claimed invention without the need for any experimentation or tinkering? For example, in the '732 measuring cup patent, the specification does not describe the proper equipment for creating the requisite sloping ramps (with indicia) in the sidewall of the cup, or how to use the equipment once it's been selected. Choosing, and using, the correct machine could well involve some trial and error, couldn't it? Is that fatal to the Hoetings' claim?

A leading Federal Circuit case on the enablement requirement, *In re Wands*, 858 F.2d 731, 735 (Fed. Cir. 1988), states that "[a] patent need not disclose what is well known in the art." Moreover, "[e]nablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. 'The key word is "undue," not "experimentation."'" *Id.* at 736-37 (quoting *In re Angstadt*, 537 F.2d 498, 504 (CCPA 1976)). The *Wands* court, indicating that the inquiry applies a "standard of reasonableness," *id.* at 737, highlighted a number of relevant factors: the nature of the invention and the breadth of the claims under review; the skill of those in the art and the state of that art when the patent was applied for; the relative predictability of the art, as well as any working examples or other guidance the patent specification provides; and the amount of experimentation required. *Id.*

Our next case, a recent one involving a pharmaceutical invention, examines the enablement question in the context of a patent enforced near the end of its life. The time to judge enablement is the filing date of the claim under review. But patentees may seek to enforce their exclusion rights against those who have developed alternative technologies, long after the patent application was first filed. As you consider the case, think about the cross-currents affecting a patentee's decision to seek a broad scope for a patent claim asserted in an infringement case. Increased breadth may make proving infringement easier, but it may also make defending the claim's validity harder. In any event, whatever the scope of the claim proves to be, § 112 requires the patentee in the patent document to enable the *full* scope of that claim: "The scope of the claims must be less than or equal to the scope of the enablement." *National Recovery Techs., Inc. v. Magnetic Separation Sys., Inc.*, 166 F.3d 1190, 1196 (Fed. Cir. 1999).

Wyeth & Cordis Corp. v. Abbott Labs.

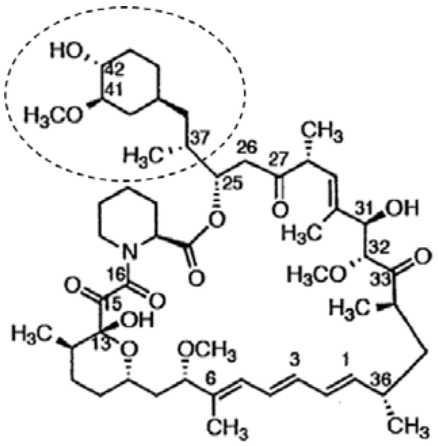
720 F.3d 1380 (Fed. Cir. 2013)

MOORE, JUDGE:

Wyeth and Cordis Corporation (Wyeth) appeal from the U.S. District Court for the District of New Jersey's grant of summary judgment that claims 1 and 2 of U.S. Patent No. 5,516,781 ('781 patent) and claim 1 of U.S. Patent No. 5,563,146 ('146 patent) are invalid for nonenablement. Because we hold that there is no genuine issue of material fact that the specification does not enable one of ordinary skill to practice the asserted claims without undue experimentation, we affirm.

BACKGROUND

The patents-in-suit relate to the use of rapamycin for the treatment and prevention of restenosis, which is the renarrowing of an artery. To open a blocked artery, a physician guides a balloon catheter to the site of accumulated plaque, and then inflates the balloon to crush the plaque. As the balloon inflates, however, it may cause injury to the arterial wall. That vascular injury causes smooth muscle cells to proliferate, which thickens the arterial wall, and, in turn, leads to restenosis.



The claims recite a method of treating or preventing "restenosis in a mammal * * * which comprises administering an antirestenosis effective amount of rapamycin to said mammal." '781 patent, claims 1 and 2; '146 patent, claim 1. In general, "rapamycin" may refer to a class of compounds. While the patents-in-suit use the term "rapamycin," the parties agree that the shared specification discloses only one rapamycin species called sirolimus. Sirolimus is naturally produced by a bacterium called *Streptomyces hygroscopicus*. The structure of sirolimus appears below and includes a substituent group at and beyond the C-37 position (dashed circle) and a macrocyclic triene ring (macrocyclic ring) indicated by the C-1 to C-36 positions.

The parties do not dispute that the effective filing date of both patents is January 9, 1992. At that time, it was known that sirolimus acts in part by binding two proteins at sites within the macrocyclic ring. It was also known that there were four additional compounds with the same macrocyclic ring as sirolimus, but different substituent groups beyond the C-37 position.

