4160-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2012-N-0212]

Tobacco Product Analysis; Scientific Workshop; Request for Comments

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of public workshop; request for comments.

The Food and Drug Administration (FDA), Center for Tobacco Products, is announcing a scientific workshop to obtain input on the chemical analysis of tobacco products. The analyses of tobacco products include developing test methods and evaluating method performance to ensure the results of the analyses are reliable and accurate. This scientific workshop will focus on understanding the testing of tobacco filler and smoke from cigarettes, roll-your-own (RYO) tobacco, and smokeless tobacco products for specific chemicals. FDA is also opening a public docket to receive comments on these topics.

Dates and Times: The public workshop will be held on July 30, 2013, from 8:30 a.m. to 5:30 p.m., and on July 31, 2013, from 8:30 a.m. to 4 p.m. Individuals who wish to attend the public workshop must register by close of business on July 1, 2013. Submit either electronic or written comments to the docket by September 30, 2013.

Location: The public workshop will be held at 9200 Corporate Blvd., Rockville, MD 20850, 1-877-287-1373.

Contact Person: Janie Kim, Office of Science, Center for Tobacco Products, Food and Drug Administration, 9200 Corporate Blvd., Rockville, MD, 20850, 1-877-287-1373, FAX: 240-276-3761, email: workshop.CTPOS@fda.hhs.gov.

Registration to Attend the Workshop and Requests for Oral Presentations: If you wish to attend the workshop, make an oral presentation at the workshop, or view the free webcast, you must register by submitting an electronic or written request by July 1, 2013. Please submit electronic requests to http://surveymonkey.com/s/3RGVYFT. A confirmation email will be sent to your registered email at least 2 weeks prior to the workshop date. Those without email access may register by contacting Janie Kim (see Contact Person). Please provide contact information for each attendee, including name, title, affiliation, address, email address, and telephone number. Registration is free, but early registration is recommended because seating is limited. FDA may limit the number of participants from each organization as well as the total number of participants based on space limitations. Registrants will receive confirmation once they have been accepted for the workshop. Onsite registration on the day of the workshop will be based on space availability. If registration reaches maximum capacity, FDA will post a notice closing registration for the workshop at http://www.fda.gov/TobaccoProducts/NewsEvents/ucm238308.htm.

There will be opportunities for audience participation at this workshop. FDA has included topics for comment in section II of this document. FDA will do its best to accommodate requests to speak during the workshop sessions, although questions from the audience may be limited. In addition, we strongly encourage submitting comments to the docket (see Comments).

If you need special accommodations due to a disability, please contact Janie Kim (see Contact Person) at least 7 days before the workshop.

Comments: Regardless of attendance at the public workshop, interested persons may submit comments on any of the topics for discussion in section II of this document by September

30, 2013. Submit electronic comments to http://www.regulations.gov. Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Room 1061, Rockville, MD 20852. 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.

SUPPLEMENTARY INFORMATION:

I. Background

In April 2012, FDA held a scientific workshop that focused on understanding how tobacco reference products and general testing methods are used to analyze tobacco products (77 FR 14814, March 13, 2012; for more information see http://www.fda.gov/TobaccoProducts/NewsEvents/ucm291530.htm). The scientific workshop that will be held on July 30 and July 31, 2013, will focus on understanding the testing of tobacco filler and smoke from cigarettes, RYO tobacco, and smokeless tobacco products for tar, nicotine, and carbon monoxide (TNCO), tobacco-specific nitrosamines (TSNAs), and polycyclic aromatic hydrocarbons (PAHs). The workshop will include discussion of the analytical methods used for measuring these constituents in tobacco products and smoke.

The workshop will include scientific experts who will present scientific and technical information on the testing of tobacco products. Such experts could include, but are not limited to, scientists from governmental agencies, academia, tobacco product manufacturers, and contract testing laboratories.

FDA is interested in receiving scientific information at the workshop and in the docket. Information from the scientific workshop may assist us in developing future scientific workshops regarding the analysis of tobacco products.

