U.S. GOVERNMENT ACCOUNTABILITY OFFICE
441 G St. N.W.
Washington, DC 20548

Decision

Matter of: U.S. Food and Drug Administration—Applicability of the Congressional Review Act to *Risk Evaluation and Mitigation Strategy (REMS) Single Shared System for Mifepristone 200 mg*

File: B-334995

Date: July 6, 2023

DIGEST

In January 2023, the U.S. Food and Drug Administration (FDA) revised the risk evaluation and mitigation strategy for the drug mifepristone. Food and Drug Administration, *Risk Evaluation and Mitigation Strategy (REMS) Single Shared System for Mifepristone 200 mg*. In the REMS, FDA determined the in-person dispensing requirement was no longer necessary but that pharmacies must be specially certified to dispense the drug.

The Congressional Review Act (CRA) requires that agencies submit rules to Congress for review before they may take effect. CRA incorporates the Administrative Procedure Act's (APA) definition of a rule, which does not include agency adjudications, such as licensing. CRA also excludes certain categories of rules from coverage, including rules of particular applicability. We conclude that FDA's approval process for new drugs and modifications to existing drug approvals, such as the REMS, are licensing actions and thus adjudications that are not subject to the CRA. Even if the REMS were to satisfy the APA definition of a rule, it would be considered a rule of particular applicability, and, therefore, would still not be subject to the CRA's submission requirement.

DECISION

In January 2023, the U.S. Food and Drug Administration (FDA) revised the risk evaluation and mitigation strategy for the drug mifepristone. Food and Drug Administration, *Approved Risk Evaluation and Mitigation Strategies (REMS), Mifepristone*, *available at* https://www.accessdata.fda.gov/scripts/cder/rems/index.cfm?event=RemsDetails.page&REMS=390 (last visited Jun. 12, 2023). We received a request for a legal decision as to whether the REMS is a rule for purposes of the Congressional Review Act (CRA). Letter from Congressional Requestors to the Comptroller General, Jan.

31, 2023. The requesters also submitted their views as to why the REMS is a rule. Letter from Congressional Requestors to Senior Attorney, GAO, Mar. 9, 2023. For the reasons discussed below, we conclude the REMS is a not a rule for purposes of CRA.

Our practice when rendering decisions is to contact the relevant agencies to obtain their legal views on the subject of the request. GAO, *Procedures and Practices for Legal Decisions and Opinions*, GAO-06-1064SP (Washington, D.C.: Sept. 2006), *available at* https://www.gao.gov/products/gao-06-1064sp. Accordingly, we reached out to FDA to obtain the agency's legal views. Letter from Assistant General Counsel, GAO, to Chief Counsel, FDA (Feb. 16, 2023). We received a response from the General Counsel of the Department of Health and Human Services (HHS) on March 15, 2023. Letter from General Counsel, HHS, to Assistant General Counsel, GAO (Mar. 15, 2023) (Response Letter).

BACKGROUND

FDA's Approval Process

Federal law prohibits anyone from introducing into interstate commerce any drug that has not been approved by FDA.[1] 21 U.S.C. §§ 331(d), 355. Anyone who violates these prohibitions may be subject to criminal penalties. 21 U.S.C. § 333. For parties seeking to introduce new drugs, they are statutorily required to file an application with FDA.[2] 21 U.S.C § 355. Applications must contain specified information such as reports of investigations demonstrating the drug's safety and effectiveness, a list of articles used as components of the drug, and such samples of the drug as the Secretary may require. 21 U.S.C § 355(b). FDA's approval process is governed by procedures, timelines, and standards laid out in statute. *E.g.,* 21 U.S.C § 355(b), (c). At the conclusion of the process, FDA must either issue an order approving or refusing to approve the application. 21 U.S.C § 355(d).

If FDA determines additional steps need to be taken to ensure the benefits of a drug outweigh its risks, FDA may require the applicant to submit a REMS for the drug. 21 U.S.C § 355-1. As part of the strategy, FDA may require a variety of materials and actions, such as communication plans and medication guides. *E.g.,* 21 U.S.C § 355-1(e)(2), (3). FDA may at any time require the drug sponsor to submit a proposal to modify the strategy if FDA determines such modification is necessary to (1) ensure the benefits of the drug outweigh the risks; (2) minimize burden on the health

[1] The statute imposes duties pertaining to the approval of drugs on the Secretary of Health and Human Services. The FDA Commissioner is statutorily authorized to perform these duties on the Secretary's behalf. 21 U.S.C. § 393(d).
[2] Alternatives to this process are available depending on the drug product type and characteristics. *See, e.g.,* 21 U.S.C § 355(j) (setting forth the approval process for generic drugs).

care delivery system; or (3) accommodate different, comparable aspects of the strategy for generic and brand name drugs. 21 U.S.C § 355-1(g)(4)(B).

