Life Sciences Webinar Series

Navigating Through the Safe Harbor: What to Know in Advance

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U.S. Research Exception

- The common law research exemption is an affirmative defense to infringement where the alleged infringer is using a patented invention for "research" purposes only. The doctrine was originated by Justice Story (of the Supreme Court) in *Whittemore v. Cutter*, 29 Fed. Cas. 1120 (C.C.D. Mass. 1813).

- The exemption is "[v]ery narrow and limited to actions performed for amusement, to satisfy idle curiosity, or for strictly philosophical inquiry." *Madey v. Duke University*, 307 F.3d 1351 (Fed. Cir. 2002). See also *Roche Products, Inc. v. Bolar Pharmaceutical Co.*, 733 F.2d 858, 863 (Fed. Cir. 1984).

U.S. Research Exception

- The exemption "does not immunize use [of a patent invention] that is in any way commercial in nature" nor "any conduct that is in keeping with the alleged infringer's legitimate business," even if that business is research or education with no commercial intent. *Madey*, 307 F.3d at 1362. While the exemption may continue to exist, it is "in a very limited form." Id. at 1360.

- The exemption is unlikely to be available to any commercial entity or academic institution. Research related to Corona Virus treatment is probably not protected.

- Hatch-Waxman Safe Harbor does not apply until "basic research" is completed and evaluation of potential FDA-approved product(s) commences. So no protection from infringement until then.

- Research exception does exist in Europe. Indeed, "basic research" may be protected. May differ from country to country. Exemption is important as Bolar amendment, which itself varies from country to country, may be limited to development of generic drugs.

The Hatch-Waxman Safe Harbor

35 U.S.C. § § 271(a), (e)(1)

INFRINGEMENT OF PATENT

(a) Except as otherwise provided in this title, whoever without authority makes, uses, offers to sell, or sells any **patented invention**, within the United States or imports into the United States any patented invention during the term of the patent therefor, infringes the patent. . . .

(e) (1) It shall not be an act of infringement to make, use, offer to sell, or sell within the United States or import into the United States a **patented invention** (other than a new animal drug or veterinary biological product (as those terms are used in the Federal Food, Drug, and Cosmetic Act and the Act of March 4, 1913) which is primarily manufactured using recombinant DNA, recombinant RNA, hybridoma technology, or other processes involving site specific genetic manipulation techniques) solely for uses reasonably related to the development and submission of information under a Federal law which regulates the manufacture, use, or sale of drugs or veterinary biological products.

THE "SAFE HARBOR"

Genesis Of Safe Harbor

- In *Roche Products, Inc. v. Bolar Pharmaceutical Co*., 733 F.2d 858 (Fed. Cir. 1984), the court found that Bolar infringed when it used Roche's patented drug substance prior to expiration of a blocking patent to prepare FDA submission to enable Bolar to market its own version of the drug after the Roche patent expired.
- This decision delayed drug introduction and allowed a patentee to maintain market exclusivity long after blocking patent(s) expired due to FDA approval process for the generic.
- The Safe Harbor was enacted to prevent this market delay by allowing testing for FDA submission without concerns of patent infringement. Without the safe harbor, generic introduction would be delayed for "about two years" after patent expiration." H.R. Rep. No. 98-857, pt. 2 at 8-9 (1984), reprinted in 1984 U.S. C.C.A.N. 2686, 2692-93.
- Safe Harbor also applies to branded pharmaceuticals products, medical devices (Types I, II and III), biologics, follow-on biologics, and biosimilars.
- Safe Harbor does not apply to new animal drugs or veterinary biological products "primarily manufactured" by recombinant DNA techniques. See *Benetec Australia, Ltd. v. Nucleonics*, Inc., 495 F.3d 1340, 1348 (Fed. Cir. 2007).

