TABLE 2—ESTIMATED ANNUAL RECORDKEEPING BURDEN [1] [2]

Activity; 21 CFR section	Number of recordkeepers	Number of records per recordkeeper	Total annual records	Average burden per recordkeeping	Total hours
Controls for low-acid canned foods; 1.502(b)	2,443	4	9,772	1	9,772
Hazard determinations, controls, and audits; 1.504, 1.506, 1.511.	56,800	87.74	4,984,036	0.38 (23 minutes)	1,917,174
Written assurances for food produced under dietary supplement current good manufacturing practices; 1.511.	11,701	2.88	33,664	2.25	75,744
Document very small importer/certain small foreign supplier status; 1.512(b)(1).	50,450	1	50,450	1	50,450
Written assurances associated with very small importer/certain small foreign supplier; 1.512(b)(3).	50,450	2.79	141,084	2.25	317,439
Total			5,219,006		2,370,579

[1] There are no capital costs or operating and maintenance costs associated with the information collection.
[2] Figures have been rounded to the nearest one hundredth.

Upon evaluation of the information collection, we are retaining the currently approved burden estimates.

Dated: April 5, 2022.

Lauren K. Roth,

Associate Commissioner for Policy.

[FR Doc. 2022–07617 Filed 4–8–22; 8:45 am]

BILLING CODE 4164–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2019–D–3049]

E8(R1) General Considerations for Clinical Studies; International Council for Harmonisation; 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 final guidance for industry entitled ''E8(R1) General Considerations for Clinical Studies.'' The guidance was prepared under the auspices of the International Council for Harmonisation (ICH), formerly the International Conference on Harmonisation. The guidance describes internationally accepted principles and practices for the design and conduct of clinical studies of drug and biological products. In addition, the guidance provides an overview of the types of clinical studies that may be performed and data sources used during the product's life cycle. The guidance is intended to promote the quality of the studies submitted to regulatory authorities, while allowing for flexibility. This guidance revises the guidance for industry ''E8 General Considerations for Clinical Trials'' issued in December 1997.

DATES: The announcement of the guidance is published in the **Federal Register** on April 11, 2022.

ADDRESSES: You may submit either electronic or written comments on Agency guidances 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–2019–D–3049 for ''E8(R1) General Considerations for Clinical Studies.'' 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, 240–402–7500.

- 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.govinfo.gov/content/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, 240–402–7500.

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

Submit written requests for single copies of this 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, or the Office of Communication, Outreach and Development, Center for Biologics Evaluation and Research (CBER), Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 71, Rm. 3128, Silver Spring, MD 20993–0002. Send one self-addressed adhesive label to assist that office in processing your requests. The guidance may also be obtained by mail by calling CBER at 1–800–835–4709 or 240–402–8010. See the **SUPPLEMENTARY INFORMATION** section for electronic access to the guidance document.

FOR FURTHER INFORMATION CONTACT: *Regarding the guidance:* Mark Levenson, Center for Drug Evaluation and Research, Food and Drug Administration, Bldg. 21, Rm. 4626, Silver Spring, MD 20993–0002, 301–796–2097, *Mark.Levenson@fda.hhs.gov;* 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.

Regarding the ICH: Jill Adleberg, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, Rm. 6364, Silver Spring, MD 20993–0002, 301–796–5259, *Jill.Adleberg@fda.hhs.gov.*

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a final guidance for industry entitled ''E8(R1) General Considerations for Clinical Studies''. The guidance was prepared under the auspices of ICH. ICH has the mission of achieving greater regulatory harmonization worldwide to ensure that safe, effective, high-quality medicines are developed, registered, and maintained in the most resource-efficient manner.

By harmonizing the regulatory requirements in regions around the world, ICH guidelines have substantially reduced duplicative clinical studies, prevented unnecessary animal studies,[1] standardized the reporting of important safety information, standardized marketing application submissions, and made many other improvements in the quality of global drug development and manufacturing and the products available to patients.

The six Founding Members of the ICH are FDA; the Pharmaceutical Research and Manufacturers of America; the European Commission; the European Federation of Pharmaceutical Industries Associations; the Japanese Ministry of Health, Labour, and Welfare; and the Japanese Pharmaceutical Manufacturers Association. The Standing Members of the ICH Association include Health Canada and Swissmedic. Additionally, the Membership of ICH has expanded to include other regulatory authorities and industry associations from around the world (refer to *https://www.ich.org/*).

