22-2153 and 23-1952

United States Court of Appeals for the Federal Circuit

SALIX PHARMACEUTICALS, LTD., SALIX PHARMACEUTICALS, INC., BAUSCH HEALTH IRELAND LTD., ALFASIGMA S.P.A.,

Plaintiffs-Appellants,

– v. –

NORWICH PHARMACEUTICALS INC.,

Defendant-Cross-Appellant.

On Appeal from the United States District Court for the District of Delaware in No. 1:20-cv-00430-RGA, Honorable Richard G. Andrews, Judge

COMBINED PETITION OF DEFENDANT-CROSS-APPELLANT FOR PANEL REHEARING OR REHEARING *EN BANC*

CHAD A. LANDMON
MATTHEW J. BECKER
MATTHEW S. MURPHY
THOMAS K. HEDEMANN
REBECCA L. CLEGG
AXINN, VELTROP & HARKRIDER LLP
90 State House Square
Hartford, Connecticut 06103
(860) 275-8100
clandmon@axinn.com
mbecker@axinn.com
mmurphy@axinn.com
thedemann@axinn.com
rclegg@axinn.com

Counsel for Defendant-Cross-Appellant

May 13, 2024

CP COUNSEL PRESS (800) 4-APPEAL • (322802)

UNITED STATES COURT OF APPEALS
FOR THE FEDERAL CIRCUIT

CERTIFICATE OF INTEREST

Case Number 22-2153, 23-1952

Short Case Caption Salix Pharmaceuticals, Ltd. v. Norwich Pharmaceuticals, I

Filing Party/Entity Norwich Pharmaceuticals Inc.

Instructions:

1. Complete each section of the form and select none or N/A if appropriate.
2. Please enter only one item per box; attach additional pages as needed, and check the box to indicate such pages are attached.
3. In answering Sections 2 and 3, be specific as to which represented entities the answers apply; lack of specificity may result in non-compliance.
4. Please do not duplicate entries within Section 5.
5. Counsel must file an amended Certificate of Interest within seven days after any information on this form changes. Fed. Cir. R. 47.4(c).

I certify the following information and any attached sheets are accurate and complete to the best of my knowledge.

Date: 10/23/2023 Signature: /s/ Chad A. Landmon

Name: Chad A. Landmon

1. Represented Entities. Fed. Cir. R. 47.4(a)(1).	**2. Real Party in Interest.** Fed. Cir. R. 47.4(a)(2).	**3. Parent Corporations and Stockholders.** Fed. Cir. R. 47.4(a)(3).
Provide the full names of all entities represented by undersigned counsel in this case.	Provide the full names of all real parties in interest for the entities. Do not list the real parties if they are the same as the entities. ☑ None/Not Applicable	Provide the full names of all parent corporations for the entities and all publicly held companies that own 10% or more stock in the entities. ☐ None/Not Applicable
Norwich Pharmaceuticals, Inc.		Alvogen Pharma US, Inc.
		Alvogen Group, Inc.
		New Alvogen Group Holdings, Inc.
		Alvogen Lux Holdings S.a.r.l.
		Aztiq Pharma Partners S.a.r.l.

☐ Additional pages attached

4. Legal Representatives. List all law firms, partners, and associates that (a) appeared for the entities in the originating court or agency or (b) are expected to appear in this court for the entities. Do not include those who have already entered an appearance in this court. Fed. Cir. R. 47.4(a)(4).

☐ None/Not Applicable ☐ Additional pages attached

Aziz Burgy, Axinn, Veltrop, & Harkrider LLP	Stacie Ropka, Axinn, Veltrop, & Harkrider LLP	Ricky Camposanto, Axinn, Veltrop, & Harkrider LLP
David Fry, Shaw Keller LLP (formerly)	Karen Keller, Shaw Keller LLP	Nate Hoeschen, Shaw Keller LLP

5. Related Cases. Other than the originating case(s) for this case, are there related or prior cases that meet the criteria under Fed. Cir. R. 47.5(a)?

☑ Yes (file separate notice; see below) ☐ No ☐ N/A (amicus/movant)

If yes, concurrently file a separate Notice of Related Case Information that complies with Fed. Cir. R. 47.5(b). **Please do not duplicate information.** This separate Notice must only be filed with the first Certificate of Interest or, subsequently, if information changes during the pendency of the appeal. Fed. Cir. R. 47.5(b).

6. Organizational Victims and Bankruptcy Cases. Provide any information required under Fed. R. App. P. 26.1(b) (organizational victims in criminal cases) and 26.1(c) (bankruptcy case debtors and trustees). Fed. Cir. R. 47.4(a)(6).

☑ None/Not Applicable ☐ Additional pages attached

TABLE OF CONTENTS

RULE 35(b) STATEMENT iv

RULE 40(a)(2) STATEMENT iv

INTRODUCTION 1

BACKGROUND 4

A. Statutory Background 4

B. Factual and Procedural Background 5

REASONS FOR GRANTING REHEARING 7

II. REHEARING IS WARRANTED TO PREVENT OVERBROAD 271(e) ORDERS THAT IMPROPERLY ENJOIN ANDAS THAT ONLY SEEK APPROVAL FOR INDICATIONS NOT COVERED BY A VALID PATENT. 9

A. The Panel Failed to Interpret Section 271(e)(4) 9

B. Furthermore, the Panel's Analysis Is Contrary to This Court's Precedent and Ignores that ANDAs Are Regularly Amended. 10

C. The District Court's Interpretation of Section 271(e)(4)(A) Is Legally Erroneous. 12

III. REHEARING IS WARRANTED TO CORRECT THE DISTRICT COURT'S OVERBROAD 271(e) ORDER. 16

CONCLUSION 18

TABLE OF AUTHORITIES

Page(s)

Cases

ArcelorMittal Atlantique et Lorraine v. AK Steel Corp.,
908 F.3d 1267 (Fed. Cir. 2018) 17

Duncan v. Walker,
533 U.S. 167 (2001).....13

Eli Lilly & Co. v. Medtronic, Inc.,
496 U.S. 661 (1990).....11

Ferring B.V. v. Watson Lab'ys, Inc.-Fla.,
764 F.3d 1382 (Fed. Cir. 2014) .....iv, 11

Ferring B.V. v. Watson Lab'ys, Inc.-Fla.,
764 F.3d 1401 (Fed. Cir. 2014) .....iv, 11

Griffin v. Oceanic Contractors, Inc.,
458 U.S. 564 (1982).....15

Salix Pharms., Ltd. v. Norwich Pharms. Inc.,
98 F.4th 1056 (Fed. Cir. 2024) .....*passim*

Teva Pharms. USA, Inc. v. Novartis Pharms. Corp.,
482 F.3d 1330 (Fed. Cir. 2007) 4, 13

Vanda Pharms. Inc. v. W.-Ward Pharms. Int'l Ltd.,
887 F.3d 1117 (Fed. Cir. 2018) .....iv, 11

Warner-Lambert Co. v. Apotex Corp.,
316 F.3d 1348 (Fed. Cir. 2003) 14

Statutes

21 U.S.C. § 355(b)(1)(A)(viii).....4

21 U.S.C. § 355(j)(2)(A)(viii).....5, 13

35 U.S.C. § 271(b) 3

35 U.S.C. § 271(e) 3, 8

35 U.S.C. § 271(e)(2).....6, 12, 13

35 U.S.C. § 271(e)(4).....*passim*

Other Authorities

21 C.F.R. § 314.53 4

21 C.F.R. § 314.94(a)(12)(i)(A)(4)(i) 4

21 C.F.R. § 314.94(a)(12)(viii)(A) 5, 14, 17

21 C.F.R. § 314.107(b)(1)(ii).....5, 14, 17

Fed. R. App. P. 40(a)(2).....iv, 3

Fed. R. Civ. P. 60(b) .....*passim*

RULE 35(b) STATEMENT

Based on my professional judgment, I believe this appeal requires an answer to a precedent-setting question of exceptional importance: Whether 35 U.S.C. § 271(e)(4)(A) requires district courts to tie the effective date of FDA approval to the indication for which the infringing ANDA seeks approval when that indication alone is the source of the infringement of a method-of-use patent.

Based on my professional judgment, I believe the panel decision is also contrary to the following precedents of this court: *Ferring B.V. v. Watson Lab'ys, Inc.-Fla.*, 764 F.3d 1401 (Fed. Cir. 2014); *Ferring B.V. v. Watson Lab'ys, Inc.-Fla.*, 764 F.3d 1382 (Fed. Cir. 2014); *Vanda Pharms. Inc. v. W.-Ward Pharms. Int'l Ltd.*, 887 F.3d 1117 (Fed. Cir. 2018).

RULE 40(a)(2) STATEMENT

Norwich respectfully submits that the following points of law or fact have been misapprehended or overlooked by the Panel with respect to its affirmance of (1) the district court's order under 35 U.S.C. § 271(e)(4)(A), and (2) the district court's denial of Norwich's motion to modify that order under Federal Rule of Civil Procedure 60(b):

1. That Norwich contended "that the district court order unfairly precludes it from receiving final approval of a *new non-infringing ANDA*. The district court did no such thing." *Salix Pharms., Ltd. v. Norwich Pharms. Inc.*, 98

F.4th 1056, 1068 (Fed. Cir. 2024) (emphasis added). Importantly, there is no misapprehension of Norwich's position if the Panel meant that Norwich's *Amended* ANDA – which does not seek the approval of the infringing HE indication or any indication listed in the Orange Book as being covered by the asserted HE Patents – is a "new non-infringing ANDA" that FDA may approve in view of the district court's 271(e) order.[1] If that was not the Panel's intention, however, the Panel misapprehended Norwich's position and the operative facts sufficiently that it failed to even consider the issue of the proper interpretation of Section 271(e)(4).

2. That Norwich's motion under Fed. R. Civ. Pro. 60(b) "assert[ed] that the amendment negated any possible infringement" and asked the district court to

[1] There are good reasons to understand the Panel as referencing Norwich's Amended ANDA when explaining that the 271(e) order does not preclude approval of a "new non-infringing ANDA." First, the Amended ANDA is the only ANDA that Norwich has contended is unfairly precluded from receiving final approval by the 271(e) order. Second, when characterizing Norwich as " suggest[ing] that the district court order unfairly precludes it from receiving final approval of a new non-infringing ANDA," the Panel added a footnote specifically referencing that FDA has both tentatively approved Norwich's Amended ANDA and acknowledged that this ANDA does not seek approval for the infringing HE Indication. *Id.*, n.10. Third, the Panel emphasized that the 271(e) order only delayed the final approval of "'this infringing ANDA' submission," *id.*, i.e., Norwich's original ANDA that, in contrast to the Amended ANDA submission, sought approval for the infringing HE Indication. Given the absence of an express statement that the order does not prevent approval of Norwich's Amended ANDA, however, Norwich is compelled to seek rehearing, if only to afford the Panel an opportunity to issue a revised opinion that leaves no doubt as to the Panel's intention.

"reconsider its own finding of infringement in light of an amended ANDA. . . ." *Id.* at 1069. In fact, Norwich sought neither a reconsideration of the court's infringement finding nor an adjudication of infringement for the Amended ANDA. Appx3999-4000. Rather, Norwich sought only a tailoring of the 271(e) order to the district court's infringement finding based upon the infringing indication.

Norwich respectfully submits that the Panel's misapprehension of these facts was determinative for its incorrect affirmance of the district court orders.

/s/ *Chad Landmon*
Chad Landmon

INTRODUCTION

It is a fundamental precept in patent law that injunctive relief may only encompass the specific infringing conduct and no other conduct. In other words, the injunction must be tailored to the infringement. Contrary to this basic principle, the district court interpreted 35 U.S.C. § 271(e)(4)(A) – the remedy provision in the Hatch-Waxman Act – to require courts to issue injunctions on ANDA approvals that, on the facts present here, are far broader in scope than the underlying infringement.

Specifically, the district court interpreted Section 271(e)(4)(A) to require a 271(e) order prohibiting FDA from approving "ANDA No. 214369," even though the court had found that only one of the two indications for which the ANDA sought approval would infringe a valid patent. As a result, FDA has declared itself unable to approve Norwich's amended ANDA submission (which must use the same ANDA number), despite acknowledging that it does not seek approval for the infringing indication and has substituted section viii statements for the Paragraph IV certifications to the patents covering that indication. The operative effect of the 271(e) order is thus equivalent to an injunction on Ford's "F-150" model based on infringement of a four-wheel drive patent; the model remains blocked even after Ford redesigns it to two-wheel drive.

This absurd outcome has no basis in the statutory language. Indeed, it is nonsensical to interpret the Hatch-Waxman Act, which Congress enacted for the express purpose of hastening the introduction of inexpensive generic alternatives, as requiring 271(e) orders that delay approval of an ANDA for any reason other than the basis for which the ANDA infringes a valid patent. That reading is antithetical to the Act's overall purpose and thwarts the section viii mechanism that Congress specifically provided to permit FDA to approve ANDAs that do not seek to market an indication covered by a method-of-use patent. Still further, it eviscerates FDA's implementing regulation that explicitly provides that ANDA applicants can amend an ANDA to carve an infringing indication and submit section viii statements to the infringed method-of-use patents *after* an infringement finding, exactly as Norwich did here.

If left undisturbed, the Panel's affirmance of the 271(e) order will have a chilling effect on the willingness of generic companies to challenge method-of-use patents covering approved indications. Where there is more than one such approved indication, generics will be forced to forgo seeking approval for more than one because an adverse infringement finding on any one indication is a death knell for the entire ANDA. The losers are patients who will be deprived of inexpensive generic alternatives for an indication that does not infringe a valid patent. The only beneficiary is Salix, who will retain its monopoly on rifaximin

for IBS-D *despite* the invalidity of its IBS-D Patents. Approval of Norwich's Amended ANDA certainly poses no unfairness to Salix, who has already enjoyed the full statutory 30-month stay, and who may assert any non-frivolous claim that the Amended ANDA infringes under Section 271(b).

The Panel erroneously affirmed the overbroad 271(e) order because it failed to engage with the relevant issue of statutory interpretation, i.e., whether Section 271(e)(4) requires that courts tie the restriction on FDA approval to the indication for which the ANDA seeks approval when that indication was the only source of the infringement. Instead, the Panel considered whether the 271(e) order prevents approval of "a new non-infringing ANDA," a question that was neither raised by a party nor implicated by the facts.[2] Moreover, in discussing this question, the Panel held – contrary to this Court's precedent – that infringement under Section 271(e) is determined solely on the basis of the initial ANDA submission. Rehearing is consequently required to correct the district court's statutory interpretation and the Panel's incorrect holding.

In addition, the Panel misapprehended the relief that Norwich sought in its Rule 60(b) motion. The Panel found no abuse of discretion in the denial of the motion on the basis that a court has discretion to "reconsider its own finding of

[2] As noted above in Norwich's Rule 40(a)(2) statement, there are good reasons to understand the Panel as referencing Norwich's Amended ANDA when explaining that the 271(e) order does not preclude approval of a "new non-infringing ANDA."

infringement in light of an amended ANDA." *Salix Pharms.*, 98 F.4th at 1069. But Norwich never asked the district court to reconsider its infringement finding, or to evaluate infringement for the Amended ANDA. Instead, Norwich sought only the tailoring of the 271(e) order to the infringement finding. Rehearing is required to determine whether, based on the actual facts, the denial of Norwich's Rule 60(b) motion was an abuse of discretion.

BACKGROUND

A. Statutory Background

The Federal Food, Drug & Cosmetic Act ("FDCA"), as amended by Hatch-Waxman, provides an abbreviated pathway to approval for generic drugs "'to enable competitors to bring cheaper, generic … drugs to market as quickly as possible.'" *Teva Pharms. USA, Inc. v. Novartis Pharms. Corp.*, 482 F.3d 1330, 1344 (Fed. Cir. 2007) (citing 149 Cong. Rec. S15885 (Nov. 25, 2003)).

Before marketing a new drug, an applicant must identify each patent listed in FDA's Orange Book as claiming the drug or a method of using the drug. *See* 21 U.S.C. § 355(b)(1)(A)(viii); 21 C.F.R. § 314.53. A company seeking FDA approval for a generic drug must file one of four patent certifications for each Orange Book-listed patent. Relevant here is the "Paragraph IV certification," which states that the patent is invalid, unenforceable, or will not be infringed by the generic drug for which the application is submitted. *See* 21 C.F.R. §

314.94(a)(12)(i)(A)(4)(i). The only exception pertains to Orange Book-listed method-of-use patents that cover an approved indication for the drug, where the applicant may forgo seeking approval for that indication and instead submit a "section viii statement" for the patents. 21 U.S.C. § 355(j)(2)(A)(viii). Unlike Paragraph IV certifications, section viii statements do not create a patent barrier to FDA approval. 21 C.F.R. § 314.107(b)(1)(ii).

Following a final court decision of infringement for a listed method-of-use patent, FDA regulation provides that an ANDA applicant may either (1) forego approval for the patented indication until patent expiration, or (2) "amend[] its ANDA such that the applicant is no longer seeking approval for a method of use claimed by the patent," i.e., convert the Paragraph IV certification to a section viii statement. 21 C.F.R. § 314.94(a)(12)(viii)(A).

B. Factual and Procedural Background

Salix Pharmaceuticals, Inc. ("Salix") is the holder of NDA No. 021361 for rifaximin tablets under the brand name Xifaxan, which is indicated for the treatment of irritable bowel syndrome with diarrhea (the "IBS-D Indication") and for the reduction of the risk of overt hepatic encephalopathy (the "HE Indication").

Norwich submitted ANDA No. 214369 seeking approval to market generic rifaximin for both the IBS-D and HE Indications. The ANDA provided Paragraph IV certifications for all the Orange Book-listed patent.

Based on the Paragraph IV certifications, Salix filed a patent suit against Norwich in the District of Delaware under 35 U.S.C. § 271(e)(2). The patents asserted at trial fell into three categories: claims directed to the HE Indication[3] (the "HE Patents"); claims directed to the IBS-D Indication[4] (the "IBS-D Patents"); and claims directed to the crystalline form of rifaximin[5] (the "Polymorph Patents"). After trial, the court ordered the parties to propose a final judgment finding that Norwich's ANDA infringed the HE Patents and that the Polymorph and IBS-D Patents were invalid. Appx3891. Norwich proposed a 271(e) order that was tailored to the infringement of the HE Indications. Appx3905.

On August 10, 2022, the court issued a Final Judgment finding the IBS-D and Polymorph Patents invalid and the HE Patents infringed. The court rejected Norwich's proposal for the 271(e) order, ordering instead "that the effective date of any final approval by [FDA] of Norwich's ANDA No. 214369 is to be a date not earlier than the date of expiration of the last to expire" of the HE Patents, i.e., October 2, 2029. Appx51.

[3] Claim 8 of U.S. Patent No. 8,642,573, claim 6 of U.S. Patent No. 9,421,195, claims 11 and 12 of U.S. Patent No. 10,335,397.

[4] Claim 2 of U.S. Patent No. 8,309,569 and claim 3 of U.S. Patent No. 10,765,667.

[5] Claim 4 of U.S. Patent No. 7,612,199 and claim 36 of U.S. Patent No. 7,902,206.

Following the above-referenced section viii provision and FDA regulation, Norwich then amended the ANDA by removing the HE Indication and providing section viii statements in place of Paragraph IV certifications for the HE Patents (the "Amended ANDA"). On September 7, 2022, Norwich moved under Federal Rule of Civil Procedure 60(b) to modify the Final Judgment to make it clear that the 271(e) order pertains to an ANDA with Paragraph IV certifications to the HE Patents. Appx3997. On May 17, 2023, the court denied Norwich's motion. Appx52-56.

On June 2, 2023, FDA granted tentative approval to Norwich's Amended ANDA. *See* D.I. 23, Ex. A to T. Zaku Declaration. FDA acknowledged that the HE Patents "do not claim any indication for which [Norwich is] seeking approval under your ANDA." *Id.* at 3-4. FDA nevertheless stated that "final approval cannot be granted until October 2, 2029 as specified in the court order." *Id.* at 3.

On April 11, 2024, the Panel affirmed the district court's 271(e) order and denial of Norwich's Rule 60(b) motion.

REASONS FOR GRANTING REHEARING

Rehearing is required because the Panel failed to interpret Section 271(e)(4)'s requirements for the scope of 271(e) orders, thereby leaving in place the district court's erroneous interpretation that results in 271(e) orders with a broader injunctive scope than the underlying infringement. Based on the district

court's 271(e) order here, FDA has refrained from approving Norwich's Amended ANDA despite acknowledging that it does not seek approval for any indication that is covered by a valid Orange-Book patent. Courts do not countenance injunctions that go beyond the infringing conduct in any other area of patent law, and there is no basis for finding that Congress intended Section 271(e)(4) to be unique in this respect. On the contrary, the statutory language, the section viii provision and overarching purpose of the Hatch-Waxman Act, FDA's implementing regulation, patent law, and plain common sense, all favor an interpretation that requires that courts tailor 271(e) orders to the actual infringement. In addition, the Panel ignored this Court's precedent in holding that infringement under Section 271(e) is based solely on the original ANDA submission.

Rehearing is also required to determine whether, based on the actual facts, the denial of Norwich's Rule 60(b) motion was an abuse of discretion. The Panel found no abuse based solely on a misapprehension of the relief that Norwich sought in the motion. Contrary to the Panel's misapprehension, Norwich did not request a reconsideration of the infringement finding for its original ANDA or an adjudication of the Amended ANDA; Norwich simply sought a tailoring of the 271(e) order to the infringement. When that misapprehension is corrected, Norwich has demonstrated that the denial of the Rule 60(b)(5) motion was based on several legal errors and should be reversed.

II. REHEARING IS WARRANTED TO PREVENT OVERBROAD 271(e) ORDERS THAT IMPROPERLY ENJOIN ANDAS THAT ONLY SEEK APPROVAL FOR INDICATIONS NOT COVERED BY A VALID PATENT.

The Panel correctly stated the issue before it as whether "§ 271(e)(4) requires courts to tie the restriction on FDA approval to the *indication* for which the ANDA seeks approval when that indication was the source of infringement." *Salix Pharms.*, 98 F.4th at 1068. Yet rather than engage with this issue of statutory interpretation, the Panel focused its brief discussion on the wholly different – and irrelevant – question of whether the district court's 271(e) order prevents approval of "a new non-infringing ANDA." *Id*. Answering that question in the negative, the Panel then erroneously affirmed the 271(e) order without seriously examining what Section 271(e)(4) requires.

A. The Panel Failed to Interpret Section 271(e)(4).

The district court erroneously interpreted Section 271(e)(4)(A) to require that the date of the ANDA approval must be tied to the "drug." It then implemented this interpretation by referencing Norwich's ANDA by its number in the 271(e) order. As a result, FDA has declared itself unable to approve Norwich's *Amended* ANDA merely because it carries the same number, despite acknowledging that the Amended ANDA submission does not seek approval for the infringing HE Indication and provides section viii statements rather than Paragraph IV certifications for the HE Patents.

The issue before the Panel was whether the district court's interpretation of Section 271(e)(4)(A) is correct, or whether, as Norwich contends, the provision requires that 271(e) orders be tailored to the underlying infringement. Here, that requires the injunctive scope of the order to be limited to the ANDA *with* the infringing HE Indication. Despite acknowledging that this was the issue before it, *see id.*, the Panel instead considered whether the 271(e) order prevents approval of "a new non-infringing ANDA." *Id.*

Neither party asked the Panel to consider this question, which is divorced from the facts of the case and irrelevant to the pertinent issue of statutory interpretation. Indeed, there was no need to examine the question the Panel posed to itself because the answer is self-evident: A brand-new ANDA could plainly not be blocked by the 271(e) order because it would be assigned a different ANDA number by FDA than the number that is referenced in the 271(e) order. The 271(e) order would therefore simply not apply. But that, of course, is irrelevant to the issue at hand and not a basis for affirming the 271(e) order. Rehearing is therefore required.

B. Furthermore, the Panel's Analysis Is Contrary to This Court's Precedent and Ignores that ANDAs Are Regularly Amended.

The Panel correctly acknowledged that Section 271(e)(4)(A) is not directed to a "drug" per se but rather to "the drug . . . involved in the infringement," i.e., to "particular uses (indications) of that drug." *Id.* It then erred, however, in holding

that "[t]he statutory scheme makes clear that it is not the potential use of Norwich's rifaximin for HE that constitutes the relevant infringement here . . . but rather it is the submission of the ANDA that included an infringing use." *Id.*

It is well-established that the Hatch-Waxman Act makes the ANDA submission an "artificial" act of infringement for purposes of vesting jurisdiction. *See, e.g.*, *Eli Lilly & Co. v. Medtronic, Inc.*, 496 U.S. 661, 676 (1990). But as this Court has explained, "once jurisdiction is established, the ultimate infringement inquiry provoked by such filing is focused on a comparison of the asserted patent claims against *the product that is likely to be sold following ANDA approval* and determined by traditional patent law principles." *Ferring B.V.*, 764 F.3d at 1408 (emphasis added). Furthermore, ANDAs evolve and change throughout the application process for any number of reasons, including alterations to FDA's approval requirements and the appearance of new dosage strengths or indications. It follows that the infringement inquiry cannot focus solely on the original submission of the ANDA and ignore subsequent amendments. *See Ferring B.V.*, 764 F.3d at 1390 (Fed. Cir. 2014) ("[O]ur own precedent conclusively establishes that sections 271(e)(2) and (4) require consideration of the amended ANDA."); *Vanda Pharms.*, 887 F.3d at 1126-27 (same).

The Panel's erroneous analysis compounds the district court's incorrect interpretation of Section 271(e)(4)(A). Absent rehearing, the result will be

overbroad 271(e) orders that are divorced from the drug product for which approval is sought and that will actually be sold.

C. The District Court's Interpretation of Section 271(e)(4)(A) Is Legally Erroneous.

The district court legally erred by interpreting Section 271(e)(4)(A) to require that the date of the ANDA approval must be tied to the "drug," which it implemented by referencing the ANDA number in the 271(e) order. As Norwich explained in its briefing, Section 271(e)(4)(A) requires courts to tie the approval date to the indication for which the ANDA seeks approval *when that indication is the source of the infringement*. *See* Cross-Appellant's Br. at 14-27; Cross-Appellant's Reply Br. at 4-19.

First, the term "the drug . . . involved in the infringement" in Section 271(e)(4)(A) is properly construed as a restriction on the scope of the 271(e) order. Section 271(e)(2)(A) provides that an ANDA infringes if it is for a drug *or* a use (i.e., an approved indication) claimed in a patent. When such infringement has occurred, Section 271(e)(4)(A) provides that the court shall "order the effective date of any approval of *the drug … involved in the infringement*" to not be earlier than expiration of the infringed patent. 35 U.S.C. § 271(e)(4)(A) (emphasis added). The statute thus mandates that the order be directed not merely to "the drug" but to the drug "involved in the infringement." Here, for example, the court found that rifaximin – "the drug" – is "involved in the infringement" when it is

used for the HE Indication. The term "involved in the infringement" thereby ensures that the 271(e) order is tailored to the actual act of infringement.

The alternative, that "the drug . . . involved in the infringement" merely serves to identify the drug to which the 271(e) order should be directed, cannot be correct because it would render the term redundant or superfluous. *See Duncan v. Walker*, 533 U.S. 167, 174 (2001) (explaining that an interpretation that renders statutory language redundant or mere surplusage is contrary to the "cardinal principle of statutory construction" of "giv[ing] effect, if possible, to every clause and word of a statute."). The redundancy arises here because the relevant drug has already been identified earlier in the Section by its reference to the "act of infringement" in Section 271(e)(2)(A). Plainly, finding an "act of infringement" requires identification of the infringing drug and there is no need to do so again in the same Section.

Second, bringing "'generic … drugs to market as quickly as possible'" is a central purpose of the Hatch-Waxman Act. *Teva*, 482 F.3d at 1344 (quoting Sen. Kennedy Remarks, 149 Cong. Rec. S15885 (Nov. 25, 2003)). This is why Congress included the section viii mechanism that permits ANDA filers to carve out indications and obtain approval without challenging method-of-use patents covering those indications. *See* 21 U.S.C. § 355(j)(2)(A)(viii). Courts engaging in statutory interpretation should consider "the whole statute . . . and the objects and

policy of the law, as indicated by its various provisions, and give it such a construction as will carry into execution the will of the Legislature." *Warner-Lambert Co. v. Apotex Corp.*, 316 F.3d 1348, 1355 (Fed. Cir. 2003). Here, the district court's interpretation resulted in a 271(e) order that delays rather than hastens the marketing of the first generic rifaximin product for IBS-D (an indication that is in the public domain with the invalidation of the IBS-D Patents), and that eviscerates the section viii mechanism that Congress put in place. *See* Cross-Appellant's Br. at 18-23; Cross-Appellant's Reply Br. at 6-8. It is therefore inconsistent with the goals and provisions of the Act.

Third, FDA regulation permits applicants to use the section viii mechanism at any time, including by amending the ANDA "[a]fter [a] finding of infringement." 21 C.F.R. § 314.94(a)(12)(viii)(A). FDA's regulations also provide that an ANDA with a section viii statement may be approved "immediately." 21 C.F.R. § 314.107(b)(1)(ii). The district court's interpretation nullifies FDA's regulation.

Fourth, there is nothing in the provisions of the Hatch-Waxman Act or its legislative history to suggest that Congress intended it to alter or abrogate any settled principles of patent law, including the general rule that injunctions should be commensurate in scope with the infringing conduct. Yet FDA has implemented the district court's 271(e) order to delay approval of Norwich's Amended ANDA

that, pursuant to Congress's section viii mechanism and FDA's regulation, does not seek approval for the infringing HE Indication and does not contain Paragraph IV certifications for the HE Patents. The district court's interpretation is therefore inconsistent with basic principles of patent law.

Fifth, "interpretations of a statute which would produce absurd results are to be avoided if alternative interpretations consistent with the legislative purpose are available." *Griffin v. Oceanic Contractors, Inc.*, 458 U.S. 564, 575 (1982). Here, the district court's interpretation has led to the absurd result that approval of Norwich's Amended ANDA is delayed by a 271(e) order that is based on infringement of a patent for which the ANDA *does not have a Paragraph IV certification* and that covers an indication for which the ANDA *does not seek approval*.[6] Furthermore, while Salix has enjoyed the full 30-month stay of FDA approval that the Hatch-Waxman Act provides for patent owners, Norwich is being denied the use of the section viii mechanism and FDA's implementing regulation.

Rehearing is required to correct the district court's incorrect statutory interpretation.

[6] Further illustrating the absurdity, FDA will continue to refrain from approving Norwich's Amended ANDA for IBS-D based on the 271(e) order even when the IBS-D Patents expire because the HE Patents expire later.

III. REHEARING IS WARRANTED TO CORRECT THE DISTRICT COURT'S OVERBROAD 271(E) ORDER.

Norwich demonstrated that the district court's denial of the Rule 60(b)(5) motion was based on several legal errors. *See* Cross-Appellant's Br. at 27-34; Cross-Appellant's Reply Br. at 19-22. The Panel did not address these errors but nevertheless affirmed because, in the Panel's view, courts have discretion whether to "reconsider its own finding of infringement in light of an amended ANDA," and the district court here had "reasonably held that consideration of the amended ANDA would be inequitable and inappropriate." *Salix Pharms.*, 98 F.4th at 1069.