II. Workshop Topics for Discussion

The scientific workshop will include discussion of the analytical methods for measuring the following constituents in tobacco products and smoke:

- TNCO in cigarette smoke;
- TSNAs (total TSNAs, N-nitrosonornicotine)(NNN), and 4-(methylnitrosamino)-1-(-pyridyl)-1-butanone (NNK)) in smoke and tobacco filler (i.e., cigarette, RYO, smokeless); and
- PAHs (benzo[a]pyrene, naphthalene, chrysene, benz[j]aceanthrylene, benzo[a]anthracene, benzo[b]fluoranthene, benzo[k]fluoranthene, benzo[c]phenanthrene, cyclopenta[cd]pyrene, dibenz[a,h]anthracene, dibenzo[a,e]pyrene, dibenzo[a,h]pyrene, dibenzo[a,i]pyrene, dibenzo[a,l]pyrene, indeno[1,2,3-cd]pyrene, and 5-methylchrysene) in smoke and tobacco filler (i.e., cigarette, RYO, smokeless).

FDA would like to engage in detailed discussions on chemical test methods to understand the principles and aspects of these analyses. Aspects of analytical methods encompass solution preparation, extraction, separation, detection, and method performance parameters with criteria.

FDA will explore all or some of the following topics during this scientific workshop:

A. TNCO in Cigarette Smoke

1. A description of the different extraction steps used when analyzing cigarette smoke for TNCO.
2. Typical concentration ranges for TNCO and the potential method adjustments to accommodate different cigarette strengths and physical parameters.

3. The optimal solvents, extraction solution, standards, and reference tobacco product(s) typically used when analyzing TNCO.

4. The method variability and whether or not it is dependent upon different products in your portfolio.

5. The specific method challenges and limitations when testing TNCO, such as environmental moisture, water measurement variability, and extraction efficiency.

6. The major sources of variability (e.g., smoking machine or regimen, sample preparation, separation, and detection).

B. TSNAs (Total, NNN, and NNK) in Tobacco Filler (Cigarette, RYO, Smokeless) and Cigarette Smoke

7. The different extraction steps used when analyzing TSNAs in tobacco filler, smokeless tobacco, and cigarette smoke particulate.

8. The optimal solvents, extraction solutions, standards, and reference tobacco product(s) needed during the extraction of TSNAs from tobacco filler or, as applicable, a Cambridge filter pad.

9. The rationale for using isotopically labeled internal standards, instead of targeted surrogates or external standards for TSNAs. The number of isotopically labeled internal standards needed to calculate the amount of TSNAs in a sample.

10. The challenges with isotopically labeled internal standards, including: (a) The commercial availability of internal standards or their analogs; (b) individual versus (vs.) mixture of internal standards; cost of internal standards; (c) deuterated vs. ^{13}C labeled internal standards; and (d) concerns of proton exchange with deuterated labeled internal standards.

11. The typical concentration ranges for total TSNAs, NNN, and NNK and any potential method adjustments to accommodate for different cigarette strengths and physical parameters.

12. The major sources of method variability, e.g., include sources from the smoking machine or regimen, sample preparation, separation, and detection of different tobacco product types and strengths.

13. The specific method challenges and limitations when testing NNN and NNK.

14. The differences in separation, detection, and limits of detection/quantitation when comparing liquid chromatography/mass spectrometry and gas chromatography/thermal energy analyzer for TSNA analysis.

C. PAHs in Tobacco Filler (Cigarette, RYO, Smokeless) and Cigarette Smoke

For the PAHs benzo[a]pyrene, naphthalene, chrysene, benz[j]aceanthrylene, benzo[a]anthracene, benzo[b]fluoranthene, benzo[k]fluoranthene, benzo[c]phenanthrene, cyclopenta[cd]pyrene, dibenz[a,h]anthracene, dibenzo[a,e]pyrene, dibenzo[a,h]pyrene, dibenzo[a,i]pyrene, dibenzo[a,l]pyrene, indeno[1,2,3-cd]pyrene, and 5-methylchrysene:

15. The different extraction steps used when analyzing PAHs in tobacco filler, smokeless tobacco, and cigarette smoke particulate and any applicable cleanup techniques used.

