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Demonstrating Food Contact Compliance of UV Initiators

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Who is Keller and Heckman?

- Founded in 1962
- Offices in Washington DC, San Francisco, Brussels and Shanghai
- Broad practice in the areas of regulatory law, litigation, and business transactions
- A pioneer in the use of interdisciplinary approaches to problem-solving
- In-house scientific staff that works closely with the firm's attorneys on matters of technical complexity
- Many of our attorneys also have experience with food and food packaging governmental agencies

Outline

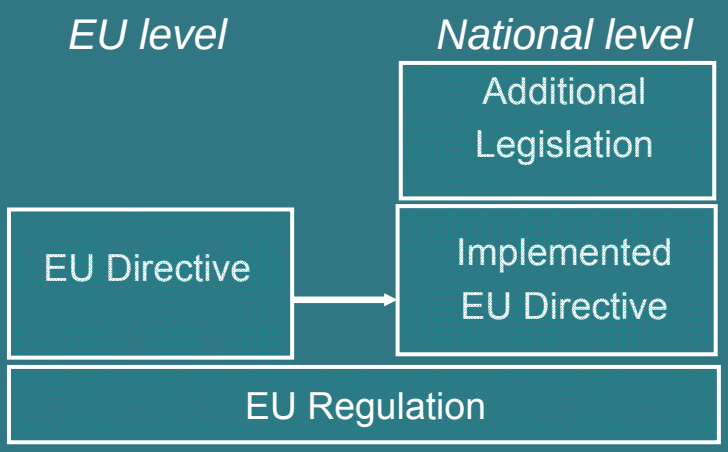
- Introduction
- EU () & USA () legislation
- Demonstrating compliance
  - Identification of possible components
  - Worst case calculation
  - Determination of toxicological limits
  - Analytical determination
- Conclusions

Why food contact legislation?

- Food contact legislation is enacted to ensure:
  - o Free circulation of goods
  - o Protection of human health
- What is covered:

  Everything that can be in contact with food contact materials: obviously packaging, but also conveyor belts, industrial food processing machinery, food utensils, etc.

EU & national legislation



EU Directives & Regulations

General
- Framework Regulation (EC)1935/2004
- GMP Regulation (EC) 2023/2006

Testing conditions

Directive 85/572/EEC, 82/711/EEC and amendments

Specific measures

Applies to one or few groups of materials

Framework Regulation (EC)1935/2004

Article 3 General safety requirements

- Not endanger public health
- No unacceptable change in composition
- No deterioration of the organoleptic characteristics

Article 15 Labeling for materials not yet in contact with food

- Text or symbol
- Instructions for manufacturer or trader

Framework Regulation (EC)1935/2004

Article 16 Declaration of compliance

- Appropriate documentation shall be made available to competent authorities
- A special measure must be published (so far measures published for plastics, ceramics and badge containing materials)

Article 17 traceability

- Traceability = ability to trace and follow a material or article through all stages of manufacture, processing and distribution
- One step forward & one step back
- Must be made available within 4 hours
- Came into force 27 October 2006

Legislative status of Inks (EU)

- No EU legislation has been drafted
- No legislation in member states present
- Expert judgment needed to state the use is safe
- Migration depends on composition of inks, curing, substrate and much more
- Mentioned in GMP Regulation
- But must always comply with Article 3 of Regulation (EC) 1935/2004

Legislative status of Adhesives (EU)

- Only EU legislation is available concerning the use of BADGE and the prohibition of BFDGE/NOGE (Regulation (EC) 1895/2005).
- Limited national legislation is existing
- Expert judgment needed to state the use is safe
- But must always comply with Article 3 of Regulation (EC) 1935/2004

FDA legislation

- Different system compared with EU
  (not more or less strict)
- Many ways to clear ingredient/material
  - Listed in the Code of Federal Regulation (CFR)
  - **Food contact notifications (FCN)**
  - GRAS (Generally recognized as safe)
  - Threshold of Regulation
  - Prior Sanctioned
  - No migration position
  - And more….