The drug sponsor is responsible for compliance with and implementation of the strategy; failure to comply with the strategy subjects the drug sponsor to potential criminal penalties for misbranded drugs. 21 U.S.C §§ 333, 352(y). Strategies may have requirements that impose duties which flow down to other parties, such as health care providers or pharmacies, even if those parties themselves are not governed by FDA. 21 U.S.C § 355-1(f)(3).

The January 2023 REMS Change

In response to litigation, FDA decided to review the REMS for mifepristone in 2021. Response Letter, at 4. During its review, FDA reviewed published literature, safety information submitted through FDA Adverse Event Reporting System reports, and information provided by advocacy groups, individuals, and the plaintiffs in ongoing litigation, as well as information submitted by the sponsors of the drugs. *Id.* After conducting the review, FDA determined the in-person dispensing requirement was no longer necessary but that pharmacies must be specially certified to dispense the drug. *Id.* at 4-5. In December 2021, FDA sent REMS Modification Notification letters to sponsors of mifepristone asking them to provide a new proposed REMS reflecting these changes.[3] *Id.* at 5. The sponsors submitted the proposals as requested, and FDA approved the revised REMS at issue in this decision on January 3, 2023. *Id.* at 5.

The Congressional Review Act

CRA, enacted in 1996 to strengthen congressional oversight of agency rulemaking, requires federal agencies to submit a report on each new rule to both houses of Congress and to the Comptroller General for review before a rule can take effect. 5 U.S.C. § 801(a)(1)(A). The report must contain a copy of the rule, "a concise general statement relating to the rule," and the rule's proposed effective date. *Id*. CRA allows Congress to review and disapprove rules issued by federal agencies for a period of 60 days using special procedures. *See* 5 U.S.C. § 802. If a resolution of disapproval is enacted, then the new rule has no force or effect. 5 U.S.C. § 801(b)(1).

CRA adopts the definition of rule under the Administrative Procedure Act (APA), 5 U.S.C. § 551(4), which states that a rule is "the whole or a part of an agency statement of general or particular applicability and future effect designed to implement, interpret, or prescribe law or policy or describing the organization, procedure, or practice requirements of an agency." 5 U.S.C. § 804(3). CRA excludes three categories of rules from coverage: (1) rules of particular applicability,

[3] As of June 21, 2023, there are currently three approved sponsors of mifepristone (two name brand and one generic).

including a rule that approves or prescribes for the future rates or wages; (2) rules relating to agency management or personnel; and (3) rules of agency organization, procedure, or practice that do not substantially affect the rights or obligations of non-agency parties. *Id.*

FDA did not submit a CRA report on the REMS to either Congress or the Comptroller General. In its response to us, FDA stated the REMS was an order under APA and thus exempt from CRA requirements. Response Letter, at 1-3. For the reasons discussed below, we conclude that the REMS is not a rule under CRA.

DISCUSSION

At issue here is whether the REMS meets the APA definition of rule. The APA provides for two methods for agencies to take legally binding actions: rulemaking, which yields a rule, and adjudication, which yields an order. 5 U.S.C. §§ 551(5), (7); B-334400, Feb. 9, 2023; B-332233, Aug. 13, 2020. The two are mutually exclusive. 5 U.S.C. §§ 551(5), (7). This means if an agency process meets the APA definition of an adjudication, then the resulting action cannot be a rule subject to CRA. The APA recognizes licensing as a form of order. *See* 5 U.S.C. § 551(6), (7). Thus a license, which is defined as "the whole or a part of an agency permit, certificate, approval, registration, charter, membership, statutory exemption or other form of permission[,]" is an order. *Id.* § 551(6).

Courts have distinguished between adjudications and rulemakings by noting that adjudications involve specific individuals in specific cases and have an immediate effect on the individuals involved, whereas rulemakings "affect[] the rights of broad classes of unspecified individuals" and "[have] legal consequences only for the future." *See Yesler Terrace Community Council v. Cisneros*, 37 F.3d 442, 448 (9th Cir. 1994) (citing cases)(citation and emphasis omitted). However, as noted in *POM Wonderful, LLC v. Federal Trade Commission*, 777 F. 3d. 478, (D.C. Cir. 2015), the "fact that an order rendered in an adjudication may affect agency policy and have general prospective application does not make it [a] rulemaking." *Id*. at 497 (citation omitted).