Patent Term Extension

Section 156 Provides "Symmetry" With Section 271(e)(1)

- Congress enacted 35 U.S.C. § 156 as part of Hatch-Waxman Act, which extends the life of patents claiming an FDA-approved product or a method of making/using that product due to the FDA approval process.
- Note: section 271(e)(1) covers "**patented** inventions"— no limitation on scope. But limitations have been added.
  - Balanced rights of patentees (§ 156) and generic manufacturers (§ 271(e)(1)).
- Because these two sections were simultaneously enacted, some courts have noted that symmetry between them is required.
- Research tools — patented inventions that are used in drug development, testing, and screening — are ***not extendable*** under section 156 and are not generally subject to regulatory approval.
- Thus, alleged infringers using research tools may not be protected by section 271(e)(1).

Supreme Court *Integra* Decision

- In *Merck KGaA v. Integra Life Sciences,* 545 U.S. 193 (2005), the Supreme Court stated:

  "[T]he statutory text [of § 271(e)(1)] makes clear that it provides a **wide berth** for the use of patented drugs in activities related to [FDA] approval."

  * * *

  "[W]e think it apparent from the statutory text that § 271(e)(1)'s exemption from infringement extends to ***all*** uses of patented inventions that are ***reasonably related*** to the development and submission of ***any*** information to the [FDA]. This necessarily includes preclinical studies of patented compounds that are appropriate for submission to the FDA in the regulatory process."

Id. at 202 (emphasis on "any" in original).

- As to the "reasonably related" requirement, the Supreme Court stated:

  "At least where a drugmaker has a **reasonable basis for believing** test that a patented compound ***may*** work, through a particular biological process, to produce a particular physiological effect, and uses the compound in research that, if successful, would be appropriate to include in a submission to the FDA, that use is 'reasonably related to the development and submission of information [to the FDA].'"

Id. at 207 *(emphasis added)*.

- Knowledge of the "particular biological process" is not required.
- *See* Coggio, "The Scope of 'Safe Harbor' Provision of the Hatch-Waxman Act In View Of *Merck v. Intergra Lifesciences,"* 16 Fordham Int'l Prop. L.J. 1 (2005).

Scope Of The Safe Harbor

In *Merck*, the Supreme Court stated:

> "[The exemption] necessarily includes **preclinical** studies of patented compounds that are appropriate for submission to the FDA in the regulatory process."

Id. at 202 (emphasis added).

> "[T]he FDA requires that applicants include in an IND summaries of the **pharmacological, toxicological, pharmacokinetic, and biological qualities of the drug** in animals. . .The primary (and, in some cases, only) way in which a drugmaker may obtain such information is through preclinical *in vitro* and *in vivo* studies."

Id. at 203 (emphasis added).

- The identification of a lead candidate is not required. Indeed, Safe Harbor can apply even if an FDA application is never filed.
- On remand, the Federal Circuit itemized 14 different uses that were all covered by the Safe Harbor. 496 F.3d 1334 (Fed. Cir. 2007).
- One will not lose Safe Harbor protection because of type of test that is performed.

The “Wide Berth” Of Protection Has Exceptions

- The Safe Harbor provides a “wide berth” of protection that immunizes the “use of a patent drug in activities related to FDA approval.” *Merck,* 545 U.S. at 202.

- However, it would be incorrect to “assume that all otherwise infringing activities are exempt if conducted during the period before regulatory approval is granted.” *Amgen Inc. v. Int’l Trade Comm.,* 565 F.3d 846, 842 (Fed. Cir. 2009), cited with approval in *Amgen Inc. v. Hospira, Inc.,* 944 F.3d 1327, 1339 n.2 (Fed. Cir. 2019).

- It would also be incorrect to assume that “simply submitting information about a drug substance lot to the FDA brings the manufacture of that lot within the Safe Harbor.” *Amgen v. Hospira,* 944 F.3d at 1340 n.3.

