FOR FURTHER INFORMATION CONTACT: Ebla Ali-Ibrahim, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, Rm. 6302, Silver Spring, MD 20993, 301–796–3691; or Stephen Ripley, Center for Biologics Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 71, Rm. 7301, Silver Spring, MD 20993–0002, 240–402–7911.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a guidance for industry entitled ''Immunogenicity Testing of Therapeutic Protein Products—Developing and Validating Assays for Anti-Drug Antibody Detection.'' This guidance finalizes the revised draft guidance for industry entitled ''Assay Development and Validation for Immunogenicity Testing of Therapeutic Protein Products'' issued in April 2016. Changes made to the guidance took into consideration comments received. In addition to editorial changes primarily for clarification, this guidance includes updated information on titration and confirmatory assays and an additional discussion of immunogenicity risk assessment.

Immune responses to therapeutic protein products have the potential to affect product pharmacokinetics, pharmacodynamics, safety, and efficacy. The clinical effects of patient immune responses are highly variable, ranging from no measurable effect to extremely harmful. Detection and analysis of ADA formation is a helpful tool in understanding potential patient immune responses. Information on immune responses observed during clinical trials, particularly the incidence of ADA induction or any implications of ADA responses affecting pharmacokinetics, pharmacodynamics, safety, and efficacy, is crucial for any therapeutic protein product development program. Accordingly, such information, if applicable, should be included in the prescribing information as a subsection of the ADVERSE REACTIONS section entitled ''Immunogenicity.''

In general, results from assays for detection of ADA facilitate understanding of the immunogenicity, pharmacokinetics, pharmacodynamics, safety, and efficacy of therapeutic protein products. However, the detection of ADA is dependent on key operating parameters of the assays (for example, sensitivity, specificity), which vary between assays. Therefore, the development of valid, sensitive, specific, and selective assays to measure ADA responses is a key aspect of therapeutic protein product development.

This guidance is being issued consistent with FDA's good guidance practices regulation (21 CFR 10.115). The guidance represents the current thinking of FDA on ''Immunogenicity Testing of Therapeutic Protein Products—Developing and Validating Assays for Anti-Drug Antibody Detection.'' It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. This guidance is not subject to Executive Order 12866.

II. Paperwork Reduction Act of 1995

This guidance refers to previously approved collections of information found in FDA regulations. These collections of information are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501–3520). The collections of information in 21 CFR part 201 have been approved under OMB control number 0910–0572; the collections of information in 21 CFR part 211 have been approved under OMB control number 0910–0139; the collections of information in 21 CFR part 312 have been approved under OMB control number 0910–0014; the collections of information in 21 CFR part 314 have been approved under OMB control number 0910–0001; the collections of information in 21 CFR part 58 have been approved under OMB control number 0910–0119; and the collections of information in 21 CFR part 601 have been approved under OMB control number 0910–0338.

III. Electronic Access

Persons with access to the internet may obtain the guidance at *https://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm, https://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/default.htm,* or *https://www.regulations.gov.*

Dated: January 16, 2019.

Leslie Kux,

Associate Commissioner for Policy.

[FR Doc. 2019–00666 Filed 1–31–19; 8:45 am]

BILLING CODE 4164–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2018–D–4726]

Abbreviated New Drug Application Submissions—Amendments and Requests for Final Approval to Tentatively Approved Abbreviated New Drug Applications; Draft Guidance for Industry; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of availability.

SUMMARY: The Food and Drug Administration (FDA or Agency) is announcing the availability of a draft guidance for industry entitled ''ANDA Submissions—Amendments and Requests for Final Approval to Tentatively Approved ANDAs.'' This guidance is intended to assist applicants in preparing and submitting amendments to tentatively approved abbreviated new drug applications (ANDAs), including requests for final approval. This guidance provides recommendations on the timing and content of amendments to tentatively approved ANDAs to facilitate submission in a timely fashion to enable final approval on the earliest lawful approval date.

DATES: Submit either electronic or written comments on the draft guidance by April 2, 2019 to ensure that the Agency considers your comment on this draft guidance before it begins work on the final version of the guidance.

