union

In 1987, the European Union established terms “of data exclusivity . . . longer than those” existing in the United States at that time.⁸⁴ For medicines approved by the European Medicines Agency, data exclusivity for ten years was enacted, although Member States could enforce periods of exclusivity from six to ten years for purposes of their internal domestic registration procedures.⁸⁵

In 2005, the European Union amended its data exclusivity law in Directive 2004/27/EC.⁸⁶ The Directive introduced an 8+2+1 formula that “grants absolute data exclusivity for eight years.”⁸⁷ During this period, the generic producer can conduct testing and pre-registration activities, but it can only apply for marketing approval following the expiration of eight years.⁸⁸ Although approval can be sought during the following two-year window, the approval can only become effective upon the expiration of the full ten years.⁸⁹ In addition to this uniform ten-year term of data exclusivity, “there is an additional one-year extension for new therapeutic indications

77. *Id.*

78. *Id.*

79. Phrma, *supra* note 37, at 22.

80. *Id.*

81. *Id.*

82. *Id.* at 21-22.

83. *Id.* at 22.

84. Brook K. Baker, *Ending Drug Registration Apartheid: Taming Data Exclusivity and Patent/Registration Linkage*, 34 AM. J. L. & MED. 303, 307 (2008).

85. *Id.*

86. Council Directive 2004/27/EC; see Junod, *Drug Exclusivity Under United States and European Union Law*, 59 FOOD & DRUG L. J. 479, 510-14 (2004).

87. Baker, *supra* note 41, at 307.

88. *Id.*

89. *Id.*

filed within the first eight years,” if the drug “provides significant clinical benefits compared to existing therapies.”⁹⁰

In summary, data exclusivity has been recognized in all developed countries as an essential incentive to the development of innovative drugs. By means of data exclusivity, drugs that are proven safe, effective, and of good quality are entitled to exclusive marketing rights from the moment of regulatory approval.⁹¹ In reliance on these rights, innovative drug developers “can choose the timing and sequence of market approvals” with confidence that their exclusive rights will not be affected.⁹² “Data exclusivity is not subject to patent-style novelty requirements and is not lost, in most countries, simply because of delays in seeking regulatory approval for the marketing of a new medicine.”⁹³

VIII. Developed Countries vs. Developing Countries

To protect their populations from the health consequences of poor-quality medicines, “all developed countries and most developing countries have” enacted “quality, safety, and efficacy standards that require prior regulatory approval before a medicine can be distributed within domestic markets.”⁹⁴ Notwithstanding, most developing countries have a severely limited ability to process drug approval applications.⁹⁵ “Although some countries cooperate in regional registration agreements,⁹⁶ and others rely on proof of foreign registration”⁹⁷ or pre-qualification by the World Health

90. *Id.* at 308; Council Directive 2004/27, *supra* note 43, at art. 10.1, ¶ 4.

91. Baker, *supra* note 41, at 308.

92. *Id.*

93. *Id.*

94. *Id.*

95. *Id.* at 309; see *Effective Drug Regulation: What Can Countries Do?*, WORLD HEALTH ORGANIZATION 13 (1999), www.who.int/medicinedocs/collect/medicinedocs/pdf/s2216e/s2216e.pdf. “Another fifty percent have varying degrees of regulatory” authority, although few “can undertake start-to-finish assessment of new product dossiers.” Baker, *supra* note 41, at n.37. The remaining one-third has very limited pharmaceutical registration capacity or none whatsoever. *Id.*

96. Baker, *supra* note 41, at 309; see Sisule F. Musungu, et al., *Utilizing TRIPS Flexibilities for Public Health Protection Through South-South Regional Frameworks*, SOUTH CENTRE 65–68 (2004), <http://apps.who.int/medicinedocs/pdf/s4968e/s4968e.pdf>. “There have been regional, sub-regional, and other harmonization efforts by the Southern African Development Community (SADC), the Pharmaceutical Product evaluation Group of the Association of South-East Asian Nations (ASEAN), the Cooperation Council for the Arab States,” the Pan American Health Organization, the “Latin American Association for Integration, and the Andean Community. European harmonization is the most advanced, though there are still ongoing efforts especially concerning Accession States.” Baker, *supra* note 41, at n.38. There has also been an attempt to “harmonize standards globally through the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use,” led by the United States, the European Union, and Japan. *Id.*