“Basic Research” Is Not Protected

- “Basic research” is not covered by the Safe Harbor. *Merck*, 545 U.S. at 206.
- No precise definition, but high through-put screening is most likely “basic research.”
- In *Isis Pharma, Inc. v. Santaris Pharma A/S Corp*., 2014 WL 794811 (S.D. Cal. Feb. 27, 2014), Santaris entered into agreements with various companies to sell its antisense drug discovery services, which were used to identify and/or screen antisense molecules for activity inhibiting a target.
  - It argued that its conduct was covered by the Safe Harbor.
  - Court denied motion for summary judgement, noting that at the pertinent time, Santaris had identified few, if any, targets that Santaris would attempt to modify using its technology.
- The Safe Harbor does not “globally embrace all experimental activity that at some point, however, may lead to an FDA process.” *Merck,* 545 U.S. at 205.
- Payments to research organizations do not negate Safe Harbor protection. *Medical Diagnostic Labs., L.L.S. v. Protagonist Therapeutics, Inc*., 298 F. Supp. 3d 1241 (N.D. Cal. 2018).

Burden Of Proof/Pleading Infringement

- Section 271(e)(1) is an affirmative defense, and the defendant has the burden of establishing it. Plaintiff is entitled to discovery to test the allegations of the defendant regarding the defense. *Ventrassist Pty Ltd. v. Heartware, Inc.* 377 F. Supp. 2d 1278, 1286-88 (S.D. Fla. 2005).
- Each alleged act of infringement must be shown to be subject to the Safe Harbor. Detailed records establishing safe harbor are necessary. Conclusory allegations will not suffice. *See In re Pharmaceutical Compositions Containing Recombinant Human Erythopoietin,* 2006 WL 2282073, No. 337-TA-68 (U.S.I.T.C. July 7, 2006). *See also Amgen, Inc. v. Hospira, Inc.,* 944 F.3d 1327 (Fed. Cir. 2019).
- In *Ventrassit Pty Ltd. v. Heartware, Inc.,* 377 F. Supp. 2d 1278 (S.D. Fla. 2005), the district court held that plaintiffs were not required to negate the safe harbor affirmative defense in its complaint.
- The complaint, however, must alleged facts that fall outside the scope of section 271(e)(1) exemption. E.g., shipment of drug samples to foreign regulatory agencies for foreign approval.

Added Benefits Of Safe Harbor Defense

- Safe Harbor defense can be useful to rebut allegation of willful infringement under *Halo*.
- For inducement under section 271(b), a defendant must "specifically intend to infringe." But an opinion of counsel on non-infringement is admissible and may negate "specific intent" requirement. *DSU Medical Corp. v. JMS Co., Ltd.,* 471 F.3d 1293 (Fed. Cir. 2006) (*en banc* in relevant part).
- An opinion of non-infringement due to safe harbor may demonstrate a good-faith belief in non-infringement to negate inducement. *Commil USA, LLC v. Cisco Sys., Inc.,* 135 S.Ct. 1920 (2015). An opinion on invalidity does not count.
- Important in pharma/biotech industry as many infringement actions are based on inducement of method-of-treatment patents under 35 U.S.C. section 271(b).
- Even if the defendant is incorrect, does opinion still establish good faith?
- Coggio, "Avoid Inducement Liability with Early Opinion of Counsel," IP Law 360 (3/21/14); Coggio and Vogel, "The Trouble with *Commil* is *DSU*," Fish Lit. Blog (1/29/15); Coggio, "*Commil v. Cisco,* - Who Really Won?" IP Law 36 (6/2/15).

Momenta I

- *Momenta Pharmaceuticals, Inc. v. Amphastar Pharmaceuticals, Inc.,* 686 F.3d 1348, 1358 (Fed. Cir. 2012) (*Momenta I*).
  - FDA required Amphastar to test each commercial batch (post approval) before sale.
  - Amphastar used Momenta's patented assay (research tool), although other tests were available.
    - No need to select non-infringing alternative.
  - Court held use was protected by Safe Harbor because resulting information was "necessary both to the continued approval of ANDA and to Amphastar's ability to market the generic drug."
    - Distinguished *Classen Immunotherapies, Inc. v. Biogen Idec*., 659 F.3d 1057, 1070 (Fed. Cir. 2011), in which the Federal Circuit held that Safe Harbor "does not apply to information that may be routinely reported to the FDA, long after marketing approval has been obtained."
    - Amphastar's post-approval activities sheltered because they were conducted to satisfy the FDA's specific requirements and thus were "anything but 'routine.'"
  - The court did not rest its decision on the fact that the assay was a research tool.
  - Court also held that actual submission of information to the FDA was not necessary.