ADDRESSES: You may submit comments on any guidance at any time as follows:

Electronic Submissions

Submit electronic comments in the following way:

- *Federal eRulemaking Portal: https://www.regulations.gov.* Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to *https://www.regulations.gov* will be posted to the docket unchanged. Because your comment will be made public, you are solely responsible for ensuring that your comment does not include any confidential information that you or a third party may not wish to be posted, such as medical information, your or anyone else's Social Security number, or confidential business information, such as a manufacturing process. Please note that if you include your name, contact information, or other information that identifies you in the body of your comments, that information will be posted on *https://www.regulations.gov.*

• If you want to submit a comment with confidential information that you do not wish to be made available to the public, submit the comment as a written/paper submission and in the manner detailed (see ''Written/Paper Submissions'' and ''Instructions'').

Written/Paper Submissions

Submit written/paper submissions as follows:

• *Mail/Hand delivery/Courier (for written/paper submissions):* Dockets Management Staff (HFA–305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.

• For written/paper comments submitted to the Dockets Management Staff, FDA will post your comment, as well as any attachments, except for information submitted, marked and identified, as confidential, if submitted as detailed in ''Instructions.''

Instructions: All submissions received must include the Docket No. FDA–2018–D–4726 for ''ANDA Submissions—Amendments and Requests for Final Approval to Tentatively Approved ANDAs.'' Received comments will be placed in the docket and, except for those submitted as ''Confidential Submissions,'' publicly viewable at *https://www.regulations.gov* or at the Dockets Management Staff between 9 a.m. and 4 p.m., Monday through Friday.

• Confidential Submissions—To submit a comment with confidential information that you do not wish to be made publicly available, submit your comments only as a written/paper submission. You should submit two copies total. One copy will include the information you claim to be confidential with a heading or cover note that states ''THIS DOCUMENT CONTAINS CONFIDENTIAL INFORMATION.'' The Agency will review this copy, including the claimed confidential information, in its consideration of comments. The second copy, which will have the claimed confidential information redacted/blacked out, will be available for public viewing and posted on *https://www.regulations.gov*. Submit both copies to the Dockets Management Staff. If you do not wish your name and contact information to be made publicly available, you can provide this information on the cover sheet and not in the body of your comments and you must identify this information as ''confidential.'' Any information marked as ''confidential'' will not be disclosed except in accordance with 21 CFR 10.20 and other applicable disclosure law. For more information about FDA's posting of comments to public dockets, see 80 FR 56469, September 18, 2015, or access the information at: *https://www.gpo.gov/fdsys/pkg/FR-2015-09-18/pdf/2015-23389.pdf.*

Docket: For access to the docket to read background documents or the electronic and written/paper comments received, go to *https://www.regulations.gov* and insert the docket number, found in brackets in the heading of this document, into the ''Search'' box and follow the prompts and/or go to the Dockets Management Staff, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.

You may submit comments on any guidance at any time (see 21 CFR 10.115(g)(5)).

Submit written requests for single copies of the draft guidance to the Division of Drug Information, Center for Drug Evaluation and Research, Food and Drug Administration, 10001 New Hampshire Ave., Hillandale Building, 4th Floor, Silver Spring, MD 20993–0002. Send one self-addressed adhesive label to assist that office in processing your requests. See the **SUPPLEMENTARY INFORMATION** section for electronic access to the draft guidance document.

FOR FURTHER INFORMATION CONTACT: Elizabeth Giaquinto Friedman, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 75, Rm. 1670, Silver Spring, MD 20993–0002, 240–402–7930, *elizabeth.giaquinto@fda.hhs.gov*.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a draft guidance for industry entitled ''ANDA Submissions—Amendments and Requests for Final Approval to Tentatively Approved ANDAs.'' This guidance is intended to assist applicants in preparing and submitting amendments to tentatively approved ANDAs, including requests for final approval. This guidance provides recommendations on the timing and content of amendments to tentatively approved ANDAs to facilitate submission in a timely fashion to enable final approval on the earliest date on which the ANDA may lawfully be approved based on patent and/or exclusivity protections (''earliest lawful ANDA approval date'').