97. See Rossi, *Free Trade Agreements and TRIPS-Plus Measures*, 1 INT’L INTELL. PROP. MGMT. 150, 156 (2006).

THE INTERNATIONAL LAWYER
A TRIANNUAL PUBLICATION OF THE ABA/SECTION OF INTERNATIONAL LAW

184 THE INTERNATIONAL LAWYER

[VOL. 51, NO. 2

Organization,⁹⁸ many countries, including Russia, “still require submission of safety” and efficacy data as a condition to domestic registration.”⁹⁹

Some developing countries have struggled to minimize the enactment of data exclusivity requirements. From their perspective, the international and domestic infrastructure for registering medicines is already exceptionally complicated and plagued with inefficiencies, delay,¹⁰⁰ and corruption.¹⁰¹ Registration-related difficulties arise from discrepancies between economic incentives for innovator and generic producers, and because of regulatory inefficiency and unaccountability at the national and international level.¹⁰² Registration-related barriers affecting generic manufacturers in developing countries include:

- a “lack of sufficient incentive[s] . . . , technical assistance,” and other measures enabling “generic companies to promptly register their therapeutic equivalents”;
- the “absence of fast-track registration procedures . . . to expedite registration of medicines that have been accepted by the WHO Prequalification Project or registered by a . . . regulatory authority in another country”;
- an “absence of efficient special authorization procedures” for “emergency access to important medicines while the formal registration process is . . . completed”; and
- a “lack of capacity, inefficiency, high costs, regulatory variations, and occasional corruption in national drug regulatory authorities that create delays and disincentives to both innovators and producers of generic equivalents.”¹⁰³

These registration-related barriers characterize the poorest and least developed countries more than they do the Russian Federation, where generic manufacturers are already incentivized to promptly register their therapeutic equivalents by the availability of a fast-track registration procedure.¹⁰⁴ To that extent, the danger to the Russian pharmaceutical industry inheres in the insufficient protection of data exclusivity, not excessive protection.

98. *Id.*; see *Prequalification of Medicines by WHO*, WORLD HEALTH ORGANIZATION, www.who.int/mediacentre/factsheets/fs278/en (last visited Jan. 2013).

99. Baker, *supra* note 41, at 309–310.

100. *Id.* at 310; see *The World Medicines Situation*, WORLD HEALTH ORGANIZATION 93–94 (2004), <http://apps.who.int/medicinedocs/collect/medicinedocs/pdf/s6160e/s6160e.pdf>.

101. Baker, *supra* note 41, at 310; see *MEASURING Transparency in Medicines Registration, Selection and Procurement: Four Country Assessment Studies*, WORLD HEALTH ORGANIZATION, 1 (2006), <http://www.who.int/medicines/areas/policy/goodgovernance/Transparency4CountryStudy.pdf>. “The combination of inefficiency, incapacity, and corruption has resulted in a” high incidence of “substandard and counterfeit drugs . . . in developing countries.” Baker, *supra* note 41, at n.42.

102. *Id.* at 310.

103. *Id.* at 311.

104. *Id.* at n.36.

IX. TRIPS

The United States and other developed economies sought the introduction of minimal standards of data exclusivity in the World Trade Organization (WTO) Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS).¹⁰⁵ Specifically, Article 39.3 of TRIPS provides:

Members, when requiring, as a condition of approving the marketing of pharmaceutical or of agricultural chemical products which utilize new chemical entities, the submission of undisclosed test or other data, the origination of which involves considerable effort, shall protect such data against unfair commercial use. In addition, Members shall protect such data against disclosure, except where necessary to protect the public, or unless steps are taken to ensure that the data are protected against unfair commercial use.¹⁰⁶

Pursuant to Article 39.3, member states incur two obligations under TRIPS: (a) to protect data relating to drug investigations acquired at considerable effort from unfair commercial use; and (b) to protect the confidentiality of such information.¹⁰⁷ This language must be interpreted consistent with the objectives and aims of the TRIPS Agreement in order to ensure the necessary protection of data exclusivity in the member states.¹⁰⁸

Article 39.3 of TRIPS does not expressly state whether it extends only to governmental regulatory authorities or also to nongovernmental organizations responsible for the registration of pharmaceutical products.¹⁰⁹ It stands to reason, however, that Article 39.3 must apply to nongovernmental organizations as well, otherwise it could be circumvented by outsourcing the administration of pharmaceutical product approval.¹¹⁰ Moreover, the legislation of several member states allows for the registration of a drug in the domestic market based on the results of examination conducted in a different state (or group of states).¹¹¹ In cases where government A relies on the results of previous examination by government

105. Agreement on Trade-Related Aspects of Intellectual Property Rights, Annex 1C, art. 8(1), Apr. 15, 1994, 33 I.L.M. 81, available at www.wto.org/english/docs_e/legal_e/27-trips.pdf (Marrakesh Agreement Establishing the World Trade Organization) (the “TRIPS Agreement”).

