



# Advancing Innovation, Competition, and Access to Therapeutic Antibodies through Patent Policy

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BIPARTISAN POLICY CENTER

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## STAFF

### **G. William Hoagland**

*Senior Vice President  
Bipartisan Policy Center*

### **Tim Swope**

*Senior Policy Analyst  
Bipartisan Policy Center*

### **Janet Marchibroda**

*Director, Health Innovation Initiative  
Bipartisan Policy Center*

### **Brian Kennedy**

*Consultant  
Bipartisan Policy Center*

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## **BIPARTISAN POLICY CENTER'S HEALTH INNOVATION INITIATIVE**

With guidance from former Senate Majority Leader William H. Frist, MD, and former Representative Bart Gordon, BPC's Health Innovation Initiative focuses on advancing innovative strategies to improve health and health care, accelerating the discovery, development, and delivery of safe and effective cures and treatments for patients as well as effectively using data and technology to improve the lives of Americans.

## **ACKNOWLEDGMENTS**

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## **DISCLAIMER**

The findings and recommendations expressed herein do not necessarily represent the views or opinions of the Bipartisan Policy Center's founders or its board of directors.

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# Introduction

Few biomedical innovations over the past three decades have been as successful and continue to offer as much promise as therapeutic antibodies.

Therapeutic antibodies—proteins that bind to specific markers on cells or tissues—can target a particular disease state.<sup>1</sup> In 1975, researchers discovered how to produce multiple antibodies with the same structure (monoclonal antibodies). This discovery shared the Nobel Prize for Medicine and Physiology in 1984, and the first therapeutic antibody was approved in 1986. Today, dozens of drugs using this breakthrough technology have been approved in the United States and Europe.

Therapeutic antibodies effectively treat a wide range of disease states, including rheumatoid arthritis, multiple sclerosis, and several types of cancer. More than 75 antibody products are available to patients in the United States.<sup>2</sup> Moreover, numerous therapeutic antibodies are in the pipeline. Expected growth offers exciting implications for treating complex, chronic, and sometimes life-threatening conditions.

Delivering on the promise of these therapies, however, requires policies that not only encourage investment in research and development, but also ensure that, once approved, these therapies will be accessible to patients.



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Patient-access issues often center on health plan coverage and utilization management techniques—such as prior authorizations or step-therapy protocols. But access to a therapy is first and foremost a question of development. Critical to that development are intellectual property (IP) protections that incentivize investment, spur competition, and, as the last three decades have proved, spawn innovation.

This brief examines the patent policies that govern therapeutic antibodies—how they work, how they differ from patent policies for other drugs, and how uncertainties and inconsistencies around their application may impact future innovation. It demonstrates why policies must keep pace with medical innovation and, finally, highlights how recent improvements to patent policies will help protect the promise of next-generation therapeutic antibodies for patients.

## Intellectual Property and Innovative Medicine

In medicine, IP protections, such as patents, have incentivized the large investment required to produce an array of therapeutic antibodies and have advanced the field of medicine. Therapies now exist for diseases that were once impossible to effectively treat, let alone cure. Moreover, effective IP protections have often incentivized the development of not just one, but several different therapeutic antibodies in the same class of medicine, creating options for physicians and patients. These options are essential, because patients may respond differently to certain mechanisms of action, become desensitized to their current treatment regimen, or face different co-morbidities, requiring different therapeutic options.

U.S. patents have traditionally driven innovation by granting inventors limited rights in exchange for inventors' publicly disclosing important inventions and advances. This includes a period of exclusivity for inventors to recover their investment and to generate capital for developing new antibodies. This approach has fostered a free flow of information, which allows further innovation.

In some instances, however, IP policies can have unintended consequences. When patent protections are broader than the scope of the invention they protect, they may actually discourage innovation. In such cases, patents don't just prevent others from copying the protected invention, as they are designed to do. They may also discourage or even block others from pursuing new inventions. This approach ultimately hurts patients by narrowing the range of potential treatments.



# Competition and Patient Access

With therapeutic antibodies, policymakers' challenge is to strike the right balance. First, they must encourage innovators by rewarding and protecting IP. Protections inspire investors' confidence that they can earn a fair rate of return, a critical first step in making new therapeutic antibodies available to patients.

Then, however, policymakers must likewise inspire competitors to continue their own independent research and development. Applying policies that are more protective than are necessary to encourage innovators can backfire if it impedes others from researching and developing new products. In striking an appropriate balance, policymakers should encourage innovation with an eye toward its ultimate beneficiaries: patients.

Clear, consistently applied patent laws can reduce the time required for new antibodies to reach patients. The Food and Drug Administration's approval process can already take a decade or more to navigate. Uncertainty surrounding U.S. patents for therapeutic antibodies can lead to litigation, causing additional delays.

Consider potentially groundbreaking treatments whose mechanisms overlap with protected therapies for entirely different diseases. Depending on how IP is defined, these therapies may be delayed or abandoned altogether. Such scenarios can also plant doubt in investors' minds. They may hesitate to fully back the development of a new drug because of the threat of IP challenges. This chain of events can undermine patients' access to drugs that could improve their quality of life or even save their lives.

