

United States

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Intellectual Property (IP) is often a company's single most valuable asset. The United States is a strong player in the global economy, in part because of its staunch protection of IP rights. Protecting these rights, as well as defending against infringement allegations of others, is critical to any company's success in an increasingly competitive global marketplace. It is imperative for all businesses to have an effective IP rights-management strategy. Pharmaceutical and biotechnology companies are adept at recognising the value of IP portfolios and devoting substantial resources to protecting and exploiting their own IP, as well as gaining access to essential IP owned by others. As a result, the law that provides for and protects IP rights in the life sciences is both highly complex and ever evolving. It is also one of the most challenging and rewarding areas of US legal practice.

This chapter provides an outline of the major applications of IP rights in life sciences in the United States. The focus is on patents because of their heightened influence in this industry. A patent gives the owner the right to exclude others from making, using, offering for sale, selling, or importing the patented inventions.¹ The exclusive patent right allows patentees to gain economic benefit from their inventions and to fund future innovation. A strong patent system is a supremely important mechanism for encouraging and fostering pharmaceutical and biotechnological research, drug discovery, therapeutic product development, investments and ultimately future innovation. Successful companies are willing to invest significant amounts of their revenues derived from sales of patent-protected products and patent licensing royalties for future research and development efforts. In this way, the future of American innovation in the life sciences depends on the nature and effectiveness of the US patent system and, more generally, US IP laws.

1. Small molecules

Small molecules are the foundational building block of the drug discovery process. Pharmaceutical and biotechnology companies involved in drug research place significant focus on patenting small molecules. Small molecules are generally defined as low-molecular-weight organic compounds that are made by chemical synthesis and that are typically assayed to test for some desired activity against a particular target or disease. They may be administered orally or formulated for intravenous, transdermal or other means of administration. Although they are not

1 35 USC § 271(a).

the only patentable aspect of a drug, protection of the compound itself as a new chemical entity often represents the most basic and valuable form of patent protection available to cover a commercial drug product.

1.1 Product and process claims

Product or composition-of-matter patents that cover active compounds, in the context of small molecules, generally specify the compound's chemical structure. See, for example, *In re Papesch* (the physical properties of a chemical compound are inseparable from its structure, and "the thing that is patented is not the formula but the compound identified by it");² *Daiichi Sankyo Co, Ltd v Matrix Labs., Ltd* (affirming patentability of a chemical compound where "the structural similarities and differences between the compounds claimed and those in the prior art" did not render the compound obvious);³ and *Takeda Chemical Indus, Ltd v Alphapharm Pty, Ltd* ("in cases involving new chemical compounds, it remains necessary to identify some reason that would have led a chemist to modify a known compound in a particular manner to establish obviousness of a new claimed compound").⁴

In addition to patenting a compound itself, a patent may be granted on methods or processes for manufacturing both old and new compounds.⁵ Patentable processes can include steps for synthesising a compound – see, for example, *In re Ochiai* (process for making chemical compound having antibiotic properties based on non-obvious starting material).⁶ But this inclusion principle only applies if the process produces a chemical compound shown to be useful: *Brenner v Manson* (holding unpatentable a process for making steroidal compounds with no disclosed use);⁷ *In re Brana* (disclosure for use of end compound requires "some desirable pharmaceutical property in a standard experimental animal");⁸ and see also 35 USC § 103(b)(1) and (2) (providing statutory requirements for patentability of biotechnological processes).

1.2 Scope of protection of claims and Markush formulae

Both product and process patent claims can provide meaningful protection in a commercial setting, because such claims may cover (ie, may be infringed by) the sale and use of a drug product, the way it is made and used, and the dosage form in which it is sold. A Markush group is a listing of specified alternatives of a group in a patent claim, typically expressed in the form 'a member selected from the group consisting of A, B, and C' (see *Abbott Labs v Baxter Pharm Prods, Inc*).⁹ Typically, one and only one member of a Markush group is required in order to infringe the claim. In some instances, a Markush-style claim will not cover multiple members of the group together.¹⁰ The risk of a Markush claim form is that if any one member of the group is found to be anticipated or obvious, the entire claim is invalid.¹¹

2 *In re Papesch* 315 F.2d 381 (CCPA 1971).