The Panel's affirmance is based on a misapprehension of the relief that Norwich sought under Rule 60(b)(5). As is plain from the proposed Order attached to Norwich's motion, Norwich never requested any "reconsideration" of the district court's infringement finding, or "consideration" of infringement with respect to the Amended ANDA. Appx3999-4000. The only relief Norwich requested were amendments to the 271(e) order to appropriately tailor it to the underlying act of infringement, i.e., the ANDA submission with the HE Indication. *Id.* It is therefore irrelevant that "[i]t is not a simple matter to determine whether an ANDA applicant has successfully carved out language from a label to turn infringement into non-infringement." *Salix Pharms.*, 98 F.4th at 1069 (quoting Rule 60(b) Order at *2). No such determination was requested or required.

The notion that Norwich was somehow seeking a "relitigation" of the infringement issue fundamentally misunderstands the section viii mechanism. Unlike Paragraph IV certifications, section viii statements to Orange-Book listed patents do not create a patent barrier to FDA approval. 21 C.F.R. § 314.107(b)(1)(ii). Indeed, the entire purpose of section viii statements is to permit ANDA applicants to forgo seeking approval for indications covered by method-of-use patents and in return avoid having FDA approval delayed by those patents. That is why FDA implemented its regulation that specifically permits applicants to substitute section viii statements for Paragraph IV certification *after* a finding of infringement. 21 C.F.R. § 314.94(a)(12)(viii)(A).

In sum, the purported "reasonable" exercise of discretion that the Panel relied on for its affirmance was based on a misapprehension of the relief sought by Norwich. Discretionary acts based on clear factual errors are reversed. *See, e.g.*, *ArcelorMittal Atlantique et Lorraine v. AK Steel Corp.*, 908 F.3d 1267, 1277 (Fed. Cir. 2018) (explaining that abuse of discretion is established when the exercise of discretion was based on "clearly erroneous fact finding"). This case should be no different, and rehearing is required to correct the overbroad 271(e) order.

CONCLUSION

For the foregoing reasons, Norwich respectfully requests rehearing or rehearing en banc.

Dated: May 13, 2024

Respectfully submitted,

/s/ Chad A. Landmon

Chad A. Landmon
Matthew Becker
Matthew Murphy
Thomas K. Hedemann
Rebecca L. Clegg
AXINN, VELTROP & HARKRIDER LLP
90 State House Square
Hartford, CT 06103
(860) 275-8100
clandmon@axinn.com
mbecker@axinn.com
mmurphy@axinn.com
thedemann@axinn.com
rclegg@axinn.com

Attorneys for Defendant-Appellant Norwich Pharmaceuticals, Inc.

ADDENDUM

ADDENDUM TABLE OF CONTENTS

Date	Docket Text	Tab No.
04/11/24	OPINION filed for the court by Lourie, Circuit Judge; Chen, Circuit Judge and Cunningham, Circuit Judge. Cunningham, Circuit Judge, dissenting in part. Precedential Opinion. Service as of this date by the Clerk of Court. [996710] [22-2153, 23-1952] [MVH] [Entered: 04/11/2024 10:51 AM] (ECF No. 71)	1
	35 U.S.C. § 271	2
	21 U.S.C. § 355	3
	21 C.F.R. § 314.94	4
	21 C.F.R. § 314.107	5

Tab 1

United States Court of Appeals for the Federal Circuit

SALIX PHARMACEUTICALS, LTD., SALIX PHARMACEUTICALS, INC., BAUSCH HEALTH IRELAND LTD., ALFASIGMA S.P.A.,
Plaintiffs-Appellants

v.

NORWICH PHARMACEUTICALS INC.,
Defendant-Cross-Appellant

2022-2153, 2023-1952

Appeals from the United States District Court for the District of Delaware in No. 1:20-cv-00430-RGA, Judge Richard G. Andrews.

Decided: April 11, 2024

WILLIAM R. PETERSON, Morgan, Lewis & Bockius LLP, Houston, TX, argued for plaintiffs-appellants. Also represented by MICHAEL J. ABERNATHY, KARON NICOLE FOWLER, MICHAEL SIKORA, Chicago, IL; JULIE S. GOLDEMBERG, Philadelphia, PA; JOSHUA DANIEL CALABRO, SHANNON KEOUGH CLARK, STEVEN C. KLINE, ALEXIS M. MCJOYNT, SCOTT K. REED, BECKY E. STEEPHENSON, Venable LLP, New York, NY.

CHAD A. LANDMON, Axinn, Veltrop & Harkrider LLP,

Hartford, CT, argued for defendant-cross-appellant. Also represented by MATTHEW BECKER, REBECCA L. CLEGG, THOMAS K. HEDEMANN, MATTHEW S. MURPHY.

IRENA ROYZMAN, Kramer Levin Naftalis & Frankel LLP, New York, NY, for amici curiae Regeneron Pharmaceuticals, Inc., Ocular Therapeutix, Inc. Also represented by CHRISTINE WILLGOOS; PAUL BRZYSKI, Washington, DC.

PAUL WHITFIELD HUGHES, III, McDermott Will & Emery LLP, Washington, DC, for amicus curiae Vanda Pharmaceuticals Inc. Also represented by CHRISTOPHER MICHAEL BRUNO, SARAH HOGARTH, APRIL ELISE WEISBRUCH.

Before LOURIE, CHEN, and CUNNINGHAM, *Circuit Judges*.

Opinion for the court filed by *Circuit Judge* LOURIE.

Opinion dissenting-in-part filed by *Circuit Judge* CUNNINGHAM.

LOURIE, *Circuit Judge*.

Salix Pharmaceuticals, Ltd., Salix Pharmaceuticals, Inc., Bausch Health Ireland Ltd., and Alfasigma S.P.A. (collectively, "Salix") appeal from a final judgment of the United States District Court for the District of Delaware holding claim 2 of U.S. Patent 8,309,569, claim 3 of U.S. Patent 10,765,667, claim 4 of U.S. Patent 7,612,199, and claim 36 of U.S. Patent 7,902,206 invalid as obvious. *See Salix Pharms., Ltd. v. Norwich Pharms., Inc.,* No. 20-cv-430, 2022 WL 3225381 (D. Del. Aug. 10, 2022) ("*Decision*").

Norwich Pharmaceuticals Inc. ("Norwich") cross-appeals from an order that issued after the district court concluded that Norwich infringed claim 8 of U.S. Patent 8,624,573, claim 6 of U.S. Patent 9,421,195, and claims 11 and 12 of U.S. Patent 10,335,397 and had failed to prove

that those claims were invalid. That order, contained within the final judgment, instructed the FDA that the effective approval date of Norwich's Abbreviated New Drug Application ("ANDA") may not precede the expiration dates of those claims. J.A. 51. Norwich also cross-appeals from a denial of its motion to modify the final judgment. *See Salix Pharms., Ltd. v. Norwich Pharms., Inc.*, No. 20-430, 2023 WL 3496373 (D. Del. May 17, 2023) ("*Rule 60(b) Order*").

For the following reasons, we affirm.

BACKGROUND

Rifaximin, the active ingredient in Salix's commercial product Xifaxan®, has been widely used as an antibiotic for decades, having been first synthesized in the early 1980s in Italy and approved there as an antibiotic in 1985. *Decision* at *8; J.A. 2532. The FDA approved Xifaxan nearly 20 years later, in 2004, as 200 mg tablets for the treatment of travelers' diarrhea. *Decision* at *1. The FDA subsequently approved 550 mg tablets for hepatic encephalopathy ("HE") in 2010 and for irritable bowel syndrome with diarrhea ("IBS-D") in 2015. *Id.*

Norwich sought to market a generic version of rifaximin and, in 2019, filed an ANDA for 550 mg tablets with the same indications as Xifaxan, certifying pursuant to 21 U.S.C. § 355(j)(2)(vii)(IV) that Salix's rifaximin patents were invalid. Salix timely sued, asserting that Norwich's ANDA infringed dozens of valid, Orange Book-listed patents. By the time of trial, the case had been streamlined to three groups of patents:

- the '573, '195, and '397 patents, directed to treating HE ("the HE patents");
- the '569 and '667 patents, directed to treating IBS-D with 550 mg rifaximin three times a day (1,650 mg/day) for 14 days ("the IBS-D patents"); and,

- the '199 and '206 patents, directed to rifaximin form ß ("the polymorph patents").

Following a bench trial, the district court held that Norwich infringed the HE patents' claims and had failed to establish their invalidity. *Decision* at *10–11. Norwich did not appeal those holdings. The court also held that Norwich's ANDA infringed the IBS-D and polymorph patents, but that those patents' claims would have been obvious over certain prior art. *Id.* at *2–3, 16–17. Salix appealed those invalidity holdings.

As part of the entered judgment, the district court ordered that the effective date of a final approval of Norwich's ANDA should not precede October 2029, which is the latest expiration date associated with the HE patents. J.A. 51. Norwich then amended its ANDA in an attempt to remove the infringing HE indication and moved to modify the judgment under Federal Rule of Civil Procedure 60(b), asserting that the amendment negated any possible infringement. The court denied Norwich's motion, and Norwich cross-appealed.

We have jurisdiction under 28 U.S.C. § 1295(a)(1).

DISCUSSION

Salix first contends that the district court's conclusion that the asserted claims of the IBS-D patents were invalid as obvious was reached in error. Subsumed within that challenge is a question of whether or not a background reference discussed by the court was properly established as prior art. Salix also contends that the court erred in holding that the asserted polymorph patent claims were invalid as obvious. Norwich's cross-appeal asserts that the court erred in the phrasing of its order precluding final approval of its ANDA until expiration of the HE patents. Norwich further asserts that the court erred in denying its motion to modify after the ANDA was amended in an attempt to avoid infringement. We address each argument in turn.

I

We turn first to Salix's contention that the district court erred in concluding that the asserted claims of the IBS-D patents would have been obvious over the asserted prior art.

Whether or not a claim would have been obvious is a question of law, based on underlying factual determinations. *Hospira, Inc. v. Fresenius Kabi USA, LLC*, 946 F.3d 1322, 1328–29 (Fed. Cir. 2020). We review the ultimate legal question of obviousness *de novo* and the underlying factual determinations for clear error. *Id.* at 1328. A finding is clearly erroneous only if we are "left with a definite and firm conviction that the district court was in error." *Id.* (citations omitted).

The IBS-D patents are directed to treating IBS-D with 550 mg rifaximin, thrice-daily (1,650 mg/day), for 14 days. For example, claim 2 of the '569 patent depends from claim 1 as follows:

> 1. A method of providing acute treatment for diarrhea-associated Irritable Bowel Syndrome (dIBS) comprising: *administering 1650 mg/day* of rifaximin for 14 days to a subject in need thereof, wherein removing the subject from treatment after the 14 days results in a durability of response, wherein the durability of response comprises about 12 weeks of adequate relief of symptoms.
>
> 2. The method of claim 1, wherein *the 1650 mg is administered at 550 mg three times per day*.

'569 patent, col. 30 ll. 4–12 (emphases added); *see also* '667 patent, col. 46 ll. 29–33, 39–40 (claims 1 & 3, similar). The key limitation on appeal is the dosage amount that appears in the claims: 550 mg, three times per day ("TID"), for a total of 1,650 mg/day.

Norwich challenged the IBS-D claims' validity by asserting as prior art references a clinical trial protocol that had been published on the ClinicalTrials.gov website in 2005 ("the Protocol")[1] and a 2006 journal article ("Pimentel").[2] The Protocol describes a Phase II study evaluating twice-daily doses of 550 mg (1,100 mg/day) and 1,100 mg (2,200 mg/day) for 14 and 28 days for the treatment of IBS-D. *See* J.A. 7051. Pimentel teaches administering 400 mg, TID (1,200 mg/day), for the treatment of IBS,[3] but further opines that the "optimal dosage of rifaximin may, in fact, be higher than that used in our study." J.A. 4644.

The district court found that those two references disclose each and every limitation of the challenged IBS-D claims, and further found that a skilled artisan would have been motivated to combine those two references to arrive at what is claimed with a reasonable expectation of success. *Decision* at *17, *19–20. The court then concluded that the challenged IBS-D claims were invalid as obvious. *Id.* at

---

[1] ClinicalTrials.gov, *History of Changes for Study: NCT00269412, Randomized, Double Blind, Placebo-Controlled Study to Assess the Efficacy and Safety of Three Different Doses of Rifaximin Administered BID either Two or Four Weeks in the Treatment of Patients with Diarrhea-Associated Irritable Bowel Syndrome* (December 22, 2005); J.A. 7047–55.

[2] M. Pimentel *et al.*, *The Effect of a Nonabsorbed Oral Antibiotic (Rifaximin) on the Symptoms of the Irritable Bowel Syndrome*, 145 ANN. INTERN. MED., 557 (2006); J.A. 4639–46.

[3] Salix did not argue a difference between a motivation to use rifaximin to treat IBS versus IBS-D. *Decision* at *19 n.3. It concedes on appeal that "[r]oughly one-third of IBS patients suffer from IBS-D," Appellants' Br. at 6, and has not otherwise suggested that treatments for IBS would not inform treatments of IBS-D.

*17–22. Salix appeals, asserting that the court erred in finding that a skilled artisan would have had a reasonable expectation of success in using the claimed 1,650 mg/day dosage to treat IBS-D. Appellants' Br. at 39–48. Whether or not there would have been a reasonable expectation of success is a question of fact, *IXI IP, LLC v. Samsung Elecs. Co.*, 903 F.3d 1257, 1262 (Fed. Cir. 2018), which we review for clear error, *Hospira*, 946 F.3d at 1328.

Salix does not appear to dispute the district court's finding that the Protocol and Pimentel "disclose all limitations of the IBS-D claims." *See Decision* at *17. Rather, it contends that even if the asserted combination of references effectively discloses the claimed 1,650 mg/day dosage, there remains insufficient evidence to support a finding of a reasonable expectation of success in using that particular dosage amount. *See*, *e.g.*, Appellants' Br. at 39–40. According to Salix, the highest prior art dosage amount that could have been supported with a reasonable expectation of success was the 1,200 mg/day dose evaluated by Pimentel. *Id.* at 40. We disagree.

The Protocol provides an outline of a planned Phase II clinical trial in which "three different doses (275, 550 and 1100 mg) of rifaximin" were to be "administered BID [*i.e.*, twice-daily] for either two or four weeks in the treatment of patients with diarrhea-associated irritable bowel syndrome." J.A. 7050 (cleaned up). As an outline of that clinical trial plan, the Protocol provides only that those three specific, twice-daily dosage regimens were to be investigated for either two or four weeks. The Protocol does not include any efficacy or safety data, nor does it mention a 1,650 mg/day dose or TID dosing.

Although we have rejected the idea that "efficacy data [are] always required for a reasonable expectation of success," *OSI Pharms., LLC v. Apotex Inc.*, 939 F.3d 1375, 1385 (Fed. Cir. 2019), we are hesitant to conclude as a general matter that the disclosure of a Phase II clinical trial

plan, standing alone, provides an expectation of success sufficient to render obvious a dosage that was not included within the planned clinical trial. *See* Appellants' Reply Br. at 13–14. But the Protocol was not asserted alone; it was asserted in combination with Pimentel.

Pimentel teaches that administration of 400 mg rifaximin, TID (1,200 mg/day), "resulted in greater improvement in IBS symptoms" and "lower bloating score[s] after treatment." J.A. 4639; *see also id.* at 4642–43 (providing supporting data). Pimentel explains that the 400 mg TID regimen was chosen "on the basis of a previous study that demonstrated the efficacy of rifaximin in bacterial overgrowth." *Id.* at 4640. However, Pimentel does not merely provide that daily rifaximin doses of 1,200 mg were likely to be successful in the treatment of IBS. Pimentel further teaches that "[r]ecent data suggest that the *optimal dosage* of rifaximin *may, in fact, be higher* than that used in our study." J.A. 4644; *Decision* at *20 (emphases added).

The district court did not clearly err in finding that a skilled artisan would have looked to both of those references, considered their limits, and had a reasonable expectation of success as to the efficacy of 550 mg TID dosing. The combined message that the skilled artisan would have discerned from the Protocol and Pimentel is that the optimal dosage for treating patients suffering from IBS disorders may be higher than 400 mg TID, and the next higher dosage unit from the Protocol was 550 mg. We see no clear error in the conclusion that there would have been a reasonable expectation of success in administering the claimed 1,650 mg/day to IBS-D patients. Indeed, certainty and absolute predictability are not required to establish a reasonable expectation of success. *See Almirall, LLC v. Amneal Pharms. LLC*, 28 F.4th 265, 275 (Fed. Cir. 2022) ("A finding of a reasonable expectation of success does not require absolute predictability of success."); *Acorda Therapeutics, Inc. v. Roxane Lab'ys, Inc.*, 903 F.3d 1310, 1333 (Fed. Cir. 2018) ("This court has long rejected a

requirement of conclusive proof of efficacy for obviousness." (cleaned up)).

Moreover, references establishing the background knowledge of a person of ordinary skill in the art are consistent with the reasonable expectation of success provided by the combination of the Protocol with Pimentel. For example, Cuoco[4] teaches the efficacy of 1,200 mg rifaximin/day for 14 days for the treatment of small intestinal bacterial overgrowth ("SIBO"). J.A. 4533. Salix has acknowledged that those of ordinary skill in the art identified "bacterial alterations" as a potential underlying cause for IBS, Appellants' Br. at 7, and the literature[5] describes SIBO as a condition that is "highly prevalent in patients with irritable bowel syndrome (IBS)," such that "SIBO decontamination is associated [with] a significant improvement of IBS symptoms." J.A. 4664. We therefore agree with the district court that references describing the treatment of SIBO would have been pertinent to the skilled artisan's considerations as to what treatments would have a potential for success in treating individuals suffering from IBS.

In addition to Cuoco, Lauritano[6] teaches an increase in rifaximin efficacy for the treatment of SIBO as doses were increased from 600 mg/day to 1,200 mg/day, providing the

---

[4] L. Cuoco & M. Salvagnini, *Small intestine bacterial overgrowth in irritable bowel syndrome: a retrospective study with rifaximin*, 52 MINERVA GASTROENTEROL. DIETOL. (2006) 89; J.A. 4533–39.

[5] E. Scarpellini et al., *High dosage rifaximin for the treatment of small intestinal bacterial overgrowth*, 25 ALIMENT. PHARMACOL. THER. 781 (2007); J.A. 4663–67 ("Scarpellini").

[6] E.C. Lauritano et al., *Rifaximin dose-finding study for the treatment of small intestinal bacterial overgrowth*, 22 ALIMENT. PHARMACOL. THER., 31 (2005); J.A. 7267–71.

trend that Pimentel described as indicating that doses higher than 1,200 mg/day may be even more optimal for the treatment of IBS. J.A. 7267 ("Higher doses of rifaximin lead to a significant gain in terms of therapeutic efficacy in [SIBO] eradication without increasing the incidence of side-effects."); *see also id.* at 4644. As evidenced by Scarpellini and Lin,[7] those in the art advanced on those findings, and subsequently evaluated higher doses. For example, Scarpellini reported that a 1,600 mg/day dose "showed a significantly higher efficacy" compared with 1,200 mg/day for the treatment of SIBO. J.A. 4663; *see also id.* at 4666 (Table 1, noting study patients included those suffering from IBS-D); *id.* at 4747 (teaching that "[a]bout 400 to about 600 mg of rifaximin may be administered TID for about 10 days" (*i.e.*, 1,200 mg/day to 1,800 mg/day) for the eradication of bacterial overgrowth).

The record further supports the finding that there would have been a reasonable expectation of success in administering higher doses of rifaximin without an intolerable increase in negative side effects. For example, Cuoco teaches that rifaximin was understood as having "a low risk of causing microbial resistance," J.A. 4533, and that rifaximin was well known for its "profile of tolerability and safety widely described in the literature," *id.* at 4538. Scarpellini further reported that the 1,600 mg/day dose provided a "similar compliance and side-effect profile" compared with the 1,200 mg/day dose. *Id.* at 4663. As the district court noted, the "[w]idespread off-label use" of rifaximin also supported the conclusion that rifaximin was safe and effective "for the treatment of IBS-D with a reasonable expectation of success." *Decision* at *19; *see also* Appellants' Br. at 17 ("There is no dispute that skilled

---

[7] International Patent Application Publication 2006/102536; J.A. 4721–47.

artisans knew of the general concept of trying off-label use of rifaximin to treat IBS-D.").

In view of the record before us, we see no clear error in the finding that a skilled artisan would have had a reasonable expectation of success in administering the claimed 1,650 mg/day regimen for the treatment of IBS-D. We therefore affirm the district court's holding that the challenged IBS-D claims would have been obvious over the cited references. *See In re Applied Materials, Inc.*, 692 F.3d 1289, 1295 (Fed. Cir. 2012) ("[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." (citation omitted)).

Salix further contends that a Press Release[8] issued by Salix in a filing with the Securities and Exchange Commission less than a year before the patents' priority date was not prior art because Norwich failed to establish that it was "by others" as required by pre-AIA 35 U.S.C. § 102(a). Appellants' Br. at 30–39. According to Salix, the district court's inclusion of that allegedly non-prior art reference in its discussion of the skilled artisan's expectation of success was harmful error. *Id.*

Although the district court cited the Press Release in its discussion of the skilled artisan's expectations, it ultimately held that the "Protocol and Pimentel [] disclose all limitations of the IBS-D claims" and that a skilled artisan "would have been motivated to combine the . . . Protocol and Pimentel [] with a reasonable expectation of success." *Decision* at *17. We therefore need not decide whether or not the Press Release was prior art because, even assuming that it was not, the Protocol and Pimentel alone established the obviousness of the claims.

---

[8] Salix Pharms., Ltd., Current Report (Form 8-K) (Sept. 5, 2007); J.A. 7477–82.

We accordingly affirm the district court's determination that Norwich established that the IBS-D claims would have been obvious in view of the Protocol and Pimentel.

II

We next turn to Salix's contention that the district court clearly erred in finding that there would have been a reasonable expectation of success in obtaining the rifaximin form ß recited in the polymorph patents' claims.

Whether or not there would have been a reasonable expectation of success is a question of fact, *IXI IP, LLC v. Samsung Elecs. Co.*, 903 F.3d 1257, 1262 (Fed. Cir. 2018), which we review for clear error, *Hospira*, 946 F.3d at 1328. We review the ultimate conclusion of obviousness *de novo*. *Id.*

The polymorph patents are directed to rifaximin form ß. For example, claim 4 of the '199 patent recites:

> 4. Rifaximin in polymorphic form ß, wherein the rifaximin has x-ray powder diffraction pattern peaks at about 5.4°; 9.0°; and 20.9°2θ and wherein the rifaximin has a water content of greater than 5%.

'199 patent, col. 10 ll. 24–27; *see also* '206 patent, col. 11 ll. 33–37, 41–43 (claims 34 & 36, similar).

Norwich challenged the polymorph claims' validity by asserting, *inter alia*, Cannata,[9] which discloses that rifaximin exists in crystalline form with "outstanding antibacterial properties." J.A. 4528; *Decision* at *6. Cannata does not discuss rifaximin's crystal structure in detail, but it does disclose several preparation protocols for rifaximin that include solvents used for crystallization. J.A. 4529–31; *see also id.* at 3408.

---

[9] U.S. Patent 4,557,866; J.A. 4526–32.

The district court held that expert testimony supported a conclusion that, in view of the prior art, (1) a skilled artisan would have had good reason to characterize the crystalline rifaximin obtained by following the Cannata protocols, (2) that such characterization was routine and could have been performed "in one day," and (3) that doing so would have led the skilled artisan to have "detected rifaximin ß." *Decision* at *6–7. The district court subsequently concluded that the challenged polymorph claims would have been obvious over the asserted prior art in view of the common knowledge of the skilled artisan. *Id.* at *7–8.

Salix first challenges the district court's conclusion of obviousness by asserting that *Grunenthal GMBH v. Alkem Laboratories Ltd.*, 919 F.3d 1333 (Fed. Cir. 2019) and *Pharmacyclics LLC v. Alvogen, Inc.*, No. 2021-2270, 2022 WL 16943006 (Fed. Cir. Nov. 15, 2022) compel the opposite result. Appellants' Br. at 49–51. Salix further contends that the court "applied the wrong test" by not following a rationale provided in the district court opinion from *Pharmacyclics*. *Id.* at 55–57. We disagree.

In *Grunenthal*, we held that it was not clear error for the district court to find that the record failed to establish by clear and convincing evidence a reasonable expectation of success in preparing the claimed polymorphic Form A of tapentadol hydrochloride. *See* 919 F.3d at 1341. In that case, the synthesis of tapentadol hydrochloride known in the prior art produced a particular form—Form B. *Id.* The district court found that there was a lack of evidence that a prior art synthesis would have resulted in the claimed Form A and that no prior art guidance existed to establish "what particular solvents, temperatures, agitation rates, etc., were likely to result" in the claimed polymorph. *Id.* at 1343. We found no clear error in that analysis. *Id.* at 1344–45.

We also affirmed a conclusion of non-obviousness of a claimed polymorph in our non-precedential *Pharmacyclics* decision, which issued after the district court released its decision in this case. *See* 2022 WL 16943006, at *10–11. But the court here acted within its discretion when it declined to follow the district court decision in *Pharmacyclics* as though it was binding precedent. *See Decision* at *7 n.1 ("Plaintiffs call to my attention [the district court's decision in] *Pharmacyclics LLC v. Alvogen Pine Brook LLC*. I have considered that case but I do not agree with it on this point."). And our later affirmance of the factual findings in *Pharmacyclics* did not retroactively override the district court's analysis here.

Moreover, a lack of clear error in *Grunenthal* and *Pharmacyclics* does not compel a conclusion of non-obviousness here. Indeed, *Grunenthal* underscored the factual nature of these types of inquiries and expressly held that it did "not rule out the possibility that polymorph patents could be found obvious." 919 F.3d at 1344–45. "The determination of obviousness is dependent on the facts of each case." *Sanofi-Synthelabo v. Apotex, Inc.*, 550 F.3d 1075, 1089 (Fed. Cir. 2008); *see also Pfizer, Inc. v. Apotex, Inc.*, 480 F.3d 1348, 1366 (Fed. Cir. 2007). In *Grunenthal* and *Pharmacyclics*, the issue was whether a skilled artisan would have had a reasonable expectation of success in *producing* a crystalline form of a compound. *See* 919 F.3d at 1341–43; 2022 WL 16943006, at *10–11. Here, the prior art included a process to produce a crystalline form of rifaximin, and the dispute centered around *characterizing* the crystalline form resulting from that process. *See Decision* at *13–14. These distinct factual predicates support the district courts' factual findings in each of these three cases under the clear error standard of review.

In *Graham v. John Deere Co. of Kansas City*, 383 U.S. 1 (1966), the Supreme Court set forth the background against which obviousness is to be assessed: "Under § 103, the scope and content of the prior art are to be determined"

and "differences between the prior art and the claims at issue are to be ascertained." *Id.* at 17. The scope and content of the prior art here includes preparations of crystalline rifaximin, which expert testimony supports would have yielded the ß form of rifaximin. *Decision* at *7; J.A. 3391–92 ("[T]he as-synthesized form of rifaximin reported by Examples 1, 6, 7, and 9 [of Cannata] were necessarily rifaximin form Beta, because of the methods used, the solvent system used, and it was later confirmed by later work, including work from the named inventors."); *id.* at 3408–09 (similar testimony); *id.* at 3393–3404 (discussing the evidence of record that supports that conclusion); *id.* at 4700–07, 4846–47, 5007–14 (providing supporting evidence for that conclusion). And the parties do not dispute that the methods for characterizing the resulting crystalline rifaximin were well known and readily available to the skilled artisan. *Decision* at *3. The difference between the prior art and the claims is thus effectively nothing more than the performance of routine characterization to identify the polymorphic forms that result from the known Cannata processes.

In this regard, Salix does not appear to dispute that there would have been a motivation to explore potential polymorphic forms of rifaximin. Appellants' Br. at 48–49. Rifaximin was, after all, a known compound with a known, useful activity. Salix further refers to the district court's finding that "polymorph ß is a commonly produced polymorph and the most stable form of rifaximin" as an "undisputed" fact. *Id.*; *see also Decision* at *7. There thus appears to be no dispute that the claimed polymorph can be readily produced from the crystallization conditions disclosed in Cannata and that it would have been well within the abilities of the skilled artisan to procure and characterize the ß form of rifaximin.

According to Salix, however, rifaximin's ß form constituted a non-obvious invention because, although skilled artisans "actually succeed[ed]" in producing and

characterizing it, they would not have "*expect*[*ed*] to succeed" because, as of the critical date, the polymorphic nature of rifaximin had not yet been reported and the identity of the ß form remained undisclosed. Appellants' Br. at 49. Salix further argues that there could have been no expectation of success because the skilled artisan would not have been able to predict what polymorphic forms might result from following the preparation protocols disclosed in the prior art. *Id.* at 20–21, 50–53. Salix's framing of the issue suggests that no unknown entity could ever be obvious, as one cannot reasonably expect what was hitherto unknown, which is incorrect.

Here, the district court found a reasonable expectation of success in characterizing the crystalline product of Cannata for potential polymorphism using routine, conventional methods and skill. *Decision* at *6–7. We see no clear error in that conclusion. Indeed, Salix has done no more than combine known elements of the prior art to verify readily accessible information concerning a compound already in the hands of those of ordinary skill in the art, and such routine efforts do not justify removing this polymorph from the public domain. *See KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 427 (2007); *see also Pfizer*, 480 F.3d at 1367–68. To be sure, we do not hold that there is always a reasonable expectation of success in accessing or characterizing polymorphs. We are simply reviewing the district court's decision before us as to its factual finding of a reasonable expectation of success, and in so doing, have not been left with a definite and firm conviction that a mistake was made in reaching that finding. *See Scanner Techs. Corp. v. ICOS Vision Sys. Corp. N.V.*, 528 F.3d 1365, 1374 (Fed. Cir. 2008).

Having found no clear error in the district court's fact findings as to the existence of a reasonable expectation of success, we affirm the court's conclusion that the polymorph patent claims were invalid as obvious. Because we affirm the court's holding that the polymorph patent claims

would have been obvious over the asserted prior art, we need not consider Norwich's separate argument that the polymorph claims would have also been invalid as inherently anticipated.

III

On cross-appeal, Norwich raises two related but distinct arguments that arose after the district court held that Norwich infringed the HE patents and failed to establish invalidity. *See Decision* at *10–16. Norwich first argues that, in issuing its final decision, the district court misinterpreted 35 U.S.C. § 271(e)(4)(A), which directs a court, following a finding of infringement, to order the FDA to defer final approval of an ANDA until the expiration of the infringed patent. According to Norwich, that statute precludes delaying final approval of an entire ANDA, and instead requires delaying only the approval of the infringing use.