106. *Id.* at art. 39.3.

107. *Id.*

108. In agreement with Article 31 of the Vienna Convention on the Law of Treaties (1969), an agreement must be interpreted in good faith and in accordance with ordinary meaning, which should be imparted to terms of the agreement in their context, and in light of the objects and aims of the agreement. Vienna Convention on the Law of Treaties, art. 31, opened for signature May 23, 1969, 1155 U.N.T.S. 331.

109. TRIPS Agreement, *supra* note 53, at art. 39.3.

110. *Id.*

111. G. Lee Skillington & Eric M. Solovy, *The Protection of Test and Other Data Required by Article 39.3 of the TRIPS Agreement*, 24 Nw. J. INT’L L. & Bus. 1, 24 – 25 (2003).

B, government A has an obligation to protect the registration data submitted to government B, which acts in the capacity as an agent of government A.¹¹²

For example, Article 39.3 extends regulatory data protection to pharmaceutical products containing “new chemical entities,” but does not indicate in which sense the drafters intended the word “new” to function in this clause, *i.e.*, whether the word refers to patentable novelty.¹¹³ But, the word “new” must be understood as a reference to chemical substances that have not already been approved by the government because interpreting the word “new” as a reference to patentable novelty would contradict the aim of Article 39.3, inasmuch as the standards of protection for undisclosed information appear in Section 7 of TRIPS, apart from the treatment of patent rights in Section 5.¹¹⁴ Consequently, “new” for purposes of Article 39.3 of TRIPS can only mean a chemical compound that previously was not registered in that WTO member state, regardless of its patentability.¹¹⁵

It is further unclear from the language of Article 39.3 whether the provision extends only to “undisclosed” data, that is, data not publicly accessible.¹¹⁶ According to Article 39.3, the protection extends not only to “undisclosed” data but also to other information the acquisition “of which involves a considerable effort.”¹¹⁷ But, in the pharmaceutical industry, the results of drug investigations are universally published, and such information is routinely used for the registration of new pharmaceutical products as well as the expedited approval of generic equivalents and biosimilars.¹¹⁸ Ethical requirements requiring the publication of clinical investigation results are also established in Paragraph 36 of the Helsinki Declaration of World Medical Association of 1964.¹¹⁹ Additionally, the label instructions of

112. *Id.* at 25.

113. *Id.*

114. *Id.* at 26.

115. *Id.*

116. Agreement on Trade-Related Aspects of Intellectual Property Rights art. 39.3, Apr. 15, 1994, Marrakesh Agreement Establishing the World Trade Organization, Annex 1C, 1869 U.N.T.S. 299, www.wto.org/english/docs_e/legal_e/27-trips.pdf.

117. *Id.*

118. See Skillington, *supra* note 54, at 24–30.

119. World Medical Association [WMA], WMA Declaration of Helsinki—Ethical Principles for Medical Research Involving Human Subjects, at ¶ 36 (June 1964), [http://irb.sinica.edu.tw/doc/regulation/DECLARATION%20OF%20HELSINKI%20\(2013\).pdf](http://irb.sinica.edu.tw/doc/regulation/DECLARATION%20OF%20HELSINKI%20(2013).pdf) [hereinafter the Helsinki Declaration]. As stated in the Helsinki Declaration, “Researchers, authors, sponsors, editors and publishers all have ethical obligations with regard to the publication and dissemination of the results of research. Researchers have a duty to make publicly available the results of their research on human subjects and are accountable for the completeness and accuracy of their reports. All parties should adhere to accepted guidelines for ethical reporting. Negative and inconclusive as well as positive results must be published or otherwise made publicly available. Sources of funding, institutional affiliations and conflicts of interest must be declared in the publication. Reports of research not in accordance with the principles of this Declaration should not be accepted for publication.” *Id.*