The parties also do not dispute that the specification discloses the immunosuppressive and antirestenotic properties of sirolimus. The specification discloses *in vitro* test data indicating that sirolimus inhibits rat smooth muscle cell proliferation. It also discloses *in vivo* test data indicating that intraperitoneal injection of sirolimus in rats reduced the thickening of the arterial wall following vascular injury.

In two separate actions, Wyeth sued the defendants for infringement of the patents-in-suit. The defendants market stent products that elute everolimus and zotarolimus, two drugs that have the same macrocyclic ring as sirolimus but different substituents at the C-42 position. After briefing and a hearing, the district court adopted Wyeth's proposed construction of "rapamycin" as "a compound containing a macrocyclic triene ring structure produced by *Streptomyces hygroscopicus*, having immuno-suppressive and anti-restenotic effects." Based in part on that construction, the court granted defendants' joint motions for summary judgment of invalidity for nonenablement and lack of written description. . . .

DISCUSSION

I.

. . . .

A patent's specification must describe the invention and "the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains * * * to make and use the same." 35 U.S.C. § 112(a). Claims are not enabled when, at the effective filing date of the patent, one of ordinary skill in the art could not practice their full scope without undue experimentation. Enablement is a question of law based on underlying facts.

II.

The central issue on appeal is whether practicing the full scope of the claims requires excessive—and thus undue—experimentation. The district court held that it does. It found that the claims cover any structural analog of sirolimus that exhibits immunosup-

pressive and antirestenotic effects. The court also found that, while the specification describes assays[*] to ascertain whether a potential rapamycin compound exhibits the recited functional effects, the only species disclosed is sirolimus. In further support of its holding of nonenablement, the court relied on the unpredictability of the chemical arts, the complexity of the invention, and the limited knowledge of treatment of restenosis using sirolimus at the time of the invention.

Wyeth argues that the district court ignored evidence that practicing the full scope of the claims would have required only routine experimentation. It contends that the claims do not cover a new genus of compounds, but rather a new use for an existing class of compounds. Wyeth argues that its experts opined that one of ordinary skill would readily know how to practice the full scope of the claims using two steps. First, a skilled artisan could ascertain whether a candidate rapamycin compound has the same macrocyclic ring as sirolimus. Second, a skilled artisan could routinely determine whether a candidate has immunosuppressive and antirestenotic effects using the assays disclosed in the specification.

Regarding the amount of experimentation, Wyeth acknowledges that one of its experts testified that there could be millions of compounds made by varying the substituent groups outside of sirolimus's macrocyclic ring. Wyeth counters that the same expert testified that the number of compounds that would exhibit the recited functional effects would be significantly smaller. According to Wyeth's expert, one of ordinary skill would have understood two relevant facts. First, in order to exhibit the recited functional effects, a compound must be permeable across cell membranes. Second, such permeability typically occurs in compounds having molecular weights below 1,000-1,200 Daltons (sirolimus's molecular weight is approximately 914 Daltons), which further limits the universe of potential rapamycin compounds.

Appellees respond that practicing the full scope of the claims would have required excessive experimentation, even if routine. They argue that the specification is silent on how to structurally modify sirolimus to yield a compound having the recited functional effects. Appellees disagree that one of ordinary skill would have known to select only compounds with a molecular weight below 1,200 Daltons. Even accepting Wyeth's molecular weight argument, however, Appellees respond that there are still tens of thousands of potential compounds that require screening. They emphasize that Wyeth's own witnesses testified that even minor alterations to the sirolimus molecule could impact its immunosuppressive and antirestenotic properties. Appellees argue that one of ordinary skill would thus need, at a minimum, to engage in a laborious iterative process to determine what candidates fall within the claimed genus, and that there is no contrary evidence in the record.

We agree with Appellees and the district court that there is no genuine dispute that practicing the full scope of the claims, measured at the time of filing, would require excessive experimentation. The scope of the claims at issue is broad. Under the district court's unchallenged construction of "rapamycin," the invention is a new method of use of a known compound (sirolimus) *and* any other compounds that meet the construction's structural and functional requirements. We also agree that there is no genuine dispute that the specification's guidance is limited to disclosures of the immunosuppressive and antirestenotic properties of sirolimus and assays to screen for those properties. Wyeth attempts to broaden the background knowledge in the art. It asserts, based in part on

[*] [*Eds. Note*: An "assay" is a test to determine the presence, absence, or character of an item.]

expert testing performed in the course of litigation, that the four compounds known to have the same macrocyclic ring as sirolimus at the effective filing date all "*have* immunosuppressive and antirestenotic effects." Appellants' Br. at 14 (emphasis added).

