Although this memorandum is marked "DRAFT", it has been referenced in FDA final memoranda and has been used in an FDA publication:

Biles, J., McNeal, T., Begley, T., Hollifield, H. (1997) Determination of Bisphenol-A in Reusable Polycarbonate Food-Contact Plastics and Migration to Food-Simulating Liquids., ***Journal of Agricultural and Food Chemistry,*** **Vol. 45(9): 3541-3544.**

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BISPHENOL-A: STATUS SUMMARY REPORT

Environmental estrogens (also referred to as estrogen mimics) are a diverse group of chemicals that have little structural similarity. What most of them do, however, is interfere with the normal biochemical function of estrogen, either by replacing it at receptor sites or blocking its action. In addition, mimics may interfere with the normal metabolism of estrogen in the body leading to possible accumulation of 16-hydroxyestrone which may result in DNA damage. Two approved indirect food additives have been identified as potential estrogen mimics: bis-phenol A and nonyl phenol. Both chemicals and their derivatives are used in a number of food applications. Bisphenol A is used primarily in polycarbonate articles and in can coatings. Nonyl phenol is used to plasticize and disperse other chemicals primarily in polyvinyl chloride applications.

This project work has focused on exposure to estrogen mimics through the food chain by way of their use in food packaging or other approved indirect additive use. The objectives are to (1) develop analytical methods to determine bisphenol-A, nonylphenol and other alkylphenols in articles approved for food contact use (2) determine the extent to which they may migrate to food under conditions of use, (3) estimate dietary exposure to these estrogen mimics and (4) provide the exposure data to FDA's toxicology experts for evaluation of possible health effects. The goal is to provide data to evaluate whether the use of estrogen mimics as indirect additives constitutes an unacceptable risk to human health and reproduction.

So far, methods have been developed for the determination of bisphenol A in foods, food simulants, and polycarbonate polymers. Specific food contact articles studied are polycarbonate baby bottles and can coatings. The baby bottles have been subjected to both accelerated package testing at 150°F for 10 days and to milder conditions thought to be typical of home use.

BPA residues in the polycarbonate bottles ranged widely as shown in Table 1.

Table 1 - RESIDUAL BPA IN POLYCARBONATE ARTICLES

Brand	ug/g	Manufacturer & origin
[redacted]	7.3 17.3 10.4	[redacted]

Residual BPA in PC bottles

[redacted] 9.5
31.3
31.8
14.0
22.5
17.1
57.7 [redacted]

Accelerated food migration tests at 150°F showed relatively enhanced migration with enfant formula, apple juice and orange juice.

Table 2 - Migration to Real Foods:
ug/g of BPA migrated @ 150°F from polycarbonate containing 14.00 ug/g of residual BPA to:

BPA Migrated by weight of Polymer (ug/g)

TIME (hrs)	[redacted]	APPLE J	GRAPE J	ORANGE J	FORMULA
24	0.56	18.9	9.8	2.3	19.9
48		40.1	12.6	28.2	7.2
72	0.55				
144	2.9	***Data not recoverable ***			
168	1.8				
192	2.9				
312	1.9				

%Recovery 112
(600 ppb level)

When similar tests are run in food simulants, it becomes apparent that there is an interaction between the ethanol solvents and polycarbonate polymer as seen in Table 3. This suggest that some foods probably interact with the polymer at elevated temperatures to increase the amount of BPA migrating.

Table 3 - MIGRATION INTO FOOD SIMULANTS

Simulant	Agitation	ug/g in bottle	ug/g migrated[a]	% migrated
Water	Y	31.3	13.7	43.7
Water	N	31.8	4.2	13.2
8% Etoh	Y	31.3	15.7	50.2
10% EtOH	N	31.8	14.5	45.7
50% EtOH	N	31.8	117.1	368.2
95% EtOH	N	31.8	42.0[b]	132.1[b]
Miglyol	Y	31.3	23.8	76.0
Miglyol	N	31.8	0.4	1.2

a = Average of three trials, corrected for recoveries.

b = 162 hour data. After 162 hours, the solutions were cloudy, not characteristic of the other solutions at any time during the experiment. The 240 hour measurement indicated a loss of BPA of 19.6 ug/g.

The migration levels of BPA drop dramatically when migration test heating conditions are reduced. For example, when polycarbonate baby bottles are sterilized for 5 min. in HPLC grade water, cooled and filled with fresh water or 10% ethanol and subsequently stored at room temperature for up to 72 hours, no measurable amount of BPA can be determined at a sensitivity of 5 ppb.

Similarly, bottles containing up to 46 ug per gram of BPA, were sterilized, then one filled with HPLC water and the other filled with 10% ethanol, and both bottles and contents heated at 100°C for 30 minutes. The bottles were brought to room temperature, and placed in a refrigerator and periodically analyzed for up to 72 hours. No measurable BPA was detected with a method of the same sensitivity as above.

These conditions are probably more likely to simulate the actual use of such articles in the home and show that such usage is likely to result in transferring little if any BPA into food.

BISPHENOL-A IN CAN COATINGS

Test portions of canned mushrooms, artichokes, green beans, mixed vegetables, and tomatoes have been tested for the presence of BPA residues. This sampling included several different imported and domestic can types and coating lacquers. BPA has been found in test portions of each, ranging from about 5 to 39 ppb. Work is continuing in this area to refine the analytical method but it does appear that these findings are consistent with those reported by Brontons et al. at the University of Granada, Spain. The levels found are in the low ug/can and vary significantly from food to food and source to source. The levels found in tomatoes were among the highest yet determined by us and demonstrates that this situation is not limited to low acid canned foods. Also, one positive finding in our tests included mushrooms "canned" in glass jars with a lacquered lid. The nondetects reported by Brontons and et al. may have more to do with the can coating type and processing conditions than food type.

Levels Found vs. EPA NOEL. All findings so far have been quite low and it is difficult to imagine dietary exposures that would exceed EPA's reference No-Observed-Effects-Level of 50 mg/kg per day. The EDI for the use of polycarbonate baby bottles assuming a non-detect level of 5 ppb is estimated at ..... The EDI of the highest canned food level reported in the Spanish study of 22ug/can (.0073 ug/g) is estimated at ..... Such comparisons should be observed with caution until the toxicology of the xenoestrogens is better understood.

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DATA TABLE FOR BPA IN CANNED FOODS

FOOD	CAN WEIGHT (gms)	CONC. IN FOOD (ppb)	BPA IN CAN (ug)
MUSHROOMS	214	15	3.21
MUSHROOMS	214	06	1.28
MUSHROOMS	225	12	2.70
TOMATOES	411	18	7.40
ARTICHOKES	396	39	15.44
MIXED VEG.	411	04	4.11