ICH works by involving technical experts from both regulators and industry parties in detailed technical harmonization work and the application of a science-based approach to harmonization through a consensus-driven process that results in the development of ICH guidelines. The regulators around the world are committed to consistently adopting these consensus-based guidelines, realizing the benefits for patients and for industry.

As a Founding Regulatory Member of ICH, FDA plays a major role in the development of each of the ICH guidelines, which FDA then adopts and issues as guidance for industry. FDA's guidance documents do not establish legally enforceable responsibilities. Instead, they describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited.

In the **Federal Register** of August 1, 2019 (84 FR 37649), FDA published a notice announcing the availability of a draft guidance entitled ''E8(R1) General Considerations for Clinical Studies.'' The notice gave interested persons an opportunity to submit comments by September 30, 2019. After consideration of the comments received and revisions to the guideline, a final draft of the guideline was submitted to the ICH Assembly and endorsed by the regulatory agencies in October 2021.

This guidance finalizes the draft guidance issued on August 1, 2019. The revised final guidance describes internationally accepted principles and practices in the design and conduct of clinical studies of drug and biological products. Changes from the 2019 draft guidance to the final guidance include a reduced emphasis on distinct phases of clinical development, the addition of examples of novel studies, and amendments to appendices. The original ICH guidance ''E8 General Considerations for Clinical Trials,'' that was issued in 1997 has not undergone revision previously. Since the 1997 guidance was issued, clinical trial design and conduct have become more complex, impacting the time and feasibility of developing drugs. In response, the revised guidance directly addresses study quality to ensure the protection of study participants and the generation of reliable and meaningful results, while promoting study efficiency. The ICH E8(R1) guidance focuses on the identification of factors that are critical to the study quality and the management of risks to those factors. Additionally, a wider range of study designs and data sources play an increasingly important role in drug development and are not adequately addressed in the original ICH E8 guidance. Hence, the revised final guidance addresses a broad range of study designs and data sources. The revised final guidance also provides updated cross-referencing to other relevant ICH guidances that inform the design, planning, and conduct of clinical research, without reproducing the detailed material found in those guidances.

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 ''E8(R1) General Considerations for Clinical Studies.'' It does not establish any rights for any person and is not binding on FDA or the

[1] We support the principles of the ''3Rs,'' to reduce, refine, and replace animal use in testing when feasible. We encourage sponsors to consult with us if it they wish to use a non-animal testing method they believe is suitable, adequate, validated, and feasible. We will consider if such an alternative method could be assessed for equivalency to an animal test method.

public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations.

II. Paperwork Reduction Act of 1995

While this guidance contains no collection of information, it does refer to previously approved FDA collections of information. Therefore, clearance by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (PRA) (44 U.S.C. 3501–3521) is not required for this guidance. The previously approved collections of information are subject to review by OMB under the PRA. The collections of information for investigational new drug applications under have been approved under OMB control number 0910–0014; the collections of information for review of new drug applications in have been approved under OMB control number 0910–0001; and the collections of information for review of biologic licensing applications in 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.regulations.gov, https://www.fda.gov/drugs/guidance-compliance-regulatory-information/guidances-drugs, https://www.fda.gov/regulatory-information/search-fda-guidance-documents,* or *https://www.fda.gov/vaccines-blood-biologics/guidance-compliance-regulatory-information-biologics/biologics-guidances.*

Dated: April 5, 2022.

Lauren K. Roth,

Associate Commissioner for Policy.

[FR Doc. 2022–07690 Filed 4–8–22; 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 Toni M. Brand, Ph.D. (Respondent), who was a graduate student in the Department of Human Oncology, University of Wisconsin-Madison (UWM), and subsequently a research fellow in the Department of Otolaryngology—Head and Neck Surgery, University of California San Francisco (UCSF). Respondent engaged in research misconduct in research supported by U.S. Public Health Service (PHS) funds, specifically National Cancer Institute (NCI), National Institutes of Health (NIH), grants P30 CA014520, K99 CA160639, T32 CA108462, and U54 CA209891, National Center for Research Resources (NCRR), NIH, grant UL1 RR025011, National Center for Translational Sciences (NCATS), NIH, grants U54 TR000021 and UL1 TR000427, National Institute of General Medical Sciences (NIGMS), NIH, grant T32 GM081061, and National Institute of Dental and Craniofacial Research (NIDCR), NIH, grant R01 DE023685. The administrative actions, including supervision for a period of four (4) years, were implemented beginning on March 23, 2022, and are detailed below.

