October 21, 2022

Centers for Medicare & Medicaid Services
7500 Security Boulevard
Baltimore, MD 21244

Re: Docket No. FDA–2021–N–0862; RIN 0910–AH62

Dear Sir/Madam:

The American Heart Association (AHA), including the American Stroke Association (ASA) and more than 40 million volunteers and supporters appreciates the opportunity to comment on the proposed rule on Nonprescription Drug Product with an Additional Condition for Nonprescription Use. While we are generally supportive, AHA has concerns related to, and recommendations to strengthen, rule clarity, equitable access, and safety.

PART 314—Applications for FDA Approval to Market a New Drug

§ 314.56 Nonprescription drug product with an additional condition for nonprescription use (ACNU)

As currently written, we have concerns that the proposed rule does not adequately ensure that the ACNU be operationalized in a manner that maximizes equitable access to those with limited health and digital literacy or other limitations who otherwise would be eligible to obtain a nonprescription drug with an ACNU. Ensuring equitable access through the offering of modalities or multiple modalities (i.e., telephonic as well as kiosk or mobile application options to accommodate those with different digital literacy or comfort levels) designed to maximize access to eligible individuals is an important factor that should be included in the criteria for approval. The rule also was silent on safeguards that would be required in the ANCU to ensure how appropriate dosage and refill determinations would be made. Requiring demonstration that the ACNU maximizes equitable access and how dosage and refill determinations

will be made should be included as part of the new drug application (NDA) and the abbreviated NDA.

If there is a technology failure in the operationalization of the ACNU, and the ACNU cannot be completed, the applicant should be required to demonstrate in the application that safeguards are in place to deny access to the drug.

While AHA agrees with the separate application requirement for nonprescription drugs with an ACNU, as noted previously, we believe that health literacy must be a significant factor in determining "[a]dequate data or other information that demonstrates the effect of the ACNU on the appropriate self-selection or appropriate actual use, or both." Moreover, the proposed rule does not address the types of consumer studies that would be needed to satisfy the data requirements for an ACNU. While the Preliminary Regulatory Impact Analysis referenced in the proposed rule refers to human factor studies, actual use studies, self-selection studies, and label comprehension studies, specific mention of the types of studies the FDA expects are omitted in the proposed rule but should be referenced in the final rule.

Drug-drug interactions also must be accounted for as part of the ACNU. Also, the self-selection or appropriate use criteria should include questions about what vitamins, complementary and alternative medicines (i.e., Red Yeast Rice), and other nonprescription medicines that the consumer is currently taking that could cause adverse reactions.

Regarding the proposed abbreviated new drug application (ANDA) requirements, when there are significant differences in efficacy or side effect profiles, such discrepancies should be addressed in the application. Furthermore, different formulations should require a separate process which might not require a de-novo application but would be more rigorous than an ANDA. This could include additional pharmacokinetic data and evidence demonstrating that consumers can safely use the product.

With respect to simultaneous marketing of nonprescription drugs with an ACNU and comparable prescription drugs, AHA agrees that an ACNU constitutes a meaningful difference and that, provided the additional precautions outlined in this comment letter are in place, the nonprescription drug product with an ACNU may be simultaneously marketed as a prescription and nonprescription with ACNU even if no other meaningful difference exists. While we believe this provision has potential to expand access for many patients, we also encourage the FDA to consider how the presence of a possibly lower-cost nonprescription drug with an ACNU may impact insurers' coverage of the prescription

drug version. Effort should be made to mitigate unintended consequences, including the proliferation of cost and coverage barriers that may impede patient access to critical prescription drugs.

§ 314.81 Other postmarketing reports

Regarding the proposed provision on "other postmarketing reports," AHA recommends the addition by the FDA of a patient-friendly website and a telephone number for patients to report issues. Such information will be essential and valuable if the FDA plans to expand this program or needs to make additional modifications.

PART 201—Labeling

§ 201.67 Labeling Requirements

With regarding to the labeling requirements, AHA would support stronger warning language for drugs that have the potential for more adverse effects as shown below in underline:

"You must complete an extra step to see if this drug is safe for you before you use it. Do not take this drug without completing this step, as it could lead to serious adverse effects leading to hospitalization and injury. See the Drug Facts labeling for more information."

Potential adverse health consequences also must be clearly articulated. Additionally, AHA recommends the addition of the following statement: "For questions or concerns, consult with your physician, pharmacist, or health care provider."

With respect to the format requirement for the required ACNU, AHA believes that it will be imperative to ensure that the instructions are written in a manner that are understandable to those with lower health literacy.

§ 201.130 Exemption from Adequate Directions for Use for a Nonprescription Drug with an ACNU

AHA also supports the exemption from the labeling requirement of nonprescription drugs provided the following is adequately described and provided at the point of purchase:
1. Name and description of the medication.
2. Dosage form, dosage, route of administration, and duration of drug therapy.
3. Special directions and pre-cautions for preparation, administration, and use by the patient.

4. Common severe side effects or adverse effects or interactions and therapeutic contraindications that may be encountered.
5. Techniques for self-monitoring of drug therapy.
6. Proper storage.
7. Action to be taken in the event of an erroneous dose, e.g. a missed dose, a double dose, etc.

FDA Request for Input re: Orange Book

AHA recommends adding these medications to the Orange Book so that if issues should arise, pharmacists can access this information easily.

AHA appreciates the opportunity to submit comments on this proposed rule. If you have any questions or require any additional information, please contact Melanie Phelps of AHA staff at (919) 306-5123 or melanie.phelps@heart.org.

Sincerely,

Michelle A. Albert, MD, MPH, FAHA
President
American Heart Association