For purposes of summary judgment, we accept as true Wyeth's claims about the state of the art. We also accept Wyeth's expert testimony that one of ordinary skill would have understood that potential rapamycin compounds should have molecular weights below 1,200 Daltons in order to be permeable across cell membranes. We also accept as true that one of ordinary skill could routinely use the assays disclosed in the specification to determine immunosuppressive and antirestenotic effects in candidate compounds. Yet, even accepting Wyeth's assertions, we find no genuine dispute that practicing the full scope of the claims would require more than routine experimentation for two reasons.

First, there is no dispute that, even if potential rapamycin compounds must have a molecular weight below 1,200 Daltons, there are still at least tens of thousands of candidates. The specification is silent about how to structurally modify sirolimus, let alone in a way that would preserve the recited utility. Second, there is no genuine dispute that it would be necessary to first synthesize and then screen *each* candidate compound using the assays disclosed in the specification to determine whether it has immunosuppressive and antirestenotic effects. There is no evidence in the record that any particular substitutions outside of the macrocyclic ring are preferable. Indeed, a Wyeth scientist confirmed the unpredictability of the art and the ensuing need to assay each candidate by testifying that, "until you test [compounds], you really can't tell whether they work or not [*i.e.*, have antirestenotic effects]." In sum, there is no genuine dispute that practicing the full scope of the claims would require synthesizing and screening each of at least tens of thousands of compounds.

The remaining question is whether having to synthesize and screen each of at least tens of thousands of candidate compounds constitutes undue experimentation. We hold that it does. Undue experimentation is a matter of degree. *Chiron Corp. v. Genentech, Inc.*, 363 F.3d 1247, 1253 (Fed. Cir. 2004). Even "a considerable amount of experimentation is permissible," as long as it is "merely routine" or the specification "provides a reasonable amount of guidance" regarding the direction of experimentation. *Johns Hopkins Univ. v. CellPro, Inc.*, 152 F.3d 1342, 1360-61 (Fed. Cir. 1998). Yet, routine experimentation is "not without bounds." *Cephalon, Inc. v. Watson Pharm., Inc.*, 707 F.3d 1330, 1339 (Fed. Cir. 2013).

Our cases have described limits on permissible experimentation in the context of enablement. For example, in *ALZA Corp. v. Andrx Pharmaceuticals, LLC*, we affirmed a judgment of nonenablement where the specification provided "only a starting point, a direction for further research." 603 F.3d 935, 941 (Fed. Cir. 2010). We concluded that one of ordinary skill "would have been required to engage in an iterative, trial-and-error process to practice the claimed invention even with the help of the * * * specification." *Id.* at 943. In *Cephalon*, although we ultimately reversed a finding of nonenablement, we noted that the defendant had not established that required experimentation "would be excessive, *e.g.*, that it would involve testing for an unreasonable length of time." 707 F.3d at 1339. Finally, in *In re Vaeck*, we affirmed the PTO's nonenablement rejection of claims reciting heterologous gene expression in as many as 150 genera of cyanobacteria. 947 F.2d 488, 495-96 (Fed. Cir. 1991). The specification disclosed only nine genera, despite cyanobacteria being a "diverse and relatively poorly understood group of microorganisms," with unpredictable heterologous gene expression. *Id.* at 496.

Here, the specification similarly discloses only a starting point for further iterative research in an unpredictable and poorly understood field. Synthesizing candidate compounds derived from sirolimus could, itself, require a complicated and lengthy series of experiments in synthetic organic chemistry. Even putting the challenges of synthesis aside, one of ordinary skill would need to assay each of at least tens of thousands of candidates. Wyeth's expert conceded that it would take technicians weeks to complete each of these assays. The specification offers no guidance or predictions about particular substitutions that might preserve the immunosuppressive and antirestenotic effects observed in sirolimus. The resulting need to engage in a systematic screening process for each of the many rapamycin candidate compounds is excessive experimentation. We thus hold that there is no genuine dispute that practicing the full scope of the claims, measured at the filing date, required undue experimentation.

We have considered the remainder of Wyeth's arguments and do not find them to be persuasive. . . .

Notes & Questions

1. Assume the specification of Wyeth's patents discussed rapamycin as a genus, as well as the specific rapamycin known as sirolimus. What claim language could Wyeth have included in a patent claim to guarantee it had at least one claim with no enablement defect? As other firms identified other therapeutically effective species of rapamycin, what would be the enforcement value, to Wyeth, of that certainly-enabled claim?