Allowing patients to realize the promise of the next generation of therapeutic antibodies, therefore, begins with effective patent policies—clear, balanced, and consistently applied.

## UNDERSTANDING ANTIBODIES

Antibodies are proteins that can be produced by the body's immune system to combat harmful substances called antigens.<sup>3</sup> Scientists discovered how to engineer individual, or "monoclonal," antibodies in 1975, setting the stage for a revolution in medicine.<sup>4</sup> Today, therapeutic antibodies are a type of biologic medicine that treats diverse diseases. The Food and Drug Administration has approved more than 75.

Utilizing antibodies, scientists have developed multiple different ways to switch on or off particular functions of the cell. These drugs are a key element of state-of-the-art cancer care,<sup>5</sup> with scientists engineering antibodies that attack cancer cells.<sup>6</sup> Antibodies also treat immune disorders, such as rheumatoid arthritis, where they can impact the disease's mechanism of action.<sup>7,8</sup> And antibodies targeting cardiovascular disease have been called the "most significant advance in clinical cardiology and lipidology in this decade."<sup>9</sup>

Antibodies are valuable because they can alter disease activity without unnecessarily disrupting other areas or functions of the body. This ability can make antibodies safer or more effective treatment options than traditional drugs. It can also have major implications for treating disease. In particular, antibodies can aid precision medicine, where drugs target a disease's genetic makeup.

The immune system is complex, and every patient is wired differently. Having different therapeutic antibodies to choose from helps clinicians find the best treatment for each individual patient.

# Historical Challenges: Broad Claims and “Work-Arounds”

Therapeutic antibodies are large, complex molecules up to 1,000 times the size of small-molecule drugs. They are produced from living cells, so their manufacturing process involves much more than chemical synthesis. Making these therapies accessible to patients requires patent policies that encourage investment and development. Yet antibodies’ complexity makes them challenging to protect with patents.

While the antibodies are large in size, not all parts are essential to their function. Of 500 amino acids in a given antibody, for example, fewer than 40 may play an important role. So, if an innovator was given patent protection only for the exact, full-antibody structure invented, a competitor could swap a single amino acid in an area that is unimportant to the overall antibody’s activity and produce a separate drug. Even though that drug could serve the very same function as the original, it would not encroach on the original patent.<sup>10</sup>

The fear of work-arounds like this has driven innovators to make broad patent claims. Innovators legitimately want to protect their investment by avoiding a market crowded with effectively identical drugs derived from their original drugs. But beyond preventing copycats, broad claims may discourage the development of distinct, innovative alternative drugs. Patent law must protect both innovation and innovative competition. Manufacturers who develop distinct drugs with similar activity provide additional treatment options and potentially lower prices for patients.

Patent law, therefore, must strike a balance between these two dynamics. But confusion about existing policies makes that a challenge.

## Lack of Clarity in the Law

The U.S. Patent and Trademark Office (USPTO) requires applicants to provide a full written description of their inventions. This ensures that inventors’ claims do not overreach the scope of their invention by requiring them to show that they have actually invented what they claim.

Over the past several years, however, the USPTO has made an exception to this rule. Rather than requiring a description of the antibody itself, the USPTO in some circumstances has accepted a description of the antibody’s target. This policy—which had been in place since 2000 until just recently—is known as the “antibody exception.”<sup>11</sup> Under the antibody exception, an innovator company could obtain a patent that prevents other companies from creating any antibody that binds to the same target.

Disagreements surrounding the antibody exception have been addressed in the U.S. court system. The U.S. Court of Appeals for the Federal Circuit (Federal Circuit Court) has interpreted the policy narrowly, often asking innovator companies to substantiate their patent claims with description beyond that of the target. That can mean providing representative examples of the antibody or describing its structural features.<sup>12</sup>

Federal Circuit Court decisions indicate that patent applicants should disclose an actual solution, not just a desired result.<sup>13</sup> This is consistent with a central tenet of the patent system—that the scope of the claim must match the contribution made to the art. Patents based on an antibody’s target might cover a vision for future antibodies rather than an existing antibody. Meanwhile, it is relatively easy for competitors to understand the scope of patents based upon an antibody’s structure to know whether they are infringing, especially compared to patents based on the antibody’s target.

Finally, narrowly defined patents allow for unique antibodies that target the same disease. They don’t reward only initial innovation; they also encourage future discoveries of new medicines for understood disease targets. This benefit is perhaps most pertinent to the patients these antibodies ultimately benefit. Instead of one breakthrough therapeutic antibody for a given condition, patients and health care providers can have multiple options. This is critical, particularly for patients who can become desensitized to a specific treatment.