Norwich's second argument arises from its decision to amend its ANDA to carve out the infringing HE use after final judgment. Following that amendment, Norwich filed a motion to modify the final judgment to allow for prompt approval of the amended ANDA that purportedly no longer sought approval for the infringing HE use. The district court denied that motion, and Norwich cross-appealed.

We address both of Norwich's concerns in turn.

A.

We first address Norwich's arguments regarding the district court's interpretation of 35 U.S.C. § 271(e)(4)(A) in ordering that a final approval of Norwich's ANDA could not be effective before the HE patents expired. J.A. 50–51.

We review issues of statutory interpretation without deference to the district court's interpretation. *Waymark Corp. v. Porta Sys. Corp.*, 245 F.3d 1364, 1366 (Fed. Cir. 2001). "The starting point in every case involving

construction of a statute is the language itself." *Blue Chip Stamps v. Manor Drug Stores*, 421 U.S. 723, 756 (1975) (Powell, J., concurring). Moreover, we "give effect, if possible, to every clause and word of [the] statute." *United States v. Menasche*, 348 U.S. 528, 538–39 (1955) (citation omitted). When a statute does not define a given word or phrase, we presume that Congress intended the word or phrase to have its ordinary meaning. *Asgrow Seed Co. v. Winterboer*, 513 U.S. 179, 187 (1995). However, "[i]n expounding a statute, we must not be guided by a single sentence or member of a sentence, but look to the provisions of the whole law, and to its object and policy." *U.S. Nat'l Bank of Or. v. Indep. Ins. Agents of Am., Inc.*, 508 U.S. 439, 455 (1993) (citation omitted).

Section 271(e)(4)(A) instructs that, following a finding of infringement, "the court shall order the effective date of any approval of the drug or veterinary biological product involved in the infringement to be a date which is not earlier than the date of the expiration of the patent which has been infringed." The order here instructed the FDA that "the effective date of any final approval . . . of Norwich's ANDA No. 214369 is to be a date not earlier than the date of expiration of the last to expire of [the HE patents] (currently October 2, 2029)." J.A. 51.

Norwich argues that the language of § 271(e)(4) requires courts to tie the restriction on FDA approval to the *indication* for which the ANDA seeks approval when that indication was the source of infringement. Cross-Appellants' Br. at 14. Norwich's ANDA originally sought approval for the treatment of both IBS-D and HE. Although only the HE indication was found to infringe a valid patent, the order restricted final approval of the entire ANDA, including the non-infringing indication, until 2029. Norwich argues that the statute requires the district court's order "to specify that the approval date pertains to Norwich's ANDA seeking approval for the infringing HE Indication." *Id.* at 18. But the district court order concerned only the

specific ANDA in question that included an infringing use, referred to the ANDA by its number, and enjoined the approval of that ANDA. J.A. 51. Norwich suggests that the district court order unfairly precludes it from receiving final approval of a new non-infringing ANDA.[10] The district court did no such thing.

Section 271(e)(4)(A) describes delaying the approval of "the drug . . . involved in the infringement." Since the FDA does not approve drugs in the abstract, but rather approves drugs for particular uses (indications) of that drug, the statute is appropriately construed as directed to approval of particular infringing uses of the drug, not all uses of the drug including non-infringing uses. The statutory scheme makes clear that it is not the potential use of Norwich's rifaximin for HE that constitutes the relevant infringement here, nor is it the unpatented drug compound itself, but rather it is the submission of the ANDA that included an infringing use. *See* 35 U.S.C. § 271(e)(2)(A) (making it an "act of infringement to submit" an ANDA "for a drug claimed in a patent or the use of which is claimed in a patent"). That the ANDA further recited a non-patent-protected indication does not negate the infringement resulting from the ANDA's submission. The order thus appropriately delayed the effective final approval date of "this infringing ANDA" submission. J.A. 48. The order appropriately said nothing that would prevent approval of a new non-infringing ANDA.

We therefore affirm the district court's order setting the effective approval date of Norwich's ANDA No. 214369

---

[10] Norwich notes that on June 2, 2023, FDA tentatively approved its amended ANDA, which purportedly lacks the HE indication. Cross-Appellant's Br. at 6. The tentative approval letter noted, however, that "final approval cannot be granted until October 2, 2029 as specified in the court order." *Id.*

to be no earlier than the date of expiration of the last to expire of the HE patents.

B.

Following entry of the final judgment, which included the resetting order barring final approval of Norwich's ANDA until 2029, Norwich amended its ANDA in an attempt to remove the infringing HE indication. Norwich then moved to modify the judgment under Federal Rule of Civil Procedure 60(b), asserting that the amendment negated any possible infringement, and that the final approval date of the ANDA, as amended, should not be tied to the HE patents. *See* Cross-Appellant's Br. at 27. The district court denied that motion, holding that Norwich "fully litigated the merits of its non-infringement and invalidity case, lost, and now seeks a way around the final judgment through Rule 60(b)." *Rule 60(b) Order* at *2. Norwich cross-appealed.

"Because denial of a Rule 60(b) motion is a procedural issue not unique to patent law, we apply the rule of the regional circuit where appeals from the district court would normally lie," *Amstar Corp. v. Envirotech Corp.*, 823 F.2d 1538, 1550 (Fed. Cir. 1987), which, here, is the Third Circuit. The Third Circuit "review[s] the denial of Rule 60(b) relief for an abuse of discretion." *Coltec Indus., Inc. v. Hobgood*, 280 F.3d 262, 269 (3d Cir. 2002); *see also Bohus v. Beloff*, 950 F.2d 919, 930 (3d Cir. 1991) (noting that Rule 60(b) motions are "extraordinary relief which should be granted only where extraordinary justifying circumstances are present" (citation omitted)).

"A district court may reconsider its own finding of infringement in light of an amended ANDA," but the court need not do so. *Ferring B.V. v. Watson Lab'ys, Inc. Fla.*, 764 F.3d 1382, 1391 (Fed. Cir. 2014). Rather, "[a]llowing an amendment is within the discretion of the district court, guided by principles of fairness and prejudice to the patentholder." *Id.* Here, the court reasonably held that

consideration of the amended ANDA would be inequitable and inappropriate. *Rule 60(b) Order* at *2. The court noted that "[i]t is not a simple matter to determine whether an ANDA applicant has successfully carved out language from a label to turn infringement into non-infringement" and that what Norwich sought in its Rule 60(b) motion "would essentially be a second litigation" following final judgment. *Id.* (noting also that, other than simply asserting that it carved out the HE indication and providing the court with the amended label, Norwich "ha[d] presented no evidence in support of its assertion" that the amended ANDA would no longer infringe the HE patents).

Norwich nevertheless argues that the amended ANDA satisfies the judgment by not seeking approval for the infringing use and that, in view of the amendment, it is no longer equitable to apply the judgment prospectively. But Rule 60(b) is permissive, holding only that the court "*may* relieve a party or its legal representative from a final judgment, order, or proceeding" under various circumstances. That is—a district court has the discretion, not the obligation, to modify a final judgment in view of a post-judgment ANDA amendment. And as the district court held, simply asserting that a patented indication has been carved out of an ANDA application does not necessarily satisfy the judgment or entitle the applicant to direct entry to the market. *See Rule 60(b) Order* at *2. We see no abuse of discretion in the district court reaching that conclusion or in subsequently denying the motion.

Norwich further argues that the district court erred by not explicitly discussing Rule 60(b)(6), which provides that a court may relieve a party from a final judgment for "any other reason that justifies relief." We disagree that the district court so erred. The court's Memorandum Order thoroughly discussed the law, the equities, the record, and the arguments before it. In so doing, the court implicitly found no additional reason that justified the relief that Norwich sought.

We therefore affirm the district court's denial of the motion to modify the final judgment.

CONCLUSION

We have considered both parties remaining arguments and find them unpersuasive. For the foregoing reasons, we affirm (1) the district court's holding that claim 2 of the '569 patent, claim 3 of the '667 patent, claim 4 of the '199 patent, and claim 36 of the '206 patent would have been invalid as obvious, (2) the district court's order setting the effective approval date of Norwich's ANDA to be no earlier than the date of expiration of the last to expire of the HE patents, and (3) the district court's denial of the motion to modify the final judgment.

AFFIRMED

COSTS

No costs.

United States Court of Appeals for the Federal Circuit

SALIX PHARMACEUTICALS, LTD., SALIX PHARMACEUTICALS, INC., BAUSCH HEALTH IRELAND LTD., ALFASIGMA S.P.A.,
Plaintiffs-Appellants

v.

NORWICH PHARMACEUTICALS INC.,
Defendant-Cross-Appellant

2022-2153, 2023-1952

Appeals from the United States District Court for the District of Delaware in No. 1:20-cv-00430-RGA, Judge Richard G. Andrews.

CUNNINGHAM, *Circuit Judge*, dissenting in part.

I join most of the majority's opinion, but I respectfully dissent from the majority's opinion concerning U.S. Patent Nos. 8,309,569 and 10,765,667 (the "IBS-D patents"). I would vacate the district court's judgment that the asserted claims of the IBS-D patents are obvious and remand for further proceedings.

I

The district court found that "[t]he asserted IBS-D claims describe a dosing regimen within the known range" and that "[a] POSA would have been motivated to combine

the RFIB 2001 Protocol[1] and Pimentel 2006[2] with a reasonable expectation of success." *Salix Pharms., Ltd. v. Norwich Pharms., Inc.,* No. 20-430-RGA, 2022 WL 3225381, at *17 (D. Del. Aug. 10, 2022) ("*Decision*") (footnotes added). Based on these findings of fact, the court concluded that "Pimentel 2006 in light of the RFIB 2001 Protocol renders the asserted claims of the IBS-D patents obvious." *Id.* at *18. After reviewing the evidence relied on by the district court, applying a clear error standard, I am "left with the definite and firm conviction that a mistake has been committed" regarding these findings. *Pfizer, Inc. v. Apotex, Inc.*, 480 F.3d 1348, 1359 (Fed. Cir. 2007) (quoting *United States v. U.S. Gypsum Co.*, 333 U.S. 364, 395 (1948)).

The evidence cited by the district court does not support its finding that a skilled artisan would have a reasonable expectation of success for the claimed dosage. *See Decision* at *17, *19. "The reasonable-expectation-of-success analysis must be tied to the scope of the claimed invention"—here, the claimed 1,650 mg/day (550 mg TID[3]) dosage for treating IBS-D. *Teva Pharms. USA, Inc. v. Corcept Therapeutics, Inc.*, 18 F.4th 1377, 1381 (Fed. Cir. 2021). The district court mainly relied on the results of the

---

[1] ClinicalTrials.gov, *History of Changes for Study: NCT00269412, Randomized, Double Blind, Placebo-Controlled Study to Assess the Efficacy and Safety of Three Different Doses of Rifaximin Administered BID Either Two or Four Weeks in the Treatment of Patients with Diarrhea-Associated Irritable Bowel Syndrome* (December 22, 2005); J.A. 7048–55.

[2] M. Pimentel et al., *The Effect of a Nonabsorbed Oral Antibiotic (Rifaximin) on the Symptoms of the Irritable Bowel Syndrome*, 145 ANNALS INTERN. MED. 557 (2006); J.A. 4639–46. The majority refers to this reference as Pimentel.

[3] TID stands for three times per day.

RFIB 2001 trial disclosed in the RFIB 2001 Press Release[4] in arriving at this conclusion. *Decision* at *19. However, there is no reason that a skilled artisan "would have known about the successful RFIB 2001 Protocol results," *id.*, as to the claimed 1,650 mg/day (550 mg TID) dosage because the RFIB 2001 Press Release only discloses an improvement in the *550 mg twice-a-day* group. J.A. 7480; *see Decision* at *19. In fact, evidence in the record suggests the opposite—that a skilled artisan might have understood the absence of discussions of the *1,100 mg twice-a-day* group to imply that higher dosage *did not* lead to similar successful results. *See* J.A. 3313–14. Indeed, the 2,200 mg/day dosage "did not achieve more responders compared to the placebo for adequate relief."[5] J.A. 3042. Thus, the court's reliance on the RFIB 2001 Press Release to establish a reasonable expectation of success was erroneous.[6]

The district court's citations to other references do not cure this error. Cuoco[7] discloses a total dose of *1,200*

---

[4] Salix Pharms., Ltd., Current Report (Form 8-K) (Sept. 5, 2007); J.A. 7477–82.

[5] Although the evidence that the 2,200 mg/day dosage did not achieve adequate relief post-dates the priority date of the patent, it clarifies what a skilled artisan would have understood from the RFIB 2001 Press Release. *See Syntex (U.S.A.) LLC v. Apotex, Inc.*, 407 F.3d 1371, 1379 (Fed. Cir. 2005) (holding district court erred in not considering a reference that post-dates the priority date when it is relevant to what "was known in the art at the relevant time").

[6] Salix also challenges the district court's finding that the RFIB 2001 Press Release was prior art. Appellant's Br. 30–39; *Decision* at *20. I agree with the majority that we do not need to reach this issue.

[7] L. Cuoco & M. Salvagnini, *Small intestine bacterial overgrowth in irritable bowel syndrome: a retrospective*

mg/day for 14 days, and Barrett[8] similarly discloses 400 mg TID for a total dosage of *1,200 mg/day*. *Decision* at *19; *see also* J.A. 4536; J.A. 4800. The district court did not explain why these references would give rise to a reasonable expectation of success for a dosage that is almost 40% higher. The reference by the district court to the "[w]idespread off-label use" of rifaximin was also unaccompanied by any discussion of dosages or citations to the record. *Decision* at *19. Likewise, it discussed market research that shows many physicians prescribe rifaximin for IBS without discussing their prescribed dosages. *Decision* at *20 (citing J.A. 7186). The cited research does not show that physicians prescribe at the 1,650 mg/day (550 mg/TID) dosage. J.A. 7186.

Although "efficacy data is [not] always required for a reasonable expectation of success," *OSI Pharms., LLC v. Apotex Inc.*, 939 F.3d 1375, 1385 (Fed. Cir. 2019), the analysis must still be tied to the scope of the claims—here, the 1,650 mg/day dosage. *See Teva*, 18 F.4th at 1381; *see also In re Cyclobenzaprine Hydrochloride Extended-Release Capsule Pat. Litig.*, 676 F.3d 1063, 1070–72 (Fed. Cir. 2012) (finding no reasonable expectation of success when the court "cited no evidence specifically indicating that a [drug with a pK profile disclosed in the prior art] would be expected to yield the same therapeutic effect as [a different pK profile as claimed]"); *Ferring B.V. v. Watson Lab'ys, Inc.-Fla.*, 764 F.3d 1401, 1407 (Fed. Cir. 2014) (finding asserted claims not to be invalid for obviousness when prior art references "disclose 500 mg [] formulations, but no

---

study with rifaximin, 52 MINERVA GASTROENTEROL. DIETOL. 89 (2006); J.A. 4533–39.

[8] G. Barrett, Abstract, *Benefits of the Antibiotic Rifaximin as Empiric Therapy in Patients with Irritable Bowel Syndrome*, 101 AM. J. GASTROENTEROL. S479 (2006); J.A. 4799–4800.

higher tablet strengths, and particularly not the claimed 650 mg formulation"). Aside from its erroneous reliance on the RFIB 2001 Press Release, the district court failed to tie its reasonable expectation of success analysis to the claimed dosage. Therefore, I would find that it clearly erred in its reasonable expectation of success analysis.

In sum, the district court clearly erred in relying on the RFIB 2001 Press Release and other references that do not teach the claimed dosage. For these reasons, I would have found the district court's finding to be clearly erroneous and would vacate the district court's judgment that the IBS-D claims were invalid as obvious.

II

In affirming the district court's judgment of obviousness, the majority relies on one additional sentence in Pimentel 2006 regarding the reasonable expectation of success analysis: "Recent data suggest that the optimal dosage of rifaximin may, in fact, be higher than that used in our study." J.A. 4644; *see* Maj. Op. 8. But the lack of discussion of any actual dosage that may be optimal, the use of the word "may," and the fact that the RFIB 2001 Protocol discloses a specific dosing regimen of 2,200 mg/day rather than 1,650 mg/day all call into question the majority's finding. Indeed, the district court only relied on this sentence in its motivation to combine analysis and did not rely on this sentence in its reasonable expectation of success analysis. *See Decision* at *18–20. The parties never made this argument before us. Therefore, I disagree that this additional sentence, when considered together with the RFIB 2001 Protocol, would give rise to a reasonable expectation of success for the claimed dosage.

The majority also discusses references not relied on by the district court in its reasonable expectation of success

analysis, including Lauritano[9], Scarpellini[10], and Lin.[11] Maj. Op. 9–10. But the district court did not make any findings on what these references teach, other than finding that the references were prior art. *See Decision* at *17–22. Nor are the majority's conclusions regarding these references uncontested. For example, Salix argues that Scarpellini and Lauritano are both directed to the treatment of small intestinal bacterial overgrowth (SIBO), not to the treatment of IBS or IBS-D, and therefore cannot establish a reasonable expectation of success. Appellant's Reply Br. 18. Although the majority may be right that Lauritano's and Scarpellini's disclosures on treating SIBO also support finding a reasonable expectation of success for treating IBS-D, *see* Maj. Op. 9–10, the district court never made this finding. *See Golden Bridge Tech., Inc. v. Nokia, Inc.*, 527 F.3d 1318, 1323 (Fed. Cir. 2008) (declining to find what a prior art reference teaches in the first instance). It merely found that "[t]he relationship between IBS and SIBO was actively being explored," and that certain prior art references "do not teach away from using rifaximin to treat IBS." *Decision* at *21. I would not make such fact-findings about Scarpellini and Lauritano in the first instance.

In summary, I would vacate the district court's judgment that the asserted claims of the IBS-D patents were obvious and remand for further proceedings. On remand, I would order the district court to consider in the first instance the teachings in the additional prior art references.

---

[9] E.C. Lauritano et al., *Rifaximin dose-finding study for the treatment of small intestinal bacterial overgrowth*, 22 ALIMENT. PHARMACOL. THER. 31 (2005); J.A. 7267–71.

[10] E. Scarpellini et al., *High dosage rifaximin for the treatment of small intestinal bacterial overgrowth*, 25 ALIMENT. PHARMACOL. THER. 781 (2007); J.A. 4663–67.

[11] International Patent Application Publication No. WO 2006/102536; J.A. 4721–47.

See ACS Hosp. Sys., Inc. v. Montefiore Hosp., 732 F.2d 1572, 1578 (Fed. Cir. 1984) ("Where the trial court fails to make findings, the judgment will normally be vacated and the action remanded for appropriate findings to be made."). Accordingly, I respectfully dissent in part.

Tab 2

KeyCite Yellow Flag - Negative Treatment
Unconstitutional or Preempted Prior Version Held Unconstitutional by Florida Prepaid Postsecondary Educ. Expense Bd. v. College Sav. Bank, U.S.N.J., June 23, 1999

KeyCite Yellow Flag - Negative Treatment
Proposed Legislation

United States Code Annotated
Title 35. Patents (Refs & Annos)
Part III. Patents and Protection of Patent Rights
Chapter 28. Infringement of Patents (Refs & Annos)

35 U.S.C.A. § 271

§ 271. Infringement of patent

Effective: March 23, 2010
Currentness

(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.

(b) Whoever actively induces infringement of a patent shall be liable as an infringer.

(c) Whoever offers to sell or sells within the United States or imports into the United States a component of a patented machine, manufacture, combination or composition, or a material or apparatus for use in practicing a patented process, constituting a material part of the invention, knowing the same to be especially made or especially adapted for use in an infringement of such patent, and not a staple article or commodity of commerce suitable for substantial noninfringing use, shall be liable as a contributory infringer.

(d) No patent owner otherwise entitled to relief for infringement or contributory infringement of a patent shall be denied relief or deemed guilty of misuse or illegal extension of the patent right by reason of his having done one or more of the following: (1) derived revenue from acts which if performed by another without his consent would constitute contributory infringement of the patent; (2) licensed or authorized another to perform acts which if performed without his consent would constitute contributory infringement of the patent; (3) sought to enforce his patent rights against infringement or contributory infringement; (4) refused to license or use any rights to the patent; or (5) conditioned the license of any rights to the patent or the sale of the patented product on the acquisition of a license to rights in another patent or purchase of a separate product, unless, in view of the circumstances, the patent owner has market power in the relevant market for the patent or patented product on which the license or sale is conditioned.

(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.

(2) It shall be an act of infringement to submit--

(A) an application under section 505(j) of the Federal Food, Drug, and Cosmetic Act or described in section 505(b)(2) of such Act for a drug claimed in a patent or the use of which is claimed in a patent,

(B) an application under section 512 of such Act or under the Act of March 4, 1913 (21 U.S.C. 151-158) for a drug or veterinary biological product which is not primarily manufactured using recombinant DNA, recombinant RNA, hybridoma technology, or other processes involving site specific genetic manipulation techniques and which is claimed in a patent or the use of which is claimed in a patent, or

(C)(i) with respect to a patent that is identified in the list of patents described in section 351(l)(3) of the Public Health Service Act (including as provided under section 351(l)(7) of such Act), an application seeking approval of a biological product, or

(ii) if the applicant for the application fails to provide the application and information required under section 351(l)(2)(A) of such Act, an application seeking approval of a biological product for a patent that could be identified pursuant to section 351(l)(3)(A)(i) of such Act,

if the purpose of such submission is to obtain approval under such Act to engage in the commercial manufacture, use, or sale of a drug, veterinary biological product, or biological product claimed in a patent or the use of which is claimed in a patent before the expiration of such patent.

(3) In any action for patent infringement brought under this section, no injunctive or other relief may be granted which would prohibit the making, using, offering to sell, or selling within the United States or importing into the United States of a patented invention under paragraph (1).

(4) For an act of infringement described in paragraph (2)--

(A) the court shall order the effective date of any approval of the drug or veterinary biological product involved in the infringement to be a date which is not earlier than the date of the expiration of the patent which has been infringed,

(B) injunctive relief may be granted against an infringer to prevent the commercial manufacture, use, offer to sell, or sale within the United States or importation into the United States of an approved drug, veterinary biological product, or biological product,

(C) damages or other monetary relief may be awarded against an infringer only if there has been commercial manufacture, use, offer to sell, or sale within the United States or importation into the United States of an approved drug, veterinary biological product, or biological product, and

(D) the court shall order a permanent injunction prohibiting any infringement of the patent by the biological product involved in the infringement until a date which is not earlier than the date of the expiration of the patent that has been infringed under paragraph (2)(C), provided the patent is the subject of a final court decision, as defined in section 351(k)(6) of the Public Health Service Act, in an action for infringement of the patent under section 351(l)(6) of such Act, and the biological product has not yet been approved because of section 351(k)(7) of such Act.

The remedies prescribed by subparagraphs (A), (B), (C), and (D) are the only remedies which may be granted by a court for an act of infringement described in paragraph (2), except that a court may award attorney fees under section 285.

(5) Where a person has filed an application described in paragraph (2) that includes a certification under subsection (b)(2)(A)(iv) or (j)(2)(A)(vii)(IV) of section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355), and neither the owner of the patent that is the subject of the certification nor the holder of the approved application under subsection (b) of such section for the drug that is claimed by the patent or a use of which is claimed by the patent brought an action for infringement of such patent before the expiration of 45 days after the date on which the notice given under subsection (b)(3) or (j)(2)(B) of such section was received, the courts of the United States shall, to the extent consistent with the Constitution, have subject matter jurisdiction in any action brought by such person under section 2201 of title 28 for a declaratory judgment that such patent is invalid or not infringed.

(6)(A) Subparagraph (B) applies, in lieu of paragraph (4), in the case of a patent--

(i) that is identified, as applicable, in the list of patents described in section 351(l)(4) of the Public Health Service Act or the lists of patents described in section 351(l)(5)(B) of such Act with respect to a biological product; and

(ii) for which an action for infringement of the patent with respect to the biological product--

(I) was brought after the expiration of the 30-day period described in subparagraph (A) or (B), as applicable, of section 351(l)(6) of such Act; or

(II) was brought before the expiration of the 30-day period described in subclause (I), but which was dismissed without prejudice or was not prosecuted to judgment in good faith.

(B) In an action for infringement of a patent described in subparagraph (A), the sole and exclusive remedy that may be granted by a court, upon a finding that the making, using, offering to sell, selling, or importation into the United States of the biological product that is the subject of the action infringed the patent, shall be a reasonable royalty.

(C) The owner of a patent that should have been included in the list described in section 351(l)(3)(A) of the Public Health Service Act, including as provided under section 351(l)(7) of such Act for a biological product, but was not timely included in such list, may not bring an action under this section for infringement of the patent with respect to the biological product.

(f)(1) Whoever without authority supplies or causes to be supplied in or from the United States all or a substantial portion of the components of a patented invention, where such components are uncombined in whole or in part, in such manner as to actively

induce the combination of such components outside of the United States in a manner that would infringe the patent if such combination occurred within the United States, shall be liable as an infringer.

(2) Whoever without authority supplies or causes to be supplied in or from the United States any component of a patented invention that is especially made or especially adapted for use in the invention and not a staple article or commodity of commerce suitable for substantial noninfringing use, where such component is uncombined in whole or in part, knowing that such component is so made or adapted and intending that such component will be combined outside of the United States in a manner that would infringe the patent if such combination occurred within the United States, shall be liable as an infringer.

(g) Whoever without authority imports into the United States or offers to sell, sells, or uses within the United States a product which is made by a process patented in the United States shall be liable as an infringer, if the importation, offer to sell, sale, or use of the product occurs during the term of such process patent. In an action for infringement of a process patent, no remedy may be granted for infringement on account of the noncommercial use or retail sale of a product unless there is no adequate remedy under this title for infringement on account of the importation or other use, offer to sell, or sale of that product. A product which is made by a patented process will, for purposes of this title, not be considered to be so made after--

(1) it is materially changed by subsequent processes; or

(2) it becomes a trivial and nonessential component of another product.

(h) As used in this section, the term "whoever" includes any State, any instrumentality of a State, and any officer or employee of a State or instrumentality of a State acting in his official capacity. Any State, and any such instrumentality, officer, or employee, shall be subject to the provisions of this title in the same manner and to the same extent as any nongovernmental entity.

(i) As used in this section, an "offer for sale" or an "offer to sell" by a person other than the patentee, or any designee of the patentee, is that in which the sale will occur before the expiration of the term of the patent.

CREDIT(S)

(July 19, 1952, c. 950, 66 Stat. 811; Pub.L. 98-417, Title II, § 202, Sept. 24, 1984, 98 Stat. 1603; Pub.L. 98-622, Title I, § 101(a), Nov. 8, 1984, 98 Stat. 3383; Pub.L. 100-418, Title IX, § 9003, Aug. 23, 1988, 102 Stat. 1563; Pub.L. 100-670, Title II, § 201(i), Nov. 16, 1988, 102 Stat. 3988; Pub.L. 100-703, Title II, § 201, Nov. 19, 1988, 102 Stat. 4676; Pub.L. 102-560, § 2(a)(1), Oct. 28, 1992, 106 Stat. 4230; Pub.L. 103-465, Title V, § 533(a), Dec. 8, 1994, 108 Stat. 4988; Pub.L. 108-173, Title XI, § 1101(d), Dec. 8, 2003, 117 Stat. 2457; Pub.L. 111-148, Title VII, § 7002(c)(1), Mar. 23, 2010, 124 Stat. 815.)

VALIDITY

<For validity of the Patent and Plant Variety Protection Remedy Clarification Act, Pub.L. 102-560, which added subsec. (h) to this section, see Florida Prepaid Postsecondary Education Expense Board v. College Savings Bank, U.S.N.J.1999, 527 U.S. 627, 119 S.Ct. 2199, 144 L.Ed. 2d 575.>

Notes of Decisions (3480)

35 U.S.C.A. § 271, 35 USCA § 271
Current through P.L. 118-46. Some statute sections may be more current, see credits for details.

Tab 3

KeyCite Yellow Flag - Negative Treatment
Unconstitutional or Preempted Negative Treatment Reconsidered by Florida ex rel. Atty. Gen. v. U.S. Dept. of Health and Human Services, 11th Cir.(Fla.), Aug. 12, 2011

KeyCite Yellow Flag - Negative Treatment
Proposed Legislation

United States Code Annotated
Title 21. Food and Drugs (Refs & Annos)
Chapter 9. Federal Food, Drug, and Cosmetic Act (Refs & Annos)
Subchapter V. Drugs and Devices
Part A. Drugs and Devices (Refs & Annos)

21 U.S.C.A. § 355

§ 355. New drugs

Effective: December 29, 2022
Currentness

(a) Necessity of effective approval of application

No person shall introduce or deliver for introduction into interstate commerce any new drug, unless an approval of an application filed pursuant to subsection (b) or (j) is effective with respect to such drug.

(b) Filing application; contents

(1)(A) Any person may file with the Secretary an application with respect to any drug subject to the provisions of subsection (a). Such persons shall submit to the Secretary as part of the application--

(i) full reports of investigations which have been made to show whether such drug is safe for use and whether such drug is effective in use;

(ii) a full list of the articles used as components of such drug;

(iii) a full statement of the composition of such drug;

(iv) a full description of the methods used in, and the facilities and controls used for, the manufacture, processing, and packing of such drug;

(v) such samples of such drug and of the articles used as components thereof as the Secretary may require;

(vi) specimens of the labeling proposed to be used for such drug;

(vii) any assessments required under section 355c of this title; and

(viii) the patent number and expiration date of each patent for which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use, or sale of the drug, and that--

(I) claims the drug for which the applicant submitted the application and is a drug substance (active ingredient) patent or a drug product (formulation or composition) patent; or

(II) claims a method of using such drug for which approval is sought or has been granted in the application.

(B) If an application is filed under this subsection for a drug, and a patent of the type described in subparagraph (A)(viii) is issued after the filing date but before approval of the application, the applicant shall amend the application to include the patent number and expiration date.

(2) An application submitted under paragraph (1) for a drug for which the investigations described in clause (A) of such paragraph and relied upon by the applicant for approval of the application were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted shall also include--

(A) a certification, in the opinion of the applicant and to the best of his knowledge, with respect to each patent which claims the drug for which such investigations were conducted or which claims a use for such drug for which the applicant is seeking approval under this subsection and for which information is required to be filed under paragraph (1) or subsection (c)--

(i) that such patent information has not been filed,

(ii) that such patent has expired,

(iii) of the date on which such patent will expire, or

(iv) that such patent is invalid or will not be infringed by the manufacture, use, or sale of the new drug for which the application is submitted; and

(B) if with respect to the drug for which investigations described in paragraph (1)(A) were conducted information was filed under paragraph (1) or subsection (c) for a method of use patent which does not claim a use for which the applicant is seeking approval under this subsection, a statement that the method of use patent does not claim such a use.

(3) Notice of opinion that patent is invalid or will not be infringed

(A) Agreement to give notice

An applicant that makes a certification described in paragraph (2)(A)(iv) shall include in the application a statement that the applicant will give notice as required by this paragraph.

