Using new scientific knowledge to update regulations in the U.S.

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Food Packaging Forum

5 October, 2017

Food Packaging Forum

US Food Additives Regulatory Program

- Administered by the Food and Drug Administration Office of Food Additive Safety
- Legal framework: Food Additive Amendment of 1958 to the Federal Food Drug and Cosmetic Act, and subsequent regulations
- Food Additives Amendment:
  - Intended to protect the public from harmful chemicals
  - Before chemicals are used in or on foods it requires
    - Testing, and
    - affirmation of safety

FDA’s definition of safety

- Reasonable certainty in the minds of competent scientists that the substance is not harmful under the intended conditions of use. In short, *“reasonable certainty of no harm”*
- It applies
  - Pre-market
  - Post-market
  - All chemicals intentionally or unintentionally added to food

Safety assessment

In performing a safety assessment, 3 factors must be considered:

1- The probable consumption of the substance and of any substance formed in or on food because of its use;

2- The cumulative effect of the substance in the diet, taking into account any chemically or pharmacologically related substance or substances in that diet; and

3- Safety factors that, in the opinion of experts, are generally recognized as appropriate

(21 CFR §170.3(i)).

Safety assessment

EXPOSURE

SAFETY/UNCERTAINTY FACTORS

CUMULATIVE EFFECTS OF CHEMICALLY OR PHARMACOLOGICALLY RELATED SUBSTANCES

CLASS

Safety assessment

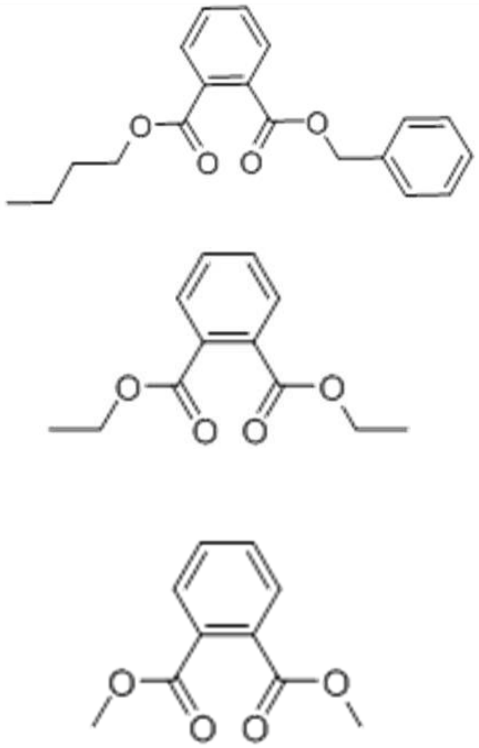
EXPOSURE

SAFETY/UNCERTAINTY FACTORS

CUMULATIVE EFFECTS OF CHEMICALLY OR PHARMACOLOGICALLY RELATED SUBSTANCES

CLASS

MEMBERS OF A CLASS



Ortho-phthalates

Safety assessment

EXPOSURE

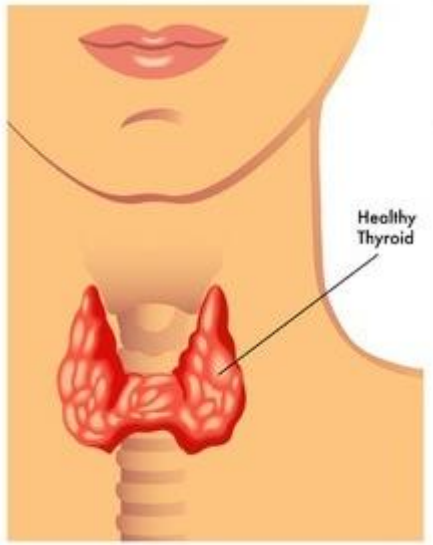
SAFETY/UNCERTAINTY FACTORS

CUMULATIVE EFFECTS OF CHEMICALLY OR PHARMACOLOGICALLY RELATED SUBSTANCES

CLASS

THESE FACTORS ALSO APPLY TO PRE- AND POST-MARKET SAFETY ASSESSMENT

MEMBERS OF A CLASS



Perchlorate
Nitrates
Thiocyanates

Progress

1958

SCIENTIFIC KNOWLEDGE
ANALYTICAL METHODS
CHEMISTRY
PREDICTION MODELING
STATISTICS
ADDITIVES ALLOWED

REGULATORY SCIENCE
TOXICITY & EXPOSURE DATA
CUMULATIVE RISK ASSESSMENT
