DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2010–D–0283]

Guidance for Industry on Chemistry, Manufacturing, and Controls Postapproval Manufacturing Changes To Be Documented in Annual Reports; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of a guidance for industry entitled ''CMC Postapproval Manufacturing Changes To Be Documented in Annual Reports.'' This guidance provides recommendations to holders of new drug applications (NDAs) and abbreviated new drug applications (ANDAs) regarding the types of changes to be documented in annual reports. Specifically, the guidance describes chemistry, manufacturing, and controls (CMC) postapproval manufacturing changes that FDA has determined will likely have a minimal potential to have an adverse effect on product quality and, therefore, should be documented by applicants in an annual report. (The guidance excludes positron emission tomography drug products.)

DATES: Submit either electronic or written comments on Agency guidances at any time.

ADDRESSES: 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, 10903 New Hampshire Ave., Bldg. 51, rm. 2201, 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 guidance document.

Submit electronic comments on the guidance to *http://www.regulations.gov.* Submit written comments to the Division of Dockets Management (HFA–305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT: Robert Iser, Office of Pharmaceutical Science, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, rm. 4178, Silver Spring, MD 20993–0002, 301–796–2400, *Robert.Iser@fda.hhs.gov.*

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a guidance for industry entitled ''CMC Postapproval Manufacturing Changes To Be Documented in Annual Reports.'' This guidance provides recommendations to holders of NDAs and ANDAs regarding the types of CMC postapproval manufacturing changes that FDA has determined will likely have a minimal potential to have an adverse effect on product quality, and therefore, should be documented by applicants in an annual report under § 314.70(d) (21 CFR 314.70(d)).

On June 25, 2010 (75 FR 36421), FDA announced the availability of the draft version of this guidance. The public comment period closed on September 23, 2010. A number of comments were received from the public, all of which the Agency considered carefully as it finalized the guidance and made appropriate changes. Any changes to the guidance were minor and made to clarify statements in the draft guidance.

In its September 2004 final report, ''Pharmaceutical Current Good Manufacturing Practices (CGMPs) for the 21st Century—A Risk-Based Approach'' (Pharmaceutical Product Quality Initiative, *http://www.fda.gov/Drugs/DevelopmentApprovalProcess/Manufacturing/QuestionsandAnswersonCurrentGoodManufacturingPracticescGMPforDrugs/ucm137175.htm),* FDA stated that to keep pace with the many advances in quality management practices in manufacturing and to enable the Agency to more effectively allocate its limited regulatory resources, FDA would implement a cooperative, risk-based approach for regulating pharmaceutical manufacturing. As part of this approach, FDA determined that to provide the most effective public health protection, its CMC regulatory review should be based on an understanding of product risk and how best to manage this risk.

The number of CMC manufacturing supplements for NDAs and ANDAs has continued to increase over the last several years. In connection with FDA's Pharmaceutical Product Quality Initiative and its risk-based approach to CMC review, FDA has evaluated the types of changes that have been submitted in CMC postapproval manufacturing supplements and determined that many of the changes being reported present low risk to the quality of the product and do not need to be submitted in supplements.

Based on its risk-based evaluation, FDA developed a list (attached as an appendix to the guidance) to provide additional current recommendations to companies regarding some postapproval manufacturing changes for NDAs and ANDAs that may be considered to have a minimal potential to have an adverse effect on product quality, and, therefore, may be classified as a change to be documented in the next annual report (i.e., notification of a change after implementation) rather than in a supplement.

This guidance is being issued consistent with FDA's good guidance practices regulation (21 CFR 10.115). The guidance represents the Agency's current thinking on CMC postapproval manufacturing changes to be documented in annual reports. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statutes and regulations.

II. Comments

Interested persons may submit either electronic comments regarding this document to *http://www.regulations.gov* or written comments to the Division of Dockets Management (see **ADDRESSES**). It is only necessary to send one set of comments. Identify comments with the docket number found in brackets in the heading of this document. Received comments may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday, and will be posted to the docket at *http://www.regulations.gov.*

III. Paperwork Reduction Act of 1995

This guidance contains collections of information that 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 have been approved under OMB control number 0910–0758. This guidance also refers to the following previously approved collections of information: (1) The submission of supplements to FDA for certain changes to an approved application in accordance with § 314.70 and 21 CFR 314.71; (2) the submission of annual reports to FDA (Form FDA 2252) in accordance with § 314.81(b)(2) (21 CFR 314.81(b)(2)); (3) the submission of supplements to an approved ANDA for changes that require FDA approval; and (4) other post-marketing reports for ANDAs in accordance with 21 CFR 314.98(c), of which the estimate for annual reports is included under § 314.81(b)(2). FDA currently has OMB approval for these collections of information under OMB control number 0910–0001.

IV. Electronic Access

Persons with access to the Internet may obtain the document at either *http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm* or *http://www.regulations.gov.*

Dated: February 27, 2014.

Leslie Kux,

Assistant Commissioner for Policy.

[FR Doc. 2014–04811 Filed 3–4–14; 8:45 am]

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Government-Owned Inventions; Availability for Licensing

AGENCY: National Institutes of Health, HHS.

ACTION: Notice.

SUMMARY: The inventions listed below are owned by an agency of the U.S. Government and are available for licensing in the U.S. in accordance with 35 U.S.C. 209 and 37 CFR Part 404 to achieve expeditious commercialization of results of federally-funded research and development. Foreign patent applications are filed on selected inventions to extend market coverage for companies and may also be available for licensing.