16. The optimal solvents, extraction solutions, standards, and reference tobacco product(s) needed during the extraction of PAHs from tobacco filler or, as applicable, a Cambridge filter pad.

17. The rationale for using isotopically labeled internal standards instead of targeted surrogates or external standards for PAHs. The number of isotopically labeled internal standards needed to calculate the amount of PAHs in a sample.

18. The challenges with isotopically labeled internal standards, including: (a) The commercial availability of internal standards or their analogs; (b) individual vs. mixture of internal standards,

cost of internal standards; (c) deuterated vs. ^{13}C labeled internal standards; and (d) concerns of proton exchange with deuterated labeled internal standards.

19. The typical concentration ranges for each of the PAHs listed in this document and any potential method adjustments to accommodate for different cigarette strengths and physical parameters.

20. The major sources of method variability, e.g., include sources from the smoking machine or regimen, sample preparation, separation, and detection of different tobacco product types and strengths.

21. The different methods necessary to separate and detect for PAHs. Provide the number of methods and steps typically used for each from extraction to detection.

22. The specific method challenges and limitations when analyzing testing PAHs, including: (a) Isomer separation and identification, (b) effects of tobacco blend, and (c) low vs. high molecular weight PAHs (volatility and sensitivity).

23. The differences in separation, detection, and limits of detection/quantitation when comparing gas chromatography/mass spectrometry, liquid chromatography/ultraviolet detection, and liquid chromatography/mass spectrometry for PAH analysis.

D. General Method Testing for TNCO, TSNAs, and PAHs in Tobacco Filler (Cigarette, RYO, Smokeless) and Cigarette Smoke

24. The solution stability for prepared solutions and procedures to ensure their integrity.

25. The typical storage conditions and shelf life (i.e., expiration dates) for tobacco product standards and samples.

26. The standard, reference, or known sample solutions used as blanks or for quality control (QC), working, and check standards when testing TNCO, TSNAs, and PAHs.

27. The system suitability and acceptance criteria for each test method. The discussion may include calibration, QC, working, bracketing, and verification standards, confirmation ion ratio for mass spectrometry, chromatographic parameters (i.e., retention times, tailing factor, or peak resolution), injector precision, and blanks.

28. The critical system suitability parameters that are critical when testing TNCO, TSNAs, and PAHs.

29. The actions taken when any system suitability criterion fails, including standards, QC, and subsequent sample analyses.

30. The typical run sequence when testing samples for TNCO, TSNAs, and PAHs.

31. The equations to calculate sample concentrations for TNCO, TSNAs, and PAHs.

32. Examples of chromatograms of reference standards and for measured TNCO, TSNAs, and PAHs in tobacco products.

E. Validation or Method Performance for TNCO, TSNAs, and PAHs in Tobacco Filler (Cigarette, RYO, Smokeless) and Cigarette Smoke

33. The specific details when evaluating each validation parameter, which may include limit of detection, limit of quantification, method detection limit, accuracy, recovery, linearity, range, precision (repeatability), and specificity.

34. The determination of each criterion for each validation parameter when evaluating TNCO, TSNAs, and PAHs.

35. The steps taken when validation parameter criteria are not met.

36. The validation parameters that are performed with reference tobacco products or standards.

37. The types and strengths of tobacco product samples used during validation and method development.

38. The process taken to revalidate a test method when changes to the method (i.e., solvent, extraction method, or column) are made.

39. The validation process when using a rotary and linear smoking machine with a non-intense and intense smoking regimen.

40. The robustness or ruggedness tests that are conducted for extraction efficiency, solution stability, and small changes in instrument parameters.

III. Transcripts

Please be advised that as soon as a transcript is available, it will be accessible at http://www.regulations.gov. It may be viewed at the Division of Dockets Management (see Comments). A transcript will also be available in either hard copy or on CD-ROM, after submission of a Freedom of Information request. Written requests are to be sent to Division of Freedom of Information (HFI-35), Office of Management Programs, Food and Drug Administration, 5600 Fishers Lane, rm. 6-30, Rockville, MD 20857.

Dated: May 24, 2013.

Leslie Kux,

Assistant Commissioner for Policy.

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