Momenta II

- *In Momenta Pharmaceuticals, Inc. v. Teva Pharmaceuticals U.S.A. Inc*., 809 F.3d 610 (Fed. Cir. 2015) (*Momenta II*), Federal Circuit reconsidered *Momenta I* decision and excluded Amphastar's use of the patented assay from the Safe Harbor because it was a "habitual" or "regular" part of the production process and not related to obtaining FDA approval.
- Post-approval conduct will only be exempted if it is truly "required" by the FDA — studies to obtain or supplement an existing filing or to modify an existing drug label.
  - "The routine record retention requirements associated with testing and other aspects of the commercial production process contrast with non-routine submissions that may occur both pre- and post-approval, such as the submission of investigational new drug applications ("INDs"), new drug applications ("NDAs"), supplemental NDAs, or other post-approval research results. . . . The routine quality control testing of each batch of generic enoxaparin as part of the post approval, commercial production process is therefore not reasonably related to the development and submission of information to the FDA, and it was clearly erroneous to conclude otherwise." *Id*. at 621.
  - Important case but decision was concerned with post-approval conduct.
  - Coggio, "Post-Approval Conduct and the Hatch-Waxman Safe Harbor," Pharmaceutical Compliance Monitor (4/1/15).

Examples Of Exempt Activities

Section 271(e)(1) Applies To . . .

- ITC actions – *Amgen, Inc. v. Int'l Trade Comm'n*, 519 F.3d 1343 (Fed. Cir. 2008).
- Medical devices (Types I, II and III) – *Abtox, Inc. v. Exition Corp*., 122 F.3d 1019 (Fed. Cir. 1997).
- Manufacture of patented items, most of which were used to generate data for the FDA – *Intermedics, Inc. v. Venitritex, Inc*., 755 F. Supp. 1269 (N.D. Cal. 1991), *aff'd*, 991 F.2d 808 (Fed. Cir. 1993).
- Submission of data to foreign regulatory agencies, where data are also submitted to the FDA — *NeoRx Corp. v. Immunomedics*, Inc., 877 F. Supp. 202 (D.N.J. 1994).
- Use of patented product to develop alternative FDA-approved manufacturing process — *Amgen, Inc. v. Hoschst Marion Roussel, Inc*., 3 F. Supp. 2d 104 (D. Mass. 1998).
- Use of FDA-generated data to prepare patent applications — *Bristol-Myers Squibb Co. v. Rhone-Poulenc Rorer, Inc.*, 2001 WL 1512597 (S.D.N.Y. 2001).

Examples Of Non-Exempt Activities

Section 271(e)(1) Does Not Apply To . . .

- Stockpiling ─ even for launch after patent expiry ─ *Amgen, Inc. v. Hospira, Inc*., 336 F. Supp. 3d 333 (D. Del. 2018), aff'd, 944 F.3d 1327 (Fed. Cir.).
- Manufacturing patented products in the U.S. for shipment to foreign regulatory authorities — *NeoRx, supra.*
- Use of product for foreign clinical trials where no indication that results would be submitted to the FDA — *NeoRx, supra*.
- "Basic research" — *Merck KGA, supra.*
- Activity must in some way relate to potential FDA approval of drug (device), supplemental approval, or label modifications.
- Activities to support non-U.S. approval are not protected.