(B) Timing of notice

An applicant that makes a certification described in paragraph (2)(A)(iv) shall give notice as required under this paragraph--

(i) if the certification is in the application, not later than 20 days after the date of the postmark on the notice with which the Secretary informs the applicant that the application has been filed; or

(ii) if the certification is in an amendment or supplement to the application, at the time at which the applicant submits the amendment or supplement, regardless of whether the applicant has already given notice with respect to another such certification contained in the application or in an amendment or supplement to the application.

(C) Recipients of notice

An applicant required under this paragraph to give notice shall give notice to--

(i) each owner of the patent that is the subject of the certification (or a representative of the owner designated to receive such a notice); and

(ii) the holder of the approved application under this subsection for the drug that is claimed by the patent or a use of which is claimed by the patent (or a representative of the holder designated to receive such a notice).

(D) Contents of notice

A notice required under this paragraph shall--

(i) state that an application that contains data from bioavailability or bioequivalence studies has been submitted under this subsection for the drug with respect to which the certification is made to obtain approval to engage in the commercial manufacture, use, or sale of the drug before the expiration of the patent referred to in the certification; and

(ii) include a detailed statement of the factual and legal basis of the opinion of the applicant that the patent is invalid or will not be infringed.

(4)(A) An applicant may not amend or supplement an application referred to in paragraph (2) to seek approval of a drug that is a different drug than the drug identified in the application as submitted to the Secretary.

(B) With respect to the drug for which such an application is submitted, nothing in this subsection or subsection (c)(3) prohibits an applicant from amending or supplementing the application to seek approval of a different strength.

(5)(A) The Secretary shall issue guidance for the individuals who review applications submitted under paragraph (1) or under section 262 of Title 42, which shall relate to promptness in conducting the review, technical excellence, lack of bias and conflict of interest, and knowledge of regulatory and scientific standards, and which shall apply equally to all individuals who review such applications.

(B) The Secretary shall meet with a sponsor of an investigation or an applicant for approval for a drug under this subsection or section 262 of Title 42 if the sponsor or applicant makes a reasonable written request for a meeting for the purpose of reaching agreement on the design and size--

(i)(I) of clinical trials intended to form the primary basis of an effectiveness claim; or

(II) in the case where human efficacy studies are not ethical or feasible, of animal and any associated clinical trials which, in combination, are intended to form the primary basis of an effectiveness claim; or

(ii) with respect to an application for approval of a biological product under section 262(k) of Title 42, of any necessary clinical study or studies.

The sponsor or applicant shall provide information necessary for discussion and agreement on the design and size of the clinical trials. Minutes of any such meeting shall be prepared by the Secretary and made available to the sponsor or applicant upon request.

(C) Any agreement regarding the parameters of the design and size of clinical trials of a new drug under this paragraph that is reached between the Secretary and a sponsor or applicant shall be reduced to writing and made part of the administrative record by the Secretary. Such agreement shall not be changed after the testing begins, except--

(i) with the written agreement of the sponsor or applicant; or

(ii) pursuant to a decision, made in accordance with subparagraph (D) by the director of the reviewing division, that a substantial scientific issue essential to determining the safety or effectiveness of the drug has been identified after the testing has begun.

(D) A decision under subparagraph (C)(ii) by the director shall be in writing and the Secretary shall provide to the sponsor or applicant an opportunity for a meeting at which the director and the sponsor or applicant will be present and at which the director will document the scientific issue involved.

(E) The written decisions of the reviewing division shall be binding upon, and may not directly or indirectly be changed by, the field or compliance division personnel unless such field or compliance division personnel demonstrate to the reviewing division why such decision should be modified.

(F) No action by the reviewing division may be delayed because of the unavailability of information from or action by field personnel unless the reviewing division determines that a delay is necessary to assure the marketing of a safe and effective drug.

(G) For purposes of this paragraph, the reviewing division is the division responsible for the review of an application for approval of a drug under this subsection or section 262 of Title 42 (including all scientific and medical matters, chemistry, manufacturing, and controls).

(6) An application submitted under this subsection shall be accompanied by the certification required under section 282(j)(5)(B) of Title 42. Such certification shall not be considered an element of such application.

(c) Period for approval of application; period for, notice, and expedition of hearing; period for issuance of order

(1) Within one hundred and eighty days after the filing of an application under subsection (b), or such additional period as may be agreed upon by the Secretary and the applicant, the Secretary shall either--

(A) approve the application if he then finds that none of the grounds for denying approval specified in subsection (d) applies, or

(B) give the applicant notice of an opportunity for a hearing before the Secretary under subsection (d) on the question whether such application is approvable. If the applicant elects to accept the opportunity for hearing by written request within thirty days after such notice, such hearing shall commence not more than ninety days after the expiration of such thirty days unless the Secretary and the applicant otherwise agree. Any such hearing shall thereafter be conducted on an expedited basis and the Secretary's order thereon shall be issued within ninety days after the date fixed by the Secretary for filing final briefs.

(2) Not later than 30 days after the date of approval of an application submitted under subsection (b), the holder of the approved application shall file with the Secretary the patent number and the expiration date of any patent described in subsection (b)(1)(A)(viii), except that a patent that is identified as claiming a method of using such drug shall be filed only if the patent claims a method of use approved in the application. If a patent described in subsection (b)(1)(A)(viii) is issued after the date of approval of an application submitted under subsection (b), the holder of the approved application shall, not later than 30 days after the date of issuance of the patent, file the patent number and the expiration date of the patent, except that a patent that claims a method of using such drug shall be filed only if approval for such use has been granted in the application. If the patent information described in subsection (b) could not be filed with the submission of an application under subsection (b) because the application was filed before the patent information was required under subsection (b) or a patent was issued after the application was approved under such subsection, the holder of an approved application shall file with the Secretary the patent number and the expiration date of any patent described in subsection (b)(1)(A)(viii). If the holder of an approved application could not file patent information under subsection (b) because it was not required at the time the application was approved, the holder shall file such information under this subsection not later than thirty days after September 24, 1984, and if the holder of an approved application could not file patent information under subsection (b) because no patent of the type for which information is required to be submitted in subsection (b)(1)(A)(viii) had been issued when an application was filed or approved, the holder shall file such information under this subsection not later than thirty days after the date the patent involved is issued. Upon the submission of patent information under this subsection, the Secretary shall publish it. Patent information that is not the type of patent information required by subsection (b)(1)(A)(viii) shall not be submitted under this paragraph.

(3) The approval of an application filed under subsection (b) which contains a certification required by paragraph (2) of such subsection shall be made effective on the last applicable date determined by applying the following to each certification made under subsection (b)(2)(A):

(A) If the applicant only made a certification described in clause (i) or (ii) of subsection (b)(2)(A) or in both such clauses, the approval may be made effective immediately.

(B) If the applicant made a certification described in clause (iii) of subsection (b)(2)(A), the approval may be made effective on the date certified under clause (iii).

(C) If the applicant made a certification described in clause (iv) of subsection (b)(2)(A), the approval shall be made effective immediately unless, before the expiration of 45 days after the date on which the notice described in subsection (b)(3) is received, an action is brought for infringement of the patent that is the subject of the certification and for which information was submitted to the Secretary under paragraph (2) or subsection (b)(1) before the date on which the application (excluding an amendment or supplement to the application) was submitted. If such an action is brought before the expiration of such days, the approval may be made effective upon the expiration of the thirty-month period beginning on the date of the receipt of the notice provided under subsection (b)(3) or such shorter or longer period as the court may order because either party to the action failed to reasonably cooperate in expediting the action, except that--

(i) if before the expiration of such period the district court decides that the patent is invalid or not infringed (including any substantive determination that there is no cause of action for patent infringement or invalidity), the approval shall be made effective on--

(I) the date on which the court enters judgment reflecting the decision; or

(II) the date of a settlement order or consent decree signed and entered by the court stating that the patent that is the subject of the certification is invalid or not infringed;

(ii) if before the expiration of such period the district court decides that the patent has been infringed--

(I) if the judgment of the district court is appealed, the approval shall be made effective on--

(aa) the date on which the court of appeals decides that the patent is invalid or not infringed (including any substantive determination that there is no cause of action for patent infringement or invalidity); or

(bb) the date of a settlement order or consent decree signed and entered by the court of appeals stating that the patent that is the subject of the certification is invalid or not infringed; or

(II) if the judgment of the district court is not appealed or is affirmed, the approval shall be made effective on the date specified by the district court in a court order under section 271(e)(4)(A) of Title 35;

(iii) if before the expiration of such period the court grants a preliminary injunction prohibiting the applicant from engaging in the commercial manufacture or sale of the drug until the court decides the issues of patent validity and infringement and if the court decides that such patent is invalid or not infringed, the approval shall be made effective as provided in clause (i); or

(iv) if before the expiration of such period the court grants a preliminary injunction prohibiting the applicant from engaging in the commercial manufacture or sale of the drug until the court decides the issues of patent validity and infringement and if the court decides that such patent has been infringed, the approval shall be made effective as provided in clause (ii).

In such an action, each of the parties shall reasonably cooperate in expediting the action.

(D) Civil action to obtain patent certainty

(i) Declaratory judgment absent infringement action

(I) In general

No action may be brought under section 2201 of Title 28 by an applicant referred to in subsection (b)(2) for a declaratory judgment with respect to a patent which is the subject of the certification referred to in subparagraph (C) unless--

(aa) the 45-day period referred to in such subparagraph has expired;

(bb) neither the owner of such patent nor the holder of the approved application under subsection (b) for the drug that is claimed by the patent or a use of which is claimed by the patent brought a civil action against the applicant for infringement of the patent before the expiration of such period; and

(cc) in any case in which the notice provided under paragraph (2)(B) relates to noninfringement, the notice was accompanied by a document described in subclause (III).

(II) Filing of civil action

If the conditions described in items (aa), (bb), and as applicable, (cc) of subclause (I) have been met, the applicant referred to in such subclause may, in accordance with section 2201 of Title 28, bring a civil action under such section against the owner or holder referred to in such subclause (but not against any owner or holder that has brought such a civil action against the applicant, unless that civil action was dismissed without prejudice) for a declaratory judgment that the patent is invalid or will not be infringed by the drug for which the applicant seeks approval, except that such civil action may be brought for a declaratory judgment that the patent will not be infringed only in a case in which the condition described in subclause (I)(cc) is applicable. A civil action referred to in this subclause shall be brought in the judicial district where the defendant has its principal place of business or a regular and established place of business.

(III) Offer of confidential access to application

For purposes of subclause (I)(cc), the document described in this subclause is a document providing an offer of confidential access to the application that is in the custody of the applicant referred to in subsection (b)(2) for the purpose of determining whether an action referred to in subparagraph (C) should be brought. The document providing the offer of confidential access shall contain such restrictions as to persons entitled to access, and on the use and disposition of any information accessed, as would apply had a protective order been entered for the purpose of protecting trade secrets and other confidential business information. A request for access to an application under an offer of confidential access shall be considered acceptance of the offer of confidential access with the restrictions as to persons entitled to access, and on the use and disposition of any information accessed, contained in the offer of confidential access, and those restrictions and other terms of the offer of confidential access shall be considered terms of an enforceable contract. Any person provided an offer of confidential access shall review the application for the sole and limited purpose of evaluating possible infringement of the patent that is the subject of the certification under subsection (b)(2)(A)(iv) and for no other purpose, and may not disclose information of no relevance to any issue of patent infringement to any person other than a person provided an offer of confidential access. Further, the application may be redacted by the applicant to remove any information of no relevance to any issue of patent infringement.

(ii) Counterclaim to infringement action

(I) In general

If an owner of the patent or the holder of the approved application under subsection (b) for the drug that is claimed by the patent or a use of which is claimed by the patent brings a patent infringement action against the applicant, the applicant may assert a counterclaim seeking an order requiring the holder to correct or delete the patent information submitted by the holder under subsection (b) or this subsection on the ground that the patent does not claim either--

(aa) the drug for which the application was approved; or

(bb) an approved method of using the drug.

(II) No independent cause of action

Subclause (I) does not authorize the assertion of a claim described in subclause (I) in any civil action or proceeding other than a counterclaim described in subclause (I).

(iii) No damages

An applicant shall not be entitled to damages in a civil action under clause (i) or a counterclaim under clause (ii).

(E)(i) Repealed. Pub.L. 117-9, § 1(b)(1)(A), Apr. 23, 2021, 135 Stat. 258

(ii) If an application submitted under subsection (b) for a drug, no active moiety (as defined by the Secretary in section 314.3 of title 21, Code of Federal Regulations (or any successor regulations)) of which has been approved in any other application under subsection (b), is approved after September 24, 1984, no application which refers to the drug for which the subsection

(b) application was submitted and for which the investigations described in subsection (b)(1)(A)(i) and relied upon by the applicant for approval of the application were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted may be submitted under subsection (b) before the expiration of five years from the date of the approval of the application under subsection (b), except that such an application may be submitted under subsection (b) after the expiration of four years from the date of the approval of the subsection (b) application if it contains a certification of patent invalidity or noninfringement described in clause (iv) of subsection (b)(2)(A). The approval of such an application shall be made effective in accordance with this paragraph except that, if an action for patent infringement is commenced during the one-year period beginning forty-eight months after the date of the approval of the subsection (b) application, the thirty-month period referred to in subparagraph (C) shall be extended by such amount of time (if any) which is required for seven and one-half years to have elapsed from the date of approval of the subsection (b) application.

(iii) If an application submitted under subsection (b) for a drug, which includes an active moiety (as defined by the Secretary in section 314.3 of title 21, Code of Federal Regulations (or any successor regulations)) that has been approved in another application approved under subsection (b), is approved after September 24, 1984, and if such application contains reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant, the Secretary may not make the approval of an application submitted under subsection (b) for the conditions of approval of such drug in the approved subsection (b) application effective before the expiration of three years from the date of the approval of the application under subsection (b) if the investigations described in subsection (b)(1)(A)(i) and relied upon by the applicant for approval of the application were not conducted by or for the applicant and if the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted.

(iv) If a supplement to an application approved under subsection (b) is approved after September 24, 1984, and the supplement contains reports of new clinical investigations (other than bioavailabilty [1] studies) essential to the approval of the supplement and conducted or sponsored by the person submitting the supplement, the Secretary may not make the approval of an application submitted under subsection (b) for a change approved in the supplement effective before the expiration of three years from the date of the approval of the supplement under subsection (b) if the investigations described in subsection (b)(1)(A)(i) and relied upon by the applicant for approval of the application were not conducted by or for the applicant and if the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted.

(v) If an application (or supplement to an application) submitted under subsection (b) for a drug, which includes an active moiety (as defined by the Secretary in section 314.3 of title 21, Code of Federal Regulations (or any successor regulations)) that has been approved in another application under subsection (b), was approved during the period beginning January 1, 1982, and ending on September 24, 1984, the Secretary may not make the approval of an application submitted under this subsection and for which the investigations described in subsection (b)(1)(A)(i) and relied upon by the applicant for approval of the application were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted and which refers to the drug for which the subsection (b) application was submitted effective before the expiration of two years from September 24, 1984.

(4) A drug manufactured in a pilot or other small facility may be used to demonstrate the safety and effectiveness of the drug and to obtain approval for the drug prior to manufacture of the drug in a larger facility, unless the Secretary makes a determination that a full scale production facility is necessary to ensure the safety or effectiveness of the drug.

(5)(A) The Secretary may rely upon qualified data summaries to support the approval of a supplemental application, with respect to a qualified indication for a drug, submitted under subsection (b), if such supplemental application complies with subparagraph (B).

(B) A supplemental application is eligible for review as described in subparagraph (A) only if--

(i) there is existing data available and acceptable to the Secretary demonstrating the safety of the drug; and

(ii) all data used to develop the qualified data summaries are submitted to the Secretary as part of the supplemental application.

(C) The Secretary shall post on the Internet website of the Food and Drug Administration and update annually--

(i) the number of applications reviewed solely under subparagraph (A) or section 262(a)(2)(E) of Title 42;

(ii) the average time for completion of review under subparagraph (A) or section 262(a)(2)(E) of Title 42;

(iii) the average time for review of supplemental applications where the Secretary did not use review flexibility under subparagraph (A) or section 262(a)(2)(E) of Title 42; and

(iv) the number of applications reviewed under subparagraph (A) or section 262(a)(2)(E) of Title 42 for which the Secretary made use of full data sets in addition to the qualified data summary.

(D) In this paragraph--

(i) the term "qualified indication" means an indication for a drug that the Secretary determines to be appropriate for summary level review under this paragraph; and

(ii) the term "qualified data summary" means a summary of clinical data that demonstrates the safety and effectiveness of a drug with respect to a qualified indication.

(d) Grounds for refusing application; approval of application; "substantial evidence" defined

If the Secretary finds, after due notice to the applicant in accordance with subsection (c) and giving him an opportunity for a hearing, in accordance with said subsection, that (1) the investigations, reports of which are required to be submitted to the Secretary pursuant to subsection (b), do not include adequate tests by all methods reasonably applicable to show whether or not such drug is safe for use under the conditions prescribed, recommended, or suggested in the proposed labeling thereof; (2) the results of such tests show that such drug is unsafe for use under such conditions or do not show that such drug is safe for use under such conditions; (3) the methods used in, and the facilities and controls used for, the manufacture, processing, and packing of such drug are inadequate to preserve its identity, strength, quality, and purity; (4) upon the basis of the information submitted to him as part of the application, or upon the basis of any other information before him with respect to such drug,

he has insufficient information to determine whether such drug is safe for use under such conditions; or (5) evaluated on the basis of the information submitted to him as part of the application and any other information before him with respect to such drug, there is a lack of substantial evidence that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the proposed labeling thereof; or (6) the application failed to contain the patent information prescribed by subsection (b); or (7) based on a fair evaluation of all material facts, such labeling is false or misleading in any particular; he shall issue an order refusing to approve the application. If, after such notice and opportunity for hearing, the Secretary finds that clauses (1) through (6) do not apply, he shall issue an order approving the application. As used in this subsection and subsection (e), the term "substantial evidence" means evidence consisting of adequate and well-controlled investigations, including clinical investigations, by experts qualified by scientific training and experience to evaluate the effectiveness of the drug involved, on the basis of which it could fairly and responsibly be concluded by such experts that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling or proposed labeling thereof. If the Secretary determines, based on relevant science, that data from one adequate and well-controlled clinical investigation and confirmatory evidence (obtained prior to or after such investigation) are sufficient to establish effectiveness, the Secretary may consider such data and evidence to constitute substantial evidence for purposes of the preceding sentence. The Secretary shall implement a structured risk-benefit assessment framework in the new drug approval process to facilitate the balanced consideration of benefits and risks, a consistent and systematic approach to the discussion and regulatory decisionmaking, and the communication of the benefits and risks of new drugs. Nothing in the preceding sentence shall alter the criteria for evaluating an application for marketing approval of a drug.

(e) Withdrawal of approval; grounds; immediate suspension upon finding imminent hazard to public health

The Secretary shall, after due notice and opportunity for hearing to the applicant, withdraw approval of an application with respect to any drug under this section if the Secretary finds (1) that clinical or other experience, tests, or other scientific data show that such drug is unsafe for use under the conditions of use upon the basis of which the application was approved; (2) that new evidence of clinical experience, not contained in such application or not available to the Secretary until after such application was approved, or tests by new methods, or tests by methods not deemed reasonably applicable when such application was approved, evaluated together with the evidence available to the Secretary when the application was approved, shows that such drug is not shown to be safe for use under the conditions of use upon the basis of which the application was approved; or (3) on the basis of new information before him with respect to such drug, evaluated together with the evidence available to him when the application was approved, that there is a lack of substantial evidence that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling thereof; or (4) the patent information prescribed by subsection (c) was not filed within thirty days after the receipt of written notice from the Secretary specifying the failure to file such information; or (5) that the application contains any untrue statement of a material fact: *Provided*, That if the Secretary (or in his absence the officer acting as Secretary) finds that there is an imminent hazard to the public health, he may suspend the approval of such application immediately, and give the applicant prompt notice of his action and afford the applicant the opportunity for an expedited hearing under this subsection; but the authority conferred by this proviso to suspend the approval of an application shall not be delegated. The Secretary may also, after due notice and opportunity for hearing to the applicant, withdraw the approval of an application submitted under subsection (b) or (j) with respect to any drug under this section if the Secretary finds (1) that the applicant has failed to establish a system for maintaining required records, or has repeatedly or deliberately failed to maintain such records or to make required reports, in accordance with a regulation or order under subsection (k) or to comply with the notice requirements of section 360(k)(2) of this title, or the applicant has refused to permit access to, or copying or verification of, such records as required by paragraph (2) of such subsection; or (2) that on the basis of new information before him, evaluated together with the evidence before him when the application was approved, the methods used in, or the facilities and controls used for, the manufacture, processing, and packing of such drug are inadequate to assure and preserve its identity, strength, quality, and purity and were not made adequate within a reasonable time after receipt of written notice from the Secretary specifying the matter complained of; or (3) that on the basis of new information before him, evaluated together with the evidence before him when the application was approved, the labeling of such drug, based on a fair evaluation of all material facts, is false or misleading in any particular and was not corrected within a reasonable time after receipt of written notice from the Secretary specifying the matter complained of. Any order under this

subsection shall state the findings upon which it is based. The Secretary may withdraw the approval of an application submitted under this section, or suspend the approval of such an application, as provided under this subsection, without first ordering the applicant to submit an assessment of the approved risk evaluation and mitigation strategy for the drug under section 355-1(g)(2)(D) of this title.

(f) Revocation of order refusing, withdrawing or suspending approval of application

Whenever the Secretary finds that the facts so require, he shall revoke any previous order under subsection (d) or (e) refusing, withdrawing, or suspending approval of an application and shall approve such application or reinstate such approval, as may be appropriate.

(g) Service of orders

Orders of the Secretary issued under this section shall be served (1) in person by any officer or employee of the department designated by the Secretary or (2) by mailing the order by registered mail or by certified mail addressed to the applicant or respondent at his last-known address in the records of the Secretary.

(h) Appeal from order

An appeal may be taken by the applicant from an order of the Secretary refusing or withdrawing approval of an application under this section. Such appeal shall be taken by filing in the United States court of appeals for the circuit wherein such applicant resides or has his principal place of business, or in the United States Court of Appeals for the District of Columbia Circuit, within sixty days after the entry of such order, a written petition praying that the order of the Secretary be set aside. A copy of such petition shall be forthwith transmitted by the clerk of the court to the Secretary, or any officer designated by him for that purpose, and thereupon the Secretary shall certify and file in the court the record upon which the order complained of was entered, as provided in section 2112 of Title 28. Upon the filing of such petition such court shall have exclusive jurisdiction to affirm or set aside such order, except that until the filing of the record the Secretary may modify or set aside his order. No objection to the order of the Secretary shall be considered by the court unless such objection shall have been urged before the Secretary or unless there were reasonable grounds for failure so to do. The finding of the Secretary as to the facts, if supported by substantial evidence, shall be conclusive. If any person shall apply to the court for leave to adduce additional evidence, and shall show to the satisfaction of the court that such additional evidence is material and that there were reasonable grounds for failure to adduce such evidence in the proceeding before the Secretary, the court may order such additional evidence to be taken before the Secretary and to be adduced upon the hearing in such manner and upon such terms and conditions as to the court may seem proper. The Secretary may modify his findings as to the facts by reason of the additional evidence so taken, and he shall file with the court such modified findings which, if supported by substantial evidence, shall be conclusive, and his recommendation, if any, for the setting aside of the original order. The judgment of the court affirming or setting aside any such order of the Secretary shall be final, subject to review by the Supreme Court of the United States upon certiorari or certification as provided in section 1254 of Title 28. The commencement of proceedings under this subsection shall not, unless specifically ordered by the court to the contrary, operate as a stay of the Secretary's order.

(i) Exemptions of drugs for research; discretionary and mandatory conditions; direct reports to Secretary

(1) The Secretary shall promulgate regulations for exempting from the operation of the foregoing subsections of this section drugs intended solely for investigational use by experts qualified by scientific training and experience to investigate the safety and effectiveness of drugs. Such regulations may, within the discretion of the Secretary, among other conditions relating to the protection of the public health, provide for conditioning such exemption upon--

(A) the submission to the Secretary, before any clinical testing of a new drug is undertaken, of reports, by the manufacturer or the sponsor of the investigation of such drug, of nonclinical tests of such drug adequate to justify the proposed clinical testing;

(B) the manufacturer or the sponsor of the investigation of a new drug proposed to be distributed to investigators for clinical testing obtaining a signed agreement from each of such investigators that patients to whom the drug is administered will be under his personal supervision, or under the supervision of investigators responsible to him, and that he will not supply such drug to any other investigator, or to clinics, for administration to human beings;

(C) the establishment and maintenance of such records, and the making of such reports to the Secretary, by the manufacturer or the sponsor of the investigation of such drug, of data (including but not limited to analytical reports by investigators) obtained as the result of such investigational use of such drug, as the Secretary finds will enable him to evaluate the safety and effectiveness of such drug in the event of the filing of an application pursuant to subsection (b); and

(D) the submission to the Secretary by the manufacturer or the sponsor of the investigation of a new drug of a statement of intent regarding whether the manufacturer or sponsor has plans for assessing pediatric safety and efficacy.

(2) Subject to paragraph (3), a clinical investigation of a new drug may begin 30 days after the Secretary has received from the manufacturer or sponsor of the investigation a submission containing such information about the drug and the clinical investigation, including--

(A) information on design of the investigation and adequate reports of basic information, certified by the applicant to be accurate reports, necessary to assess the safety of the drug for use in clinical investigation; and

(B) adequate information on the chemistry and manufacturing of the drug, controls available for the drug, and primary data tabulations from nonclinical tests or human studies.

(3)(A) At any time, the Secretary may prohibit the sponsor of an investigation from conducting the investigation (referred to in this paragraph as a "clinical hold") if the Secretary makes a determination described in subparagraph (B). The Secretary shall specify the basis for the clinical hold, including the specific information available to the Secretary which served as the basis for such clinical hold, and confirm such determination in writing.

(B) For purposes of subparagraph (A), a determination described in this subparagraph with respect to a clinical hold is that--

(i) the drug involved represents an unreasonable risk to the safety of the persons who are the subjects of the clinical investigation, taking into account the qualifications of the clinical investigators, information about the drug, the design of the clinical investigation, the condition for which the drug is to be investigated, and the health status of the subjects involved; or

(ii) the clinical hold should be issued for such other reasons as the Secretary may by regulation establish (including reasons established by regulation before November 21, 1997).

(C) Any written request to the Secretary from the sponsor of an investigation that a clinical hold be removed shall receive a decision, in writing and specifying the reasons therefor, within 30 days after receipt of such request. Any such request shall include sufficient information to support the removal of such clinical hold.

(4) Regulations under paragraph (1) shall provide that such exemption shall be conditioned upon the manufacturer, or the sponsor of the investigation, requiring that experts using such drugs for investigational purposes certify to such manufacturer or sponsor that they will inform any human beings to whom such drugs, or any controls used in connection therewith, are being administered, or their representatives, that such drugs are being used for investigational purposes and will obtain the consent of such human beings or their representatives, except where it is not feasible, it is contrary to the best interests of such human beings, or the proposed clinical testing poses no more than minimal risk to such human beings and includes appropriate safeguards as prescribed to protect the rights, safety, and welfare of such human beings. Nothing in this subsection shall be construed to require any clinical investigator to submit directly to the Secretary reports on the investigational use of drugs. The Secretary shall update such regulations to require inclusion in the informed consent documents and process a statement that clinical trial information for such clinical investigation has been or will be submitted for inclusion in the registry data bank pursuant to subsection (j) of section 282 of Title 42.

(j) Abbreviated new drug applications

(1) Any person may file with the Secretary an abbreviated application for the approval of a new drug.

(2)(A) An abbreviated application for a new drug shall contain--

(i) information to show that the conditions of use prescribed, recommended, or suggested in the labeling proposed for the new drug have been previously approved for a drug listed under paragraph (7) (hereinafter in this subsection referred to as a "listed drug");

(ii)(I) if the listed drug referred to in clause (i) has only one active ingredient, information to show that the active ingredient of the new drug is the same as that of the listed drug;

(II) if the listed drug referred to in clause (i) has more than one active ingredient, information to show that the active ingredients of the new drug are the same as those of the listed drug, or

(III) if the listed drug referred to in clause (i) has more than one active ingredient and if one of the active ingredients of the new drug is different and the application is filed pursuant to the approval of a petition filed under subparagraph (C), information to show that the other active ingredients of the new drug are the same as the active ingredients of the listed drug, information to show that the different active ingredient is an active ingredient of a listed drug or of a drug which does not meet the requirements of section 321(p) of this title, and such other information respecting the different active ingredient with respect to which the petition was filed as the Secretary may require;

(iii) information to show that the route of administration, the dosage form, and the strength of the new drug are the same as those of the listed drug referred to in clause (i) or, if the route of administration, the dosage form, or the strength of the new drug is different and the application is filed pursuant to the approval of a petition filed under subparagraph (C), such

information respecting the route of administration, dosage form, or strength with respect to which the petition was filed as the Secretary may require;

(iv) information to show that the new drug is bioequivalent to the listed drug referred to in clause (i), except that if the application is filed pursuant to the approval of a petition filed under subparagraph (C), information to show that the active ingredients of the new drug are of the same pharmacological or therapeutic class as those of the listed drug referred to in clause (i) and the new drug can be expected to have the same therapeutic effect as the listed drug when administered to patients for a condition of use referred to in clause (i);

(v) information to show that the labeling proposed for the new drug is the same as the labeling approved for the listed drug referred to in clause (i) except for changes required because of differences approved under a petition filed under subparagraph (C) or because the new drug and the listed drug are produced or distributed by different manufacturers;

(vi) the items specified in clauses (ii) through (vi) of subsection (b)(1)(A);

(vii) a certification, in the opinion of the applicant and to the best of his knowledge, with respect to each patent which claims the listed drug referred to in clause (i) or which claims a use for such listed drug for which the applicant is seeking approval under this subsection and for which information is required to be filed under subsection (b) or (c)--

(I) that such patent information has not been filed,

(II) that such patent has expired,

(III) of the date on which such patent will expire, or

(IV) that such patent is invalid or will not be infringed by the manufacture, use, or sale of the new drug for which the application is submitted; and

(viii) if with respect to the listed drug referred to in clause (i) information was filed under subsection (b) or (c) for a method of use patent which does not claim a use for which the applicant is seeking approval under this subsection, a statement that the method of use patent does not claim such a use.

The Secretary may not require that an abbreviated application contain information in addition to that required by clauses (i) through (viii).

(B) Notice of opinion that patent is invalid or will not be infringed

(i) Agreement to give notice

An applicant that makes a certification described in subparagraph (A)(vii)(IV) shall include in the application a statement that the applicant will give notice as required by this subparagraph.

(ii) Timing of notice

An applicant that makes a certification described in subparagraph (A)(vii)(IV) shall give notice as required under this subparagraph--

(I) if the certification is in the application, not later than 20 days after the date of the postmark on the notice with which the Secretary informs the applicant that the application has been filed; or

(II) if the certification is in an amendment or supplement to the application, at the time at which the applicant submits the amendment or supplement, regardless of whether the applicant has already given notice with respect to another such certification contained in the application or in an amendment or supplement to the application.