THE INTERNATIONAL LAWYER
A TRIANNUAL PUBLICATION OF THE ABA/SECTION OF INTERNATIONAL LAW

2018]

SETBACKS IN REGULATORY DATA PROTECTION 187

pharmaceutical products are required to include information about the results of investigations involving the product.¹²⁰

The protection of regulatory data pursuant to Article 39.3, therefore, would lose all meaning, and would suffer from an internal contradiction, if regulatory data protection terminated every time part of the information became publicly accessible. Article 39.3 is intended to create an incentive for developers to offer safe and effective pharmaceutical products in the maximum possible number of markets.¹²¹ If protection were afforded only to undisclosed results, then, after registration of the product in the first members state where protection was sought and publication of the investigative data in that country, the developer would lose the possibility to obtain protection of its data in all other member states, and consequently would lose the incentive to offer pharmaceutical products in the markets of those countries.¹²²

Moreover, if data exclusivity terminated every time information became publicly accessible, developers would be vulnerable to unfair commercial practices by competitors, who could publish investigative data obtained, for example, through industrial espionage, or violation of a confidentiality agreement, for the purpose of depriving the developer of the opportunity to avail itself of regulatory data protection. Developers would lose the incentive to conduct investigations if they knew that any event resulting in the disclosure of the data would cut short the period of exclusivity.

Similarly, to qualify for protection under Article 39.3 of TRIPS, the acquisition of data must “involve considerable effort.”¹²³ But, the effort need not have been expended in the country where subsequent registration is sought if it was expended in the country where registration was originally approved.¹²⁴ Thus, the development and marketing of *any* new pharmaceutical product requires “considerable effort” in terms of the financial and time commitments required to conduct preclinical investigations and clinical trials.

In cases where “considerable effort” is established, WTO member states must protect such data from “unfair commercial use.” Interpreting that phrase in context as required by Article 31 of the Vienna Convention, the

120. Federal Law of the Russian Federation on Circulations of Medicine, art. 27, 2010, No. 61-FZ.

121. TRIPS Agreement, *supra* note 55, at art. 39.3.

122. *Id.* The strategy of the developer in that instance would lie in the introduction of the product in markets with the highest-income consumers and the longest period of data exclusivity, that is, in the European Union and the United States, but not in the marketing of developing countries. *See id.* That is because, if Article 39.3 is interpreted in such a way that any publication of undisclosed data in country A bars data exclusivity in country B, then innovative drug developers will always choose an EU country or the United States, where they would obtain data exclusivity first, inasmuch as the period of protection is longer there, instead of registering their drugs in Russia where the period of protection is shorter. *See id.*

123. TRIPS Agreement, *supra* note 55, at art. 39.3.

124. G. Lee Skillington & Eric M. Solovy, *The Protection of Test and Other Data Required by Article 39.3 of the TRIPS Agreement*, 24 Nw. J. INT'L L. & BUS. 1, 28–29 (2003).

unauthorized use of data from prior preclinical investigations and clinical trials to support an application for registration of a generic equivalent prior to expiration of the data exclusivity meets both criteria, i.e., it is both unfair and a commercial use.¹²⁵

The term “unfair” in Article 39.3 of TRIPS must likewise be interpreted in the context of the “considerable efforts” by the developer to obtain the data.¹²⁶ In this context, producers of generics are “free riders”¹²⁷ vis-à-vis innovative drug developers inasmuch as they exploit the results of research and investigation in which they did not invest.¹²⁸ Moreover, due to the expense of preclinical investigations and clinical trials, producers of generics are advantageously situated from the very beginning in comparison to the developers because they can offer lower prices for their products.¹²⁹ And the use of such data by the generic manufacturer has an unquestionably commercial character inasmuch as it is directed at the marketing and sale of the manufacturer’s own product and corresponding profit.

The TRIPS Agreement does not provide for a universal period of data exclusivity.¹³⁰ The average period of protection in the member states is between five and twelve years.¹³¹ As noted above, the countries of the European Union recognize a ten-year period of exclusivity; in Canada, data is protected for eight years; in Russia and China, the period of exclusivity is six years; and it is five years in Egypt, Chile, New Zealand, Malaysia, Mexico, Morocco, Peru, Jordan, Oman, Singapore, Taiwan, and Vietnam.¹³² In some of these countries, however, meaningful regulatory data protection exists on paper but not in practice.