3 *Daiichi Sankyo Co, Ltd v Matrix Labs., Ltd* 619 F.3d 1346, 1352 (Fed. Cir. 2010).

4 *Takeda Chemical Indus, Ltd v Alphapharm Pty, Ltd* 492 F.3d 1350, 1357 (Fed. Cir. 2007).

5 See 35 USC § 101 – patentable subject matter includes "any new and useful process".

6 *In re Ochiai* 71 F.3d 1565, 1570 (Fed. Cir. 1995).

7 *Brenner v Manson* 383 US 519 (1966).

8 *In re Brana* 51 F.3d 1560, 1567 (Fed. Cir. 1995).

9 *Abbott Labs v Baxter Pharm Prods, Inc* 334 F.3d 1274, 1280 (Fed. Cir. 2003).

1.3 Metabolites

A metabolite is a compound formed in the patient's body upon ingestion of a drug. A new metabolite compound is formed when an ingested drug undergoes a chemical conversion in the digestion process.¹² A company may infringe a claim to a metabolite if it markets a product that, when ingested, metabolises to form the claimed metabolite.¹³ A patent claiming either the active ingredient of a drug or a method of using that ingredient does not necessarily also cover its metabolites.¹⁴ A metabolite may not be patentable if the metabolite is inherently formed as a natural result of a prior-art drug's administration.¹⁵

2. Second-generation inventions

Second-generation patents can provide an additional period of patent protection, and accordingly an increased term of market exclusivity and enhanced commercial value, for a pharmaceutical product.

2.1 Combinations

A combination of two or more drug products may be eligible for its own patent protection, where administration of the combination to treat a desired condition provides a synergistic improvement over the effect that would have been expected by administering either product alone or the two products together. Administration of a formulation comprising two or more active compounds, or the co-administration of the multiple active compounds, can be patented even if each of the underlying products were known, so long as the combination was not obvious.¹⁶ By contrast, a combination of two active ingredients to treat co-occurring conditions may not be patentable if the prior art teaches the combination of interchangeable ingredients for at least one of the conditions.¹⁷

2.2 Enantiomers

Enantiomers are compounds that are mirror images of each other. They are a type of stereoisomer, which refers to one of a set of two or more compounds that are composed of the same constituent atoms, connected in the same sequence, but

10 *Ibid* at 1280 to 1281, holding that where a claim recites a Markush group preceded by the indefinite article 'a' and does not include qualifying language, the claim covers a single recited member of the Markush group.

11 *Ecolochem, Inc v Southern California Edison Co* 91 F.3d 169, 1996 WL 297601, *2 (Fed. Cir. 1996), citing *In re Skoll* 523 F.2d 1392, 1397 (CCPA 1975).

12 *Schering Corp v Geneva Pharms* 339 F.3d 1373, 1375 (Fed. Cir. 2003).

13 See *Hoechst-Roussel Pharms, Inc v Lehman* 109 F.3d 756, 759 (Fed. Cir. 1997); see also *Zenith Labs, Inc v Bristol-Myers Squibb Co* 19 F.3d 1418, 1421 to 1422 (Fed. Cir. 1994) (noting a compound claim could cover a metabolite formed upon ingestion).

14 *Hoechst-Roussel Pharms., Inc* 109 F.3d at 759.

15 *Schering Corp* 339 F.3d at 1382.

16 See, for example, *Knoll Pharm Co v Teva Pharms USA, Inc* 367 F.3d 1381, 1384–85 (Fed. Cir. 2004), where a combination of the opioid hydrocodone and the analgesic ibuprofen was found non-obvious over the prior art based on the unexpected result of achieving a 'surprising' benefit from the combination in treating pain relief and muscle repair after exercise.