(iii) Recipients of notice

An applicant required under this subparagraph to give notice shall give notice to--

(I) each owner of the patent that is the subject of the certification (or a representative of the owner designated to receive such a notice); and

(II) the holder of the approved application under subsection (b) for the drug that is claimed by the patent or a use of which is claimed by the patent (or a representative of the holder designated to receive such a notice).

(iv) Contents of notice

A notice required under this subparagraph shall--

(I) state that an application that contains data from bioavailability or bioequivalence studies has been submitted under this subsection for the drug with respect to which the certification is made to obtain approval to engage in the commercial manufacture, use, or sale of the drug before the expiration of the patent referred to in the certification; and

(II) include a detailed statement of the factual and legal basis of the opinion of the applicant that the patent is invalid or will not be infringed.

(C) If a person wants to submit an abbreviated application for a new drug which has a different active ingredient or whose route of administration, dosage form, or strength differ from that of a listed drug, such person shall submit a petition to the Secretary seeking permission to file such an application. The Secretary shall approve or disapprove a petition submitted under this subparagraph within ninety days of the date the petition is submitted. The Secretary shall approve such a petition unless the Secretary finds--

(i) that investigations must be conducted to show the safety and effectiveness of the drug or of any of its active ingredients, the route of administration, the dosage form, or strength which differ from the listed drug; or

(ii) that any drug with a different active ingredient may not be adequately evaluated for approval as safe and effective on the basis of the information required to be submitted in an abbreviated application.

(D)(i) An applicant may not amend or supplement an application to seek approval of a drug referring to a different listed drug from the listed drug identified in the application as submitted to the Secretary.

(ii) With respect to the drug for which an application is submitted, nothing in this subsection prohibits an applicant from amending or supplementing the application to seek approval of a different strength.

(iii) Within 60 days after December 8, 2003, the Secretary shall issue guidance defining the term "listed drug" for purposes of this subparagraph.

(3)(A) The Secretary shall issue guidance for the individuals who review applications submitted under paragraph (1), which shall relate to promptness in conducting the review, technical excellence, lack of bias and conflict of interest, and knowledge of regulatory and scientific standards, and which shall apply equally to all individuals who review such applications.

(B) The Secretary shall meet with a sponsor of an investigation or an applicant for approval for a drug under this subsection if the sponsor or applicant makes a reasonable written request for a meeting for the purpose of reaching agreement on the design and size of bioavailability and bioequivalence studies needed for approval of such application. The sponsor or applicant shall provide information necessary for discussion and agreement on the design and size of such studies. Minutes of any such meeting shall be prepared by the Secretary and made available to the sponsor or applicant.

(C) Any agreement regarding the parameters of design and size of bioavailability and bioequivalence studies of a drug under this paragraph that is reached between the Secretary and a sponsor or applicant shall be reduced to writing and made part of the administrative record by the Secretary. Such agreement shall not be changed after the testing begins, except--

(i) with the written agreement of the sponsor or applicant; or

(ii) pursuant to a decision, made in accordance with subparagraph (D) by the director of the reviewing division, that a substantial scientific issue essential to determining the safety or effectiveness of the drug has been identified after the testing has begun.

(D) A decision under subparagraph (C)(ii) by the director shall be in writing and the Secretary shall provide to the sponsor or applicant an opportunity for a meeting at which the director and the sponsor or applicant will be present and at which the director will document the scientific issue involved.

(E) The written decisions of the reviewing division shall be binding upon, and may not directly or indirectly be changed by, the field or compliance office personnel unless such field or compliance office personnel demonstrate to the reviewing division why such decision should be modified.

(F) No action by the reviewing division may be delayed because of the unavailability of information from or action by field personnel unless the reviewing division determines that a delay is necessary to assure the marketing of a safe and effective drug.

(G) For purposes of this paragraph, the reviewing division is the division responsible for the review of an application for approval of a drug under this subsection (including scientific matters, chemistry, manufacturing, and controls).

(4) Subject to paragraph (5), the Secretary shall approve an application for a drug unless the Secretary finds--

(A) the methods used in, or the facilities and controls used for, the manufacture, processing, and packing of the drug are inadequate to assure and preserve its identity, strength, quality, and purity;

(B) information submitted with the application is insufficient to show that each of the proposed conditions of use have been previously approved for the listed drug referred to in the application;

(C)(i) if the listed drug has only one active ingredient, information submitted with the application is insufficient to show that the active ingredient is the same as that of the listed drug;

(ii) if the listed drug has more than one active ingredient, information submitted with the application is insufficient to show that the active ingredients are the same as the active ingredients of the listed drug, or

(iii) if the listed drug has more than one active ingredient and if the application is for a drug which has an active ingredient different from the listed drug, information submitted with the application is insufficient to show--

(I) that the other active ingredients are the same as the active ingredients of the listed drug, or

(II) that the different active ingredient is an active ingredient of a listed drug or a drug which does not meet the requirements of section 321(p) of this title,

or no petition to file an application for the drug with the different ingredient was approved under paragraph (2)(C);

(D)(i) if the application is for a drug whose route of administration, dosage form, or strength of the drug is the same as the route of administration, dosage form, or strength of the listed drug referred to in the application, information submitted in the application is insufficient to show that the route of administration, dosage form, or strength is the same as that of the listed drug, or

(ii) if the application is for a drug whose route of administration, dosage form, or strength of the drug is different from that of the listed drug referred to in the application, no petition to file an application for the drug with the different route of administration, dosage form, or strength was approved under paragraph (2)(C);

(E) if the application was filed pursuant to the approval of a petition under paragraph (2)(C), the application did not contain the information required by the Secretary respecting the active ingredient, route of administration, dosage form, or strength which is not the same;

(F) information submitted in the application is insufficient to show that the drug is bioequivalent to the listed drug referred to in the application or, if the application was filed pursuant to a petition approved under paragraph (2)(C), information submitted in the application is insufficient to show that the active ingredients of the new drug are of the same pharmacological or therapeutic class as those of the listed drug referred to in paragraph (2)(A)(i) and that the new drug can be expected to have the same therapeutic effect as the listed drug when administered to patients for a condition of use referred to in such paragraph;

(G) information submitted in the application is insufficient to show that the labeling proposed for the drug is the same as the labeling approved for the listed drug referred to in the application except for changes required because of differences approved under a petition filed under paragraph (2)(C) or because the drug and the listed drug are produced or distributed by different manufacturers;

(H) information submitted in the application or any other information available to the Secretary shows that (i) the inactive ingredients of the drug are unsafe for use under the conditions prescribed, recommended, or suggested in the labeling proposed for the drug, or (ii) the composition of the drug is unsafe under such conditions because of the type or quantity of inactive ingredients included or the manner in which the inactive ingredients are included;

(I) the approval under subsection (c) of the listed drug referred to in the application under this subsection has been withdrawn or suspended for grounds described in the first sentence of subsection (e), the Secretary has published a notice of opportunity for hearing to withdraw approval of the listed drug under subsection (c) for grounds described in the first sentence of subsection (e), the approval under this subsection of the listed drug referred to in the application under this subsection has been withdrawn or suspended under paragraph (6), or the Secretary has determined that the listed drug has been withdrawn from sale for safety or effectiveness reasons;

(J) the application does not meet any other requirement of paragraph (2)(A); or

(K) the application contains an untrue statement of material fact.

(5)(A) Within one hundred and eighty days of the initial receipt of an application under paragraph (2) or within such additional period as may be agreed upon by the Secretary and the applicant, the Secretary shall approve or disapprove the application.

(B) The approval of an application submitted under paragraph (2) shall be made effective on the last applicable date determined by applying the following to each certification made under paragraph (2)(A)(vii):

(i) If the applicant only made a certification described in subclause (I) or (II) of paragraph (2)(A)(vii) or in both such subclauses, the approval may be made effective immediately.

(ii) If the applicant made a certification described in subclause (III) of paragraph (2)(A)(vii), the approval may be made effective on the date certified under subclause (III).

(iii) If the applicant made a certification described in subclause (IV) of paragraph (2)(A)(vii), the approval shall be made effective immediately unless, before the expiration of 45 days after the date on which the notice described in paragraph (2)(B) is received, an action is brought for infringement of the patent that is the subject of the certification and for which information was submitted to the Secretary under subsection (b)(1) or (c)(2) before the date on which the application (excluding an amendment or supplement to the application), which the Secretary later determines to be substantially complete, was submitted. If such an action is brought before the expiration of such days, the approval shall be made effective upon the expiration of the thirty-month period beginning on the date of the receipt of the notice provided under paragraph (2)(B)(i) or such shorter or longer period as the court may order because either party to the action failed to reasonably cooperate in expediting the action, except that--

(I) if before the expiration of such period the district court decides that the patent is invalid or not infringed (including any substantive determination that there is no cause of action for patent infringement or invalidity), the approval shall be made effective on--

(aa) the date on which the court enters judgment reflecting the decision; or

(bb) the date of a settlement order or consent decree signed and entered by the court stating that the patent that is the subject of the certification is invalid or not infringed;

(II) if before the expiration of such period the district court decides that the patent has been infringed--

(aa) if the judgment of the district court is appealed, the approval shall be made effective on--

(AA) the date on which the court of appeals decides that the patent is invalid or not infringed (including any substantive determination that there is no cause of action for patent infringement or invalidity); or

(BB) the date of a settlement order or consent decree signed and entered by the court of appeals stating that the patent that is the subject of the certification is invalid or not infringed; or

(bb) if the judgment of the district court is not appealed or is affirmed, the approval shall be made effective on the date specified by the district court in a court order under section 271(e)(4)(A) of Title 35;

(III) if before the expiration of such period the court grants a preliminary injunction prohibiting the applicant from engaging in the commercial manufacture or sale of the drug until the court decides the issues of patent validity and infringement

and if the court decides that such patent is invalid or not infringed, the approval shall be made effective as provided in subclause (I); or

(IV) if before the expiration of such period the court grants a preliminary injunction prohibiting the applicant from engaging in the commercial manufacture or sale of the drug until the court decides the issues of patent validity and infringement and if the court decides that such patent has been infringed, the approval shall be made effective as provided in subclause (II).

In such an action, each of the parties shall reasonably cooperate in expediting the action.

(iv) 180-day exclusivity period

(I) Effectiveness of application

Subject to subparagraph (D), if the application contains a certification described in paragraph (2)(A)(vii)(IV) and is for a drug for which a first applicant has submitted an application containing such a certification, the application shall be made effective on the date that is 180 days after the date of the first commercial marketing of the drug (including the commercial marketing of the listed drug) by any first applicant.

(II) Definitions

In this paragraph:

(aa) 180-day exclusivity period

The term "180-day exclusivity period" means the 180-day period ending on the day before the date on which an application submitted by an applicant other than a first applicant could become effective under this clause.

(bb) First applicant

As used in this subsection, the term "first applicant" means an applicant that, on the first day on which a substantially complete application containing a certification described in paragraph (2)(A)(vii)(IV) is submitted for approval of a drug, submits a substantially complete application that contains and lawfully maintains a certification described in paragraph (2)(A)(vii)(IV) for the drug.

(cc) Substantially complete application

As used in this subsection, the term "substantially complete application" means an application under this subsection that on its face is sufficiently complete to permit a substantive review and contains all the information required by paragraph (2)(A).

(dd) Tentative approval

(AA) In general

The term "tentative approval" means notification to an applicant by the Secretary that an application under this subsection meets the requirements of paragraph (2)(A), but cannot receive effective approval because the application does not meet the requirements of this subparagraph, there is a period of exclusivity for the listed drug under subparagraph (F) or section 355a of this title, or there is a 7-year period of exclusivity for the listed drug under section 360cc of this title.

(BB) Limitation

A drug that is granted tentative approval by the Secretary is not an approved drug and shall not have an effective approval until the Secretary issues an approval after any necessary additional review of the application.

(v) 180-day exclusivity period for competitive generic therapies

(I) Effectiveness of application

Subject to subparagraph (D)(iv), if the application is for a drug that is the same as a competitive generic therapy for which any first approved applicant has commenced commercial marketing, the application shall be made effective on the date that is 180 days after the date of the first commercial marketing of the competitive generic therapy (including the commercial marketing of the listed drug) by any first approved applicant.

(II) Limitation

The exclusivity period under subclause (I) shall not apply with respect to a competitive generic therapy that has previously received an exclusivity period under subclause (I).

(III) Definitions

In this clause and subparagraph (D)(iv):

(aa) The term "competitive generic therapy" means a drug--

(AA) that is designated as a competitive generic therapy under section 356h of this title; and

(BB) for which there are no unexpired patents or exclusivities on the list of products described in section 355(j)(7)(A) of this title at the time of submission.

(bb) The term "first approved applicant" means any applicant that has submitted an application that--

(AA) is for a competitive generic therapy that is approved on the first day on which any application for such competitive generic therapy is approved;

(BB) is not eligible for a 180-day exclusivity period under clause (iv) for the drug that is the subject of the application for the competitive generic therapy; and

(CC) is not for a drug for which all drug versions have forfeited eligibility for a 180-day exclusivity period under clause (iv) pursuant to subparagraph (D).

(C) Civil action to obtain patent certainty

(i) Declaratory judgment absent infringement action

(I) In general

No action may be brought under section 2201 of Title 28 by an applicant under paragraph (2) for a declaratory judgment with respect to a patent which is the subject of the certification referred to in subparagraph (B)(iii) unless--

(aa) the 45-day period referred to in such subparagraph has expired;

(bb) neither the owner of such patent nor the holder of the approved application under subsection (b) for the drug that is claimed by the patent or a use of which is claimed by the patent brought a civil action against the applicant for infringement of the patent before the expiration of such period; and

(cc) in any case in which the notice provided under paragraph (2)(B) relates to noninfringement, the notice was accompanied by a document described in subclause (III).

(II) Filing of civil action

If the conditions described in items (aa), (bb), and as applicable, (cc) of subclause (I) have been met, the applicant referred to in such subclause may, in accordance with section 2201 of Title 28, bring a civil action under such section against the owner or holder referred to in such subclause (but not against any owner or holder that has brought such a civil action against the applicant, unless that civil action was dismissed without prejudice) for a declaratory judgment that the patent is invalid or will not be infringed by the drug for which the applicant seeks approval, except that such civil action may be brought for a declaratory judgment that the patent will not be infringed only in a case in which the condition described in subclause (I)(cc) is applicable. A civil action referred to in this subclause shall be brought in the judicial district where the defendant has its principal place of business or a regular and established place of business.

(III) Offer of confidential access to application

For purposes of subclause (I)(cc), the document described in this subclause is a document providing an offer of confidential access to the application that is in the custody of the applicant under paragraph (2) for the purpose of determining whether an action referred to in subparagraph (B)(iii) should be brought. The document providing the offer of confidential access shall contain such restrictions as to persons entitled to access, and on the use and disposition of any information accessed, as would apply had a protective order been entered for the purpose of protecting trade

secrets and other confidential business information. A request for access to an application under an offer of confidential access shall be considered acceptance of the offer of confidential access with the restrictions as to persons entitled to access, and on the use and disposition of any information accessed, contained in the offer of confidential access, and those restrictions and other terms of the offer of confidential access shall be considered terms of an enforceable contract. Any person provided an offer of confidential access shall review the application for the sole and limited purpose of evaluating possible infringement of the patent that is the subject of the certification under paragraph (2)(A)(vii)(IV) and for no other purpose, and may not disclose information of no relevance to any issue of patent infringement to any person other than a person provided an offer of confidential access. Further, the application may be redacted by the applicant to remove any information of no relevance to any issue of patent infringement.

(ii) Counterclaim to infringement action

(I) In general

If an owner of the patent or the holder of the approved application under subsection (b) for the drug that is claimed by the patent or a use of which is claimed by the patent brings a patent infringement action against the applicant, the applicant may assert a counterclaim seeking an order requiring the holder to correct or delete the patent information submitted by the holder under subsection (b) or (c) on the ground that the patent does not claim either--

(aa) the drug for which the application was approved; or

(bb) an approved method of using the drug.

(II) No independent cause of action

Subclause (I) does not authorize the assertion of a claim described in subclause (I) in any civil action or proceeding other than a counterclaim described in subclause (I).

(iii) No damages

An applicant shall not be entitled to damages in a civil action under clause (i) or a counterclaim under clause (ii).

(D) Forfeiture of 180-day exclusivity period

(i) Definition of forfeiture event

In this subparagraph, the term “forfeiture event”, with respect to an application under this subsection, means the occurrence of any of the following:

(I) Failure to market

The first applicant fails to market the drug by the later of--

(aa) the earlier of the date that is--

(AA) 75 days after the date on which the approval of the application of the first applicant is made effective under subparagraph (B)(iii); or

(BB) 30 months after the date of submission of the application of the first applicant; or

(bb) with respect to the first applicant or any other applicant (which other applicant has received tentative approval), the date that is 75 days after the date as of which, as to each of the patents with respect to which the first applicant submitted and lawfully maintained a certification qualifying the first applicant for the 180-day exclusivity period under subparagraph (B)(iv), at least 1 of the following has occurred:

(AA) In an infringement action brought against that applicant with respect to the patent or in a declaratory judgment action brought by that applicant with respect to the patent, a court enters a final decision from which no appeal (other than a petition to the Supreme Court for a writ of certiorari) has been or can be taken that the patent is invalid or not infringed.

(BB) In an infringement action or a declaratory judgment action described in subitem (AA), a court signs a settlement order or consent decree that enters a final judgment that includes a finding that the patent is invalid or not infringed.

(CC) The patent information submitted under subsection (b) or (c) is withdrawn by the holder of the application approved under subsection (b).

(II) Withdrawal of application

The first applicant withdraws the application or the Secretary considers the application to have been withdrawn as a result of a determination by the Secretary that the application does not meet the requirements for approval under paragraph (4).

(III) Amendment of certification

The first applicant amends or withdraws the certification for all of the patents with respect to which that applicant submitted a certification qualifying the applicant for the 180-day exclusivity period.

(IV) Failure to obtain tentative approval

The first applicant fails to obtain tentative approval of the application within 30 months after the date on which the application is filed, unless the failure is caused by a change in or a review of the requirements for approval of the application imposed after the date on which the application is filed.

(V) Agreement with another applicant, the listed drug application holder, or a patent owner

The first applicant enters into an agreement with another applicant under this subsection for the drug, the holder of the application for the listed drug, or an owner of the patent that is the subject of the certification under paragraph (2)(A)(vii)(IV), the Federal Trade Commission or the Attorney General files a complaint, and there is a final decision of the Federal Trade Commission or the court with regard to the complaint from which no appeal (other than a petition to the Supreme Court for a writ of certiorari) has been or can be taken that the agreement has violated the antitrust laws (as defined in section 12 of Title 15, except that the term includes section 45 of Title 15 to the extent that that section applies to unfair methods of competition).

(VI) Expiration of all patents

All of the patents as to which the applicant submitted a certification qualifying it for the 180-day exclusivity period have expired.

(ii) Forfeiture

The 180-day exclusivity period described in subparagraph (B)(iv) shall be forfeited by a first applicant if a forfeiture event occurs with respect to that first applicant.

(iii) Subsequent applicant

If all first applicants forfeit the 180-day exclusivity period under clause (ii)--

(I) approval of any application containing a certification described in paragraph (2)(A)(vii)(IV) shall be made effective in accordance with subparagraph (B)(iii); and

(II) no applicant shall be eligible for a 180-day exclusivity period.

(iv) Special forfeiture rule for competitive generic therapy

The 180-day exclusivity period described in subparagraph (B)(v) shall be forfeited by a first approved applicant if the applicant fails to market the competitive generic therapy within 75 days after the date on which the approval of the first approved applicant's application for the competitive generic therapy is made effective.

(E) If the Secretary decides to disapprove an application, the Secretary shall give the applicant notice of an opportunity for a hearing before the Secretary on the question of whether such application is approvable. If the applicant elects to accept the opportunity for hearing by written request within thirty days after such notice, such hearing shall commence not more than ninety days after the expiration of such thirty days unless the Secretary and the applicant otherwise agree. Any such hearing shall thereafter be conducted on an expedited basis and the Secretary's order thereon shall be issued within ninety days after the date fixed by the Secretary for filing final briefs.

(F)(i) Repealed. Pub.L. 117-9, § 1(b)(1)(B), Apr. 23, 2021, 135 Stat. 258

(ii) If an application submitted under subsection (b) for a drug, no active moiety (as defined by the Secretary in section 314.3 of title 21, Code of Federal Regulations (or any successor regulations)) of which has been approved in any other application under subsection (b), is approved after September 24, 1984, no application may be submitted under this subsection which refers to the drug for which the subsection (b) application was submitted before the expiration of five years from the date of the approval of the application under subsection (b), except that such an application may be submitted under this subsection after the expiration of four years from the date of the approval of the subsection (b) application if it contains a certification of patent invalidity or noninfringement described in subclause (IV) of paragraph (2)(A)(vii). The approval of such an application shall be made effective in accordance with subparagraph (B) except that, if an action for patent infringement is commenced during the one-year period beginning forty-eight months after the date of the approval of the subsection (b) application, the thirty-month period referred to in subparagraph (B)(iii) shall be extended by such amount of time (if any) which is required for seven and one-half years to have elapsed from the date of approval of the subsection (b) application.

(iii) If an application submitted under subsection (b) for a drug, which includes an active moiety (as defined by the Secretary in section 314.3 of title 21, Code of Federal Regulations (or any successor regulations)) that has been approved in another application approved under subsection (b), is approved after September 24, 1984, and if such application contains reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant, the Secretary may not make the approval of an application submitted under this subsection for the conditions of approval of such drug in the subsection (b) application effective before the expiration of three years from the date of the approval of the application under subsection (b) for such drug.

(iv) If a supplement to an application approved under subsection (b) is approved after September 24, 1984, and the supplement contains reports of new clinical investigations (other than bioavailability studies) essential to the approval of the supplement and conducted or sponsored by the person submitting the supplement, the Secretary may not make the approval of an application submitted under this subsection for a change approved in the supplement effective before the expiration of three years from the date of the approval of the supplement under subsection (b).

(v) If an application (or supplement to an application) submitted under subsection (b) for a drug, which includes an active moiety (as defined by the Secretary in section 314.3 of title 21, Code of Federal Regulations (or any successor regulations)) that has been approved in another application under subsection (b), was approved during the period beginning January 1, 1982, and ending on September 24, 1984, the Secretary may not make the approval of an application submitted under this subsection which refers to the drug for which the subsection (b) application was submitted or which refers to a change approved in a supplement to the subsection (b) application effective before the expiration of two years from September 24, 1984.

(6) If a drug approved under this subsection refers in its approved application to a drug the approval of which was withdrawn or suspended for grounds described in the first sentence of subsection (e) or was withdrawn or suspended under this paragraph or which, as determined by the Secretary, has been withdrawn from sale for safety or effectiveness reasons, the approval of the drug under this subsection shall be withdrawn or suspended--

(A) for the same period as the withdrawal or suspension under subsection (e) or this paragraph, or

(B) if the listed drug has been withdrawn from sale, for the period of withdrawal from sale or, if earlier, the period ending on the date the Secretary determines that the withdrawal from sale is not for safety or effectiveness reasons.

(7)(A)(i) Within sixty days of September 24, 1984, the Secretary shall publish and make available to the public--

(I) a list in alphabetical order of the official and proprietary name of each drug which has been approved for safety and effectiveness under subsection (c) before September 24, 1984;

(II) the date of approval if the drug is approved after 1981 and the number of the application which was approved; and

(III) whether in vitro or in vivo bioequivalence studies, or both such studies, are required for applications filed under this subsection which will refer to the drug published.

(ii) Every thirty days after the publication of the first list under clause (i) the Secretary shall revise the list to include each drug which has been approved for safety and effectiveness under subsection (c) or approved under this subsection during the thirty-day period.

(iii) When patent information submitted under subsection (c) respecting a drug included on the list is to be published by the Secretary, the Secretary shall, in revisions made under clause (ii), include such information for such drug.

(iv) For each drug included on the list, the Secretary shall specify any exclusivity period that is applicable, for which the Secretary has determined the expiration date, and for which such period has not yet expired, under--

(I) clause (ii), (iii), or (iv) of subsection (c)(3)(E);

(II) clause (iv) or (v) of paragraph (5)(B);

(III) clause (ii), (iii), or (iv) of paragraph (5)(F);

(IV) section 355a of this title;

(V) section 355f of this title;

(VI) section 360cc(a) of this title; or

(VII) subsection (u).

(v)(I) With respect to an application submitted pursuant to subsection (b)(2) for a drug that is subject to section 353(b) of this title for which the sole difference from a listed drug relied upon in the application is a difference in inactive ingredients not permitted under clause (iii) or (iv) of section 314.94(a)(9) of title 21, Code of Federal Regulations (or any successor regulations), the Secretary shall make an evaluation with respect to whether such drug is a therapeutic equivalent (as defined in section 314.3

of title 21, Code of Federal Regulations (or any successor regulations)) to another approved drug product in the prescription drug product section of the list under this paragraph as follows:

(aa) With respect to such an application submitted after December 29, 2022, the evaluation shall be made with respect to a listed drug relied upon in the application pursuant to subsection (b)(2) that is a pharmaceutical equivalent (as defined in section 314.3 of title 21, Code of Federal Regulations (or any successor regulations)) to the drug in the application pursuant to subsection (b)(2) at the time of approval of such application or not later than 180 days after the date of such approval, provided that the request for such an evaluation is made in the original application (or in a resubmission to a complete response letter), and all necessary data and information are submitted in the original application (or in a resubmission in response to a complete response letter) for the therapeutic equivalence evaluation, including information to demonstrate bioequivalence, in a form and manner prescribed by the Secretary.

(bb) With respect to such an application approved prior to or on December 29, 2022, the evaluation shall be made not later than 180 days after receipt of a request for a therapeutic equivalence evaluation submitted as part of a supplement to such application; or with respect to an application that was submitted prior to December 29, 2022, but not approved as of December 29, 2022, the evaluation shall be made not later than 180 days after the date of approval of such application if a request for such evaluation is submitted as an amendment to the application, provided that--

(AA) such request for a therapeutic equivalence evaluation is being sought with respect to a listed drug relied upon in the application, and the relied upon listed drug is in the prescription drug product section of the list under this paragraph and is a pharmaceutical equivalent (as defined in section 314.3 of title 21, Code of Federal Regulations (or any successor regulations)) to the drug for which a therapeutic equivalence evaluation is sought; and

(BB) the amendment or supplement, as applicable, containing such request, or the relevant application, includes all necessary data and information for the therapeutic equivalence evaluation, including information to demonstrate bioequivalence, in a form and manner prescribed by the Secretary.

(II) When the Secretary makes an evaluation under subclause (I), the Secretary shall, in revisions made to the list pursuant to clause (ii), include such information for such drug.

(B) A drug approved for safety and effectiveness under subsection (c) or approved under this subsection shall, for purposes of this subsection, be considered to have been published under subparagraph (A) on the date of its approval or September 24, 1984, whichever is later.

(C) If the approval of a drug was withdrawn or suspended for grounds described in the first sentence of subsection (e) or was withdrawn or suspended under paragraph (6) or if the Secretary determines that a drug has been withdrawn from sale for safety or effectiveness reasons, it may not be published in the list under subparagraph (A) or, if the withdrawal or suspension occurred after its publication in such list, it shall be immediately removed from such list--

(i) for the same period as the withdrawal or suspension under subsection (e) or paragraph (6), or

(ii) if the listed drug has been withdrawn from sale, for the period of withdrawal from sale or, if earlier, the period ending on the date the Secretary determines that the withdrawal from sale is not for safety or effectiveness reasons.

A notice of the removal shall be published in the Federal Register.

(D) In the case of a listed drug for which the list under subparagraph (A)(i) includes a patent for such drug, and any claim of the patent has been cancelled or invalidated pursuant to a final decision issued by the Patent Trial and Appeal Board of the United States Patent and Trademark Office or by a court, from which no appeal has been, or can be, taken, if the holder of the applicable application approved under subsection (c) determines that a patent for such drug, or any patent information for such drug, no longer meets the listing requirements under this section--

(i) the holder of such approved application shall notify the Secretary, in writing, within 14 days of such decision of such cancellation or invalidation and request that such patent or patent information, as applicable, be amended or withdrawn in accordance with the decision issued by the Patent Trial and Appeal Board or a court;

(ii) the holder of such approved application shall include in any notification under clause (i) information related to such patent cancellation or invalidation decision and submit such information, including a copy of such decision, to the Secretary; and

(iii) the Secretary shall, in response to a notification under clause (i), amend or remove patent or patent information in accordance with the relevant decision from the Patent Trial and Appeals Board or court, as applicable, except that the Secretary shall not remove from the list any patent or patent information before the expiration of any 180-day exclusivity period under paragraph (5)(B)(iv) that relies on a certification described in paragraph (2)(A)(vii)(IV).

(8) For purposes of this subsection:

(A)(i) The term "bioavailability" means the rate and extent to which the active ingredient or therapeutic ingredient is absorbed from a drug and becomes available at the site of drug action.

(ii) For a drug that is not intended to be absorbed into the bloodstream, the Secretary may assess bioavailability by scientifically valid measurements intended to reflect the rate and extent to which the active ingredient or therapeutic ingredient becomes available at the site of drug action.

(B) A drug shall be considered to be bioequivalent to a listed drug if--

(i) the rate and extent of absorption of the drug do not show a significant difference from the rate and extent of absorption of the listed drug when administered at the same molar dose of the therapeutic ingredient under similar experimental conditions in either a single dose or multiple doses; or

(ii) the extent of absorption of the drug does not show a significant difference from the extent of absorption of the listed drug when administered at the same molar dose of the therapeutic ingredient under similar experimental conditions in either a single dose or multiple doses and the difference from the listed drug in the rate of absorption of the drug is intentional, is reflected in its proposed labeling, is not essential to the attainment of effective body drug concentrations on chronic use, and is considered medically insignificant for the drug.

(C) For a drug that is not intended to be absorbed into the bloodstream, the Secretary may establish alternative, scientifically valid methods to show bioequivalence if the alternative methods are expected to detect a significant difference between the drug and the listed drug in safety and therapeutic effect.

(9) The Secretary shall, with respect to each application submitted under this subsection, maintain a record of--

(A) the name of the applicant,

(B) the name of the drug covered by the application,

(C) the name of each person to whom the review of the chemistry of the application was assigned and the date of such assignment, and

(D) the name of each person to whom the bioequivalence review for such application was assigned and the date of such assignment.

The information the Secretary is required to maintain under this paragraph with respect to an application submitted under this subsection shall be made available to the public after the approval of such application.

(10)(A) If the proposed labeling of a drug that is the subject of an application under this subsection differs from the listed drug due to a labeling revision described under clause (i), the drug that is the subject of such application shall, notwithstanding any other provision of this chapter, be eligible for approval and shall not be considered misbranded under section 352 of this title if--

(i) a revision to the labeling of the listed drug has been approved by the Secretary within 90 days of when the application is otherwise eligible for approval under this subsection;

(ii) the sponsor of the application agrees to submit revised labeling for the drug that is the subject of the application not later than 60 days after approval under this subsection of the application;

(iii) the labeling revision described under clause (i) does not include a change to the "Warnings" section of the labeling; and

(iv) such application otherwise meets the applicable requirements for approval under this subsection.