Supplying Active Ingredient

Pre-Approval - - OK

- API suppliers are not ANDA filers as they do not "submit" the ANDA and thus do not infringe under section 271(e)(2).
- Safe harbor protects third parties that supply API to generic filers to develop product for FDA filing. *Shire LLC v. Amneal Pharm.,* 802 F. 3d 1301, 1310 (Fed. Cir. 2015).
- Prior to the Federal Circuit decision in *Shire*, the law had been confusing. *Compare Ortho-McNeil Pharmaceutical Inc. v. Mylan Laboratories Inc.,* 267 F. Supp. 545 (N.D. W. Va. 2003) *with Shire LLC v. Mylan Inc.,* 202 WL 2072665 (D.N.J. June 7, 2012).
- Thus, one who manufactures an sells an API for use in FDA trials is not subject to infringement. Same should be true for branded pharmaceuticals.
- Safe Harbor covers one who "makes, uses, offers to sell or **sells** any patented invention." 35 U.S.C. § 271(e)(1).

Supplying Active Ingredient/"Joint" Submissions

Post-Approval Conduct Is Trickier

- Only a "submitter" of FDA application is liable under § 271(e)(2) as an infringer.
  - If the supplier will provide commercial API quantities after approval, it may be liable for inducement and can still be sued pre-approval. *Smithkline Beecham Corp v. Geneva Pharmaceuticals, Inc.*, 287 F. Supp. 2d 576, 585-86 (E.D. Pa. 2002).
- Some decisions have held the corporate relationship between the ANDA filer and the API supplier can make both liable as "submitters."
  - *Astra Zeneca Pharmaceuticals LP v. Aurobindo Pharma Ltd*., 2009 WL 483131 (D. Del. Feb. 25, 2009) (employee of U.S. company signed on behalf of foreign parent)
  - *Wyeth v. Lupin, Ltd*., 505 F. Supp. 2d 303 (D. Md. 2007) (parent and wholly-owned U.S. subsidiary both liable).
  - See Coggio and Vogel, "Safe Harbor Protects Supplier of Active Ingredient for ANDA," IP Law 360 (Sept. 29, 2015); Coggio and Vogel, "Hatch-Waxman Actions: Who Do You (Can You) Sue?" Pharmaceutical Compliance Monitor (6/3/15).

Stockpiling

- Stockpiling is not protected. *Biogen, Inc. v. Scheing AG,* 954 F. Supp (D. Mass. 1996).

- Recently, Amgen was awarded $70 million for patent infringement due to Hosira's stockpiling of "nearly a billion dollars" in product in anticipation of FDA approval. *Amgen, Inc. v. Hospira, Inc.,* 336 F. Supp. 3d 333 (D. Del. 2018), *aff'd,* 944 F.3d 1327 (Fed. Cir. 2019). Amgen's patent had expired. No commercial sales ever occurred.

- Production of commercial size batches may be subject to safe harbor if required by FDA to support approval. *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 3 F. Supp. 2d 104, 108, 110 (D. Mass. 1998). See also *NeoRx Corp v. Immunomedics, Inc.,* 877 F. Supp. 202 (D.N.J. 1994) (4th commercial batch – in excess of 3 required for FDA approval – protected).

Stockpiling

- The Amgen patents covered methods of manufacturing, not the final product or its formulation.
- The Federal Circuit affirmed that 7 of the 21 batches were covered by the safe harbor. Each of the batches must be separately examined.
- Was each act of manufacture for a use reasonably related to developing and submitting informative to the FDA?
- Two batches were used to qualify Hospira's process to make the drug and five were used for a mandatory pre-approval FDA inspection. All other batches were not protected as they were not required by FDA.
- Simply submitting testing results to the FDA does not automatically confer Safe Harbor protection.
- Hospira's own documents show that certain batches were for "commercial inventory." This designation was later changed by Hospira.

Stockpiling—Support In Legislative History?

Congress Aimed To Give Immediate Access To Drugs

- Act's legislative history demonstrates that goal of Safe Harbor was to give the public immediate access to generic products after patent expiration.
  - "It is the Committee's view that experimental activity does not have any adverse economic impact on the patent owner's exclusivity during the life of a patent, but preventing of such activity would extend the patent owner's commercial exclusivity beyond the patent expiration date. H.R. Rep. No. 98-857, pt. 1 at 46 (1984).

