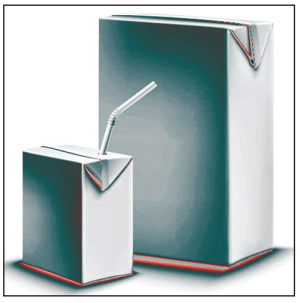
By George G. Misko, Esq.

FDA's Multiple "Conditions of Use"



Defining key regulatory terms for package testing

The U.S. Food and Drug Administration (FDA)'s use of the term "Conditions of Use" can be confusing. FDA employs the term in its food additive regulations to describe the typical temperature conditions under which food products may be used in contact with packaging materials intended to process or hold food. However, in its guidance documents, "Conditions of Use" describe the temperature and duration at which a material should be tested to simulate the manner in which the material is intended to be used. To add to the confusion, FDA also references the term "Conditions of Use" when describing the extractive testing required to establish compliance for many food packaging materials under the food additive regulations.

To make matters even worse, the Conditions of Use employed in the food additive regulations for food contact substances were modified by FDA in the context of the Food Contact Notification (FCN) program so that there is now an incongruity as to the conditions described in the regulations versus the FCNs. The purpose of this article is to attempt to explain the various ways in which FDA talks about Conditions of Use for placing regulatory limits on the use of some food contact materials, for extractive testing compliance purposes and for migration testing needed to support an FCN.

"Conditions of Use" Defined in the Regulations

For food contact substances (FCSs) cleared by the food additive regulations, any temperature restriction on intended use is generally specified by reference to the Conditions of Use as defined in Title 21 *Code of Federal Regulations* (C.F.R.) Section 176.170(c), Table 2, which are as follows:

- Condition of Use A, High temperature heat-sterilized (e.g., > 212 °F)
- Condition of Use B, Boiling water sterilized
- Condition of Use C, Hot filled or pasteurized above 150 °F
- Condition of Use D, Hot filled or pasteurized below 150 °F
- Condition of Use E, Room temperature filled and stored (no thermal treatment in the container)
- Condition of Use F, Refrigerated storage (no thermal treatment in the container)
- Condition of Use G, Frozen storage (no thermal treatment in the container)
- Condition of Use H, Frozen or refrigerated storage: Ready-prepared foods intended to be reheated in container at time of use

Even though Section 176.170 is a regulation pertaining only to paper and paperboard food packaging, the first column of Table 2 (set forth above) has been used as a convenient reference in many other regulations and, until April 2006, in FCNs for all types of FCSs. Conditions of Use A–H are also set out in Section 175.300 ("Resinous and polymeric coatings") and Section 177.1210 ("Closures for sealing gaskets"). In addition to defining Conditions of Use, each of the noted regulations also includes an extractive test that tracks the relevant Condition of Use under which the additive is permitted to be used along with identification of the appropriate food simulants that should be used to conduct the testing and the duration of the test.

It is important to note that while the times and temperatures specified for testing in these regulations are more or

Reprinted from Food Safety Magazine, October/November 2015, with permission of the publishers.

less severe according to the intended Condition of Use, these testing conditions are applicable only for the purpose of demonstrating that materials or articles that consist of substances explicitly cleared in a particular regulation comply with the requirements of that regulation; these conditions do *not* necessarily reflect actual use conditions. Accordingly, when another regulation lists an FCS as permitted for use under Conditions of Use A–H, as defined in 21 C.F.R. Section 176.170(c), Table 2, this cross-reference does not in any way suggest that extraction testing in accordance with Section 176.170 is required, or that such testing would be sufficient to determine whether, or to what extent, substances may reasonably be expected to migrate to food when used as intended.

> "…'Conditions of Use' describe the temperature and duration at which a material should be tested to simulate the manner in which the material is intended to be used."