X. Russian Legislation

Russia became a member of the WTO on August 22, 2012, taking on the obligation to bring its national legislation into conformance with the

125. *Id.* at 28; Vienna Convention on the Law of Treaties, art. 31, opened for signature May 23, 1969, 1155 U.N.T.S. 331.

126. TRIPS Agreement, *supra* note 55, at art 39.3.

127. The term “free-rider” (*bezbiletnik* in Russian) is a party who received benefit from the efforts undertaken by another party without paying for them. See Jennifer E. Sturiale, *Hatch-Waxman Patent Litigation and Inter Partes Review: A New Sort of Competition*, 69 ALA. L. REV. 59, 72-73 (2017) (discussing free rider problem).

128. Skillington, *supra* note 59, at 30.

129. *Id.* at 8.

130. TRIPS Agreement, *supra* note 55. An earlier draft of TRIPS provided for a five-year minimum period for exclusivity of data, which was deleted from the final version of the Agreement. See Gargi Chakrabarti, *Need of Data Exclusivity: Impact on Access to Medicine*, 19 J. OF INTELL. PROP. RTS. 325, 333 (2014).

131. U.S. Chamber of Commerce Global Intellectual Property Center, *Heading in a Different Direction? The European Medicine Agency’s Policy on the Public Release of Clinical Trials Data*, (2014) at 11-12, <http://www.theglobalipcenter.com/wp-content/uploads/2014/05/EMA-Study-COMplete.pdf>.

132. *Id.*

THE INTERNATIONAL LAWYER
A TRIANNUAL PUBLICATION OF THE ABA/SECTION OF INTERNATIONAL LAW

2018]

SETBACKS IN REGULATORY DATA PROTECTION 189

requirements of TRIPS.¹³³ As stated in the Report of the Working Group on Accession of the Russian Federation to the WTO:

The representative of the Russian Federation confirmed that the Russian Federation had enacted legislation and would adopt regulations on the protection of undisclosed information and test data, in compliance with Article 39.3 of the WTO TRIPS Agreement, providing that undisclosed information submitted to obtain marketing approval, i.e., registration of pharmaceutical products, would provide for a period of at least six years of protection against unfair commercial use starting from the date of grant of marketing approval in the Russian Federation. During this period of protection against unfair commercial use, no person or entity (public or private), other than the person or entity who submitted such undisclosed data, could without the explicit consent of the person or entity who submitted such undisclosed data rely, directly or indirectly, on such data in support of an application for product approval/registration. Notice of subsequent applications for registration would be provided in accord with established procedures. During the six year period, any subsequent application for marketing approval or registration would not be granted, unless the subsequent applicant submitted his own data (or data used with the authorization of the right-holder) meeting the same requirements as the first applicant, and products registered without submission of such data would be removed from the market until requirements were met. Further, he confirmed that the Russian Federation would protect such data against any disclosure, except where necessary to protect the public or unless steps were taken to ensure that the data were protected against unfair commercial use.¹³⁴

In its 2012 Report to the WTO, the Russian Federation confirmed that it would provide protection against the disclosure and unfair commercial use of undisclosed data and investigative results submitted in support of an application for approval of new drugs for a period of six years.¹³⁵ The representative of the Russian Federation specifically pointed out that during this period of exclusivity applicants for approval of generic and biosimilar pharmaceutical products must submit the same information about the results of clinical investigations establishing safety and effectiveness that was required of the first party who filed an application for such registration, and that products submitted for registration without the filing of such data will be prohibited from the market.¹³⁶

133. *Russian Federation*, WORLD TRADE ORGANIZATION, https://www.wto.org/english/thewto_e/acc_e/a1_russie_e.htm (last visited Oct. 13, 2017).

134. Working Party on the Accession of the Russian Federation, *Report of The Working Party on The Accession of The Russian Federation to the World Trade Organization*, ¶ 1295, WTO Doc. WT/ACC/RUS/70 (Nov. 17, 2011).

135. *Id.* ¶ 1295–96.

136. *Id.* ¶ 1296.