* * *

  - [The Committee on Energy and Commerce] reasoned that without [§ 271(e)(1)] generic manufacturers would be required to engage in . . . bioequivalency tests after the expiration of the patent. This would result in delays of about two years after the expiration of the patent before a generic could go on the market." H.R. Rep. 98-857, pt. 2 at 8-9 (1984).

  - Coggio and Vogel, "Should Stockpiling Be Protected?" Fish Litigation Blog (9/11/18); Coggio and Vogel, "Is Stockpiling Protected by the Hatch-Waxman Safe Harbor?" Law 360 (11/21/14).

Research Tools

- In *Merck v. Integra,* the Supreme Court stated: “We therefore need not – and do not – express a view about whether, or to what extent, § 271(e)(1) exempts from infringement the use of ‘research tools’ in the development of information for the regulatory process.” 545 U.S. at 205 n.7.

- *Proveris Sci. Corp. v. Innovasystems, Inc.,* 536 F.3d 1256 (Fed. Cir. 2008) is classified as the leading decision on research tools and the Safe Harbor.

- There, defendant asserted Safe Harbor protection for its sales of optical spray machines used in analyzing the product subject to FDA approval. The devices were only used on securing FDA approved of the final product.

- The Federal Circuit held that, although the devices were only used in developing data for FDA submissions, they were “not itself subject to FDA premarket approval process.” *Id.* at 1265. Thus, section 271(e)(1) did not apply.

- The court then continued the Proveris patent “is not eligible for the benefit of the patent term extension afforded by 35 U.S.C. § 156(l)” and is not limited by section 271(e)(1).

Research Tools

- Decisions on research tools and Safe Harbor are not consistent. For decisions holding that the Safe Harbor did not apply, *see PSN Ill, LLC. v. Abbot Labs,* 2011 U.S. Dist. LEXIS 108055 (N.D. Ill. 2011) (patented receptors used in drug development); *ISIS Pharms. Inc. v. Santaris Pharma A/S Corp.,* 2012 U.S. Dist. EXIS 134107 (S.D. Cal. 2012) (methods of modifying compounds).

- For a decision holding that the Safe Harbor did not apply, *see Teva Pharms U.S.A., Inc. v. Sandoz, Inc.,* 2013 U.S. Dist. LEXIS 99121 (S.D.N.Y. 2013) (patented markers).

- But the *Proveris* decision was cited with approval by the Federal Circuit in *Momenta II*: "[R]esearch tools or devices that are not themselves subject to FDA approval may not be covered." 809 F.2d at 619.

Research Tools—Need Statutory Symmetry?

- In *Eli Lilly and Co. v. Medtronic, Inc*., 496 U.S. 661 (1990), the Supreme Court recognized possible exceptions where research tool patents would be subject to Section 271(e)(1), even though the controlling patent was not extendable under Section 156. Thus, symmetry was not required.

- Statutory symmetry is preferable but not required. *Abtox, Inc. v. Exiron Corp*., 122 F. 3d 1019, 1027 (Fed. Cir.), *amended*, 131 F. 3d 1009 (Fed. Cir. 1997).

- Some district court decisions do not require symmetry. *See, e.g*., *Classen Immunotherapies Inc. v. Shionogi, Inc.,* 2014 WL 323941 (D. Md. 2014); *Teva Pharm. USA, Inc. v. Sandoz Inc.,* 2013 WL 3732867, at *7 (S.D.N.Y. July 16, 2013).

- Other district courts require symmetry between the two sections. *See, e.g*., *Isis Pharm., Inc. v. Santaris Pharma A/S Corp*., 2014 WL 794811, at *11-*12 (S.D. Cal. Feb. 27, 2014).