The Expanded Conditions of Use

Many FCNs and regulatory clearances include a reference to a Condition of Use. Prior to April 2006, all of the referenced Conditions of Use were found in 21 C.F.R. Section 176.170(c), Table 2. Then in April 2006, FDA expanded its list of Conditions of Use to include Conditions I (Irradiation) and J (Cooking at temperatures exceeding 250 °F), but it did not do so by proposing to amend Table 2 in 21 C.F.R. Section 176.170 or otherwise modifying the food additive regulations. Instead, the revised list of Conditions of Use was simply published on FDA's website.[1] Shortly thereafter, this expanded list was used by the agency as the reference for permitted Conditions of Use relative to new FCNs, instead of the FDA continuing to reference Section 176.170, Table 2.

Migration Testing Requirements of FDA's *Chemistry Guidance*

In December 2007, FDA issued an updated guidance document on chemistry issues related to preparing FCN submissions, *Guidance for Industry, Preparation of Premarket Submissions for Food Contact Substances: Chemistry Recommendations*.[2] The purpose of the guidance document is to explain the migration testing needed to clear a food contact substance for a particular intended use. The update addressed the new Conditions of Use I and J. With respect to the use of packaging materials with food that is subject to cooking, the previous *Chemistry Guidance*, published in 2002, had merely recommended that migration testing be conducted "under the most severe conditions of temperature and time anticipated for the proposed use." The 2007 edition of the *Chemistry Guidance* specifically recommends conducting migration testing at the maximum intended cooking temperature for the longest intended cooking time, using a food oil or a fatty food simulant, that is, the update spelled out more clearly what is meant by the "most severe conditions."

A table describing all of FDA's Conditions of Use categories is included in Appendix V of the 2007 *Chemistry Guidance*. Notably, whereas Condition of Use A is defined in Section 176.170(c) of the food additive regulations as "High temperature heat-sterilized (e.g., > 212 °F)," in Appendix V of the 2007 *Chemistry Guidance*, Condition of Use A is described as "High temperature, heat sterilized or retorted [~121 °C (250 °F)]." Condition of Use A is the category applicable to retorting food in a container. Thus, because retorting is normally done at 250 °F and above, it makes sense that FDA would reference the more precise temperature of 250 °F in the guidance document, rather than referencing temperatures "over 212 °F," which is the boiling point of water (i.e., the temperature applicable to Condition of Use B).

The 2007 *Chemistry Guidance* also contains updated migration testing information for microwave-only containers. FDA confirmed that tests performed for broad coverage under the protocol for Condition of Use H (reheating ready-to-eat prepared foods) are adequate to cover microwave-only containers in addition to conventional oven reheating of ready-to-eat prepared foods. However, where such containers are intended to cook food in a microwave, the agency expects the testing to be conducted in accordance with the admonition noted above, which in this case is use of a food oil or fatty food simulant at 266 °F for 15 minutes and an aqueous food simulant at 212 °F for 15 minutes. The guidance also includes specific protocols on testing for dual ovenable and microwave heat susceptor packaging.

Condition of Use I – Irradiation of Packaged Food

FDA's Good Manufacturing Practice (GMP) requirements for the irradiation of prepackaged food mandate that the packaging materials be cleared for such use under Section 179.45 of the regulations, be the subject of an exemption from the need for regulation under the Threshold of Regulation (TOR) or be the subject of an effective FCN.

Condition of Use I applies only to materials used during irradiation of prepackaged food and not to packaging materials that are irradiated as part of their manufacturing process to promote cross-linking or some other physical attribute. The latter use of irradiation may be considered acceptable without FDA preclearance or authorization, provided that no chemical compounds are created during irradiation that could affect the suitable purity of the materials for use with food.

Interestingly enough, although FDA created Condition of Use I, the *Chemistry Guidance* does not describe the kinds of migration tests that must be done. Rather, FDA states, "We do not have protocols for studies on FCSs that are intended to be irradiated with ionizing radiation. Please consult with FDA to discuss recommended protocols for this use."