THE INTERNATIONAL LAWYER
A TRIANNUAL PUBLICATION OF THE ABA/SECTION OF INTERNATIONAL LAW

In order to conform its domestic legislation to Article 39.3 of TRIPS, Federal Law No. FZ-61, “On the Circulation of Medicines,” was enacted on October 11, 2010.¹³⁷ Article 18.6 of the 2010 law prohibited the unauthorized receipt, disclosure, commercial use, and use in an application for government registration of information about the results of preclinical investigations and clinical trials of pharmaceutical products submitted by an applicant for government registration of such products during the course of six years from the date of government registration of the pharmaceutical product.¹³⁸ An explanatory note to the law indicated that the requirement was directed at the development of the domestic pharmaceutical industry and increasing the level of innovation.¹³⁹

The language in Article 18.6 of the 2010 law raised several issues. First, it was not clear from the language whether data exclusivity extended to the first registered product, and second, it was unclear whether the producers of generics could file applications for registration of their products during the period of data exclusivity.¹⁴⁰ In other words, the language of the law in 2010 failed to clarify whether the six-year period was for *marketing* exclusivity or *registration* exclusivity.¹⁴¹

On January 1, 2016, amendments to Article 18 of the Law on Circulation of Medicines went into effect.¹⁴² Under the amended law, which was purportedly enacted to bring Russian legislation into compliance with TRIPS, regulatory data protection is expressly extended to data about the reference medicine, where a reference medicine is defined as “a medicine which previously has never been registered in Russia, whose quality, efficacy and safety have been confirmed by the results of preclinical and clinical trials and which is used for the assessment of bioequivalence or therapeutic equivalence, quality, efficacy and safety of a generic (or biosimilar) medicine.”¹⁴³

The January 2016 amendments to Article 18, however, undermine the scope of regulatory data protection by allowing a registration application for a generic or biosimilar to be filed upon the expiration of only four years following the marketing authorization for a reference small molecule drug

137. Federal Law of the Russian Federation on Circulations of Medicine, 2010, No. 61-FZ.

138. *Id.* at art. 18.6.

139. *Zakonoprojekt ? 426962-5:O vnesenii izmeneniy v Federal'nyy zakon "Ob obrashchenii lekarstvennykh sredstv"* [Bill No. 426962-5: On Amending the Federal Law “On the Circulation of Medicines”], GOSUDARSTVENNAYA DUMA FEDERAL'NOGO SOBRANIYA ROSSIYSKOY FEDERATSII [THE STATE DUMA OF THE FEDERAL ASSEMBLY OF THE RUSSIAN FEDERATION], [http://asozd2.duma.gov.ru/main.nsf/\(Spravka\)?OpenAgent&RN=426962-5](http://asozd2.duma.gov.ru/main.nsf/(Spravka)?OpenAgent&RN=426962-5) (last visited Oct. 29, 2017) (containing the explanatory record).

140. Federal Law of the Russian Federation on Circulations of Medicine, *supra* note 65, at art. 18.6.

141. *Id.*

142. Lisa L. Mueller, *Current State of Data Protection and Exclusivity in Russia*, THE NATIONAL LAW REVIEW (Dec. 30, 2015), <https://www.natlawreview.com/article/current-state-data-protection-and-exclusivity-russia>.

143. *Id.*

and three years after marketing authorization of a reference biologic medicine.¹⁴⁴ The 2016 amendments separate the six-year period of data exclusivity into “registration exclusivity” (commonly known as “data exclusivity”) and “marketing exclusivity.”¹⁴⁵

As such, the amended Russian law provides four years of registration exclusivity plus two years of marketing exclusivity for generic drugs and three years of registration exclusivity plus three years of marketing exclusivity for biosimilars.¹⁴⁶ During the period of “registration” or “data exclusivity,” the Ministry of Health will not examine an application for registration of a generic product pursuant to the abbreviated procedure.¹⁴⁷ During the remaining period of “marketing exclusivity”—two years for generics and three years for biosimilars—the Ministry of Health may examine an application, but may not register the product prior to expiration of the marketing exclusivity.¹⁴⁸

Although the new law extends the protection of data exclusivity to the prior registered reference drug, the law now extends only to the unauthorized “commercial use” of such data.¹⁴⁹ References to the unauthorized “receipt,” “disclosure,” and “use in an application for government registration” of such data are absent from the amended language.¹⁵⁰ The new law prohibits only the unauthorized commercial use of the results of preclinical investigations and clinical trials of pharmaceutical products submitted by an applicant for government registration of such products during the course of six years from the date of government registration of the medicinal preparation.¹⁵¹