17 *McNeil-PPC, Inc v L Perrigo Co* 337 F.3d 1362, 1369–70 (Fed. Cir. 2003), where the combination of the anti-diarrhoeal agent loperamide and anti-gas agent simethicone was judged to be obvious where conditions were known to occur together and anti-diarrhoeal agents had been prescribed with simethicone.

differing in spatial arrangement. Enantiomers can exist in mixtures of various isomers that differ in form, or they can be isolated into a pure form in which only a single enantiomer exists. An equal mixture of two enantiomers is called a 'racemate'.¹⁸ Enantiomers, while having the same atoms as other isomeric forms, can impart particular properties and provide grounds for new patent protection.¹⁹

2.3 Selection inventions

A selection invention is based on selecting one or more species within a broader genus already disclosed in the prior art. The patentability of a species as a selection invention depends on it having new and non-obvious benefits over the prior-art generic disclosure, such as specific dose ranges of a pharmaceutical formulation, optimal units of enzyme, or particular functions of a subset of compounds. The reasoning behind selection inventions is that art disclosing a genus does not necessarily disclose every species that is a member of that genus, particularly if the genus is large, so the identification of a species with advantageous properties may constitute a separate invention.²⁰

Recently, the Supreme Court's 'obviousness' analysis in *KSR Int'l Co v Teleflex Inc.*²¹ has made it more difficult to patent selection inventions even in situations where the prior art does not explicitly teach the advantageous properties of the claimed selection.

2.4 Methods of use and secondary indications

A novel, non-obvious pharmaceutical compound can be patent-protected both for its composition and for its use. Additional protection can be conferred on pharmaceutical products by patenting new methods of use, or new or secondary indications for a drug. A secondary method of using an existing drug can be patented if using the drug in that way or for that indication would be an unexpected property (see, for example, *In re Schoenwald*²²) but not if the new use is merely the recognition of a drug's inherent properties (*Bristol-Myers Squibb Co v Ben Venue Labs* – newly discovered results of a known process directed to the same purpose are not patentable because such results are inherent).²³

18 See *Pfizer, Inc v Ranbaxy Labs, Ltd* 457 F.3d 1284, 1286 (Fed. Cir. 2006)

19 See, for example, *Sanofi-Synthelabo v Apotex, Inc* 470 F.3d 1368, 1380 (Fed. Cir. 2006) (rejecting the argument that enantiomers are unpatentable over disclosures of their racemates); *Forest Labs, Inc v Ivax Pharms, Inc* 501 F.3d 1263, 1269 (Fed. Cir. 2007) (substantially pure (+)-enantiomer of citalopram not anticipated by or obvious over racemic citalopram, based on difficulty of separating the constituent enantiomers and the unexpected properties of (+)-citalopram); *Ortho-McNeil Pharm v Lupin Pharms* 603 F.3d 1377, 1381 (Fed. Cir. 2010) (the enantiomer levofloxacin is a 'different drug product' that is separately patentable from its racemate ofloxacin).

20 See *In re Jones* 958 F.2d 347, 383 (Fed. Cir. 1992) ("... [a] disclosure of millions of compounds does not render obvious a claim to three compounds, particularly when that disclosure indicates a preference leading away from the claimed compounds"); see also *In re Bell* 991 F.2d 781, 784 (Fed. Cir. 1993) (claimed DNA sequence coding for human insulin-like growth factors not obvious over known protein because of the 'nearly infinite' number of sequences that could code for the protein); but cf, *In re Petering* 301 F.2d 676 (CCPA 1962) (claimed compound was anticipated by prior-art disclosure of generic class of about 20 compounds that sufficiently described all 20).

21 *KSR Int'l Co v Teleflex Inc.* 550 US 398 (2007).

22 *In re Schoenwald* 964 F.2d 1122 (Fed. Cir. 1992).

23 *Bristol-Myers Squibb Co v Ben Venue Labs* 48 246 F.3d 1368 (Fed. Cir. 2001).

Method-of-use claims are also vulnerable to obviousness-type double-patenting challenges over composition-of-matter patents that describe methods for using the composition. See, for example, *Sun Pharm. Indus, Ltd, v Eli Lilly and Co* (holding invalid for obviousness-type double patenting a method of use claim for a pharmaceutical product where the composition was previously claimed and the use was disclosed but not claimed in a prior patent).²⁴

2.5 Methods of treatment

Method-of-treatment claims are a form of process claim. They have been permitted even where the compound and a method of using the compound are both known, so long as the claimed method of treatment is limited to a specific purpose not taught in the prior art. Importantly, someone of ordinary skill in the art for a method-of-treatment claim is not limited to one skilled as a treating physician and can include a skilled worker who develops new drugs or treatments.²⁵ While the Supreme Court's decision in *Bilski v Kappos* provides guidance on the patent-eligibility of process claims if they comply with the 'machine-or-transformation' test,²⁶ it leaves open many issues with respect to method-of-treatment patents in the life sciences arena.²⁷