SAFETY RE-EVALUATIONS

TO DATE

Safe chemicals in the food supply

EXPOSURE

TOLERABLE DAILY INTAKE

SAFE

Unsafe chemicals in the food supply

EXPOSURE

TOLERABLE DAILY INTAKE

SAFE

EXPOSURE

UNSAFE

Unsafe chemicals in the food supply

EXPOSURE

TOLERABLE DAILY INTAKE

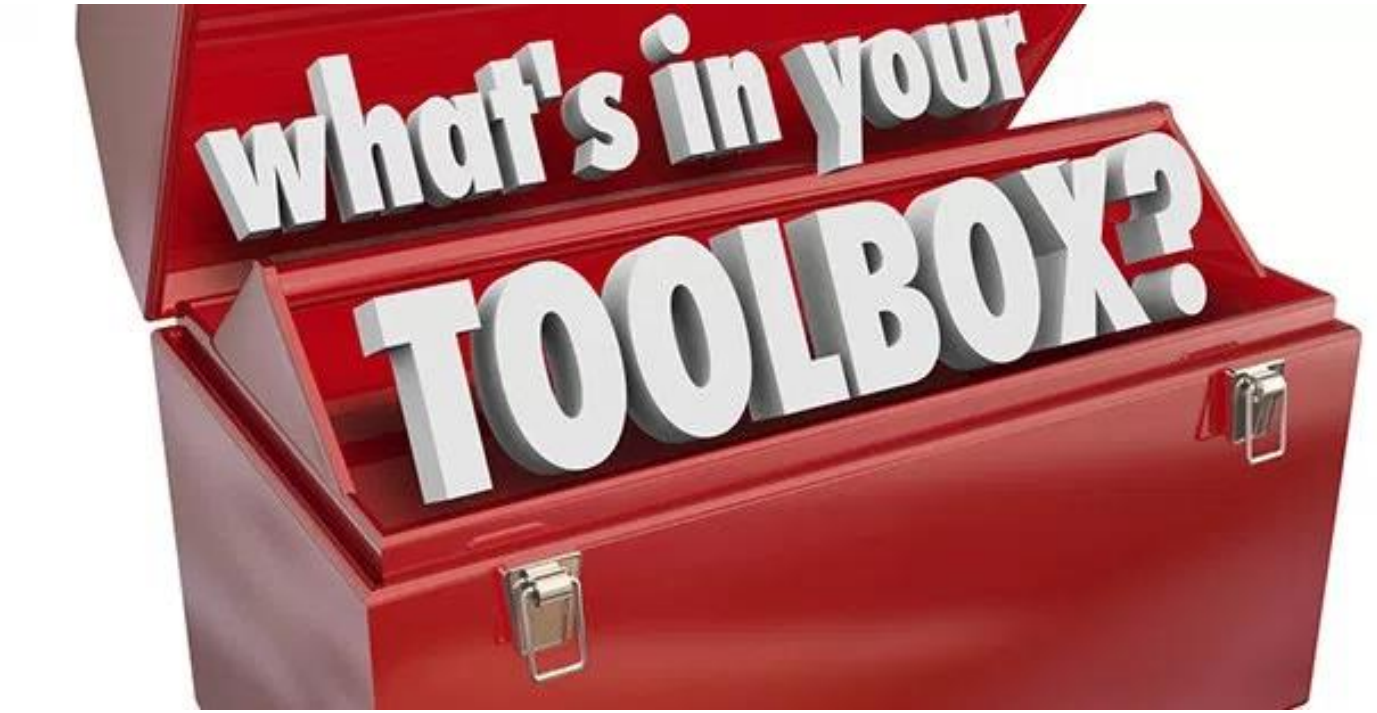
SAFE

HAZARD

TOLERABLE DAILY INTAKE??

UNSAFE

In the absence of a post-market safety review program, how do we use new scientific knowledge to eliminate additives of concern from the food supply?



Food additive petition rule making process

- Historically used by industry to get chemicals approved
- Any person u organization can submit a FAP
- FDA has specific and enforceable timelines:
  - 30 days after filing the petition: announcement in the *Federal Register*
  - 180 days after filing: final rule and publication in *FR*
- FDA is willing to review drafts and provide feedback to petitioners, including in-person consultation before the official submission
- FDA final decision is effective immediately, the day its announced in the *Federal Register*
- Opportunities for public comment and legal challenges

21 CFR 171

FAPs request FDA to do 1 of these 3 things

- Approve an additive
- Revoke an additive approval because the use(s) has been abandoned
  - BPA – baby bottles and sippy cups (sponsored by American Chemical Council)
  - Perchlorate – closure-sealing gaskets (sponsored by Soc. Plastic Industry; accepted May 2017)
  - PFOS-type compounds – paper and paperboard (sponsored by 3M Corporation; under review by FDA)
- Revoke an approval because the additive is unsafe
  - ≥ C8 Perfluoroalkyl ethyl chemicals – paper and paperboard (accepted Jan 2016)
  - Perchlorate – closure-sealing gaskets, food contact material for dry food (rejected May 2017; ongoing objection and legal challenge)
  - Ortho-phthalates – 28 chemicals, long list of uses (ongoing review)

Revoke an approval because the additive is unsafe

1- Demonstration that the safety standard of **reasonable certainty of no harm** is no longer met

- Precedent
  - FDA statements/ruling/opinions/memos
  - EPA
- Exposure and toxicity data
  - Biomonitoring
  - Scientific literature
  - EFSA/ECHA/EU Member States agencies opinions/risk assessments