FOR FURTHER INFORMATION CONTACT: Wanda K. Jones, Dr. P.H., Acting Director, Office of Research Integrity, 1101 Wootton Parkway, Suite 240, 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:

Toni M. Brand, Ph.D., University of Wisconsin-Madison and University of California San Francisco: Based on the reports of investigations conducted by UWM and UCSF and additional analysis conducted by ORI in its oversight review, ORI found that Dr. Toni M. Brand, who was a graduate student in the Department of Human Oncology, UWM, and subsequently a research fellow in the Department of Otolaryngology—Head and Neck Surgery, UCSF, engaged in research misconduct in research supported by PHS funds, specifically NCI, NIH, grants P30 CA014520, K99 CA160639, T32 CA108462, and U54 CA209891, NCRR, NIH, grant UL1 RR025011, NCATS, NIH, grants U54 TR000021 and UL1 TR000427, NIGMS, NIH, grant T32 GM081061, and NIDCR, NIH, grant R01 DE023685.

ORI found that Respondent engaged in research misconduct by knowingly or recklessly falsifying or fabricating western blot data, by reusing and relabeling data to represent expression of proteins in control experiments measuring the purity of cytoplasmic and nuclear cell fractionation, measurements of proteins of interest, and measurements of the same protein under different experimental conditions or loading controls, included in twenty-four (24) figures in the following grant application submitted to NIDCR, NIH, her Ph.D. Thesis Dissertation, and seven (7) published papers:

- K99 DE027699–01, ''Targeting HPV-driven immunosuppressive signaling pathways in head and neck cancer,'' submitted to NIDCR, NIH, on June 8, 2017.
- Ph.D. Thesis Dissertation, ''Investigations of Nuclear HER family receptors in cancer and resistance to cetuximab therapy,'' Department of Human Oncology, UWM, March 21, 2014 (hereafter referred to as ''Thesis'').
- Mapping C-terminal transactivation domains of the nuclear HER family receptor tyrosine kinase HER3. *PLoS One* 2013 Aug 8;8(8):e71518; doi: 10.1371/journal.pone.0071518. eCollection 2013 (hereafter referred to as ''*PLoS One* 2013'').
- Nuclear EGFR as a molecular target in cancer. *Radiother Oncol.* 2013 Sep;108(3):370–7; doi: 10.1016/j.radonc.2013.06.010 (hereafter referred to as ''*Radiother Oncol.* 2013''). Corrected in: *Radiother Oncol.* 2019 Jan;130:195; doi: 10.1016/j.radonc.2018.10.011.
- Nuclear epidermal growth factor receptor is a functional molecular target in triple-negative breast cancer. *Mol Cancer Ther.* 2014 May;13(5):1356–68; doi: 10.1158/1535–7163.MCT–13–1021 (hereafter referred to as ''*Mol Cancer Ther.* 2014''). Corrected in: *Mol Cancer Ther.* 2019 Apr;18(4):868; doi: 10.1158/1535–7163.MCT–18–1183.
- AXL mediates resistance to cetuximab therapy. *Cancer Res.* 2014 Sep 15;74(18):5152–64; doi: 10.1158/0008–5472.CAN–14–0294 (hereafter referred to as ''*Cancer Res.* 2014'').
- The receptor tyrosine kinase AXL mediates nuclear translocation of the epidermal growth factor receptor. *Sci Signal.* 2017 Jan 3;10(460):eaag1064; doi: 10.1126/scisignal.aag1064 (hereafter referred to as ''*Sci Signal.* 2017''). Retracted in: *Sci Signal.* 2021 Nov 9;14(708):eabn0168; doi: 10.1126/scisignal.abn0168.
- Human Papillomavirus Regulates HER3 Expression in Head and Neck Cancer: Implications for Targeted HER3 Therapy in HPV + Patients. *Clin Cancer Res.* 2017 Jun 15;23(12):3072–3083; doi: 10.1158/1078–0432.CCR–16–2203 (hereafter referred to as ''*Clin Cancer Res.* 2017''). Corrected in: *Clin Cancer Res.* 2021 Jul 15;27(14):4129; doi: 10.1158/1078–0432.CCR–21–2141.
- Cross-talk Signaling between HER3 and HPV16 E6 and E7 Mediates Resistance to PI3K Inhibitors in Head and Neck Cancer. *Cancer Res.* 2018 May 1;78(9):2383–95; doi: 10.1158/0008–5472.CAN–17–1672 (hereafter referred to as ''*Cancer Res.* 2018'').