

PIND 159180

EXEMPT

Jonathan P. Piccini, MD, MHS, FACC, FAHA, FHRS
Associate Professor of Medicine
Duke University Medical Center
P O Box 3816
Durham, NC 27710

Dear Dr. Piccini:

We have received, on October 18, 2021, your email submission dated October 18, 2021. This submission contains a Pre-IND exemption request for dronedarone.

After reviewing the information contained in your submission, we have concluded that your study, "Pragmatic Randomized Clinical Trial of Early Dronedarone versus Usual Care to Change and Improve Outcomes in Persons with First-Detected Atrial Fibrillation (CHANGE AFIB)", meets all of the requirements for exemption from the investigational new drug (IND) regulations and, therefore, an IND is not required to conduct your investigation.

The IND regulations [21 CFR 312.2(b)] state that the clinical investigation of a drug product, including a biological product, that is lawfully marketed in the United States, is exempt from the requirements for an IND if all of the following apply:

- (1) The investigation is not intended to be reported to FDA as a well-controlled study in support of a new indication for use, nor intended to be used to support any other significant change in the labeling for the drug.
- (2) The investigation is not intended to support a significant change in the advertising for a prescription drug product.
- (3) The investigation does not involve a change in route of administration, dosage level, or patient population, or other factor that significantly increases the risks (or decreases the acceptability of risks) associated with use of the drug product.
- (4) The investigation is conducted in compliance with the requirements for institutional review (21 CFR 56) and informed consent (21 CFR 50).
- (5) The investigation is conducted in compliance with the requirements of 21 CFR 312.7, i.e., the drug may not be represented as safe or effective, nor may it be commercially distributed, for the purposes for which it is under investigation.

In addition, 21 CFR 312.2(b)(5) exempts from the IND requirements a clinical investigation that involves use of a placebo if the investigation does not otherwise require submission of an IND.

We remind you that exemption from the requirements for an IND does not in any way exempt you from complying with the requirements for informed consent under 21 CFR 50.20 or from initial and continuing Institutional Review Board review under 21 CFR 56. You are also responsible for complying with the applicable provisions of sections 402(i) and 402(j) of the Public Health Service Act (PHS Act) [42 U.S.C. §§ 282(i) and (j)], which was amended by Title VIII of the Food and Drug Administration Amendments Act of 2007 (FDAAA) (Public Law No. 110-85, 121 Stat. 904).

Title VIII of FDAAA amended the PHS Act by adding new section 402(j) [42 USC § 282(j)], which expanded the current database known as ClinicalTrials.gov to include mandatory registration and reporting of results for applicable clinical trials of human drugs (including biological products) and devices. Please note that, if in the future you submit an application under sections 505, 515, or 520(m) of the FDCA [21 USC §§ 355, 360(e), or 360(j)(m)], or under section 351 of the PHS Act (21 U.S.C. § 262), or you submit a report under section 510(k) of the FDCA [21 USC § 360(k)], the application or submission must be accompanied by a certification that all applicable requirements of section 402(j) of the PHS Act [42 USC § 282(j)] have been met. Where available, such certification must include the appropriate National Clinical Trial (NCT) control numbers [42 USC § 282(j)(5)(B)]. Additional information regarding the certification is available at FDA.gov.¹ Additional information regarding Title VIII of FDAAA is available at NIH.gov.² Additional information on registering your clinical trial(s) is available at the Protocol Registration System website.³

For additional information about IND regulations, you can check our web site.⁴

For archival and documentation purposes only, we have assigned a Pre-Investigational New Drug Application (PIND) number for this drug product. Send any future communication or inquiries concerning this PIND to the following address:

Food and Drug Administration
Center for Drug Evaluation and Research
Central Document Room
5901-B Ammendale Rd.
Beltsville, MD 20705-1266

¹ <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/form-fda-3674-certifications-accompany-drug-biological-product-and-device-application-submissions>

² <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-08-014.html>

³ <http://prsinfo.clinicaltrials.gov/>

⁴ <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcr/CFRSearch.cfm>

If you have any questions, please call Edward Fromm, Chief, Project Management Staff, at (301) 796-1072.

Sincerely,

{See appended electronic signature page}

Norman Stockbridge, MD, PhD
Director
Division of Cardiology and Nephrology
Office of Cardiology, Hematology, Endocrinology,
and Nephrology
Center for Drug Evaluation and Research

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

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