(B) If, after a labeling revision described in subparagraph (A)(i), the Secretary determines that the continued presence in interstate commerce of the labeling of the listed drug (as in effect before the revision described in subparagraph (A)(i)) adversely impacts the safe use of the drug, no application under this subsection shall be eligible for approval with such labeling.

(11)(A) Subject to subparagraph (B), the Secretary shall prioritize the review of, and act within 8 months of the date of the submission of, an original abbreviated new drug application submitted for review under this subsection that is for a drug--

(i) for which there are not more than 3 approved drug products listed under paragraph (7) and for which there are no blocking patents and exclusivities; or

(ii) that has been included on the list under section 356e of this title.

(B) To qualify for priority review under this paragraph, not later than 60 days prior to the submission of an application described in subparagraph (A) or that the Secretary may prioritize pursuant to subparagraph (D), the applicant shall provide complete, accurate information regarding facilities involved in manufacturing processes and testing of the drug that is the subject of the application, including facilities in corresponding Type II active pharmaceutical ingredients drug master files referenced in an application and sites or organizations involved in bioequivalence and clinical studies used to support the application, to enable the Secretary to make a determination regarding whether an inspection of a facility is necessary. Such information shall include the relevant (as determined by the Secretary) sections of such application, which shall be unchanged relative to the date of the submission of such application, except to the extent that a change is made to such information to exclude a facility that was not used to generate data to meet any application requirements for such submission and that is not the only facility intended to conduct one or more unit operations in commercial production. Information provided by an applicant under this subparagraph shall not be considered the submission of an application under this subsection.

(C) The Secretary may expedite an inspection or reinspection under section 374 of this title of an establishment that proposes to manufacture a drug described in subparagraph (A).

(D) Nothing in this paragraph shall prevent the Secretary from prioritizing the review of other applications as the Secretary determines appropriate.

(12) The Secretary shall publish on the internet website of the Food and Drug Administration, and update at least once every 6 months, a list of all drugs approved under subsection (c) for which all patents and periods of exclusivity under this chapter have expired and for which no application has been approved under this subsection.

(13) Upon the request of an applicant regarding one or more specified pending applications under this subsection, the Secretary shall, as appropriate, provide review status updates indicating the categorical status of the applications by each relevant review discipline.

(k) Records and reports; required information; regulations and orders; access to records

(1) In the case of any drug for which an approval of an application filed under subsection (b) or (j) is in effect, the applicant shall establish and maintain such records, and make such reports to the Secretary, of data relating to clinical experience and other data or information, received or otherwise obtained by such applicant with respect to such drug, as the Secretary may by general regulation, or by order with respect to such application, prescribe on the basis of a finding that such records and reports are necessary in order to enable the Secretary to determine, or facilitate a determination, whether there is or may be ground for invoking subsection (e). Regulations and orders issued under this subsection and under subsection (i) shall have due regard for the professional ethics of the medical profession and the interests of patients and shall provide, where the Secretary deems it to be appropriate, for the examination, upon request, by the persons to whom such regulations or orders are applicable, of similar information received or otherwise obtained by the Secretary.

(2) Every person required under this section to maintain records, and every person in charge or custody thereof, shall, upon request of an officer or employee designated by the Secretary, permit such officer or employee at all reasonable times to have access to and copy and verify such records.

(3) Active postmarket risk identification

(A) Definition

In this paragraph, the term "data" refers to information with respect to a drug approved under this section or under section 262 of Title 42, including claims data, patient survey data, standardized analytic files that allow for the pooling and analysis of data from disparate data environments, and any other data deemed appropriate by the Secretary.

(B) Development of postmarket risk identification and analysis methods

The Secretary shall, not later than 2 years after September 27, 2007, in collaboration with public, academic, and private entities--

(i) develop methods to obtain access to disparate data sources including the data sources specified in subparagraph (C);

(ii) develop validated methods for the establishment of a postmarket risk identification and analysis system to link and analyze safety data from multiple sources, with the goals of including, in aggregate--

(I) at least 25,000,000 patients by July 1, 2010; and

(II) at least 100,000,000 patients by July 1, 2012; and

(iii) convene a committee of experts, including individuals who are recognized in the field of protecting data privacy and security, to make recommendations to the Secretary on the development of tools and methods for the ethical and scientific uses for, and communication of, postmarketing data specified under subparagraph (C), including recommendations on the development of effective research methods for the study of drug safety questions.

(C) Establishment of the postmarket risk identification and analysis system

(i) In general

The Secretary shall, not later than 1 year after the development of the risk identification and analysis methods under subparagraph (B), establish and maintain procedures--

(I) for risk identification and analysis based on electronic health data, in compliance with the regulations promulgated under section 264(c) of the Health Insurance Portability and Accountability Act of 1996, and in a manner that does not disclose individually identifiable health information in violation of paragraph (4)(B);

(II) for the reporting (in a standardized form) of data on all serious adverse drug experiences (as defined in section 355-1(b) of this title) submitted to the Secretary under paragraph (1), and those adverse events submitted by patients, providers, and drug sponsors, when appropriate;

(III) to provide for active adverse event surveillance using the following data sources, as available:

(aa) Federal health-related electronic data (such as data from the Medicare program and the health systems of the Department of Veterans Affairs);

(bb) private sector health-related electronic data (such as pharmaceutical purchase data and health insurance claims data); and

(cc) other data as the Secretary deems necessary to create a robust system to identify adverse events and potential drug safety signals;

(IV) to identify certain trends and patterns with respect to data accessed by the system;

(V) to provide regular reports to the Secretary concerning adverse event trends, adverse event patterns, incidence and prevalence of adverse events, and other information the Secretary determines appropriate, which may include data on comparative national adverse event trends; and

(VI) to enable the program to export data in a form appropriate for further aggregation, statistical analysis, and reporting.

(ii) Timeliness of reporting

The procedures established under clause (i) shall ensure that such data are accessed, analyzed, and reported in a timely, routine, and systematic manner, taking into consideration the need for data completeness, coding, cleansing, and standardized analysis and transmission.

(iii) Private sector resources

To ensure the establishment of the active postmarket risk identification and analysis system under this subsection not later than 1 year after the development of the risk identification and analysis methods under subparagraph (B), as required under clause (i), the Secretary may, on a temporary or permanent basis, implement systems or products developed by private entities.

(iv) Complementary approaches

To the extent the active postmarket risk identification and analysis system under this subsection is not sufficient to gather data and information relevant to a priority drug safety question, the Secretary shall develop, support, and participate in complementary approaches to gather and analyze such data and information, including--

(I) approaches that are complementary with respect to assessing the safety of use of a drug in domestic populations not included, or underrepresented, in the trials used to approve the drug (such as older people, people with comorbidities, pregnant women, or children); and

(II) existing approaches such as the Vaccine Adverse Event Reporting System and the Vaccine Safety Datalink or successor databases.

(v) Authority for contracts

The Secretary may enter into contracts with public and private entities to fulfill the requirements of this subparagraph.

(4) Advanced analysis of drug safety data

(A) Purpose

The Secretary shall establish collaborations with public, academic, and private entities, which may include the Centers for Education and Research on Therapeutics under section 299b-1 of Title 42, to provide for advanced analysis of drug safety data described in paragraph (3)(C) and other information that is publicly available or is provided by the Secretary, in order to--

(i) improve the quality and efficiency of postmarket drug safety risk-benefit analysis;

(ii) provide the Secretary with routine access to outside expertise to study advanced drug safety questions; and

(iii) enhance the ability of the Secretary to make timely assessments based on drug safety data.

(B) Privacy

Such analysis shall not disclose individually identifiable health information when presenting such drug safety signals and trends or when responding to inquiries regarding such drug safety signals and trends.

(C) Public process for priority questions

At least biannually, the Secretary shall seek recommendations from the Drug Safety and Risk Management Advisory Committee (or any successor committee) and from other advisory committees, as appropriate, to the Food and Drug Administration on--

(i) priority drug safety questions; and

(ii) mechanisms for answering such questions, including through--

(I) active risk identification under paragraph (3); and

(II) when such risk identification is not sufficient, postapproval studies and clinical trials under subsection (o)(3).

(D) Procedures for the development of drug safety collaborations

(i) In general

Not later than 180 days after the date of the establishment of the active postmarket risk identification and analysis system under this subsection, the Secretary shall establish and implement procedures under which the Secretary may routinely contract with one or more qualified entities to--

(I) classify, analyze, or aggregate data described in paragraph (3)(C) and information that is publicly available or is provided by the Secretary;

(II) allow for prompt investigation of priority drug safety questions, including--

(aa) unresolved safety questions for drugs or classes of drugs; and

(bb) for a newly-approved drugs, [2] safety signals from clinical trials used to approve the drug and other preapproval trials; rare, serious drug side effects; and the safety of use in domestic populations not included, or underrepresented, in the trials used to approve the drug (such as older people, people with comorbidities, pregnant women, or children);

(III) perform advanced research and analysis on identified drug safety risks;

(IV) focus postapproval studies and clinical trials under subsection (o)(3) more effectively on cases for which reports under paragraph (1) and other safety signal detection is not sufficient to resolve whether there is an elevated risk of a serious adverse event associated with the use of a drug; and

(V) carry out other activities as the Secretary deems necessary to carry out the purposes of this paragraph.

(ii) Request for specific methodology

The procedures described in clause (i) shall permit the Secretary to request that a specific methodology be used by the qualified entity. The qualified entity shall work with the Secretary to finalize the methodology to be used.

(E) Use of analyses

The Secretary shall provide the analyses described in this paragraph, including the methods and results of such analyses, about a drug to the sponsor or sponsors of such drug.

(F) Qualified entities

(i) In general

The Secretary shall enter into contracts with a sufficient number of qualified entities to develop and provide information to the Secretary in a timely manner.

(ii) Qualification

The Secretary shall enter into a contract with an entity under clause (i) only if the Secretary determines that the entity has a significant presence in the United States and has one or more of the following qualifications:

(I) The research, statistical, epidemiologic, or clinical capability and expertise to conduct and complete the activities under this paragraph, including the capability and expertise to provide the Secretary de-identified data consistent with the requirements of this subsection.

(II) An information technology infrastructure in place to support electronic data and operational standards to provide security for such data.

(III) Experience with, and expertise on, the development of drug safety and effectiveness research using electronic population data.

(IV) An understanding of drug development or risk/benefit balancing in a clinical setting.

(V) Other expertise which the Secretary deems necessary to fulfill the activities under this paragraph.

(G) Contract requirements

Each contract with a qualified entity under subparagraph (F)(i) shall contain the following requirements:

(i) Ensuring privacy

The qualified entity shall ensure that the entity will not use data under this subsection in a manner that--

(I) violates the regulations promulgated under section 264(c) of the Health Insurance Portability and Accountability Act of 1996;

(II) violates sections 552 or 552a of Title 5 with regard to the privacy of individually-identifiable beneficiary health information; or

(III) discloses individually identifiable health information when presenting drug safety signals and trends or when responding to inquiries regarding drug safety signals and trends.

Nothing in this clause prohibits lawful disclosure for other purposes.

(ii) Component of another organization

If a qualified entity is a component of another organization--

(I) the qualified entity shall establish appropriate security measures to maintain the confidentiality and privacy of such data; and

(II) the entity shall not make an unauthorized disclosure of such data to the other components of the organization in breach of such confidentiality and privacy requirement.

(iii) Termination or nonrenewal

If a contract with a qualified entity under this subparagraph is terminated or not renewed, the following requirements shall apply:

(I) Confidentiality and privacy protections

The entity shall continue to comply with the confidentiality and privacy requirements under this paragraph with respect to all data disclosed to the entity.

(II) Disposition of data

The entity shall return any data disclosed to such entity under this subsection to which it would not otherwise have access or, if returning the data is not practicable, destroy the data.

(H) Competitive procedures

The Secretary shall use competitive procedures (as defined in section 132 of Title 41) to enter into contracts under subparagraph (G).

(I) Review of contract in the event of a merger or acquisition

The Secretary shall review the contract with a qualified entity under this paragraph in the event of a merger or acquisition of the entity in order to ensure that the requirements under this paragraph will continue to be met.

(J) Coordination

In carrying out this paragraph, the Secretary shall provide for appropriate communications to the public, scientific, public health, and medical communities, and other key stakeholders, and to the extent practicable shall coordinate with the activities of private entities, professional associations, or other entities that may have sources of drug safety data.

(5) The Secretary shall--

(A) conduct regular screenings of the Adverse Event Reporting System database and post a quarterly report on the Adverse Event Reporting System Web site of any new safety information or potential signal of a serious risk identified by Adverse [3] Event Reporting System within the last quarter; and [4]

(B) on an annual basis, review the entire backlog of postmarket safety commitments to determine which commitments require revision or should be eliminated, report to the Congress on these determinations, and assign start dates and estimated completion dates for such commitments; and

(C) make available on the Internet website of the Food and Drug Administration--

(i) guidelines, developed with input from experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs, that detail best practices for drug safety surveillance using the Adverse Event Reporting System; and

(ii) criteria for public posting of adverse event signals.

(l) Public disclosure of safety and effectiveness data and action package

(1) Safety and effectiveness data and information which has been submitted in an application under subsection (b) for a drug and which has not previously been disclosed to the public shall be made available to the public, upon request, unless extraordinary circumstances are shown--

(A) if no work is being or will be undertaken to have the application approved,

(B) if the Secretary has determined that the application is not approvable and all legal appeals have been exhausted,

(C) if approval of the application under subsection (c) is withdrawn and all legal appeals have been exhausted,

(D) if the Secretary has determined that such drug is not a new drug, or

(E) upon the effective date of the approval of the first application under subsection (j) which refers to such drug or upon the date upon which the approval of an application under subsection (j) which refers to such drug could be made effective if such an application had been submitted.

(2) Action package for approval

(A) Action package

The Secretary shall publish the action package for approval of an application under subsection (b) or section 262 of Title 42 on the Internet Web site of the Food and Drug Administration--

(i) not later than 30 days after the date of approval of such applications--

(I) for a drug, no active moiety (as defined by the Secretary in section 314.3 of title 21, Code of Federal Regulations (or any successor regulations)) of which has been approved in any other application under this section; or

(II) for a biological product, no active ingredient of which has been approved in any other application under section 262 of Title 42; and

(ii) not later than 30 days after the third request for such action package for approval received under section 552 of Title 5 for any other drug or biological product.

(B) Immediate publication of summary review

Notwithstanding subparagraph (A), the Secretary shall publish, on the Internet Web site of the Food and Drug Administration, the materials described in subparagraph (C)(iv) not later than 48 hours after the date of approval of the drug, except where such materials require redaction by the Secretary.

(C) Contents

An action package for approval of an application under subparagraph (A) shall be dated and shall include the following:

(i) Documents generated by the Food and Drug Administration related to review of the application.

(ii) Documents pertaining to the format and content of the application generated during drug development.

(iii) Labeling submitted by the applicant.

(iv) A summary review that documents conclusions from all reviewing disciplines about the drug, noting any critical issues and disagreements with the applicant and within the review team and how they were resolved, recommendations for action, and an explanation of any nonconcurrence with review conclusions.

(v) The Division Director and Office Director's decision document which includes--

(I) a brief statement of concurrence with the summary review;

(II) a separate review or addendum to the review if disagreeing with the summary review; and

(III) a separate review or addendum to the review to add further analysis.

(vi) Identification by name of each officer or employee of the Food and Drug Administration who--

(I) participated in the decision to approve the application; and

(II) consents to have his or her name included in the package.

(D) Review

A scientific review of an application is considered the work of the reviewer and shall not be altered by management or the reviewer once final.

(E) Confidential information

This paragraph does not authorize the disclosure of any trade secret, confidential commercial or financial information, or other matter listed in section 552(b) of Title 5.

(m) "Patent" defined

For purposes of this section, the term "patent" means a patent issued by the United States Patent and Trademark Office.

(n) Scientific advisory panels

(1) For the purpose of providing expert scientific advice and recommendations to the Secretary regarding a clinical investigation of a drug or the approval for marketing of a drug under this section or section 262 of Title 42, the Secretary shall establish panels of experts or use panels of experts established before November 21, 1997, or both.

(2) The Secretary may delegate the appointment and oversight authority granted under section 394 of this title to a director of a center or successor entity within the Food and Drug Administration.

(3) The Secretary shall make appointments to each panel established under paragraph (1) so that each panel shall consist of--

(A) members who are qualified by training and experience to evaluate the safety and effectiveness of the drugs to be referred to the panel and who, to the extent feasible, possess skill and experience in the development, manufacture, or utilization of such drugs;

(B) members with diverse expertise in such fields as clinical and administrative medicine, pharmacy, pharmacology, pharmacoeconomics, biological and physical sciences, and other related professions;

(C) a representative of consumer interests, and a representative of interests of the drug manufacturing industry not directly affected by the matter to be brought before the panel; and

(D) two or more members who are specialists or have other expertise in the particular disease or condition for which the drug under review is proposed to be indicated.

Scientific, trade, and consumer organizations shall be afforded an opportunity to nominate individuals for appointment to the panels. No individual who is in the regular full-time employ of the United States and engaged in the administration of this chapter may be a voting member of any panel. The Secretary shall designate one of the members of each panel to serve as chairman thereof.

(4) The Secretary shall, as appropriate, provide education and training to each new panel member before such member participates in a panel's activities, including education regarding requirements under this chapter and related regulations of the Secretary, and the administrative processes and procedures related to panel meetings.

(5) Panel members (other than officers or employees of the United States), while attending meetings or conferences of a panel or otherwise engaged in its business, shall be entitled to receive compensation for each day so engaged, including traveltime, at rates to be fixed by the Secretary, but not to exceed the daily equivalent of the rate in effect for positions classified above grade GS-15 of the General Schedule. While serving away from their homes or regular places of business, panel members may be allowed travel expenses (including per diem in lieu of subsistence) as authorized by section 5703 of Title 5, for persons in the Government service employed intermittently.

(6) The Secretary shall ensure that scientific advisory panels meet regularly and at appropriate intervals so that any matter to be reviewed by such a panel can be presented to the panel not more than 60 days after the matter is ready for such review. Meetings of the panel may be held using electronic communication to convene the meetings.

(7) Within 90 days after a scientific advisory panel makes recommendations on any matter under its review, the Food and Drug Administration official responsible for the matter shall review the conclusions and recommendations of the panel, and notify the affected persons of the final decision on the matter, or of the reasons that no such decision has been reached. Each such final decision shall be documented including the rationale for the decision.

(o) Postmarket studies and clinical trials; labeling

(1) In general

A responsible person may not introduce or deliver for introduction into interstate commerce the new drug involved if the person is in violation of a requirement established under paragraph (3) or (4) with respect to the drug.

(2) Definitions

For purposes of this subsection:

(A) Responsible person

The term "responsible person" means a person who--

(i) has submitted to the Secretary a covered application that is pending; or

(ii) is the holder of an approved covered application.

(B) Covered application

The term "covered application" means--

(i) an application under subsection (b) for a drug that is subject to section 353(b) of this title; and

(ii) an application under section 262 of Title 42.

(C) New safety information; serious risk

The terms "new safety information", "serious risk", and "signal of a serious risk" have the meanings given such terms in section 355-1(b) of this title.

(3) Studies and clinical trials

(A) In general

For any or all of the purposes specified in subparagraph (B), the Secretary may, subject to subparagraph (D), require a responsible person for a drug to conduct a postapproval study or studies of the drug, or a postapproval clinical trial or trials of the drug, on the basis of scientific data deemed appropriate by the Secretary, including information regarding chemically-related or pharmacologically-related drugs.

(B) Purposes of study or clinical trial

The purposes referred to in this subparagraph with respect to a postapproval study or postapproval clinical trial are the following:

(i) To assess a known serious risk related to the use of the drug involved.

(ii) To assess signals of serious risk related to the use of the drug.

(iii) To identify an unexpected serious risk when available data indicates the potential for a serious risk.

(C) Establishment of requirement after approval of covered application

The Secretary may require a postapproval study or studies or postapproval clinical trial or trials for a drug for which an approved covered application is in effect as of the date on which the Secretary seeks to establish such requirement only if the Secretary becomes aware of new safety information.

(D) Determination by Secretary

(i) Postapproval studies

The Secretary may not require the responsible person to conduct a study under this paragraph, unless the Secretary makes a determination that the reports under subsection (k)(1) and the active postmarket risk identification and analysis system as available under subsection (k)(3) will not be sufficient to meet the purposes set forth in subparagraph (B).

(ii) Postapproval clinical trials

The Secretary may not require the responsible person to conduct a clinical trial under this paragraph, unless the Secretary makes a determination that a postapproval study or studies will not be sufficient to meet the purposes set forth in subparagraph (B).

(E) Notification; timetables; periodic reports

(i) Notification

The Secretary shall notify the responsible person regarding a requirement under this paragraph to conduct a postapproval study or clinical trial by the target dates for communication of feedback from the review team to the responsible person regarding proposed labeling and postmarketing study commitments as set forth in the letters described in section 101(c) of the Food and Drug Administration Amendments Act of 2007.

(ii) Timetable; periodic reports

For each study or clinical trial required to be conducted under this paragraph, the Secretary shall require that the responsible person submit a timetable for completion of the study or clinical trial. With respect to each study required to be conducted under this paragraph or otherwise undertaken by the responsible person to investigate a safety issue, the Secretary shall require the responsible person to periodically report to the Secretary on the status of such study including whether any difficulties in completing the study have been encountered. With respect to each clinical trial required to be conducted under this paragraph or otherwise undertaken by the responsible person to investigate a safety issue, the Secretary shall require the responsible person to periodically report to the Secretary on the status of such clinical trial including whether enrollment has begun, the number of participants enrolled, the expected completion date, whether any difficulties completing the clinical trial have been encountered, and registration information with respect to the requirements under section 282(j) of Title 42. If the responsible person fails to comply with such timetable or violates any other requirement of this subparagraph, the responsible person shall be considered in violation of this subsection, unless the responsible person demonstrates good cause for such noncompliance or such other violation. The Secretary shall determine what constitutes good cause under the preceding sentence.

(F) Dispute resolution

The responsible person may appeal a requirement to conduct a study or clinical trial under this paragraph using dispute resolution procedures established by the Secretary in regulation and guidance.

(4) Safety labeling changes requested by Secretary

(A) New safety or new effectiveness information

If the Secretary becomes aware of new information, including any new safety information or information related to reduced effectiveness, that the Secretary determines should be included in the labeling of the drug, the Secretary shall promptly notify the responsible person or, if the same drug approved under subsection (b) is not currently marketed, the holder of an approved application under subsection (j).

(B) Response to notification

Following notification pursuant to subparagraph (A), the responsible person or the holder of the approved application under subsection (j) shall within 30 days--

(i) submit a supplement proposing changes to the approved labeling to reflect the new safety information, including changes to boxed warnings, contraindications, warnings, precautions, or adverse reactions, or new effectiveness information; or

(ii) notify the Secretary that the responsible person or the holder of the approved application under subsection (j) does not believe a labeling change is warranted and submit a statement detailing the reasons why such a change is not warranted.

(C) Review

Upon receipt of such supplement, the Secretary shall promptly review and act upon such supplement. If the Secretary disagrees with the proposed changes in the supplement or with the statement setting forth the reasons why no labeling change is necessary, the Secretary shall initiate discussions to reach agreement on whether the labeling for the drug should be modified to reflect the new safety or new effectiveness information, and if so, the contents of such labeling changes.

(D) Discussions

Such discussions shall not extend for more than 30 days after the response to the notification under subparagraph (B), unless the Secretary determines an extension of such discussion period is warranted.

(E) Order

Within 15 days of the conclusion of the discussions under subparagraph (D), the Secretary may issue an order directing the responsible person or the holder of the approved application under subsection (j) to make such a labeling change as the Secretary deems appropriate to address the new safety or new effectiveness information. Within 15 days of such an order, the responsible person or the holder of the approved application under subsection (j) shall submit a supplement containing the labeling change.

(F) Dispute resolution

Within 5 days of receiving an order under subparagraph (E), the responsible person or the holder of the approved application under subsection (j) may appeal using dispute resolution procedures established by the Secretary in regulation and guidance.

(G) Violation

If the responsible person or the holder of the approved application under subsection (j) has not submitted a supplement within 15 days of the date of such order under subparagraph (E), and there is no appeal or dispute resolution proceeding pending, the responsible person or holder shall be considered to be in violation of this subsection. If at the conclusion of any dispute resolution procedures the Secretary determines that a supplement must be submitted and such a supplement is not submitted within 15 days of the date of that determination, the responsible person or holder shall be in violation of this subsection.

(H) Public health threat

Notwithstanding subparagraphs (A) through (F), if the Secretary concludes that such a labeling change is necessary to protect the public health, the Secretary may accelerate the timelines in such subparagraphs.

(I) Rule of construction

This paragraph shall not be construed to affect the responsibility of the responsible person or the holder of the approved application under subsection (j) to maintain its label in accordance with existing requirements, including subpart B of part 201 and sections 314.70 and 601.12 of title 21, Code of Federal Regulations (or any successor regulations).

(5) Non-delegation

Determinations by the Secretary under this subsection for a drug shall be made by individuals at or above the level of individuals empowered to approve a drug (such as division directors within the Center for Drug Evaluation and Research).

(p) Risk evaluation and mitigation strategy

(1) In general

A person may not introduce or deliver for introduction into interstate commerce a new drug if--

(A)(i) the application for such drug is approved under subsection (b) or (j) and is subject to section 353(b) of this title; or

(ii) the application for such drug is approved under section 262 of Title 42; and

(B) a risk evaluation and mitigation strategy is required under section 355-1 of this title with respect to the drug and the person fails to maintain compliance with the requirements of the approved strategy or with other requirements under section 355-1 of this title, including requirements regarding assessments of approved strategies.

(2) Certain postmarket studies

The failure to conduct a postmarket study under section 356 of this title, subpart H of part 314, or subpart E of part 601 of title 21, Code of Federal Regulations (or any successor regulations), is deemed to be a violation of paragraph (1).

(q) Petitions and civil actions regarding approval of certain applications

(1) In general

(A) Determination

The Secretary shall not delay approval of a pending application submitted under subsection (b)(2) or (j) of this section or section 262(k) of Title 42 because of any request to take any form of action relating to the application, either before or during consideration of the request, unless--

(i) the request is in writing and is a petition submitted to the Secretary pursuant to section 10.30 or 10.35 of title 21, Code of Federal Regulations (or any successor regulations); and

(ii) the Secretary determines, upon reviewing the petition, that a delay is necessary to protect the public health.

Consideration of the petition shall be separate and apart from review and approval of any application.

(B) Notification

If the Secretary determines under subparagraph (A) that a delay is necessary with respect to an application, the Secretary shall provide to the applicant, not later than 30 days after making such determination, the following information:

(i) Notification of the fact that a determination under subparagraph (A) has been made.

(ii) If applicable, any clarification or additional data that the applicant should submit to the docket on the petition to allow the Secretary to review the petition promptly.

(iii) A brief summary of the specific substantive issues raised in the petition which form the basis of the determination.

(C) Format

The information described in subparagraph (B) shall be conveyed via either, at the discretion of the Secretary--

(i) a document; or

(ii) a meeting with the applicant involved.

(D) Public disclosure

Any information conveyed by the Secretary under subparagraph (C) shall be considered part of the application and shall be subject to the disclosure requirements applicable to information in such application.

(E) Denial based on intent to delay

If the Secretary determines that a petition or a supplement to the petition was submitted with the primary purpose of delaying the approval of an application and the petition does not on its face raise valid scientific or regulatory issues, the Secretary may deny the petition at any point based on such determination. The Secretary may issue guidance to describe the factors that will be used to determine under this subparagraph whether a petition is submitted with the primary purpose of delaying the approval of an application.

(F) Final agency action

The Secretary shall take final agency action on a petition not later than 150 days after the date on which the petition is submitted. The Secretary shall not extend such period for any reason, including--

(i) any determination made under subparagraph (A);

(ii) the submission of comments relating to the petition or supplemental information supplied by the petitioner; or

(iii) the consent of the petitioner.

(G) Extension of 30-month period

If the filing of an application resulted in first-applicant status under subsection (j)(5)(D)(i)(IV) and approval of the application was delayed because of a petition, the 30-month period under such subsection is deemed to be extended by a period of time equal to the period beginning on the date on which the Secretary received the petition and ending on the date of final agency action on the petition (inclusive of such beginning and ending dates), without regard to whether the Secretary grants, in whole or in part, or denies, in whole or in part, the petition.

(H) Certification

The Secretary shall not consider a petition for review unless the party submitting such petition does so in written form and the subject document is signed and contains the following certification: "I certify that, to my best knowledge and belief: (a) this petition includes all information and views upon which the petition relies; (b) this petition includes representative data and/or information known to the petitioner which are unfavorable to the petition; and (c) I have taken reasonable steps to ensure that any representative data and/or information which are unfavorable to the petition were disclosed to me. I further certify that the information upon which I have based the action requested herein first became known to the party on whose behalf this petition is submitted on or about the following date: _____. If I received or expect to receive payments, including cash and other forms of consideration, to file this information or its contents, I received or expect to receive those payments from the following persons or organizations: _____. I verify under penalty of perjury that the foregoing is true and correct as of the date of the submission of this petition.", with the date on which such information first became known to such party and the names of such persons or organizations inserted in the first and second blank space, respectively.

(I) Verification

The Secretary shall not accept for review any supplemental information or comments on a petition unless the party submitting such information or comments does so in written form and the subject document is signed and contains the following verification: "I certify that, to my best knowledge and belief: (a) I have not intentionally delayed submission of this document or its contents; and (b) the information upon which I have based the action requested herein first became known to me on or about _____. If I received or expect to receive payments, including cash and other forms of consideration, to file this information or its contents, I received or expect to receive those payments from the following persons or organizations: _____. I verify under penalty of perjury that the foregoing is true and correct as of the date of the submission of this petition.", with the date on which such information first became known to the party and the names of such persons or organizations inserted in the first and second blank space, respectively.

(2) Exhaustion of administrative remedies

(A) Final agency action within 150 days

The Secretary shall be considered to have taken final agency action on a petition if--

(i) during the 150-day period referred to in paragraph (1)(F), the Secretary makes a final decision within the meaning of section 10.45(d) of title 21, Code of Federal Regulations (or any successor regulation); or

(ii) such period expires without the Secretary having made such a final decision.

(B) Dismissal of certain civil actions

If a civil action is filed against the Secretary with respect to any issue raised in the petition before the Secretary has taken final agency action on the petition within the meaning of subparagraph (A), the court shall dismiss without prejudice the action for failure to exhaust administrative remedies.