If an ANDA meets the substantive requirements for approval but cannot be finally approved by FDA because of unexpired patents or exclusivities, FDA will tentatively approve the ANDA. Under section 505 of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 355), a drug product that is the subject of a tentatively approved ANDA is not an approved drug and may not be marketed without final Agency approval. In addition, under section 301 of the FD&C Act (21 U.S.C. 331), the introduction or delivery for introduction into interstate commerce of such a drug product before the final approval date is prohibited.

An ANDA applicant may submit amendments to a tentatively approved application that propose changes to the application, request final approval, or propose changes *and* request final approval. As described in the draft guidance, an amendment may delay FDA's final approval of the ANDA until after the earliest lawful ANDA approval date, depending on the nature of the changes proposed in the amendment and any related deficiencies identified upon review. The draft guidance is intended to assist applicants in preparing an amendment for submission in a timely fashion to obtain final approval on the earliest lawful approval date. In particular, applicants that wish to request final approval should determine whether changes are necessary before requesting this final approval, review any changes that have been made to their application since the tentative approval was granted, and consider the possible review goal dates that may be assigned to the request for final approval to request final approval in a timely fashion.

This draft guidance is being issued consistent with FDA's good guidance practices regulation (21 CFR 10.115). The draft guidance, when finalized, will represent the current thinking of FDA on ''ANDA Submissions—Amendments and Requests for Final Approval to Tentatively Approved ANDAs.'' It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. This guidance is not subject to Executive Order 12866.

II. Paperwork Reduction Act of 1995

This draft guidance refers to previously approved collections of information found in FDA regulations. These collections of information are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (PRA) (44 U.S.C. 3501–3520). The collection of information for the submission of ANDAs under 21 CFR part 314, subpart C has been approved under OMB control number 0910–0001. In accordance with the PRA, prior to publication of any final guidance document, FDA intends to solicit public

comment and obtain OMB approval for any information collections recommended in this guidance that are new or that would represent material modifications to those previously approved collections of information found in FDA regulations or guidances.

III. Electronic Access

Persons with access to the internet may obtain the draft guidance at either *http://www.fda.gov/Drugs/GuidanceCompliance RegulatoryInformation/Guidances/default.htm* or *https://www.regulations.gov*.

Dated: January 11, 2019.

Leslie Kux,

Associate Commissioner for Policy.

[FR Doc. 2019–00680 Filed 1–31–19; 8:45 am]

BILLING CODE 4164–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Office of the Secretary

Findings of Research Misconduct

AGENCY: Office of the Secretary, HHS.

ACTION: Notice.

SUMMARY: Findings of research misconduct have been made against Srikanth Santhanam, Ph.D. (Respondent), staff scientist in the Division of Gastroenterology, Department of Internal Medicine, Washington University in St. Louis (WUSTL). Dr. Santhanam engaged in research misconduct in research supported by National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), National Institutes of Health (NIH), grants R01 DK109384, R03 DK100737, P30 DK052574, and T32 DK077653; National Institute of Allergy and Infectious Diseases (NIAID), NIH, grants R01 AI126587 and U01 AI1095776; and National Cancer Institute (NCI), NIH, grants R21 CA206039 and P30 CA091842. The administrative actions, including supervision for a period of two (2) years, were implemented beginning on December 14, 2018, and are detailed below.

FOR FURTHER INFORMATION CONTACT: Wanda K. Jones, Dr.P.H., Interim Director, Office of Research Integrity, 1101 Wootton Parkway, Suite 750, Rockville, MD 20852, (240) 453–8200.