XI. Novartis AG v. BioIntegrator

In 2014, the Swiss company Novartis Pharma AG brought an action against the Russian company BioIntegrator.¹⁵² Having developed an innovative drug named Fingolimod for the treatment of diffuse sclerosis, marketed under the brand name Gilenya, Novartis registered the drug with the Russian Ministry of Health.¹⁵³ BioIntegrator, before the period of exclusivity for Gilenya expired, filed an application to register a generic

144. Vladimir Sokov, et al., *Amendments to the Law on Circulation of Medicines*, TERRALEX (Mar. 16, 2015), <https://terrallex.org/publication/p0f578a7d0a/amendments-to-the-law-on-circulation-of-medicines>.

145. Mueller, *supra* note 66.

146. *Id.*; see Federal Law of the Russian Federation on Circulations of Medicine, *supra* note 65, at art. 18.

147. See Mueller, *supra* note 66.

148. See *id.*

149. *Id.*

150. *Id.*

151. *Id.*

152. Novartis AG v. BioIntegrator, Verhovnyi Sud Rossiiskoi Federatsii [Verkh. Sud RF] [Russian Federation Supreme Court] 2016, No. A40-188378/2014).

153. See *id.*

THE INTERNATIONAL LAWYER
A TRIANNUAL PUBLICATION OF THE ABA/SECTION OF INTERNATIONAL LAW

192 THE INTERNATIONAL LAWYER

[VOL. 51, NO. 2

equivalent of Fingolimod, marketed under the name Neskler, pursuant to the abbreviated procedure for generic and biosimilar drugs.¹⁵⁴ Novartis then brought a court action seeking a declaration that BioIntegrator's application for approval of its generic drug was invalid, and an order prohibiting the Ministry of Health and BioIntegrator from using the results of Novartis's preclinical investigations and clinical trials for its product.¹⁵⁵

The Moscow Arbitration Court, in a decision dated March 20, 2015, sidestepped a discussion of data exclusivity per se and focused, instead, on the time when the defendant filed its application.¹⁵⁶ The court held that data exclusivity protection did not apply because the application for registration of the generic was filed prior to August 22, 2012, the date when Russia became a member of the WTO.¹⁵⁷

On appeal to the Ninth Circuit Arbitration Court of Appeals by Novartis, the appellate court rejected the decision of the lower court in a decision dated August 14, 2015, finding that the original application for registration of the generic drug, although filed prior to the effective date of the law, was filed by a different legal entity, ZAO "Research Institute of Chemical Diversity," and that the law did not allow for the assignment of the right to file an application for registration of a pharmaceutical product from one entity to another.¹⁵⁸ In the opinion of the appellate court, affirmed by the court of cassation, the application of BioIntegrator, having been filed after the effective date of the law, was independent from the earlier application filed by the Research Institute, and, accordingly, was subject to the provisions on data exclusivity.¹⁵⁹

In granting Novartis's petition, the appellate court analyzed the scope of information protected by data exclusivity. The court held that exclusivity "extends to any information about the applicant's conduct of preclinical investigations and clinical trials involved in the application for government registration of the product regardless of whether it was published or not."¹⁶⁰ BioIntegrator then appealed to the Intellectual Property Court of the Russian Federation (IPC).¹⁶¹

The IPC, in a decision dated December 17, 2015, reversed the appellate courts and reinstated the decision of the Moscow Arbitration Court, holding that "the prohibition set forth by Part 6, Article 18 of the Law 'On the Circulation of Medicines' does not apply to information published in

154. *See id.*

155. *See id.*

156. *See id.*

157. *Novartis AG v. BioIntegrator*, Verhovnyi Sud Rossiiskoi Federatsii [Verkh. Sud RF] [Russian Federation Supreme Court] 2016, No. A40-188378/2014).

158. *See id.*

159. *See id.*

160. *IP Court Interpreted Some Aspects of Data Exclusivity*, LIDINGS (Dec. 29, 2015), <http://www.lidings.com/eng/legalupdates2?id=257>.

161. *See Mueller, supra* note 66.