(C) Administrative record

For purposes of judicial review related to the approval of an application for which a petition under paragraph (1) was submitted, the administrative record regarding any issue raised by the petition shall include--

(i) the petition filed under paragraph (1) and any supplements and comments thereto;

(ii) the Secretary's response to such petition, if issued; and

(iii) other information, as designated by the Secretary, related to the Secretary's determinations regarding the issues raised in such petition, as long as the information was considered by the agency no later than the date of final agency action as defined under subparagraph (2)(A), and regardless of whether the Secretary responded to the petition at or before the approval of the application at issue in the petition.

(3) Annual report on delays in approvals per petitions

The Secretary shall annually submit to the Congress a report that specifies--

(A) the number of applications that were approved during the preceding 12-month period;

(B) the number of such applications whose effective dates were delayed by petitions referred to in paragraph (1) during such period;

(C) the number of days by which such applications were so delayed; and

(D) the number of such petitions that were submitted during such period.

(4) Exceptions

(A) This subsection does not apply to--

(i) a petition that relates solely to the timing of the approval of an application pursuant to subsection (j)(5)(B)(iv); or

(ii) a petition that is made by the sponsor of an application and that seeks only to have the Secretary take or refrain from taking any form of action with respect to that application.

(B) Paragraph (2) does not apply to a petition addressing issues concerning an application submitted pursuant to section 262(k) of Title 42.

(5) Definitions

(A) Application

For purposes of this subsection, the term "application" means an application submitted under subsection (b)(2) or (j) of this section or section 262(k) of Title 42.

(B) Petition

For purposes of this subsection, other than paragraph (1)(A)(i), the term "petition" means a request described in paragraph (1)(A)(i).

(r) Postmarket drug safety information for patients and providers

(1) Establishment

Not later than 1 year after September 27, 2007, the Secretary shall improve the transparency of information about drugs and allow patients and health care providers better access to information about drugs by developing and maintaining an Internet Web site that--

(A) provides links to drug safety information listed in paragraph (2) for prescription drugs that are approved under this section or licensed under section 262 of Title 42; and

(B) improves communication of drug safety information to patients and providers.

(2) Internet Web site

The Secretary shall carry out paragraph (1) by--

(A) developing and maintaining an accessible, consolidated Internet Web site with easily searchable drug safety information, including the information found on United States Government Internet Web sites, such as the United States National Library of Medicine's Daily Med and Medline Plus Web sites, in addition to other such Web sites maintained by the Secretary;

(B) ensuring that the information provided on the Internet Web site is comprehensive and includes, when available and appropriate--

(i) patient labeling and patient packaging inserts;

(ii) a link to a list of each drug, whether approved under this section or licensed under such section 262, for which a Medication Guide, as provided for under part 208 of title 21, Code of Federal Regulations (or any successor regulations), is required;

(iii) a link to the registry and results data bank provided for under subsections (i) and (j) of section 282 of Title 42;

(iv) the most recent safety information and alerts issued by the Food and Drug Administration for drugs approved by the Secretary under this section, such as product recalls, warning letters, and import alerts;

(v) publicly available information about implemented RiskMAPs and risk evaluation and mitigation strategies under subsection (o);

(vi) guidance documents and regulations related to drug safety; and

(vii) other material determined appropriate by the Secretary;

(C) providing access to summaries of the assessed and aggregated data collected from the active surveillance infrastructure under subsection (k)(3) to provide information of known and serious side-effects for drugs approved under this section or licensed under such section 262;

(D) preparing and making publicly available on the Internet website established under paragraph (1) best practices for drug safety surveillance activities for drugs approved under this section or section 262 of Title 42;

(E) enabling patients, providers, and drug sponsors to submit adverse event reports through the Internet Web site;

(F) providing educational materials for patients and providers about the appropriate means of disposing of expired, damaged, or unusable medications; and

(G) supporting initiatives that the Secretary determines to be useful to fulfill the purposes of the Internet Web site.

(3) Posting of drug labeling

The Secretary shall post on the Internet Web site established under paragraph (1) the approved professional labeling and any required patient labeling of a drug approved under this section or licensed under such section 262 not later than 21 days after the date the drug is approved or licensed, including in a supplemental application with respect to a labeling change.

(4) Private sector resources

To ensure development of the Internet Web site by the date described in paragraph (1), the Secretary may, on a temporary or permanent basis, implement systems or products developed by private entities.

(5) Authority for contracts

The Secretary may enter into contracts with public and private entities to fulfill the requirements of this subsection.

(6) Review

The Advisory Committee on Risk Communication under section 360bbb-6 of this title shall, on a regular basis, perform a comprehensive review and evaluation of the types of risk communication information provided on the Internet Web site established under paragraph (1) and, through other means, shall identify, clarify, and define the purposes and types of information available to facilitate the efficient flow of information to patients and providers, and shall recommend ways for the Food and Drug Administration to work with outside entities to help facilitate the dispensing of risk communication information to patients and providers.

(s) Referral to advisory committee

The Secretary shall--

(1) refer a drug or biological product to a Food and Drug Administration advisory committee for review at a meeting of such advisory committee prior to the approval of such drug or biological if it is--

(A) a drug, no active moiety (as defined by the Secretary in section 314.3 of title 21, Code of Federal Regulations (or any successor regulations)) of which has been approved in any other application under this section; or

(B) a biological product, no active ingredient of which has been approved in any other application under section 262 of Title 42; or

(2) if the Secretary does not refer a drug or biological product described in paragraph (1) to a Food and Drug Administration advisory committee prior to such approval, provide in the action letter on the application for the drug or biological product a summary of the reasons why the Secretary did not refer the drug or biological product to an advisory committee prior to approval.

(t) Database for authorized generic drugs

(1) In general

(A) Publication

The Commissioner shall--

(i) not later than 9 months after September 27, 2007, publish a complete list on the Internet Web site of the Food and Drug Administration of all authorized generic drugs (including drug trade name, brand company manufacturer, and the date the authorized generic drug entered the market); and

(ii) update the list quarterly to include each authorized generic drug included in an annual report submitted to the Secretary by the sponsor of a listed drug during the preceding 3-month period.

(B) Notification

The Commissioner shall notify relevant Federal agencies, including the Centers for Medicare & Medicaid Services and the Federal Trade Commission, when the Commissioner first publishes the information described in subparagraph (A) that the information has been published and that the information will be updated quarterly.

(2) Inclusion

The Commissioner shall include in the list described in paragraph (1) each authorized generic drug included in an annual report submitted to the Secretary by the sponsor of a listed drug after January 1, 1999.

(3) Authorized generic drug

In this section, the term "authorized generic drug" means a listed drug (as that term is used in subsection (j)) that--

(A) has been approved under subsection (c); and

(B) is marketed, sold, or distributed directly or indirectly to retail class of trade under a different labeling, packaging (other than repackaging as the listed drug in blister packs, unit doses, or similar packaging for use in institutions), product code, labeler code, trade name, or trade mark than the listed drug.

(u) Certain drugs containing single enantiomers

(1) In general

For purposes of subsections (c)(3)(E)(ii) and (j)(5)(F)(ii), if an application is submitted under subsection (b) for a non-racemic drug containing as an active moiety (as defined by the Secretary in section 314.3 of title 21, Code of Federal Regulations (or any successor regulations)) a single enantiomer that is contained in a racemic drug approved in another application under subsection (b), the applicant may, in the application for such non-racemic drug, elect to have the single enantiomer not be considered the same active moiety as that contained in the approved racemic drug, if--

(A)(i) the single enantiomer has not been previously approved except in the approved racemic drug; and

(ii) the application submitted under subsection (b) for such non-racemic drug--

(I) includes full reports of new clinical investigations (other than bioavailability studies)--

(aa) necessary for the approval of the application under subsections (c) and (d); and

(bb) conducted or sponsored by the applicant; and

(II) does not rely on any clinical investigations (other than bioavailability studies) that are part of an application submitted under subsection (b) for approval of the approved racemic drug; and

(B) the application submitted under subsection (b) for such non-racemic drug is not submitted for approval of a condition of use--

(i) in a therapeutic category in which the approved racemic drug has been approved; or

(ii) for which any other enantiomer of the racemic drug has been approved.

(2) Limitation

(A) No approval in certain therapeutic categories

Until the date that is 10 years after the date of approval of a non-racemic drug described in paragraph (1) and with respect to which the applicant has made the election provided for by such paragraph, the Secretary shall not approve such non-racemic drug for any condition of use in the therapeutic category in which the racemic drug has been approved.

(B) Labeling

If applicable, the labeling of a non-racemic drug described in paragraph (1) and with respect to which the applicant has made the election provided for by such paragraph shall include a statement that the non-racemic drug is not approved, and has not been shown to be safe and effective, for any condition of use of the racemic drug.

(3) Definition

(A) In general

For purposes of this subsection, the term "therapeutic category" means a therapeutic category identified in the list developed by the United States Pharmacopeia pursuant to section 1395w-104(b)(3)(C)(ii) of Title 42 and as in effect on September 27, 2007.

(B) Publication by Secretary

The Secretary shall publish the list described in subparagraph (A) and may amend such list by regulation.

(4) Availability

The election referred to in paragraph (1) may be made only in an application that is submitted to the Secretary after September 27, 2007, and before October 1, 2027.

(v) Antibiotic drugs submitted before November 21, 1997

(1) Antibiotic drugs approved before November 21, 1997

(A) In general

Notwithstanding any provision of the Food and Drug Administration Modernization Act of 1997 or any other provision of law, a sponsor of a drug that is the subject of an application described in subparagraph (B)(i) shall be eligible for, with respect to the drug, the 3-year exclusivity period referred to under clauses (iii) and (iv) of subsection (c)(3)(E) and under clauses (iii) and (iv) of subsection (j)(5)(F), subject to the requirements of such clauses, as applicable.

(B) Application; antibiotic drug described

(i) Application

An application described in this clause is an application for marketing submitted under this section after October 8, 2008, in which the drug that is the subject of the application contains an antibiotic drug described in clause (ii).

(ii) Antibiotic drug

An antibiotic drug described in this clause is an antibiotic drug that was the subject of an application approved by the Secretary under section 357 of this title (as in effect before November 21, 1997).

(2) Antibiotic drugs submitted before November 21, 1997, but not approved

(A) In general

Notwithstanding any provision of the Food and Drug Administration Modernization Act of 1997 or any other provision of law, a sponsor of a drug that is the subject of an application described in subparagraph (B)(i) may elect to be eligible for, with respect to the drug--

(i)(I) the 3-year exclusivity period referred to under clauses (iii) and (iv) of subsection (c)(3)(E) and under clauses (iii) and (iv) of subsection (j)(5)(F), subject to the requirements of such clauses, as applicable; and

(II) the 5-year exclusivity period referred to under clause (ii) of subsection (c)(3)(E) and under clause (ii) of subsection (j)(5)(F), subject to the requirements of such clauses, as applicable; or

(ii) a patent term extension under section 156 of Title 35, subject to the requirements of such section.

(B) Application; antibiotic drug described

(i) Application

An application described in this clause is an application for marketing submitted under this section after October 8, 2008, in which the drug that is the subject of the application contains an antibiotic drug described in clause (ii).

(ii) Antibiotic drug

An antibiotic drug described in this clause is an antibiotic drug that was the subject of 1 or more applications received by the Secretary under section 357 of this title (as in effect before November 21, 1997), none of which was approved by the Secretary under such section.

(3) Limitations

(A) Exclusivities and extensions

Paragraphs (1)(A) and (2)(A) shall not be construed to entitle a drug that is the subject of an approved application described in subparagraphs [5] (1)(B)(i) or (2)(B)(i), as applicable, to any market exclusivities or patent extensions other than those exclusivities or extensions described in paragraph (1)(A) or (2)(A).

(B) Conditions of use

Paragraphs (1)(A) and (2)(A)(i) shall not apply to any condition of use for which the drug referred to in subparagraph (1)(B)(i) or (2)(B)(i), as applicable, was approved before October 8, 2008.

(4) Application of certain provisions

Notwithstanding section 125, or any other provision, of the Food and Drug Administration Modernization Act of 1997, or any other provision of law, and subject to the limitations in paragraphs (1), (2), and (3), the provisions of the Drug Price Competition and Patent Term Restoration Act of 1984 shall apply to any drug subject to paragraph (1) or any drug with respect to which an election is made under paragraph (2)(A).

(w) Deadline for determination on certain petitions

The Secretary shall issue a final, substantive determination on a petition submitted pursuant to subsection (b) of section 314.161 of title 21, Code of Federal Regulations (or any successor regulations), no later than 270 days after the date the petition is submitted.

(x) Date of approval in the case of recommended controls under the CSA

(1) In general

In the case of an application under subsection (b) with respect to a drug for which the Secretary provides notice to the sponsor that the Secretary intends to issue a scientific and medical evaluation and recommend controls under the Controlled Substances Act, approval of such application shall not take effect until the interim final rule controlling the drug is issued in accordance with section 201(j) of the Controlled Substances Act.

(2) Date of approval

For purposes of this section, with respect to an application described in paragraph (1), the term "date of approval" shall mean the later of--

(A) the date an application under subsection (b) is approved under subsection (c); or

(B) the date of issuance of the interim final rule controlling the drug.

(y) Contrast agents intended for use with applicable medical imaging devices

(1) In general

The sponsor of a contrast agent for which an application has been approved under this section may submit a supplement to the application seeking approval for a new use following the authorization of a premarket submission for an applicable medical imaging device for that use with the contrast agent pursuant to section 360j(p)(1) of this title.

(2) Review of supplement

In reviewing a supplement submitted under this subsection, the agency center charged with the premarket review of drugs may--

(A) consult with the center charged with the premarket review of devices; and

(B) review information and data submitted to the Secretary by the sponsor of an applicable medical imaging device pursuant to section 360e, 360(k), or 360c(f)(2) of this title so long as the sponsor of such applicable medical imaging device has provided to the sponsor of the contrast agent a right of reference.

(3) Definitions

For purposes of this subsection--

(A) the term "new use" means a use of a contrast agent that is described in the approved labeling of an applicable medical imaging device described in section 360j(p) of this title, but that is not described in the approved labeling of the contrast agent; and

(B) the terms "applicable medical imaging device" and "contrast agent" have the meanings given such terms in section 360j(p) of this title.

(z) [6] Nonclinical test defined

For purposes of this section, the term "nonclinical test" means a test conducted in vitro, in silico, or in chemico, or a nonhuman in vivo test, that occurs before or during the clinical trial phase of the investigation of the safety and effectiveness of a drug. Such test may include the following:

(1) Cell-based assays.

(2) Organ chips and microphysiological systems.

(3) Computer modeling.

(4) Other nonhuman or human biology-based test methods, such as bioprinting.

(5) Animal tests.

(z) [6] Diversity action plan for clinical studies

(1) With respect to a clinical investigation of a new drug that is a phase 3 study, as defined in section 312.21(c) of title 21, Code of Federal Regulations (or successor regulations), or, as appropriate, another pivotal study of a new drug (other than bioavailability or bioequivalence studies), the sponsor of such drug shall submit to the Secretary a diversity action plan.

(2) Such diversity action plan shall include--

(A) the sponsor's goals for enrollment in such clinical study;

(B) the sponsor's rationale for such goals; and

(C) an explanation of how the sponsor intends to meet such goals.

(3) The sponsor shall submit to the Secretary such diversity action plan, in the form and manner specified by the Secretary in guidance, as soon as practicable but not later than the date on which the sponsor submits the protocol to the Secretary for such a phase 3 study or other pivotal study of the drug. The sponsor may submit modifications to the diversity action plan. Any such modifications shall be in the form and manner specified by the Secretary in guidance.

(4)(A) On the initiative of the Secretary or at the request of a sponsor, the Secretary may waive any requirement in paragraph (1), (2), or (3) if the Secretary determines that a waiver is necessary based on what is known or what can be determined about the prevalence or incidence of the disease or condition for which the new drug is under investigation (including in terms of the patient population that may use the drug), if conducting a clinical investigation in accordance with a diversity action plan would otherwise be impracticable, or if such waiver is necessary to protect public health during a public health emergency.

(B) The Secretary shall issue a written response granting or denying a request from a sponsor for a waiver within 60 days of receiving such request.

(5) No diversity action plan shall be required for a submission described in section 360bbb of this title.

CREDIT(S)

(June 25, 1938, c. 675, § 505, 52 Stat. 1052; Pub.L. 86-507, § 1(18), June 11, 1960, 74 Stat. 201; Pub.L. 87-781, Title I, §§ 102(b) to (d), 103(a), (b), 104(a) to (d)(2), Oct. 10, 1962, 76 Stat. 781, 784, 785; Pub.L. 92-387, § 4(d), Aug. 16, 1972, 86 Stat. 562; Pub.L. 98-417, Title I, §§ 101, 102(a) to (b)(5), 103, 104, Sept. 24, 1984, 98 Stat. 1585, 1592, 1593, 1597; Pub.L. 102-282, § 5, May 13, 1992, 106 Stat. 161; Pub.L. 103-80, § 3(n), Aug. 13, 1993, 107 Stat. 777; Pub.L. 105-115, Title I, §§ 115, 117, 119, 120, 124(a), Nov. 21, 1997, 111 Stat. 2313, 2315, 2316, 2318, 2324; Pub.L. 106-113, Div. B, § 1000(a)(9) [Title IV, § 4732(b)(11)], Nov. 29, 1999, 113 Stat. 1536, 1501A-584; Pub.L. 107-109, § 15(c)(1), Jan. 4, 2002, 115 Stat. 1420; Pub.L. 108-155, § 2(b)(1), Dec. 3, 2003, 117 Stat. 1941; Pub.L. 108-173, Title XI, §§ 1101(a), (b), 1102(a), 1103(a), Dec. 8, 2003, 117 Stat. 2448, 2452, 2457, 2460; Pub.L. 110-85, Title VII, § 701(b), Title VIII, § 801(b)(3)(A), (B), Title IX, §§ 901(a), 903, 905(a), 914(a), 915, 916, 918, 920, 921, Title XI, § 1113, Sept. 27, 2007, 121 Stat. 903, 921, 922, 943, 944, 953, 957, 960, 961, 976; Pub.L. 110-316, Title III, § 301, Aug. 14, 2008, 122 Stat. 3524; Pub.L. 110-379, § 4(a), Oct. 8, 2008, 122 Stat. 4076; Pub.L. 111-31, Div. A, Title I, § 103(e), June 22, 2009, 123 Stat. 1837; Pub.L. 111-148, Title VII, § 7002(d)(1), Title X, § 10609, Mar. 23, 2010, 124 Stat. 816, 1014; Pub.L. 112-144, Title IX, § 905, Title XI, §§ 1101, 1134(a), 1135, July 9, 2012, 126 Stat.

1092, 1108, 1123; Pub.L. 113-5, Title III, § 301, Mar. 13, 2013, 127 Stat. 179; Pub.L. 114-89, § 2(a)(1), Nov. 25, 2015, 129 Stat. 698; Pub.L. 114-255, Div. A, Title III, §§ 3024(b), 3031(a), 3075(a), (b), 3101(a)(2)(B), 3102(1), Dec. 13, 2016, 130 Stat. 1099, 1138, 1152, 1156; Pub.L. 115-52, Title VI, § 601, Title VII, § 706(b), Title VIII, §§ 801, 802, 808, Title IX, § 901(a), Aug. 18, 2017, 131 Stat. 1048, 1059, 1068, 1069, 1074, 1076; Pub.L. 115-271, Title III, § 3041(b), Oct. 24, 2018, 132 Stat. 3942; Pub.L. 116-290, § 2(a) to (d)(1), (g), Jan. 5, 2021, 134 Stat. 4889, 4892; Pub.L. 117-9, § 1(a)(1), (b)(1), Apr. 23, 2021, 135 Stat. 256, 258; Pub.L. 117-180, Div. F, Title V, § 5004, Sept. 30, 2022, 136 Stat. 2167; Pub.L. 117-229, Div. C, Title III, § 305, Dec. 16, 2022, 136 Stat. 2312; Pub.L. 117-328, Div. FF, Title III, §§ 3105, 3209(a), 3222, 3224, 3601(a), Dec. 29, 2022, 136 Stat. 5807, 5821, 5829, 5831, 5860.)

Notes of Decisions (649)

Footnotes

1 So in original. Probably should be “bioavailability”.

2 So in original. Probably should be “drug,”.

3 So in original. Probably should be preceded by “the”.

4 So in original. The word “and” probably should not appear.

5 So in original. Probably should be “subparagraph”.

6 So in original. Two subsecs. (z) have been enacted.

21 U.S.C.A. § 355, 21 USCA § 355
Current through P.L. 118-46. Some statute sections may be more current, see credits for details.

End of Document

Tab 4

Code of Federal Regulations
Title 21. Food and Drugs
Chapter I. Food and Drug Administration, Department of Health and Human Services (Refs & Annos)
Subchapter D. Drugs for Human Use
Part 314. Applications for FDA Approval to Market a New Drug (Refs & Annos)
Subpart C. Abbreviated Applications (Refs & Annos)

21 C.F.R. § 314.94

§ 314.94 Content and format of an ANDA.

Effective: December 5, 2016
Currentness

ANDAs are required to be submitted in the form and contain the information required under this section. Three copies of the ANDA are required, an archival copy, a review copy, and a field copy. FDA will maintain guidance documents on the format and content of ANDAs to assist applicants in their preparation.

(a) ANDAs. Except as provided in paragraph (b) of this section, the applicant must submit a complete archival copy of the ANDA that includes the following:

(1) Application form. The applicant must submit a completed and signed application form that contains the information described under § 314.50(a)(1), (a)(3), (a)(4), and (a)(5). The applicant must state whether the submission is an ANDA under this section or a supplement to an ANDA under § 314.97.

(2) Table of contents. The archival copy of the ANDA is required to contain a table of contents that shows the volume number and page number of the contents of the submission.

(3) Basis for ANDA submission. An ANDA must refer to a listed drug. Ordinarily, that listed drug will be the drug product selected by the Agency as the reference standard for conducting bioequivalence testing. The ANDA must contain:

(i) The name of the reference listed drug, including its dosage form and strength. For an ANDA based on an approved petition under § 10.30 of this chapter and § 314.93, the reference listed drug must be the same as the listed drug referenced in the approved petition.

(ii) A statement as to whether, according to the information published in the list, the reference listed drug is entitled to a period of marketing exclusivity under section 505(j)(5)(F) of the Federal Food, Drug, and Cosmetic Act.

(iii) For an ANDA based on an approved petition under § 10.30 of this chapter and § 314.93, a reference to the FDA–assigned docket number for the petition and a copy of FDA's correspondence approving the petition.

(4) Conditions of use.

(i) A statement that the conditions of use prescribed, recommended, or suggested in the labeling proposed for the drug product have been previously approved for the reference listed drug.

(ii) A reference to the applicant's annotated proposed labeling and to the currently approved labeling for the reference listed drug provided under paragraph (a)(8) of this section.

(5) Active ingredients.

(i) For a single-active-ingredient drug product, information to show that the active ingredient is the same as that of the reference single-active-ingredient listed drug, as follows:

(A) A statement that the active ingredient of the proposed drug product is the same as that of the reference listed drug.

(B) A reference to the applicant's annotated proposed labeling and to the currently approved labeling for the reference listed drug provided under paragraph (a)(8) of this section.

(ii) For a combination drug product, information to show that the active ingredients are the same as those of the reference listed drug except for any different active ingredient that has been the subject of an approved petition, as follows:

(A) A statement that the active ingredients of the proposed drug product are the same as those of the reference listed drug, or if one of the active ingredients differs from one of the active ingredients of the reference listed drug and the ANDA is submitted under the approval of a petition under § 314.93 to vary such active ingredient, information to show that the other active ingredients of the drug product are the same as the other active ingredients of the reference listed drug, information to show that the different active ingredient is an active ingredient of another listed drug or of a drug that does not meet the definition of “new drug” in section 201(p) of the Federal Food, Drug, and Cosmetic Act, and such other information about the different active ingredient that FDA may require.

(B) A reference to the applicant's annotated proposed labeling and to the currently approved labeling for the reference listed drug provided under paragraph (a)(8) of this section.

(6) Route of administration, dosage form, and strength.

(i) Information to show that the route of administration, dosage form, and strength of the drug product are the same as those of the reference listed drug except for any differences that have been the subject of an approved petition, as follows:

(A) A statement that the route of administration, dosage form, and strength of the proposed drug product are the same as those of the reference listed drug.

(B) A reference to the applicant's annotated proposed labeling and to the currently approved labeling for the reference listed drug provided under paragraph (a)(8) of this section.

(ii) If the route of administration, dosage form, or strength of the drug product differs from the reference listed drug and the ANDA is submitted under an approved petition under § 314.93, such information about the different route of administration, dosage form, or strength that FDA may require.

(7) Bioequivalence.

(i) Information that shows that the drug product is bioequivalent to the reference listed drug upon which the applicant relies. A complete study report must be submitted for the bioequivalence study upon which the applicant relies for approval. For all other bioequivalence studies conducted on the same drug product formulation as defined in § 314.3(b), the applicant must submit either a complete or summary report. If a summary report of a bioequivalence study is submitted and FDA determines that there may be bioequivalence issues or concerns with the product, FDA may require that the applicant submit a complete report of the bioequivalence study to FDA; or

(ii) If the ANDA is submitted pursuant to a petition approved under § 314.93, the results of any bioavailability or bioequivalence testing required by the Agency, or any other information required by the Agency to show that the active ingredients of the proposed drug product are of the same pharmacological or therapeutic class as those in the reference listed drug and that the proposed drug product can be expected to have the same therapeutic effect as the reference listed drug. If the proposed drug product contains a different active ingredient than the reference listed drug, FDA will consider the proposed drug product to have the same therapeutic effect as the reference listed drug if the applicant provides information demonstrating that:

(A) There is an adequate scientific basis for determining that substitution of the specific proposed dose of the different active ingredient for the dose of the member of the same pharmacological or therapeutic class in the reference listed drug will yield a resulting drug product whose safety and effectiveness have not been adversely affected.

(B) The unchanged active ingredients in the proposed drug product are bioequivalent to those in the reference listed drug.

(C) The different active ingredient in the proposed drug product is bioequivalent to an approved dosage form containing that ingredient and approved for the same indication as the proposed drug product or is bioequivalent to a drug product offered for that indication which does not meet the definition of “new drug” under section 201(p) of the Federal Food, Drug, and Cosmetic Act.

(iii) For each in vivo or in vitro bioequivalence study contained in the ANDA:

(A) A description of the analytical and statistical methods used in each study; and

(B) With respect to each study involving human subjects, a statement that the study either was conducted in compliance with the institutional review board regulations in part 56 of this chapter, or was not subject to the regulations under § 56.104 or § 56.105 of this chapter, and that it was conducted in compliance with the informed consent regulations in part 50 of this chapter.

(8) Labeling—

(i) Listed drug labeling. A copy of the currently approved labeling (including, if applicable, any Medication Guide required under part 208 of this chapter) for the listed drug referred to in the ANDA, if the ANDA relies on a reference listed drug.

(ii) Copies of proposed labeling. Copies of the label and all labeling for the drug product including, if applicable, any Medication Guide required under part 208 of this chapter (4 copies of draft labeling or 12 copies of final printed labeling).

(iii) Statement on proposed labeling. A statement that the applicant's proposed labeling including, if applicable, any Medication Guide required under part 208 of this chapter is the same as the labeling of the reference listed drug except for differences annotated and explained under paragraph (a)(8)(iv) of this section.

(iv) Comparison of approved and proposed labeling. A side-by-side comparison of the applicant's proposed labeling including, if applicable, any Medication Guide required under part 208 of this chapter with the approved labeling for the reference listed drug with all differences annotated and explained. Labeling (including the container label, package insert, and, if applicable, Medication Guide) proposed for the drug product must be the same as the labeling approved for the reference listed drug, except for changes required because of differences approved under a petition filed under § 314.93 or because the drug product and the reference listed drug are produced or distributed by different manufacturers. Such differences between the applicant's proposed labeling and labeling approved for the reference listed drug may include differences in expiration date, formulation, bioavailability, or pharmacokinetics, labeling revisions made to comply with current FDA labeling guidelines or other guidance, or omission of an indication or other aspect of labeling protected by patent or accorded exclusivity under section 505(j)(5)(F) of the Federal Food, Drug, and Cosmetic Act.

(9) Chemistry, manufacturing, and controls.

(i) The information required under § 314.50(d)(1), except that the information required under § 314.50(d)(1)(ii)(c) must contain the proposed or actual master production record, including a description of the equipment, to be used for the manufacture of a commercial lot of the drug product.

(ii) Inactive ingredients. Unless otherwise stated in paragraphs (a)(9)(iii) through (a)(9)(v) of this section, an applicant must identify and characterize the inactive ingredients in the proposed drug product and provide information demonstrating that such inactive ingredients do not affect the safety or efficacy of the proposed drug product.

(iii) Inactive ingredient changes permitted in drug products intended for parenteral use. Generally, a drug product intended for parenteral use must contain the same inactive ingredients and in the same concentration as the reference listed drug identified by the applicant under paragraph (a)(3) of this section. However, an applicant may seek approval of a drug product that differs from the reference listed drug in preservative, buffer, or antioxidant provided that the applicant identifies and characterizes the differences and provides information demonstrating that the differences do not affect the safety or efficacy of the proposed drug product.

(iv) Inactive ingredient changes permitted in drug products intended for ophthalmic or otic use. Generally, a drug product intended for ophthalmic or otic use must contain the same inactive ingredients and in the same concentration as the reference listed drug identified by the applicant under paragraph (a)(3) of this section. However, an applicant may seek approval of a drug product that differs from the reference listed drug in preservative, buffer, substance to adjust tonicity, or thickening agent provided that the applicant identifies and characterizes the differences and provides information demonstrating that the differences do not affect the safety or efficacy of the proposed drug product, except that, in a product intended for ophthalmic use, an applicant may not change a buffer or substance to adjust tonicity for the purpose of claiming a therapeutic advantage over or difference from the listed drug, e.g., by using a balanced salt solution as a diluent as opposed to an isotonic saline solution, or by making a significant change in the pH or other change that may raise questions of irritability.

(v) Inactive ingredient changes permitted in drug products intended for topical use. Generally, a drug product intended for topical use, solutions for aerosolization or nebulization, and nasal solutions shall contain the same inactive ingredients as the reference listed drug identified by the applicant under paragraph (a)(3) of this section. However, an ANDA may include different inactive ingredients provided that the applicant identifies and characterizes the differences and provides information demonstrating that the differences do not affect the safety or efficacy of the proposed drug product.

(10) Samples. The information required under § 314.50(e)(1) and (e)(2)(i). Samples need not be submitted until requested by FDA.

(11) Other. The information required under § 314.50(g).

(12) Patent certification—

(i) Patents claiming drug substance, drug product, or method of use.