Post-*Bilski*, the Federal Circuit has held that method-of-treatment claims involving the administration of drugs are patent-eligible as being transformative to the human body.²⁸

2.6 Formulations and physical forms

Formulation patents are one of the most popular forms of second-generation patents, typically covering both the active and inactive ingredients in tablet, capsule or other final dosage form. Active ingredients are typically mixed with inactive ingredients to make a pharmaceutical formulation that can be suitably administered to a patient. New formulations are important to drug design and development and may come in numerous physical forms, such as solid tablets, liquid or gel capsules, liquids, ointments and aerosols.

Formulation patents may also encompass a new route or schedule of administration, such as controlled- or sustained-release forms.²⁹ Notably, formulation patents may be vulnerable to 'design around' opportunities by competitors, particularly if the patent claims narrowly capture specific ingredients, drug release rates or routes of administration.³⁰

24 *Sun Pharm. Indus, Ltd, v Eli Lilly and Co*. 611 F.3d 1381 (Fed. Cir. 2010).

25 *Daiichi Sankyo Co v Apotex, Inc*. 501 F.3d 1254 (Fed. Cir. 2007).

26 *Bilski v Kappos* 130 SCt 3218 (2010).

27 *Ibid.* at 3228, noting "new technologies may call for new inquiries" for process claims.

28 *Prometheus Labs, Inc v Mayo Collaborative Services* 628 F.3d 1347, 1256 to 1157 (Fed. Cir. 2010), cert granted; *Mayo Collaborative Services et al. v Prometheus Labs, Inc* (US June 20 2011) (No 10-1150).

29 See, for example, *Abbott Labs v Sandoz, Inc* 544 F.3d 1341, 1352 (Fed. Cir. 2008) (extended-release formulations of the antibiotic drug clarithromycin having the pharmacokinetic properties in the claims were not taught in prior art); *Alza Corp v Mylan Labs* 464 F.3d 1286, 1293-4 (Fed. Cir. 2006) (claims to sustained-release oxybutynin formulation found obvious, based on the reasonable expectation that oxybutynin would be colonically absorbed and thus motivation existed to produce the claimed extended-release formulation).

30 *Ibid.* at 1297, for example: in vitro dissolution rates were sufficiently dissimilar from *in vivo* extended-release properties to avoid infringement.

2.7 Reach-through claims

Reach-through claims refer to claims that cover products obtained by the use of research tools (ie, research or screening techniques that can be used to identify and evaluate drug candidates). The goal of patents covering research tools is to have the claims 'reach through' to apply to the ultimate drug product that is sold, so as to collect royalties from that sale or at least from pre-clinical drug discovery efforts.

However, US courts have cast doubt on the patentability and enforcement of claims to products identified only by reference to the material or means used to find or identify them.³¹ This case law also intersects with both the common-law research exemption³² and the statutory experimental-use exemption under 35 USC § 271(e)(1).³³ There is an ongoing debate over the extent to which life sciences companies should be allowed, as a matter of public policy, to operate within the scope of research tool patents in order to develop new drug products.

3. DNA, biologicals and personalised medicine

Biologics are large organic molecules that distinguish themselves from small molecules by virtue of their having been synthesised from living organisms. They are also typically administered by injection or intravenous infusion. This feature means that the legal framework both for approving a follow-on biologic drug and for finding infringement of a biologic drug product is different from that of a small-molecule drug.

3.1 Discoveries

Discoveries in the biotech area generally begin with the study of genes, nucleic acid sequences of DNA or RNA, amino acid sequences of proteins and resulting biological products. While the field of biology differs from chemistry, DNA is considered "a chemical compound, albeit a complex one" for the purposes of patenting.³⁴ The breadth of patentable subject-matter for biological inventions, as famously described in *Diamond v Chakrabarty*,³⁵ a case relating to genetically modified bacteria, includes "anything under the sun that is made by man."