THE INTERNATIONAL LAWYER
A TRIANNUAL PUBLICATION OF THE ABA/SECTION OF INTERNATIONAL LAW

2018]

SETBACKS IN REGULATORY DATA PROTECTION 193

specialized printed journals.”¹⁶² The IPC rejected Novartis’s suit on the grounds that the data about the effectiveness of the generic product submitted by BioIntegrator to the Ministry of Health was based on information that had previously been published in scientific journals describing the results of clinical trials in connection with Gilenya.¹⁶³ The IPC held that the Russian data exclusivity statute protects only *undisclosed* data, and that as soon as information is published, it may be freely used for the registration of generics.¹⁶⁴

The IPC’s decision in *Novartis* is problematic because it allows a generic producer to rely indirectly on the innovator’s registration by referencing the data reported in scientific journals about the product following its approval, and thereby to seek marketing approval for its own follow-on product during the period of regulatory data protection. The *Novartis* decision is in conflict with the Russian Law on Circulation of Medicines *and* TRIPS, and, further, is conducive to bad faith conduct by producers of generic drugs. First, Article 18.6 of the law prohibits the use of *any* information developed at considerable effort in relation to preclinical investigations and clinical trials submitted in an application for registration of a pharmaceutical product. That is, the law refers not to the use of specific documents in the application package but expressly extends to all information used in the government registration.¹⁶⁵

Second, publishing the results of investigations and trials is universal in the pharmaceutical industry. The unconditional publication of such information ensures the openness, transparency, and accountability of such results and provides doctors and patients with maximum access to information about pharmaceutical products. Following the interpretation of the IPC to its conclusion would require a finding that Article 18.6 of the law, at the moment of its enactment, failed to extend any protection whatsoever inasmuch as *all* of the information about the investigative results, which previously had to be submitted as part of the application for registration of the original product, was already published and would not be subject to protection.

Despite decisions from the lower courts holding the Russian Ministry of Health to WTO standards in its interpretation of regulatory data protection requirements,¹⁶⁶ the decision of the IPC in *Novartis* is a harmful precedent to innovative drug developers and generic manufacturers alike. Concerns

162. *See id.*

163. *See id.*

164. *See id.*

165. *IP Court Interpreted Some Aspects of Data Exclusivity*, LIDINGS (Dec. 29, 2015), <http://www.lidings.com/eng/legalupdates2?id=257>.

166. In the recent *Trakten* case, for example, a Russian generic producer named Farnasintez filed an application with the Ministry of Health for registration of *Trakten*, a generic version of *Atripla*, an innovative drug for the treatment of HIV registered by Gilead Sciences International, Ltd. The Ministry of Health rejected the application on the grounds that it covered a reference drug and was impermissibly filed prior to expiration of the four-year period of data exclusivity. The Ministry’s decision was affirmed on March 31, 2017 by the Arbitration

stemming from the decision are amplified by statutory amendments to the Law on Circulation of Medicines, proposed in October 2016 by the Russian Ministry of Health that would codify the ruling in *Novartis*.

XII. Conclusion

The enactment of regulatory data protection by the Russian Federation in 2012 was a positive step towards fulfilling Russia's obligations under Article 39.3 of TRIPS, promising a supportive environment for pharmaceutical products in Russia. But the *Novartis* decision, the 2016 amendment to the Law on Circulation of Medicines, and the pending legislative proposal to codify the *Novartis* decision call that commitment into question, as they significantly curtail the statutory protection of data exclusivity that is essential to the development of the Russian pharmaceutical industry. Without sufficient regulatory data protection, producers of generic drugs, after government approval of an innovative drug, can immediately market a generic copy of the innovative drug and deprive the innovator of the opportunity to recoup its investment in development, investigation, and registration of the drug.

Such are the realities governing decisions of foreign companies and Russian producers regarding the marketing of innovative pharmaceutical products in Russia. The Russian pharmaceutical market is potentially attractive for foreign investors, witnessed by the fact that the majority of foreign pharmaceutical companies have local manufacturing operations in Russia in one form or another. The current insufficiency of regulatory data protection resulting from the IPC's interpretation in *Novartis* could discourage Russian domestic pharmaceutical companies from investment in the development and investigation of innovative pharmaceutical preparations, damage Russia's localization efforts, and drive away foreign investors.

Court of Moscow, and again by the 9th Arbitrage Court of Appeal on June 16, 2017. *See* Case No. A40-657/2017-121-10.re.