Feinstein Institutes for Medical Research
Northwell Health

PROTOCOL: INTERVENTION STUDY (CLINICAL TRIALS)

Title: Impact of Vitamin D Therapy on Thyroid Function and Antibody Levels in Pediatric Graves' Disease: A Pilot Feasibility Trial

Protocol Number: 25-0285

Principal Investigator:
Name Sharon Hyman, MD
Title Pediatric Endocrinologist
Address 1991 Marcus Ave, Suite M100, New Hyde Park NY 11042
Phone number 516 472 3750
Email address

Investigational Product Name(s): ergocalciferol

PIND 176865

Regulatory Sponsor (Sponsor-Investigator or IND/IDE holder, if applicable): NA Name
Address
Phone number
Email address

Date of FDA IND Exemption: 4/30/2025

Template version: xx,xx, 202

U.S. FOOD & DRUG ADMINISTRATION

PIND 176865

EXEMPT

Sharon Hyman, MD
Cohen Childrens Medical Center
1991 Marcus Ave
Suite M100
New Hyde Park, NY 11042

Dear Dr. Hyman:

We have received your submission dated April 10, 2025, for vitamin D2 (ergocalciferol). This submission contains an investigational new drug (IND) exemption request for the use of vitamin D2 (ergocalciferol) in a proposed clinical study.

After reviewing the information contained in your submission, we have concluded that your study entitled, “Impact of Vitamin D Therapy on Thyroid Function and Antibody Levels in Pediatric Graves’ Disease: A Pilot Feasibility Trial”, 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]

[1] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/form-fda-3674-certificationsaccompany-drug-biological-product-and-device-applicationssubmissions
[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/cfcfr/CFRSearch.cfm

U.S. Food and Drug Administration
Silver Spring, MD 20993
www.fda.gov

SUBMISSION REQUIREMENTS

For archival and documentation purposes only, we have assigned a Pre-Investigational New Drug Application (PIND) number for this drug product. Cite the PIND number listed above at the top of the first page of any communications concerning this application.

Electronic submissions:
You may choose to submit future amendments, that are not in eCTD format, to your PIND electronically via the FDA CDER NextGen Portal. You will need to request an

account in order to log in and utilize the portal. For additional information, see FDA.gov.[5,6]

If you choose to submit future amendments to your PIND electronically in eCTD format, the FDA Electronic Submissions Gateway (ESG) is the central transmission point, and you should obtain an ESG account. For additional information, see FDA.gov.[7]

Paper submissions:
FDA will also accept submissions in paper and on certain physical media (e.g. CDs, DVDs (up to 6 pieces), external hard drives); a printed copy of the cover letter should be included with submissions on electronic media. Send all submissions, electronic or paper, including those sent by overnight mail or courier, to the following address:

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

All regulatory documents submitted in paper should be three-hole punched on the left side of the page and bound. The left margin should be at least three-fourths of an inch to assure text is not obscured in the fastened area. Standard paper size (8-1/2 by 11 inches) should be used; however, it may occasionally be necessary to use individual pages larger than standard paper size. Non-standard, large pages should be folded and mounted to allow the page to be opened for review without disassembling the jacket and refolded without damage when the volume is shelved. Shipping unbound documents may result in the loss of portions of the submission or an unnecessary delay in processing which could have an adverse impact on the review of the submission. For additional information, see FDA.gov.[8]

If you have any questions, contact Elisabeth Hanan, Chief, Project Management Staff, at 240-402-0350 or Elisabeth.Hanan@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Theresa E. Kehoe, MD

[5] https://edm.fda.gov/
[6] https://www.fda.gov/media/128774/download
[7] http://www.fda.gov/ForIndustry/ElectronicSubmissionsGateway
[8] https://www.fda.gov/drugs/investigational-new-drug-ind-application/information-sponsor-investigatorssubmitting-investigational-new-drug-applications-inds

Director
Division of General Endocrinology
Office of Cardiology, Hematology, Endocrinology,
and Nephrology Office of New Drugs
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/

THERESA E KEHOE
04/30/2025 12:13:05 PM

PIND 176865

EXEMPT

Sharon Hyman, MD
Cohen Childrens Medical Center
1991 Marcus Ave
Suite M100
New Hyde Park, NY 11042

Dear Dr. Hyman:

We have received your submission dated April 10, 2025, for vitamin D2 (ergocalciferol). This submission contains an investigational new drug (IND) exemption request for the use of vitamin D2 (ergocalciferol) in a proposed clinical study.

After reviewing the information contained in your submission, we have concluded that your study entitled, “Impact of Vitamin D Therapy on Thyroid Function and Antibody Levels in Pediatric Graves’ Disease: A Pilot Feasibility Trial”, 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]

SUBMISSION REQUIREMENTS

For archival and documentation purposes only, we have assigned a Pre-Investigational New Drug Application (PIND) number for this drug product. Cite the PIND number listed above at the top of the first page of any communications concerning this application.

Electronic submissions:
You may choose to submit future amendments, that are not in eCTD format, to your PIND electronically via the FDA CDER NextGen Portal. You will need to request an

[1] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/form-fda-3674-certifications-accompany-drug-biological-product-and-device-applicationssubmissions
[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/cfcfr/CFRSearch.cfm

account in order to log in and utilize the portal. For additional information, see FDA.gov.[5,6]

If you choose to submit future amendments to your PIND electronically in eCTD format, the FDA Electronic Submissions Gateway (ESG) is the central transmission point, and you should obtain an ESG account. For additional information, see FDA.gov.[7]

Paper submissions:
FDA will also accept submissions in paper and on certain physical media (e.g. CDs, DVDs (up to 6 pieces), external hard drives); a printed copy of the cover letter should be included with submissions on electronic media. Send all submissions, electronic or paper, including those sent by overnight mail or courier, to the following address:

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

All regulatory documents submitted in paper should be three-hole punched on the left side of the page and bound. The left margin should be at least three-fourths of an inch to assure text is not obscured in the fastened area. Standard paper size (8-1/2 by 11 inches) should be used; however, it may occasionally be necessary to use individual pages larger than standard paper size. Non-standard, large pages should be folded and mounted to allow the page to be opened for review without disassembling the jacket and refolded without damage when the volume is shelved. Shipping unbound documents may result in the loss of portions of the submission or an unnecessary delay in processing which could have an adverse impact on the review of the submission. For additional information, see FDA.gov.[8]

[5] https://edm.fda.gov/
[6] https://www.fda.gov/media/128774/download
[7] http://www.fda.gov/ForIndustry/ElectronicSubmissionsGateway
[8] https://www.fda.gov/drugs/investigational-new-drug-ind-application/information-sponsor-investigators-submitting-investigational-new-drug-applications-inds

If you have any questions, contact Elisabeth Hanan, Chief, Project Management Staff, at 240-402-0350 or Elisabeth.Hanan@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Theresa E. Kehoe, MD
Director
Division of General Endocrinology
Office of Cardiology, Hematology, Endocrinology, and Nephrology
Office of New Drugs
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/

THERESA E KEHOE
04/30/2025 12:13:05 PM