3.2 Gene patents and industrial application

There is no explicit industrial application requirement for patents under US law. The utility requirement under 35 USC § 101 can be analogised to the industrial-use requirement that exists for patenting genes in other jurisdictions. US case law has held that an isolated and purified DNA sequence that is complete and encodes for a specific (eg, human) protein constitutes patentable subject matter,³⁶ whereas an incomplete gene sequence is not.³⁷ In 2010, however, a US district court held invalid

31 See, for example, *Univ. of Rochester v GD Searle & Co* 375 F.3d 1303 (Fed. Cir. 2004); *Housey Pharms, Inc v Astrazeneca UK Ltd* 366 F.3d 1348, 1350 (Fed. Cir. 2004); *Bayer AG v Housey Pharms, Inc.* 340 F.3d 1367 (Fed. Cir. 2003).

32 See *Madey v Duke Univ.* 307 F.3d 1351 (Fed. Cir. 2002).

33 See *Merck KGaA v Integra LifeSciences I Ltd* 545 US 193 (2005).

34 *Amgen, Inc v Chugai Pharm Co* 927 F.2d 1200 (Fed. Cir. 1991).

35 *Diamond v Chakrabarty* 447 US 303, 309 (1980).

36 See, for example, *Amgen, Inc v Chugai Pharm Co* 927 F.2d 1200 (Fed. Cir. 1991) and *Fiers v Revel* 984 F.2d 1164 (Fed. Cir. 1993).

claims to isolated DNA sequences of two breast cancer genes on the basis that isolated DNA is no different from DNA that exists in nature and thus constitutes unpatentable subject matter under Section 101.³⁸ The case was widely watched and a recent Federal Circuit decision reversed the district court's decision on the DNA claims, reasoning that US law permits patents on human-engineered gene sequences such as cDNA because it recognises that, like other chemical compounds, the purification of DNA transforms it into something different in character.³⁹

The case to watch regarding these types of diagnostic claims will be the *Prometheus* case,⁴⁰ now pending before the US Supreme Court (and scheduled for oral argument during the October 2011 Term).

3.3 Stem cells and other organic material

There is no explicit *ordre public* or morality restriction on patentable inventions in the United States. Aside from the judicial prohibitions on patenting natural phenomena, laws of nature, abstract ideas and naturally-occurring substances, US law generally allows for a broader scope of patentable invention than many European countries. For example, the Wisconsin Alumni Research Foundation (WARF) obtained a number of US patents directed to purified and isolated stem cells – for example, US Patent Nos 5,843,780 (purified preparation of primate embryonic stem cells), 6,200,806 (purified preparation of pluripotent human embryonic stem cells) and 7,029,913 (proliferating and stably undifferentiated human embryonic stem cells cultured *in vitro*). These and other WARF patents have been contested in *inter partes* re-examination proceedings before the Board of Appeals and Interferences of the US Patent and Trademark Office, with some claims being withdrawn and others being upheld. Proceedings are ongoing and the patentability of these types of claim remains uncertain.

3.4 Bioinformatics systems

One burgeoning area of law relating to the life sciences industry is that of biotechnology inventions derived from non-wet lab techniques such as computer-assisted screening of new drugs, genes and other biological materials. The patentability of such subject matter depends on the extent to which the computer application can be claimed in terms of an apparatus rather than a type of mathematical algorithm.⁴¹ The patentability of biological screens and related diagnostics will undoubtedly continue to be the subject of much litigation in the wake of *Bilski v Kappos*.⁴²

37 See *In re Fisher* 421 F.3d 1365 (Fed. Cir. 2005) (partial sequence in form of expressed sequence tags lacks utility unless gene function is identified) and *Regents of the University of California v Eli Lilly & Co* 119 F.3d 1559 (1997) (claim to a plasmid containing cDNA coding for human insulin held invalid where only rat cDNA sequence was disclosed).

38 *Association for Molecular Pathology et al. v United States Patent and Trademark Office et al.* 94 USPQ 2d 1683 (SDNY March 29 2010).

39 See *The Association For Molecular Pathology v US Patent and Trademark Office et al.* No 2010–1406, 2011 WL 3211513, *20–21 (Fed. Cir July 29 2011) (holding claims to isolated DNA patent-eligible, while diagnostic/method claims involving screening DNA sequences are patent-eligible only if they involve a transformative step beyond simply ‘comparing’ or ‘analysing’ two gene sequences).

40 *Mayo Collaborative Services et al. v Prometheus Labs, Inc.* (US June 20 2011) (No 10-1150).