To date, there are no effective FCNs covering the use of irradiation, although there are several TOR exemptions. Of particular interest, the agency determined that no regulations are necessary for the irradiation of otherwise compliant food packaging materials, provided that the radiation processing is done in compliance with 21 C.F.R. Section 179; the packaging materials are subjected to radiation not exceeding 4.5 kGy; and the packaged food is irradiated either in a verifiably oxygen-free environment or while frozen and contained under vacuum. This exemption is applicable to food contact materials listed in 21 C.F.R. Sections 174 through 186, as well as those listed in FDA's Inventory of Effective FCS Notifications and Inventory of TOR Exemptions.[3,4]

> "The adoption of Condition of Use J raised some concerns about temperature restrictions on food contact substances previously cleared by FDA."

Temperature Restrictions on Cleared FCSs

The adoption of Condition of Use J raised some concerns about temperature restrictions on FCSs previously cleared by FDA, especially those used in microwaveable food packaging. With respect to FCSs cleared through a food additive regulation, FDA has not promulgated an overarching regulation establishing a temperature limitation on any specific food additive regulation. Thus, unless a specific food additive regulation sets out a temperature limit with respect to the substance that is the subject of the regulation, that substance may be used in cooking applications, provided that such use conforms to GMP requirements in 21 C.F.R. Section 174.5 (i.e., used in a manner that does not affect the suitable purity of the finished product for its intended use). Establishing the suitable purity of the finished product with respect to certain FCSs may require additional testing to establish that no significant migration to food results from the actual intended use.

In FCN submissions, even prior to the 2007 revision of the *Chemistry Guidance*, FDA typically required migration testing at temperatures higher than 250 °F for FCSs intended for use in applications where they would be subjected to higher temperatures. The purpose of this requirement was to establish that there was not a significant change in the nature or amount of potential migrants, as opposed to the migrants obtained by extraction at 250 °F, the phase of migration testing recommended for establishing a clearance for Condition of Use A.

For substances cleared through the FCN process prior to the adoption of Condition of Use J, the submitters of the notifications should be able, at a minimum, to interpret the notifications as covering the temperatures of use supported by the highest temperature of the migration testing. Companies that have effective notifications may want to consider having FDA add a reference to Condition of Use J if the previously submitted migration data or new data support the higher temperature use. If there are no additional data, then there may be some risk that the clearance will be considered not to include Condition of Use J.

Discussions and presentations made by FDA staff provide further direction. For aqueous foods, no further testing should be required if the substance is cleared for use under Conditions of Use A, B or H. For single-service packaging for fatty foods intended to be cooked in a conventional oven at temperatures exceeding 250 °F, the packaging material should be exposed at the maximum temperature and time at which it is expected to be used, or it should be tested at 350 °F for 2 hours using a fatty food simulant, such as corn oil or Miglyol 812. Testing at 350 °F for 2 hours covers use of the FCS at higher temperatures (i.e., not limited to use at 350 °F).

FDA's recommended test procedure for repeated-use food contact articles generally is to extract the samples at the highest-use temperature for 240 hours (10 days) and divide the amount extracted by the amount of food that will contact the article over its useful life to determine exposure to the FCS.

Identifying the correct Conditions of Use for testing purposes is critical to obtaining the desired clearance from FDA and establishing compliance with extractive testing requirements in the regulations. Unfortunately, FDA has not made this easy to understand with the overlapping and sometimes inconsistent use of similar terminology. ■

***George G. Misko, Esq.**, is a partner in the Washington, DC, office of Keller and Heckman LLP. He can be reached at misko@khlaw.com.*

References

1. www.fda.gov/Food/IngredientsPackagingLabeling/PackagingFCS/FoodTypesConditionsofUse/ucm109358.htm.
2. www.fda.gov/Food/GuidanceRegulation/GuidanceDocumentsRegulatoryInformation/IngredientsAdditivesGRASPackaging/ucm081818.htm.
3. www.fda.gov/Food/IngredientsPackagingLabeling/PackagingFCS/Notifications/default.htm.
4. www.fda.gov/Food/IngredientsPackagingLabeling/PackagingFCS/ThresholdRegulationExemptions/default.htm.