In B-332233, we found the Federal Communications Commission's (FCC) approval of license modifications to be a licensing action and thus an adjudication. The FCC grants applications by reviewing the facts and information provided by the applicant as well as considering other information known to the agency to determine if the application should be granted. In that decision, we found that FCC granted applications filed by the existing licensee, Ligado Networks, LLC, thereby modifying Ligado's licenses to permit the conduct of a new activity, and establishing certain conditions and such action constituted an adjudication and not a rule. Before approving the modifications and imposing conditions, FCC conduced a fact-intensive inquiry into the merits of Ligado's applications, including by soliciting public comments and considering reports commissioned by Ligado and other federal agencies on potential impacts. Additionally, in B-334400, we determined an EPA

action denying 69 small refinery exemption petitions was an adjudication even though it may have had some characteristics of a rulemaking, such as an impact on a broad group. The EPA acts on exemption requests by reviewing the facts presented by the applicant and considering the statutory requirements to determine if the requests should be granted. In that decision EPA applied its interpretation of the applicable statutory standard to deny multiple petitions in a single action. We found that the EPA action was still an adjudication as EPA was acting on exemption requests that amounted to licensing applications.

Here, as in the FCC and EPA cases, FDA performed a licensing action. Specifically, through a process similar to those we considered in the prior cases, FDA reviewed and approved the REMS, which changed the conditions under which mifepristone could be distributed. By statute, no drug is permitted to enter interstate commerce unless FDA determines the drug satisfies the statutory requirements, thus granting approval for the sponsor to manufacture and sell the drug. *See* 21 U.S.C. §§ 331, 355. And, by statute, FDA may require a drug sponsor to submit a proposal to modify a REMS where necessary, which, similar to EPA, FDA did here after reviewing the relevant facts against the statutory criteria. *See* 21 U.S.C § 355-1(g); *see also supra p.* 3. FDA followed the statutory process for issuing modifications for existing approvals when it modified the REMS. Similar to FCC's fact-intensive inquiry which led it to establish certain conditions for Ligado's licenses, FDA considered an array of information, including published literature, information provided by advocacy groups, and information submitted by the sponsors of the drugs, before determining that a REMS modification was needed. The resulting action is akin to FCC's approval of license modifications stemming from the applications submitted by Ligado.

Applying our analysis from the EPA case, the fact that the REMS contains requirements that are prospective or may impact a broad group does not convert the adjudicatory process into a rulemaking. To the contrary, consistent with the distinguishing characteristics courts have identified, FDA's process involved a review and approval of applications submitted by specific companies, and the resulting REMS had an immediate effect on those companies, as they became directly responsible for implementation and compliance with the REMS upon its approval. As adjudications are not subject to CRA, CRA does not apply to the REMS.[4]

Even if the REMS met the APA definition of a rule, the REMS would still not be subject to CRA as it would fall within the first exception for rules of particular applicability. In B-330843, Oct. 22, 2019, we stated rules of particular applicability

[4] As additional support, FDA's organic statute uses licensing language. *See* 21 U.S.C. § 355(d) ("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.") (emphasis added). This same analysis applies for modifications to approved drugs.

are those rules that are addressed to an identified entity and also address actions that entity may or may not take, taking into account facts and circumstances specific to that the entity. *Id.* at 8. In that decision, we found that a regulatory guidance document issued by the Board of Governors of the Federal Reserve System (FRB) did not fall within the exemption because, while the document was addressed to eight specifically named banks, it did not address specific actions to be taken by each bank and did not factor in each bank's specific facts and circumstances. Instead, FRB asked each to bank to engage in recovery planning and stated what that would look like generally. *Id.* FRB left it to each bank to decide on the details and specific actions necessary. *Id.*

Here, only sponsors of mifepristone are responsible for implementation of and compliance with the REMS, and no one can manufacture and distribute mifepristone without FDA approval. Therefore, while the REMS does not specifically name the sponsors as addressees, the "mifepristone sponsors" referenced in the REMS consist of a closed class. Response Letter at 4-5. Thus, when the REMS addresses the mifepristone sponsors, it addresses specific and easily identifiable parties. If this were an open class where anyone could enter the class independent of FDA's determination, then it would be a rule of general applicability.