2. Wyeth's predecessor in interest first filed the application that led to the patents in suit in January 1992. Both the patents enforced here issued in 1996, under an earlier patent-term statute providing protection for 17 years from the issue date; in other words, they expired the year of the Federal Circuit decision (2013). Wyeth and Cordis sued Abbott and others in this case in 2008, when the art had progressed beyond the 1992 inventions to include anti-restenosis compounds other than sirolimus.

3. Cordis, Wyeth's exclusive licensee, competes against Abbott and others in the market for drug eluting stents. All sell stents that release an anti-restenosis compound, thus enabling their customers to practice something like the claimed method. But the stent makers differ in what compound their stents release. The first-generation ingredient, sirolimus, is synonymous with "rapamycin," the term used in Wyeth's claims. But "rapamycin" can also be treated as the name for a class of compounds with a common core structure, a class that includes second-generation ingredients like everolimus and zotarolimus (used by the defendants in their stents). If "rapamycin" means *only* sirolimus, there is no enablement problem with Wyeth's claims, but there is also no literal infringement by Abbott. If "rapamycin" means the class of compounds that includes sirolimus, everolimus, and others, there is literal infringement by Abbott, but there is also a fatal enablement problem with the claims. Wyeth asked for, and received, a claim construction for "rapamycin" that ultimately proved to be its undoing.

4. The court emphasizes that "a Wyeth scientist confirmed the unpredictability of the art." Predictability is a relative term, of course. One can hazard an educated guess about even the most mysterious happenings, and even the most mundane events offer the occasional surprise. Still, patent law relies on the conventional view that mechanical and electrical arts are more predictable than chemical and biological arts, and that mature arts are more predictable than newly pioneered arts. In this case, the claimed restenosis prevention methods were doubly less predictable as of 1992—from a biochemical art in its infancy. Predictability plays a role not only in the enablement inquiry, but also in determining whether an invention would have been obvious to the phosita at the time

the patentee filed her application. Keep an eye out for the discussion of predictability in the nonobviousness unit later in this Chapter.

B. The Written Description Requirement

The first subsection of 35 U.S.C. § 112 not only requires an enabling disclosure, it also provides that "[t]he specification shall contain a written description of the invention." This separate *written description* requirement polices another aspect of the public's bargain with the inventor: The public wants to ensure not only that it receives an enabling disclosure, but also that it is dealing with the proper bargaining partner, *i.e.*, the person who truly invented the claimed invention.

Why do we need a separate disclosure requirement to ensure that we are dealing with the right inventor? After all, if the patentee's written description enables a phosita to make and use the claimed invention, isn't it plain that the patentee is the one who invented the claimed subject matter? The answer, it turns out, is "no." This is easiest to see when we consider the fact that, during prosecution, we allow the patent applicant to amend his or her claims. We do not, however, permit the applicant to add new material to the written disclosure. 35 U.S.C. § 132(a). As an applicant amends claims over time, a gap can open—by accident, or by design—between what he described as his invention on the original filing date and what he now claims (and, if successful in obtaining a patent on the amended claims, will be able to exclude others from doing without permission).

The written description requirement's chief role is to ensure that any claims the applicant introduces after the start of patent prosecution are supported by the originally filed disclosure. The Federal Circuit applies a possession standard to analyze compliance with the requirement:

> The purpose of the "written description" requirement is broader than to merely explain how to "make and use"; the applicant must also convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the "written description" inquiry, *whatever is now claimed.*

Vas-Cath Inc. v. Mahurkar, 935 F.2d 1555, 1563-64 (Fed. Cir. 1991).

The written description requirement can also invalidate even an originally filed claim, if the supporting disclosure fails to show that the inventor possessed the claimed invention at the time the application was filed. *See Ariad Pharms., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336 (Fed. Cir. 2010) (en banc). Consider, for example, the so-called "super aspirin" pain relievers Vioxx, Celebrex, and Bextra, that achieved great fame and notoriety in the late 1990s. The active ingredient in this family of drugs is a compound that selectively inhibits an inflammation-causing enzyme (COX-2) without inhibiting a similar enzyme (COX-1) that protects the stomach lining. Regular aspirin inhibits both COX-2 and COX-1, indiscriminately. *University of Rochester v. G.D. Searle & Co.*, 358 F.3d 916, 917-18 (Fed. Cir. 2004). In one of the earliest-filed patent applications in this area, the University of Rochester included the following originally filed claim in 1992:

> 1. A method for selectively inhibiting [COX]-2 activity in a human host, comprising administering a non-steroidal compound that selectively inhibits activity of the [COX]-2 gene product to a human host in need of such treatment.

Id. at 918. It was undisputed, however, that in the University's supporting disclosure, no compounds that would perform the claimed method were disclosed, nor was there any evidence that such a compound was known at the time the Rochester scientists filed the