(A) An appropriate patent certification or statement with respect to each patent issued by the U.S. Patent and Trademark Office that, in the opinion of the applicant and to the best of its knowledge, claims the reference listed drug or that claims a use of such listed drug for which the applicant is seeking approval under section 505(j) of the Federal Food, Drug, and Cosmetic Act and for which information is required to be filed under section 505(b) and (c) of the Federal Food, Drug, and Cosmetic Act and § 314.53. For each such patent, the applicant must provide the patent number and certify, in its opinion and to the best of its knowledge, one of the following circumstances:

(1) That the patent information has not been submitted to FDA. The applicant must entitle such a certification "Paragraph I Certification";

(2) That the patent has expired. The applicant must entitle such a certification "Paragraph II Certification";

(3) The date on which the patent will expire. The applicant must entitle such a certification "Paragraph III Certification"; or

(4)(i) That the patent is invalid, unenforceable, or will not be infringed by the manufacture, use, or sale of the drug product for which the ANDA is submitted. The applicant must entitle such a certification "Paragraph IV Certification". This certification must be submitted in the following form:

I, (name of applicant), certify that Patent No. _____ (is invalid, unenforceable, or will not be infringed by the manufacture, use, or sale of) (name of proposed drug product) for which this ANDA is submitted.

(ii) The certification must be accompanied by a statement that the applicant will comply with the requirements under § 314.95(a) with respect to providing a notice to each owner of the patent or its representative and to the NDA holder (or, if the NDA holder does not reside or maintain a place of business within the United States, its attorney, agent, or other authorized official) for the listed drug, with the requirements under § 314.95(b) with respect to sending the notice, and with the requirements under § 314.95(c) with respect to the content of the notice.

(B) If the ANDA refers to a listed drug that is itself a licensed generic product of a patented drug first approved under section 505(b) of the Federal Food, Drug, and Cosmetic Act, an appropriate patent certification or statement under paragraph (a)(12)(i) and/or (iii) of this section with respect to each patent that claims the first-approved patented drug or that claims a use for such drug.

(ii) No relevant patents. If, in the opinion of the applicant and to the best of its knowledge, there are no patents described in paragraph (a)(12)(i) of this section, a certification in the following form:

In the opinion and to the best knowledge of (name of applicant), there are no patents that claim the listed drug referred to in this ANDA or that claim a use of the listed drug.

(iii) Method-of-use patent.

(A) If patent information is submitted under section 505(b) or (c) of the Federal Food, Drug, and Cosmetic Act and § 314.53 for a patent claiming a method of using the listed drug, and the labeling for the drug product for which the applicant is seeking approval does not include an indication or other condition of use that is covered by the method-of-use patent, a statement explaining that the method-of-use patent does not claim a proposed indication or other condition of use.

(B) If the labeling of the drug product for which the applicant is seeking approval includes an indication or other condition of use that, according to the patent information submitted under section 505(b) or (c) of the Federal Food, Drug, and Cosmetic Act and § 314.53 or in the opinion of the applicant, is claimed by a method-of-use patent, an applicable certification under paragraph (a)(12)(i) of this section.

(iv) [Reserved by 81 FR 69649]

(v) Licensing agreements. If the ANDA is for a drug or method of using a drug claimed by a patent and the applicant has a licensing agreement with the patent owner, the applicant must submit a paragraph IV certification as to that patent and a statement that the applicant has been granted a patent license. If the patent owner consents to approval of the ANDA (if otherwise eligible for approval) as of a specific date, the ANDA must contain a written statement from the patent owner that it has a licensing agreement with the applicant and that it consents to approval of the ANDA as of a specific date.

(vi) Untimely filing of patent information.

(A) If a patent on the listed drug is issued and the holder of the approved NDA for the listed drug does not file with FDA the required information on the patent within 30 days of issuance of the patent, an applicant who submitted an ANDA for that drug that contained an appropriate patent certification or statement before the submission of the patent information is not required to submit a patent certification or statement to address the patent or patent information that is late-listed with respect to the pending ANDA. Except as provided in § 314.53(f)(1), an NDA holder's amendment to the description of the approved method(s) of use claimed by the patent will be considered untimely filing of patent information unless:

(1) The amendment to the description of the approved method(s) of use claimed by the patent is submitted within 30 days of patent issuance;

(2) The amendment to the description of the approved method(s) of use claimed by the patent is submitted within 30 days of approval of a corresponding change to product labeling; or

(3) The amendment to the description of the approved method(s) of use claimed by the patent is submitted within 30 days of a decision by the U.S. Patent and Trademark Office or by a Federal district court, the Court of Appeals for the Federal Circuit, or the U.S. Supreme Court that is specific to the patent and alters the construction of a method-of-use claim(s) of the patent, and the amendment contains a copy of the decision.

(B) An applicant whose ANDA is submitted after the NDA holder's untimely filing of patent information, or whose pending ANDA was previously submitted but did not contain an appropriate patent certification or statement at the time of the patent submission, must submit a certification under paragraph (a)(12)(i) of this section and/or a statement under paragraph (a)(12)(iii) of this section as to that patent.

(vii) Disputed patent information. If an applicant disputes the accuracy or relevance of patent information submitted to FDA, the applicant may seek a confirmation of the correctness of the patent information in accordance with the procedures under § 314.53(f). Unless the patent information is withdrawn, the applicant must submit an appropriate certification or statement for each listed patent.

(viii) Amended certifications. A patent certification or statement submitted under paragraphs (a)(12)(i) through (iii) of this section may be amended at any time before the approval of the ANDA. If an applicant with a pending ANDA voluntarily makes a patent certification for an untimely filed patent, the applicant may withdraw the patent certification for the untimely

filed patent. An applicant must submit an amended certification as an amendment to a pending ANDA. Once an amendment is submitted to change a certification, the ANDA will no longer be considered to contain the prior certification.

(A) After finding of infringement. An applicant who has submitted a paragraph IV certification and is sued for patent infringement must submit an amendment to change its certification if a court enters a final decision from which no appeal has been or can be taken, or signs and enters a settlement order or consent decree in the action that includes a finding that the patent is infringed, unless the final decision, settlement order, or consent decree also finds the patent to be invalid. In its amendment, the applicant must certify under paragraph (a)(12)(i)(A)(3) of this section that the patent will expire on a specific date or, with respect to a patent claiming a method of use, the applicant may instead provide a statement under paragraph (a)(12)(iii) of this section if the applicant amends its ANDA such that the applicant is no longer seeking approval for a method of use claimed by the patent. Once an amendment for the change has been submitted, the ANDA will no longer be considered to contain a paragraph IV certification to the patent. If a final judgment finds the patent to be invalid and infringed, an amended certification is not required.

(B) After request to remove a patent or patent information from the list. If the list reflects that an NDA holder has requested that a patent or patent information be removed from the list and no ANDA applicant is eligible for 180–day exclusivity based on a paragraph IV certification to that patent, the patent or patent information will be removed and any applicant with a pending ANDA (including a tentatively approved ANDA) who has made a certification with respect to such patent must submit an amendment to withdraw its certification. In the amendment, the applicant must state the reason for withdrawing the certification or statement (that the patent has been removed from the list). If the list reflects that an NDA holder has requested that a patent or patent information be removed from the list and one or more first applicants are eligible for 180–day exclusivity based on a paragraph IV certification to that patent, the patent will remain listed until any 180–day exclusivity based on that patent has expired or has been extinguished. After any applicable 180–day exclusivity has expired or has been extinguished, the patent or patent information will be removed and any applicant with a pending ANDA (including a tentatively approved ANDA) who has made a certification with respect to such patent must submit an amendment to withdraw its certification. Once an amendment to withdraw the certification has been submitted, the ANDA will no longer be considered to contain a paragraph IV certification to the patent. If removal of a patent from the list results in there being no patents listed for the listed drug identified in the ANDA, the applicant must submit an amended certification reflecting that there are no relevant patents.

(C) Other amendments.

(1) Except as provided in paragraphs (a)(12)(vi) and (a)(12)(viii)(C)(2) of this section:

(i) An applicant must amend a submitted certification or statement if, at any time before the date of approval of the ANDA, the applicant learns that the submitted certification or statement is no longer accurate; and

(ii) An applicant must submit an appropriate patent certification or statement under paragraph (a)(12)(i) and/or (iii) of this section if, after submission of the ANDA, a new patent is issued by the U.S. Patent and Trademark Office that, in the opinion of the applicant and to the best of its knowledge, claims the reference listed drug or that claims an approved use for such reference listed drug and for which information is required to be filed under section 505(b) and (c) of the Federal Food, Drug, and Cosmetic Act and § 314.53. For a paragraph IV certification, the certification must not be submitted earlier than the first working day after the day the patent is published in the list.

(2) An applicant is not required to submit a supplement to change a submitted certification when information on a patent on the listed drug is submitted after the approval of the ANDA.

(13) Financial certification or disclosure statement. An ANDA must contain a financial certification or disclosure statement as required by part 54 of this chapter.

(b) Drug products subject to the Drug Efficacy Study Implementation (DESI) review. If the ANDA is for a duplicate of a drug product that is subject to FDA's DESI review (a review of drug products approved as safe between 1938 and 1962) or other DESI-like review and the drug product evaluated in the review is a listed drug, the applicant must comply with the provisions of paragraph (a) of this section.

(c) [Reserved]

(d) Format of an ANDA.

(1) The applicant must submit a complete archival copy of the ANDA as required under paragraphs (a) and (c) of this section. FDA will maintain the archival copy during the review of the ANDA to permit individual reviewers to refer to information that is not contained in their particular technical sections of the ANDA, to give other Agency personnel access to the ANDA for official business, and to maintain in one place a complete copy of the ANDA.

(i) Format of submission. An applicant may submit portions of the archival copy of the ANDA in any form that the applicant and FDA agree is acceptable, except as provided in paragraph (d)(1)(ii) of this section.

(ii) Labeling. The content of labeling required under § 201.100(d)(3) of this chapter (commonly referred to as the package insert or professional labeling), including all text, tables, and figures, must be submitted to the agency in electronic format as described in paragraph (d)(1)(iii) of this section. This requirement applies to the content of labeling for the proposed drug product only and is in addition to the requirements of paragraph (a)(8)(ii) of this section that copies of the formatted label and all proposed labeling be submitted. Submissions under this paragraph must be made in accordance with part 11 of this chapter, except for the requirements of § 11.10(a), (c) through (h), and (k), and the corresponding requirements of § 11.30.

(iii) Electronic format submissions. Electronic format submissions must be in a form that FDA can process, review, and archive. FDA will periodically issue guidance on how to provide the electronic submission (e.g., method of transmission, media, file formats, preparation and organization of files).

(2) For ANDAs, the applicant must submit a review copy of the ANDA that contains two separate sections. One section must contain the information described under paragraphs (a)(2) through (6) and (8) and (9) of this section and section 505(j)(2)(A)(vii) of the Federal Food, Drug, and Cosmetic Act and a copy of the analytical procedures and descriptive information needed by FDA's laboratories to perform tests on samples of the proposed drug product and to validate the applicant's analytical procedures. The other section must contain the information described under paragraphs (a)(3), (7), and (8) of this section. Each of the sections in the review copy is required to contain a copy of the application form described under paragraph (a) of this section.

(3) [Reserved]

(4) The applicant may obtain from FDA sufficient folders to bind the archival, the review, and the field copies of the ANDA.

(5) The applicant must submit a field copy of the ANDA that contains the technical section described in paragraph (a)(9) of this section, a copy of the application form required under paragraph (a)(1) of this section, and a certification that the field copy is a true copy of the technical section described in paragraph (a)(9) of this section contained in the archival and review copies of the ANDA.

Credits

[57 FR 29353, July 1, 1992; 58 FR 47352, Sept. 8, 1993; 59 FR 50364, Oct. 3, 1994; 63 FR 5252, Feb. 2, 1998; 63 FR 66399, Dec. 1, 1998; 64 FR 401, Jan. 5, 1999; 64 FR 26657, May 17, 1999; 65 FR 56479, Sept. 19, 2000; 67 FR 77672, Dec. 19, 2002; 68 FR 69019, Dec. 11, 2003; 69 FR 18766, April 8, 2004; 74 FR 2861, Jan. 16, 2009; 76 FR 13880, March 15, 2011; 81 FR 69649, Oct. 6, 2016]

SOURCE: 73 FR 39607; 39 FR 11718, March 29, 1974; 50 FR 7493, Feb. 22, 1985; 50 FR 21238, May 23, 1985; 54 FR 39636, Sept. 27, 1989; 55 FR 37322, Sept. 11, 1990; 57 FR 17983, April 28, 1992; 58 FR 47351, Sept. 8, 1993; 59 FR 13200, March 21, 1994; 62 FR 51516, Oct. 1, 1997; 63 FR 26698, May 13, 1998; 63 FR 59712, Nov. 5, 1998; 64 FR 401, Jan. 5, 1999; 65 FR 64617, Oct. 30, 2000; 72 FR 58999, Oct. 18, 2007; July 10, 2008; 79 FR 33088, June 10, 2014; 80 FR 38938, July 8, 2015; 81 FR 69636, Oct. 6, 2016; 88 FR 45066, July 14, 2023, unless otherwise noted.

AUTHORITY: 21 U.S.C. 321, 331, 351, 352, 353, 355, 355a, 355f, 356, 356a, 356b, 356c, 356e, 360cc, 371, 374, 379e, 379k–1.

Notes of Decisions (92)

Current through May 7, 2024, 89 FR 38835. Some sections may be more current. See credits for details.

End of Document

Tab 5

Code of Federal Regulations
Title 21. Food and Drugs
Chapter I. Food and Drug Administration, Department of Health and Human Services (Refs & Annos)
Subchapter D. Drugs for Human Use
Part 314. Applications for FDA Approval to Market a New Drug (Refs & Annos)
Subpart D. FDA Action on Applications and Abbreviated Applications (Refs & Annos)

21 C.F.R. § 314.107

§ 314.107 Date of approval of a 505(b)(2) application or ANDA.

Effective: December 5, 2016
Currentness

(a) General. A drug product may be introduced or delivered for introduction into interstate commerce when the 505(b)(2) application or ANDA for the drug product is approved. A 505(b)(2) application or ANDA for a drug product is approved on the date FDA issues an approval letter under § 314.105 for the 505(b)(2) application or ANDA.

(b) Effect of patent(s) on the listed drug. As described in paragraphs (b)(1) and (2) of this section, the status of patents listed for the listed drug(s) relied upon or reference listed drug, as applicable, must be considered in determining the first possible date on which a 505(b)(2) application or ANDA can be approved. The criteria in paragraphs (b)(1) and (2) of this section will be used to determine, for each relevant patent, the date that patent will no longer prevent approval. The first possible date on which the 505(b)(2) application or ANDA can be approved will be calculated for each patent, and the 505(b)(2) application or ANDA may be approved on the last applicable date.

(1) Timing of approval based on patent certification or statement. If none of the reasons in § 314.125 or § 314.127, as applicable, for refusing to approve the 505(b)(2) application or ANDA applies, and none of the reasons in paragraph (d) of this section for delaying approval applies, the 505(b)(2) application or ANDA may be approved as follows:

(i) Immediately, if the applicant certifies under § 314.50(i) or § 314.94(a)(12) that:

(A) The applicant is aware of a relevant patent but the patent information required under section 505(b) or (c) of the Federal Food, Drug, and Cosmetic Act has not been submitted to FDA; or

(B) The relevant patent has expired; or

(C) The relevant patent is invalid, unenforceable, or will not be infringed, except as provided in paragraphs (b)(3) and (c) of this section, and the 45–day period provided for in section 505(c)(3)(C) and (j)(5)(B)(iii) of the Federal Food, Drug, and Cosmetic Act has expired; or

(D) There are no relevant patents.

(ii) Immediately, if the applicant submits an appropriate statement under § 314.50(i) or § 314.94(a)(12) explaining that a method-of-use patent does not claim an indication or other condition of use for which the applicant is seeking approval, except that if the applicant also submits a paragraph IV certification to the patent, then the 505(b)(2) application or ANDA may be approved as provided in paragraph (b)(1)(i)(C) of this section.

(iii) On the date specified, if the applicant certifies under § 314.50(i) or § 314.94(a)(12) that the relevant patent will expire on a specified date.

(2) Patent information filed after submission of 505(b)(2) application or ANDA. If the holder of the approved NDA for the listed drug submits patent information required under § 314.53 after the date on which the 505(b)(2) application or ANDA was submitted to FDA, the 505(b)(2) applicant or ANDA applicant must comply with the requirements of § 314.50(i)(4) and (6) and § 314.94(a)(12)(vi) and (viii) regarding submission of an appropriate patent certification or statement. If the applicant submits an amendment certifying under § 314.50(i)(1)(i)(A)(4) or § 314.94(a)(12)(i)(A)(4) that the relevant patent is invalid, unenforceable, or will not be infringed, and complies with the requirements of § 314.52 or § 314.95, the 505(b)(2) application or ANDA may be approved immediately upon submission of documentation of receipt of notice of paragraph IV certification under § 314.52(e) or § 314.95(e). The 45–day period provided for in section 505(c)(3)(C) and (j)(5)(B)(iii) of the Federal Food, Drug, and Cosmetic Act does not apply in these circumstances.

(3) Disposition of patent litigation—

(i) Approval upon expiration of 30–month period or 7 ½ years from date of listed drug approval.

(A) Except as provided in paragraphs (b)(3)(ii) through (viii) of this section, if, with respect to patents for which required information was submitted under § 314.53 before the date on which the 505(b)(2) application or ANDA was submitted to FDA (excluding an amendment or supplement to the 505(b)(2) application or ANDA), the applicant certifies under § 314.50(i) or § 314.94(a)(12) that the relevant patent is invalid, unenforceable, or will not be infringed, and the patent owner or its representative or the exclusive patent licensee brings suit for patent infringement within 45 days of receipt of the notice of certification from the applicant under § 314.52 or § 314.95, the 505(b)(2) application or ANDA may be approved 30 months after the later of the date of the receipt of the notice of certification by any owner of the listed patent or by the NDA holder (or its representative(s)) unless the court has extended or reduced the period because of a failure of either the plaintiff or defendant to cooperate reasonably in expediting the action; or

(B) If the patented drug product qualifies for 5 years of exclusive marketing under § 314.108(b)(2) and the patent owner or its representative or the exclusive patent licensee brings suit for patent infringement during the 1–year period beginning 4 years after the date of approval of the patented drug and within 45 days of receipt of the notice of certification from the applicant under § 314.52 or § 314.95, the 505(b)(2) application or ANDA may be approved at the expiration of the 7 ½ years from the date of approval of the NDA for the patented drug product.

(ii) Federal district court decision of invalidity, unenforceability, or non-infringement. If before the expiration of the 30–month period, or 7 ½ years where applicable, the district court decides that the patent is invalid, unenforceable, or not infringed (including any substantive determination that there is no cause of action for patent infringement or invalidity), the 505(b)(2) application or ANDA may be approved on:

(A) The date on which the court enters judgment reflecting the decision; or

(B) The date of a settlement order or consent decree signed and entered by the court stating that the patent that is the subject of the certification is invalid, unenforceable, or not infringed.

(iii) Appeal of Federal district court judgment of infringement. If before the expiration of the 30–month period, or 7 ½ years where applicable, the district court decides that the patent has been infringed, and if the judgment of the district court is appealed, the 505(b)(2) application or ANDA may be approved on:

(A) The date on which the mandate is issued by the court of appeals entering judgment that the patent is invalid, unenforceable, or not infringed (including any substantive determination that there is no cause of action for patent infringement or invalidity); or

(B) The date of a settlement order or consent decree signed and entered by the court of appeals stating that the patent that is the subject of the certification is invalid, unenforceable, or not infringed.

(iv) Affirmation or non-appeal of Federal district court judgment of infringement. If before the expiration of the 30–month period, or 7 ½ years where applicable, the district court decides that the patent has been infringed, and if the judgment of the district court is not appealed or is affirmed, the 505(b)(2) application or ANDA may be approved no earlier than the date specified by the district court in an order under 35 U.S.C. 271(e)(4)(A).

(v) Grant of preliminary injunction by Federal district court. If before the expiration of the 30–month period, or 7 ½ years where applicable, the district court grants a preliminary injunction prohibiting the applicant from engaging in the commercial manufacture or sale of the drug product until the court decides the issues of patent validity and infringement, and if the court later decides that:

(A) The patent is invalid, unenforceable, or not infringed, the 505(b)(2) application or ANDA may be approved as provided in paragraph (b)(3)(ii) of this section; or

(B) The patent is infringed, the 505(b)(2) application or ANDA may be approved as provided in paragraph (b)(3)(iii) or (iv) of this section, whichever is applicable.

(vi) Written consent to approval by patent owner or exclusive patent licensee. If before the expiration of the 30–month period, or 7 ½ years where applicable, the patent owner or the exclusive patent licensee (or their representatives) agrees in writing that the 505(b)(2) application or ANDA may be approved any time on or after the date of the consent, approval may be granted on or after that date.

(vii) Court order terminating 30–month or 7 ½ -year period. If before the expiration of the 30–month period, or 7 ½ years where applicable, the court enters an order requiring the 30–month or 7 ½ -year period to be terminated, the 505(b)(2) application or ANDA may be approved in accordance with the court's order.

(viii) Court order of dismissal without a finding of infringement. If before the expiration of the 30–month period, or 7 ½ years where applicable, the court(s) enter(s) an order of dismissal, with or without prejudice, without a finding of infringement in each pending suit for patent infringement brought within 45 days of receipt of the notice of paragraph IV certification sent by the 505(b)(2) or ANDA applicant, the 505(b)(2) application or ANDA may be approved on or after the date of the order.

(4) Tentative approval. FDA will issue a tentative approval letter when tentative approval is appropriate in accordance with this section. In order for a 505(b)(2) application or ANDA to be approved under paragraph (b)(3) of this section, the applicant must receive an approval letter from the Agency. Tentative approval of an NDA or ANDA does not constitute "approval" of an NDA or ANDA and cannot, absent an approval letter from the Agency, result in an approval under paragraph (b)(3) of this section.

(c) Timing of approval of subsequent ANDA.

(1) If an ANDA contains a paragraph IV certification for a relevant patent and the ANDA is not that of a first applicant, the ANDA is regarded as the ANDA of a subsequent applicant. The ANDA of a subsequent applicant will not be approved during the period when any first applicant is eligible for 180–day exclusivity or during the 180–day exclusivity period of a first applicant. Any applicable 180–day exclusivity period cannot extend beyond the expiration of the patent upon which the 180–day exclusivity period was based.

(2) A first applicant must submit correspondence to its ANDA notifying FDA within 30 days of the date of its first commercial marketing of its drug product or the reference listed drug. If an applicant does not notify FDA, as required in this paragraph (c)(2), of this date, the date of first commercial marketing will be deemed to be the date of the drug product's approval.

(3) If FDA concludes that a first applicant is not actively pursuing approval of its ANDA, FDA may immediately approve an ANDA(s) of a subsequent applicant(s) if the ANDA(s) is otherwise eligible for approval.

(d) Delay due to exclusivity. The Agency will also delay the approval of a 505(b)(2) application or ANDA if delay is required by the exclusivity provisions in § 314.108; section 527 of the Federal Food, Drug, and Cosmetic Act and § 316.31 of this chapter; section 505A of the Federal Food, Drug, and Cosmetic Act; or section 505E of the Federal Food, Drug, and Cosmetic Act. When the approval of a 505(b)(2) application or ANDA is delayed under this section and § 314.108; section 527 of the Federal Food, Drug, and Cosmetic Act and § 316.31 of this chapter; section 505A of the Federal Food, Drug, and Cosmetic Act; or section 505E of the Federal Food, Drug, and Cosmetic Act, the 505(b)(2) application or ANDA will be approved on the latest of the days specified under this section and § 314.108; section 527 of the Federal Food, Drug, and Cosmetic Act and § 316.31 of this chapter; section 505A of the Federal Food, Drug, and Cosmetic Act; or section 505E of the Federal Food, Drug, and Cosmetic Act, as applicable.

(e) Notification of court actions or written consent to approval.

(1) The applicant must submit the following information to FDA, as applicable:

(i) A copy of any judgment by the court (district court or mandate of the court of appeals) or settlement order or consent decree signed and entered by the court (district court or court of appeals) finding a patent described in paragraph (b)(3) of this section invalid, unenforceable, or not infringed, or finding the patent valid and infringed;

(ii) Written notification of whether or not any action by the court described in paragraph (e)(1)(i) of this section has been appealed within the time permitted for an appeal;

(iii) A copy of any order entered by the court terminating the 30–month or 7 ½ -year period as described in paragraph (b)(3)(i), (ii), (vii), or (viii) of this section;

(iv) A copy of any written consent to approval by the patent owner or exclusive patent licensee described in paragraph (b)(3)(vi) of this section;

(v) A copy of any preliminary injunction described in paragraph (b)(3)(v) of this section, and a copy of any subsequent court order lifting the injunction; and

(vi) A copy of any court order pursuant to 35 U.S.C. 271(e)(4)(A) ordering that a 505(b)(2) application or ANDA may be approved no earlier than the date specified (irrespective of whether the injunction relates to a patent described in paragraph (b)(3) of this section).

(2) All information required by paragraph (e)(1) of this section must be sent to the applicant's NDA or ANDA, as appropriate, within 14 days of the date of entry by the court, the date of appeal or expiration of the time for appeal, or the date of written consent to approval, as applicable.

(f) Forty-five day period after receipt of notice of paragraph IV certification—

(1) Computation of 45–day time clock. The 45–day clock described in paragraph (b)(3) of this section as to each recipient required to receive notice of paragraph IV certification under § 314.52 or § 314.95 begins on the day after the date of receipt of the applicant's notice of paragraph IV certification by the recipient. When the 45th day falls on Saturday, Sunday, or a Federal holiday, the 45th day will be the next day that is not a Saturday, Sunday, or a Federal holiday.

(2) Notification of filing of legal action.

(i) The 505(b)(2) or ANDA applicant must notify FDA in writing within 14 days of the filing of any legal action filed within 45 days of receipt of the notice of paragraph IV certification by any recipient. A 505(b)(2) applicant must send

the notification to its NDA. An ANDA applicant must send the notification to its ANDA. The notification to FDA of the legal action must include:

(A) The 505(b)(2) application or ANDA number.

(B) The name of the 505(b)(2) or ANDA applicant.

(C) The established name of the drug product or, if no established name exists, the name(s) of the active ingredient(s), the drug product's strength, and dosage form.

(D) A statement that an action for patent infringement, identified by court, case number, and the patent number(s) of the patent(s) at issue in the action, has been filed in an appropriate court on a specified date.

(ii) A patent owner or NDA holder (or its representative(s)) may also notify FDA of the filing of any legal action for patent infringement. The notice should contain the information and be sent to the offices or divisions described in paragraph (f)(2)(i) of this section.

(iii) If the 505(b)(2) or ANDA applicant, the patent owner(s), the NDA holder, or its representative(s) does not notify FDA in writing before the expiration of the 45–day time period or the completion of the Agency's review of the 505(b)(2) application or ANDA, whichever occurs later, that a legal action for patent infringement was filed within 45 days of receipt of the notice of paragraph IV certification, the 505(b)(2) application or ANDA may be approved upon expiration of the 45–day period (if the 505(b)(2) or ANDA applicant confirms that a legal action for patent infringement has not been filed) or upon completion of the Agency's review of the 505(b)(2) application or ANDA, whichever is later.

(3) Waiver. If the patent owner or NDA holder who is an exclusive patent licensee (or its representative(s)) waives its opportunity to file a legal action for patent infringement within 45 days of a receipt of the notice of certification and the patent owner or NDA holder who is an exclusive patent licensee (or its representative(s)) submits to FDA a valid waiver before the 45 days elapse, the 505(b)(2) application or ANDA may be approved upon completion of the Agency's review of the NDA or ANDA. FDA will only accept a waiver in the following form:

(Name of patent owner or NDA holder who is an exclusive patent licensee or its representative(s)) has received notice from (name of applicant) under (section 505(b)(3) or 505(j)(2)(B) of the Federal Food, Drug, and Cosmetic Act) and does not intend to file an action for patent infringement against (name of applicant) concerning the drug (name of drug) before (date on which 45 days elapse). (Name of patent owner or NDA holder who is an exclusive patent licensee) waives the opportunity provided by (section 505(c)(3)(C) or 505(j)(5)(B)(iii) of the Federal Food, Drug, and Cosmetic Act) and does not object to FDA's approval of (name of applicant)'s (505(b)(2) application or ANDA) for (name of drug) with an approval date on or after the date of this submission.

(g) Conversion of approval to tentative approval. If FDA issues an approval letter in error or a court enters an order requiring, in the case of an already approved 505(b)(2) application or ANDA, that the date of approval be delayed, FDA will convert the approval to a tentative approval if appropriate.

Credits

[59 FR 50367, Oct. 3, 1994; 63 FR 59712, Nov. 5, 1998; 65 FR 43235, July 13, 2000; 73 FR 39609, July 10, 2008; 74 FR 9766, March 6, 2009; 81 FR 69655, Oct. 6, 2016]

SOURCE: 73 FR 39607; 39 FR 11718, March 29, 1974; 50 FR 7493, Feb. 22, 1985; 50 FR 21238, May 23, 1985; 54 FR 39636, Sept. 27, 1989; 55 FR 37322, Sept. 11, 1990; 57 FR 17983, April 28, 1992; 58 FR 47351, Sept. 8, 1993; 59 FR 13200, March 21, 1994; 62 FR 51516, Oct. 1, 1997; 63 FR 26698, May 13, 1998; 63 FR 59712, Nov. 5, 1998; 64 FR 401, Jan. 5, 1999; 65 FR 64617, Oct. 30, 2000; 72 FR 58999, Oct. 18, 2007; July 10, 2008; 79 FR 33088, June 10, 2014; 80 FR 38938, July 8, 2015; 81 FR 69636, Oct. 6, 2016; 88 FR 45066, July 14, 2023, unless otherwise noted.

AUTHORITY: 21 U.S.C. 321, 331, 351, 352, 353, 355, 355a, 355f, 356, 356a, 356b, 356c, 356e, 360cc, 371, 374, 379e, 379k–1.

Notes of Decisions (105)

Current through May 7, 2024, 89 FR 38835. Some sections may be more current. See credits for details.

End of Document

FORM 19. Certificate of Compliance with Type-Volume Limitations **Form 19**
July 2020

UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT

CERTIFICATE OF COMPLIANCE WITH TYPE-VOLUME LIMITATIONS

Case Number: 22-2153, 23-1952

Short Case Caption: Salix Pharmaceuticals, Ltd. v. Norwich Pharmaceuticals Inc.

Instructions: When computing a word, line, or page count, you may exclude any items listed as exempted under Fed. R. App. P. 5(c), Fed. R. App. P. 21(d), Fed. R. App. P. 27(d)(2), Fed. R. App. P. 32(f), or Fed. Cir. R. 32(b)(2).

The foregoing filing complies with the relevant type-volume limitation of the Federal Rules of Appellate Procedure and Federal Circuit Rules because it meets one of the following:

☑ the filing has been prepared using a proportionally-spaced typeface and includes 3,894 words.

☐ the filing has been prepared using a monospaced typeface and includes _____ lines of text.

☐ the filing contains _____ pages / _____ words / _____ lines of text, which does not exceed the maximum authorized by this court's order (ECF No. _____).

Date: 05/13/2024

Signature: /s/ Chad A. Landmon

Name: Chad A. Landmon

Save for Filing