SUPPLEMENTARY INFORMATION: Notice is hereby given that the Office of Research Integrity (ORI) has taken final action in the following case:

Srikanth Santhanam, Ph.D., Washington University in St. Louis:

Based on the respondent's voluntary admission and additional analysis conducted by ORI in its oversight review, ORI found that Dr. Srikanth Santhanam, staff scientist in the Division of Gastroenterology, Department of Internal Medicine, WUSTL, engaged in research misconduct in research supported by NIDDK, NIH, grants R01 DK109384, R03 DK100737, P30 DK052574, and T32 DK077653; NIAID, NIH, grants R01 AI126587 and U01 AI1095776; and NCI, NIH, grants R21 CA206039 and P30 CA09184.

In addition to making a voluntary admission, Respondent cooperated fully with WUSTL and ORI and has expressed remorse for his actions.

ORI found that Respondent engaged in research misconduct by falsifying data that were included in a manuscript and a revision submitted to *Cancer Research,* entitled ''IDO1 and kynurenine pathway metabolites activate PI3K-Akt signaling in the neoplastic colon epithelium to promote cancer cell proliferation and inhibit apoptosis.''

ORI found that Respondent intentionally, knowingly, and/or recklessly falsely labeled figures in both the original submission and the revised submission of the manuscript. Specifically, Respondent falsely reported:

- In Figure 2A and resubmission Figure 3A, that the cytoplasmic and nuclear fraction bands for kynurenine (Kyn) and quinolinic acid (QA) and the nuclear fraction bands for β-Catenin were from a single experiment when they were from unrelated experiments
- in resubmission Figures 4A, 8A, and 8B, the descriptions of Western blot analyses, which he labeled as showing the effect of Kyn and QA on HCT116 cells (Figure 4A), mouse AOM/DSS tumor organoids (Figure 8A) and human FAP tumor organoids (Figure 8B, pPRAS40 only), when in fact he used HT29 cells for each test
- in resubmission Figure 4B, that bands labeled as representing pAKT S473 were actually PRAS40
- in Figure S2C, resubmission Figure 3C, and resubmission Figure S3A, that bands labeled as representing total AKT actually came from an unknown source
- in resubmission Figure 7B, that the bands labeled as representing staurosporine-induced apoptosis were actually the same protein samples used to show TNF-α induced apoptosis in Figure 7A
- in resubmission Figures 3A, 3B, and 4A, that the cell lines used were between 3 and 10 passages old, when in fact they were passaged more than 10 times.

As a result of the admission, the corresponding author contacted the journal immediately; the manuscript was not reviewed.

Dr. Santhanam entered into a Voluntary Settlement Agreement (Agreement) and voluntarily agreed:

(1) To have his research supervised for a period of two (2) years beginning on December 14, 2018; Respondent agreed that prior to submission of an application for U.S. Public Health Service (PHS) support for a research project on which Respondent's participation is proposed and prior to Respondent's participation in any capacity on PHS-supported research, Respondent shall ensure that a plan for supervision of Respondent's duties is submitted to ORI for approval; the supervision plan must be designed to ensure the scientific integrity of Respondent's research contribution; Respondent agreed that he shall not participate in any PHS-supported research until such a supervision plan is submitted to and approved by ORI; Respondent agreed to maintain responsibility for compliance with the agreed upon supervision plan;

(2) that for a period of two (2) years beginning on December 14, 2018, any institution employing him shall submit, in conjunction with each application for PHS funds, or report, manuscript, or abstract involving PHS-supported research in which Respondent is involved, a certification to ORI that the data provided by Respondent are based on actual experiments or are otherwise legitimately derived and that the data, procedures, and methodology are accurately reported in the application, report, manuscript, or abstract;

(3) that if no supervisory plan is provided to ORI, Respondent will provide certification to ORI at the conclusion of the supervision period that he has not engaged in, applied for, or had his name included on any application, proposal, or other request for PHS funds without prior notification to ORI; and

(4) to exclude himself from serving in any advisory capacity to PHS including, but not limited to, service on any PHS advisory committee, board, and/or peer review committee, or as a consultant for a period of two (2) years beginning on December 14, 2018.

Wanda K. Jones,

Interim Director, Office of Research Integrity.

[FR Doc. 2019–00667 Filed 1–31–19; 8:45 am]

BILLING CODE 4150–31–P