2- Legal supporting arguments

≥ C8 Perfluoroalkyl ethyl substances

Table 1: Three classes of long-chain perfluorocarboxylates that NRDC is requesting FDA to remove from 21 C.F.R. § 176.170

Class	Description of indirect additive[a]	Company Requesting Approval	Year Approved	Max. Estimated Exposure[b]
1	Diethanolamine salts of mono- and bis (1*H*,1*H*,2*H*,2*H* perfluoroalkyl) phosphates where the alkyl group is even-numbered in the range C8-C18 and the salts have a fluorine content of 52.4% to 54.4% as determined on a solids basis	DuPont	1967	0.013 mg / person / day
2	Pentanoic acid, 4,4-bis [(*gamma-omega*-perfluoro-C8-20-alkyl)thio] derivatives, compounds with diethanolamine (CAS Reg. No. 71608-61-2)	Ciba-Geigy[c] (now BASF)	1983	0.05 mg / person / day
3	Perfluoroalkyl substituted phosphate ester acids, ammonium salts formed by the reaction of 2,2-bis[([gamma], [omega]-perfluoro C4-20 alkylthio) methyl]-1,3-propanediol, polyphosphoric acid and ammonium hydroxide	Ciba-Geigy[c] (now BASF)	1996 & 1997	0.13 mg / person / day

[a] See Appendix 2 for details on each class.
[b] See Appendix 3.
[c] Ciba-Geigy transferred this business to Ciba Specialty Chemicals in 1996. BASF purchased it in 2008.

1- FDA memos

- 2007: **carcinogenicity** was a concern for chemicals structurally similar to PFOA
- 2010: due to considerable data gaps on toxic effects of PFCs as a class, significant questions regarding safe levels of exposure

2- 2014 EPA analysis of health effects and exposure to PFOA. Estimated reference dose: 10 to 100 times lower than estimated exposure from food contact uses for the class

3- 2014 Systematic review conclusion: sufficient human evidence developmental exposures to PFOA reduce fetal growth

4- Extensive literature searches

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1- The three food contact substances belong to a class of **chemically related substances**
2- PFOA and similar LC PFCs **also belong to the same class**

The members of the class will likely have similar toxic effects including

- adversely affecting fetal and neonatal development,
- the male, and likely female, reproductive systems
- cause cancer

Given the dearth of toxicology studies on these three classes of chemicals, without evidence showing that these chemicals impact the human body differently than PFOA, there is no longer “a reasonable certainty in the minds of competent scientists that the substance is not harmful under the intended conditions of use”

FDA's rationale for accepting the PFCs FAP

- We also concluded that there is a lack of data specific to the three subject FCSs subject to the petition to address these questions
- We concluded that data for subsets of long-chain PFCs (demonstrating biopersistence and reproductive and developmental toxicity) are applicable to long-chain PFCs on a general basis and that this data raises significant questions as to the safety of the authorized uses of the three FCSs subject to the petition

For these reasons, in the **absence of data specific to the three FCSs** to address reproductive and developmental **toxicity**, adequate **migration** data to determine dietary exposure to the FCSs from the food-contact use, and sufficient data to account for a **consumer's systemic exposure resulting from chronic dietary exposure** to these FCSs, we conclude that there is no longer a reasonable certainty of no harm for the food contact use of these FCSs.

List of Subjects in 21 CFR Part 176

Food additives, Food packaging.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs and re-delegated to the Director, Center for Food Safety and Applied Nutrition, 21 CFR part 176 is amended as follows:

PART 176—INDIRECT FOOD ADDITIVES: PAPER AND PAPERBOARD COMPONENTS

■ 1. The authority citation for 21 CFR part 176 continues to read as follows:

Authority: 21 U.S.C. 321, 342, 346, 348, 379e.

§ 176.170 [Amended]

■ 2. Amend § 176.170 in the table in paragraph (a)(5) by removing the entries for ''Diethanolamine salts of mono- and bis,'' ''Pentanoic acid,'' and ''Perfluoroalkyl substituted phosphate ester acids.''

Dated: December 29, 2015.

Susan Bernard,

Director, Office of Regulations, Policy and Social Sciences, Center for Food Safety and Applied Nutrition.

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Perchlorate and o-phthalates FAPs

- Perchlorate, thiocyanate and nitrates, all found in the diet, must be assessed as a class of pharmacologically-related substances
- The 28 o-phthalates allowed by FDA must be assessed as a class of chemically and pharmacologically related substances; more than half lack toxicity and exposure data
- PFCs precedent: In the absence of toxicity data, the information available for a subset of members of the class is applicable to the whole class

Conclusions

Until:

- A systematic re-evaluation program is developed
- A priority setting criteria is implemented
- FDA gets access to the information it needs: chemical uses, usage, toxicity, exposure
- Cumulative risk assessment methods are utilized
- Testing and exposure guidance are updated

Food additive petitions are the preferred tool to update regulations

Thank you!

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