Since 2010, and most recently in October 2017, the Federal Circuit Court has ruled consistently that inventors of antibodies must follow the same written description requirements as other inventions.<sup>14,15,16,17</sup> Several legal experts have commented that the USPTO guidelines have been more lenient than Federal Circuit Court opinions.<sup>18,19,20</sup>



Previous studies have assessed how Federal Circuit Court decisions impact actual practices at the USPTO.<sup>21,22</sup> Following these study methods, the Bipartisan Policy Center reviewed 778 Patent Trial and Appeal Board decisions from 2014 through February 2018.<sup>23</sup> Of the 778 decisions reviewed, 51 were associated with antibodies and written description. Fifteen of the 51 decisions directly argued antibody exception issues. The vast majority — or 49 of the 51 decisions — followed Federal Circuit Court precedent, requiring that patent applicants disclose examples or specify common structural features of the antibodies in question. Two of the 51 decisions demonstrated a broader interpretation consistent with the antibody exception. These studies confirm the prevailing confusion about antibody patent policies. They also reflect a continued lack of clarity in requirements.

Lack of clarity isn't just inconvenient for manufacturers. Uncertainty increases the risk associated with investing in antibody development. Putting a damper on development means limiting vital treatment options for patients.

The Bipartisan Policy Center had the opportunity to meet with several members of the USPTO staff in late 2017 to share key elements of this report, including our findings.

## Recent Changes in USPTO Policy Will Improve Clarity

On February 22, 2018, the USPTO issued a memorandum to its Patent Examining Corps, clarifying its guidance regarding the written description requirement for claims drawn to antibodies.<sup>24,25,26</sup> The USPTO's memorandum signals its intention to bring its guidance and related training materials into alignment with recent Federal Circuit Court decisions, thereby improving clarity and reducing uncertainty in therapeutic antibody development.

The USPTO's recent clarifications, along with actions to support full implementation, will have a positive impact on innovation, competition, and access in this vital field of human health.

## Conclusion

Patients today face complex barriers to treatment, including—in some cases—high costs and restrictions to access. However, access to life-changing therapies also depends on patent policies that encourage competition and continued discovery.

Patients have welcomed an array of groundbreaking treatments in recent years in the form of therapeutic antibodies, which hold exceptional promise for still more patients and the treatment of more disease states. Recent USPTO action will help patients see this promise come to fruition.

With straightforward, consistently applied policies in place, manufacturers can have the confidence to invest in the research and development of new therapeutic antibodies. Patients, meanwhile, will have access to more options for managing, or even curing, their conditions.



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## APPENDIX: LIST OF INTERVIEWEES AND ROUNDTABLE PARTICIPANTS

BPC would like to acknowledge and thank the individuals who participated in interviews, meetings, or roundtable discussions regarding patent policies for therapeutic antibodies. It is important to note that while these individuals provided important input to our work, BPC's final report was not specifically reviewed or endorsed by such individuals.

### **Bruce Artim**

*Director, Federal Affairs  
Eli Lilly and Company*

### **Clifton Bingham**

*Director  
Johns Hopkins Arthritis Center,  
Professor of Medicine  
Johns Hopkins University School of Medicine*

### **Marc Boutin**

*Chief Executive Officer  
National Health Council*

### **Catie Coman**

*Co-Founder  
Health Advocacy Partners*

### **Tonya Combs**

*Senior Director-General Patent Counsel, Lilly BioMedicines  
Eli Lilly and Company*

### **John Conway**

*Global Head of Intellectual Property Department  
Sanofi*

### **Larry Coury**

*Senior Director, Dispute Resolution  
Regeneron*

### **Michael Eck**

*Professor, Biological Chemistry and Molecular Pharmacology  
Harvard Medical School;  
Professor, Cancer Biology  
Dana-Farber Cancer Institute*

### **Group Discussion with the Following Individuals at the U.S. Patent and Trademark Office:**

*Tamara Foley, Attorney-Advisor, Office of Governmental Affairs  
Vanessa Ford, Supervisory Patent Examiner, Art Unit 1645  
Brian Hanlon, Director, Office of Patent Legal Administration  
Ali Salimi, Legal Advisor, Office of Patent Legal Administration  
Daniel Sullivan, Director of Technology Center 1600 – Biotechnology  
and Organic Chemistry*

### **Jorge Goldstein**

*Director  
Sterne Kessler Goldstein Fox*

### **The Honorable Lawrence LaMotte**

*Vice President, Public Policy  
Immune Deficiency Foundation;  
Coordinator  
Patients for Biologic Safety and Access*

### **Joe Liebeschuetz**

*Partner, Silicon Valley  
Alston & Bird*

### **Oskar Liivak**

*Professor of Law  
Cornell University Law School*

### **Deborah Martin**

*Vice President and Assistant General Counsel  
Pfizer*

### **Edward Patz**

*James and Alice Chen Professor of Radiology  
Duke University School of Medicine*

### **Lana Skirboll**

*Vice President, Global Policy  
Sanofi*

### **Gilbert Voy**

*Vice President and Deputy General Patent Counsel  
Eli Lilly and Company*

### **Tonya Winders**

*Allergy and Asthma Network  
President and Chief Executive Officer*

### **Cris Woolston**

*Deputy Head of Science Policy  
Sanofi*

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