Infringement Of Research Tools—Remedies

- Cannot enjoin sales of commercial product. No "fruit-of-the-poisonous-tree" doctrine. *See John Hopkins University v. Cellpro, Inc*., 152 F.3d 1342, 1367 (Fed. Cir. 1998).
- Lost profits on sale of commercial product is highly unlikely. *See Panduit Corp. v. Stahin Bros. Fibre Winks*, 575 F.2d 1152, 1156 (6th Cir. 1978) (Markey, C.J.)
- "Infringing" data will not be destroyed, but can be submitted to FDA. *See Pfizer, Inc. v. Int'l Rectifier Corp.*, 217 U.S.P.O. (BNA) 157, 163 (C.D. Cal. 1982).
- Reach-through royalties are not patent misuse, but are unlikely unless defendant has agreed to them. See *Bayer A.G. v. Houser Pharmaceuticals, Inc*., 228 F. Supp. 2d 467, 470 (D. Del. 2002) (alternative license was offered). Previous course of conduct by defendant my support reach-through award.
- Injunction (preliminary/permanent) barring continued use of a research tool is questionable. *See eBay, Inc. v. Merc Exchange*, 547 U.S. 388 (2006).
  - If patentee is in business of licensing its research tools, injunction more possible. *See Commonwealth Sci. Indus v. Buffalo Tech. Inc.,* 492 F. Supp. 2d 600 (E.D. Tex. 2007).

Companion Diagnostics

- Companion diagnostics are becoming vital to FDA approval of related drugs.
- The FDA Guidance - "In Vitro Companion Diagnostic Devices" — indicates that a diagnostic test is "essential" for certain drug products to meet their goals (p. 7), and the data for the drug and the diagnostic should be developed and cleared by FDA contemporaneously (p. 8). Indeed, in certain circumstances, the FDA may not approve a drug if its companion diagnostic is not also approved.
- Under *Momenta II*, "[Research tools or devices that are not themselves subject to FDA approval may not be covered." 809 F. 3d at 619 *(citing Proveris).* Thus, even though companion diagnostic assays or kits are research tools, Safe Harbor protection may apply.
- The drug and the companion diagnostic are, in essence, one product. As such, the diagnostic - even if it were considered a research tool - should not be evaluated apart from the drug itself. Since the testing of the drug is certainly protected by the Safe Harbor, that "wide birth" of protection should also extent to the necessary companion diagnostic.
- *See* Coggio, "Research Tools and the Hatch-Waxman Safe Harbor," 22 Biotechnology Law Report 1 (Nov. 1, 2014).

Genetically-Engineered Animals

FDA Guidance

- In its 2017 draft guidance entitled “Regulation of Intentionally Altered Genomic DNA in Animals” (Guidance No. 187), FDA considers “animals whose genomics have been intentionally altered using modern molecular techniques” to be “**new animal drugs**.”

- FDA’s Green Book confirms that FDA has regulated genetically-engineered animals as drugs. See NADA Nos. 141-294 (goats), 141-453 (chickens), and 141-454 (salmon).

- Recall the wording of section 271(e)(1) which specifically excludes “new animal drugs” “primarily manufactured” using “genetic manipulation techniques,” from the Safe Harbor.
    - Accordingly, research using CRISPR to create animal models or the use of such animals in research, development, drug testing may be excluded from the protection of the safe harbor.

- *See also “Q&A on FDA Regulations of Intentionally Altered Genomic DNA in Animals.” (10/13/17).*

Summary

- Safe Harbor is very broad.
- Safe Harbor is a defense that must be proven by defendant.
    - Covers drugs, biologics, biosimilars, medical devices, and possibly research tools.
    - The vast majority of reported decisions have found that the Safe Harbor applies.
- Safe Harbor applies where a drug maker/researcher has “a reasonable basis for believing” that a patented compound “may work.”
    - Certainty is not required.
- Research must be “reasonably related” to “development and submission” of information to the FDA.
    - Information can be used for other purposes without losing protection, e.g., marketing, foreign filings, etc.
- Submission to the FDA of documents underlying protected research is not required.
- Validation batches are covered — particularly important for biologics.
- “Basic research” – whatever that is - is not protected.
- Companion diagnostics are protected.
- Stockpiling is not protected.
- Limited post-approval activities can be protected, even if drug has been commercialized.
- Genetically-engineered animals may not be protected.

Thank You!

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