Further, FDA requested and approved the REMS modification after studying mifepristone's safety and effectiveness based on the statutory criteria.[5] Response Letter, at 4-5. FDA approved specific changes and rejected others based on the results of this study. *Id.* Given these facts, FDA changed the REMS based on the specific facts and circumstances pertaining to mifepristone. Thus, the REMS modification would be a rule addressed to specific parties—the drug sponsors, addressing actions the drug sponsors may take based on the specific facts and circumstances pertaining to mifepristone, meaning it would fall within the first exception.

Note, although the REMS appears to impose duties and obligations on pharmacies, doctors and patients, only the mifepristone sponsors are directly subject to the REMS at issue, as only they are responsible for its implementation. 21 U.S.C. § 355-1(f); Response Letter, at 5-6. While the statute contemplates that a REMS could contain requirements for pharmacies and doctors, those entities are not directly subject to enforcement of those requirements by FDA. *See* 21 U.S.C. §§ 331, 352, and 505-1 (referencing "sponsors"). Rather, it is the sponsors who are required to distribute the drug in accordance with the REMS. *Id.* If the sponsors fail to distribute mifepristone as required by the REMS, they can be subject to civil and criminal penalties; however, these penalties do not flow down to any pharmacy, doctor, or patient. *See* 21 U.S.C. §§ 331, 355, 502. Accordingly, the pharmacies, doctors, and patients are not among the intended range of the REMS for purposes of applying the first exception.

[5] We note that FDA made the policy choice to alter the REMS at its own initiative. The statute allows FDA to do this. 21 U.S.C § 355-1(g)(4).

This conclusion is further supported by CRA's legislative history. The legislative history states that most "agency actions that grant an approval, license, registration, or similar authority to a particular person or particular entities. . .or allow the manufacture, distribution, sale, or use of a substance or product" fall within the exception. 142 Cong. Rec. S3683-01, S3687 (daily ed. Apr. 18, 1996). The legislative history also specifically names "drug and medical device approvals" as an example of a rule of particular applicability. *Id.*

Because the REMS falls within the APA definition of license,[6] but even if considered to be a rule, would fall within the exception for rules of particular applicability, it is not subject to the CRA's requirements.

CONCLUSION

FDA reviewed the REMS for mifepristone under the mandated statutory criteria for the licensing process. After review, it approved a revised REMS which changed the conditions by which mifepristone could be distributed. These changes were done as part of a licensing, which is an adjudication. Even if the action were considered to be a rule, it would be a rule of particular applicability. For these reasons, the REMS is not a rule for purposes of CRA and, thus, not subject to the requirement that it be submitted to Congress and the Comptroller General before it may take effect.

Edda Emmanuelli Perez

Edda Emmanuelli Perez
General Counsel

[6] It was noted in a supplemental letter from the requesters that FDA referred to the REMS revision as a regulation. Letter from Congressional Requestors to Senior Attorney, GAO, Mar. 9, 2023. While we consider an agency's characterization of its action as a rule or an order, that characterization is not dispositive. B-333501, Dec. 14, 2021, at 4. The key consideration when we analyze whether an agency action is a rule, is to apply the definitions found in the APA.

List of Congressional Requestors

Marco Rubio
U.S. Senator

Andrew S. Clyde
Member of Congress

Cindy Hyde-Smith
U.S. Senator

Christopher H. Smith
Member of Congress

Michael S. Lee
U.S. Senator

Mary E. Miller
Member of Congress

Thom Tillis
U.S. Senator

Andy Biggs
Member of Congress

Roger Marshall, M.D.
U.S. Senator

Debbie Lesko
Member of Congress

Mike Braun
U.S. Senator

Barry Loudermilk
Member of Congress

Rick Scott
U.S. Senator

Doug Lamborn
Member of Congress

Roger F. Wicker
U.S. Senator

Bill Johnson
Member of Congress

Ben Cline
Member of Congress

Paul A Gosar, D.D.S.
Member of Congress

Troy Balderson
Member of Congress

Randy K. Weber
Member of Congress

Josh Brecheen
Member of Congress

Jeff Duncan
Member of Congress

Mike Bost
Member of Congress

Jefferson Van Drew
Member of Congress

Mike Ezell
Member of Congress

Jim Banks
Member of Congress

Andy Ogles
Member of Congress

Marjorie Taylor Greene
Member of Congress

Alex X. Mooney
Member of Congress

Diana Harshbarger
Member of Congress

Lance Gooden
Member of Congress

Bob Good
Member of Congress

Trent Kelly
Member of Congress

Michael Guest
Member of Congress

Russ Fulcher
Member of Congress

Daniel Webster
Member of Congress