using the process specified in the final rule should also result in the agency having more complete information on what substances are being used in food-contact articles. This information will permit the agency to take action in the event that data become available that raise significant questions as to whether the continued use of a substance in a food-contact article is safe.

16. One comment stated that the 0.5 ppb threshold was too low for the use of pigments in food-contact articles because such pigments are less toxic than other chemicals. Because these pigments are relatively insoluble, they would also have lower bioavailability.

FDA does not believe that it is feasible to establish specific thresholds of regulation for each of the many types of chemicals used in food-contact articles. Such an approach, with many different thresholds, would be cumbersome. Moreover, as discussed in a previous comment, the toxicological properties of chemicals within a class can vary greatly. Therefore, it would be extremely difficult to establish a single threshold for all the chemicals within a given class. Because of this difficulty, FDA is not taking any action in response to this comment.

The agency believes that it may be feasible in the future to establish a higher threshold based on a substance's toxicological properties rather than based on its type or on the class of chemicals to which it belongs. For example, as discussed in a previous comment, it may be possible in the future to establish separate thresholds for substances that either have been shown to be noncarcinogenic by appropriate 2-year bioassays or, based on the results of short-term toxicity testing (e.g., mutagenicity and acute oral feeding studies), are likely to have a low carcinogenic potency if they are, in fact, carcinogenic.

17. One comment requested that FDA specifically address whether biocides would be eligible for consideration under the threshold of regulation regime. Because such substances must be registered with the Environmental Protection Agency (EPA) in accordance with the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA) (7 U.S.C. 136 *et al.*), and must undergo an extensive review for safety and efficacy, the comment stated that biocides are well suited for an abbreviated review under FDA's threshold of regulation process.

As long as the criteria specified in this final rule are met, FDA will grant exemptions from regulation as food additives for biocides that become components of food-contact articles.

18. Two comments requested that FDA clarify how the presence of a ''barrier'' (one that would limit the migration of a packaging substance into food) would be factored into threshold of regulation decisions. In particular, the comment asked whether, in cases where there is a functional barrier, and no migration can be detected, FDA would still consider the validated detection limit of the method used to analyze for the substance in its dietary exposure estimate.

The key factor in FDA's decision to grant an exemption from regulation for a substance used in a food-contact article is whether the dietary concentration of the substance resulting from its use is below the threshold. Thus, if the presence of a functional barrier limits the migration of the substance into food such that the resulting dietary concentration is below the threshold, FDA will grant an exemption for the intended use of that substance, provided that the other criteria specified in this final rule are met.

In most cases, the effectiveness of a material to act as a barrier to migration will depend not only on the physical and chemical properties of the barrier material and the potential migrant but also on the thickness of the barrier layer and the conditions of use (e.g., temperature, food type, contact time). Therefore, it is usually not possible to draw any conclusions regarding the effectiveness of a barrier material in the absence of migration data. In such cases, requests for exemptions from the food additive regulations would need to contain data showing that the barrier material precludes all but minimal migration of the substance into food (i.e., the resulting dietary concentration is at or below the threshold). FDA will consider the validated detection limit of the method used to analyze for the substance in arriving at its dietary exposure estimate.

There are a number of specific situations, however, where FDA would not require data to show that a barrier material precludes all but minimal migration of the substance into food. For example, some packaging materials such as aluminum foil, when used as the inner layer of laminates, have been generally recognized as being able to provide an effective barrier to migration of the outer layer components into food under a variety of conditions. In such cases, it would not be necessary for the requestor to carry out and submit extraction studies designed to show the effectiveness of the barrier layer. Another example involves those cases in which FDA has reviewed the barrier material and has established specific conditions under which the material would indeed function as a barrier. In these cases, the agency will be able to make decisions on similar constructions in the absence of any additional extraction studies, as long as the conditions of use do not differ significantly from those the agency reviewed.

19. One comment inquired as to whether the final rule establishing a threshold of regulation for substances used in food-contact articles will be applicable to regulated direct animal feed additives that are intended to be used as components of articles that may contact animal feed (i.e., indirect animal feed additives).

This final rule will allow those substances exempted under § 170.39 to be used in articles contacting animal feed as long as the intended conditions of use of the substance are those for which the exemption was issued. This result follows from §§ 174.6 and § 570.14 (21 CFR 570.14) of FDA's regulations. Under § 174.6 *Threshold of regulation for substances used in food-contact articles*, FDA will exempt substances from regulation as food additives whose use in food-contact articles meet the criteria in § 170.39. Authority to use substances exempted under § 174.6 in articles contacting animal feed is set out in § 570.14 *Indirect food additives resulting from packaging materials for animal feed and pet food*, which states that the regulations providing for the use of food-packaging materials in parts 174 through 179 (21 CFR parts 174 through 179) are applicable to packaging materials used in animal feed and pet food.

Moreover, in cases where the exemption request concerns the use of a substance in an article that is used only in contact with animal feed, the criteria used by FDA to determine whether an exemption from regulation is warranted will be those specified in new § 170.39. Because § 570.14 contains a cross-reference that includes § 174.6, in accordance with that provision, FDA can review a request for exemption of a substance used only in contact with animal feed under § 170.39.

Sections 170.39, 174.6, and 570.14, however, will not provide for the use in articles contacting animal feed, at a level that is 1 percent or less of their ADI, of substances that are currently regulated for direct use in animal feed in part 573 (21 CFR part 573). To provide for such a review, FDA will have to adopt a regulation similar to § 170.39 that applies to direct animal feed additives that have not been