FOR FURTHER INFORMATION CONTACT: Licensing information and copies of the U.S. patent applications listed below may be obtained by writing to the indicated licensing contact at the Office of Technology Transfer, National Institutes of Health, 6011 Executive Boulevard, Suite 325, Rockville, Maryland 20852–3804; telephone: 301–496–7057; fax: 301–402–0220. A signed Confidential Disclosure Agreement will be required to receive copies of the patent applications.

Software for 3D Spectral Fingerprint Based Consensus Modeling Using Orthogonal PLS and Tanimoto Similarity KNN Techniques

Description of Technology: This technology is a software tool for improving molecular modeling. The software addresses data matrices processed in rows instead of columns and the result of these approaches are combined. To process data in rows, the technique uses a measure of similarity known as ''Tanimoto Similarity'' operating on pairs of objects. The property values of the top most similar objects are normalized and used as coefficients to predict the property of interest. These predictions can then be used in combination with the predictions obtained by multivariate techniques to improve the quality of the consensus model in comparison to the individual predictions. Since, in the case of multivariate techniques, the information is accessed in columns, while for the similarity based technique it is accessed in rows, the two types of techniques provide complementary information. Thus, more useful information can be extracted from the same data matrix. Also contemplated is the use of consensus modeling by letting two algorithms (PLS and KNN) operate on descriptor matrices of different size. If each of these matrices is processed by a different model building algorithm and a consensus model between two or more such individual models is built, the resulting model would benefit from both: i) the partial orthogonality of the modeling techniques and ii) the complementarity of the information contained in 3D–SDAR matrices of different granularity.

Potential Commercial Applications:

- Drug Design
- Drug Development

Competitive Advantages:

- Matrix processing of molecules of biological interest
- High Fit-Activity Prediction capacity

Development Stage:

- Early-stage
- In vitro data available

Inventors: Svetoslav H. Slavov, Jon G. Wilkes, Rick Beger, Dan A. Buzatu, Bruce A. Pearce (all of FDA)

Publications:

1. Slavov SH, et al. ^{13}C NMR-distance matrix descriptors: optimal abstract 3D space granularity for predicting estrogen binding. J Chem Inform Model. 2012 Jul 23;52(7):1845–64. [PMID 22681591]

2. Slavov SH, et al. Complementary PLS and KNN algorithms for improved 3D–QSDAR consensus modeling of AhR binding. J Cheminform. 2013 Nov 21;5(1):47–62. [PMID 24257141]

3. Stoyanova-Slavova IB, et al. PLS and KNN algorithms for improved 3D–QSDAR consensus modeling of acute toxicity. Environ Toxicol Chem. 2014 Jan 27 (Epub ahead of print). [PMID 24464801]

Intellectual Property: HHS Reference No. E–015–2014/0—Software Materials. Patent protection is not being pursued for this technology.

Related Technologies:

- HHS Reference No. E–209–1999/1—US Patent 6,898,533 issued 24 May 2005
- HHS Reference No. E–297–2001/0—US Patent 7,996,156 issued 09 Aug 2011

Licensing Contact: Michael Shmilovich, Esq., CLP; 301–435–6019; *shmilovm@mail.nih.gov.*

Collaborative Research Opportunity: The Food and Drug Administration is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize Molecular Modeling/Drug Design. For collaboration opportunities, please contact Ashley Groves at 870–543–7956.

Multivalent, Multiple-Antigenic-Peptides for Serological Detection of HIV–1 Groups -M, -N, -O, and HIV–2

Description of Technology: This CDC-developed invention pertains to multivalent antigenic peptides (MAPs) that can be used in a variety of HIV/AIDS diagnostics. There are two types of HIV: HIV–1 and HIV–2. HIV–1 is subdivided into groups M, N, and O, while HIV–2 is subdivided into subtypes A and B. Within HIV -1 group M, several different subtypes and numerous forms of recombinant viruses exist. To detect all types, groups, and subtypes of HIV by serological methods, a mixture of antigens derived from different viral strains representing different HIV types and subtypes is needed. However, due to the competition and dilution effect, mixing multiple antigens may reduce the amount of individual antigen bound to the solid phase and lead to a reduction in assay sensitivity.

It is known that MAPs, which contain multiple branches of an oligopeptide sequence, are more antigenic than the corresponding single chain linear peptides. The MAPs encompassed by this technology contain multiple branches of oligopeptides of different sequences, derived from HIV–1 group M, N, O, and HIV–2. Thus, depending on the peptide sequences incorporated, a single MAP can be used to detect HIV–1 group M alone, HIV–2 alone, or to simultaneously detect HIV–1 groups M, N, O, and HIV–2 with high sensitivity and specificity.

Potential Commercial Applications:

- Diagnostic test for HIV–1 and/or HIV–2 infection
- Blood and plasma donation screening
- HIV/AIDS surveillance and monitoring programs

Competitive Advantages:

- Lateral flow assays for HIV detection and discrimination
- On-site, point-of-care testing and diagnosis
- Easily formulated as an ELISA kit for commercial or research applications
- Technology can be used to develop a rapid, low-cost method of determining HIV status for home-use or low-resource settings

Development Stage: In vitro data available

Inventor: Chou-Pong Pau (CDC)

Publications:

1. Granade TC, et al. Rapid detection and differentiation of antibodies to HIV–1 and HIV–2 using multivalent antigens and magnetic immunochromatography testing. Clin Vaccine Immunol. 2010 Jun;17(6):1034–9. [PMID 20410326]

2. Pau C, et al. Chimeric multiple antigenic peptides for the simultaneously detection of specific antibodies to HTV–1 groups M, N, O, and HIV–2. J Immunol Methods. 2007 Jan 10;318(1–2):59–64. [PMID 17169369]