Legislative status of Inks (USA)

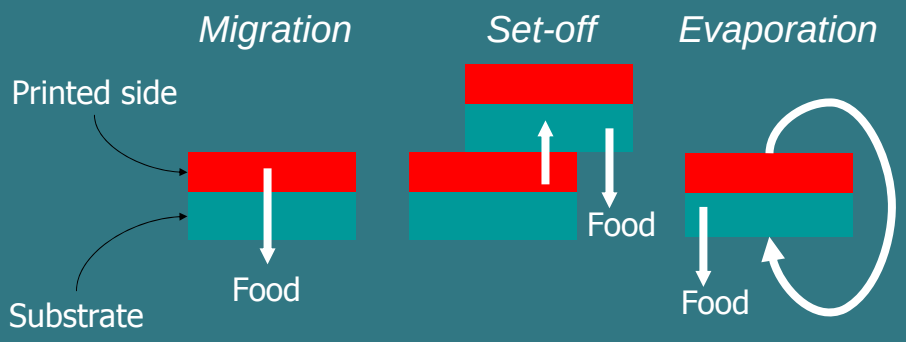
- No specific legislation is available
- Positive list for colorants in 21 CFR 178.3297
- FCN can be submitted
- Expert judgment needed to state the use is safe
- Safety use in the diet must be demonstrated
- A migration of 1.5 µg per day (3 kg of food consumed per day is considered to be safe) for compounds with no toxicological and carcinogenic concern

Legislative status of adhesives (USA)

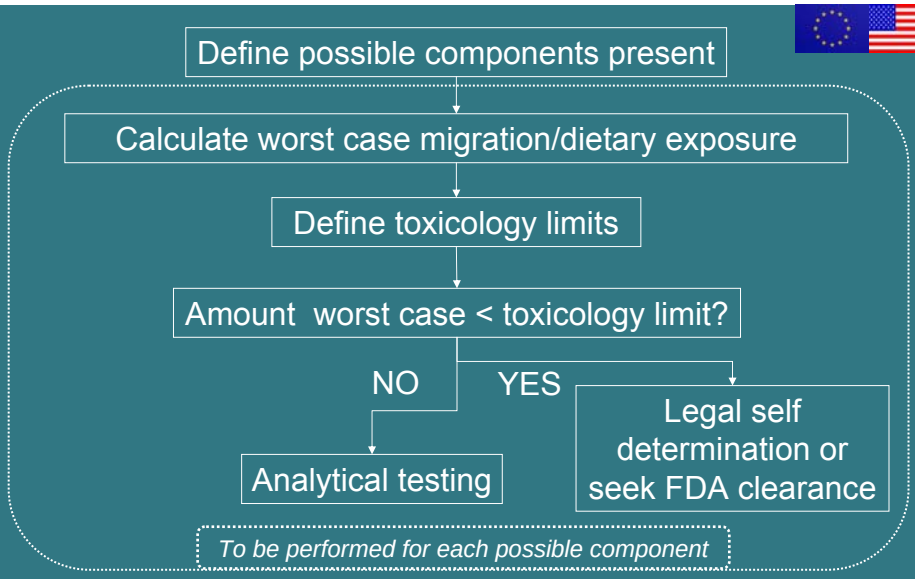
- Regulated in 21 CFR 175.105 (for use behind a barrier only!!)
- Some UV initiators are mentioned in 21 CFR 175.105
- FCN can be submitted
- Expert judgment needed to state the use is safe
- Safety use in the diet must be demonstrated

Migration of ink components to the food

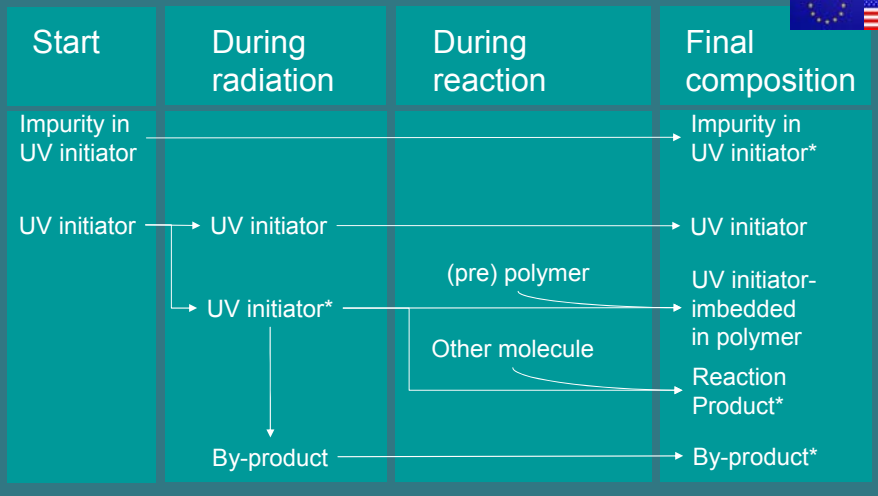
Components may migrate in different ways to the food:



Keller & Heckman approach

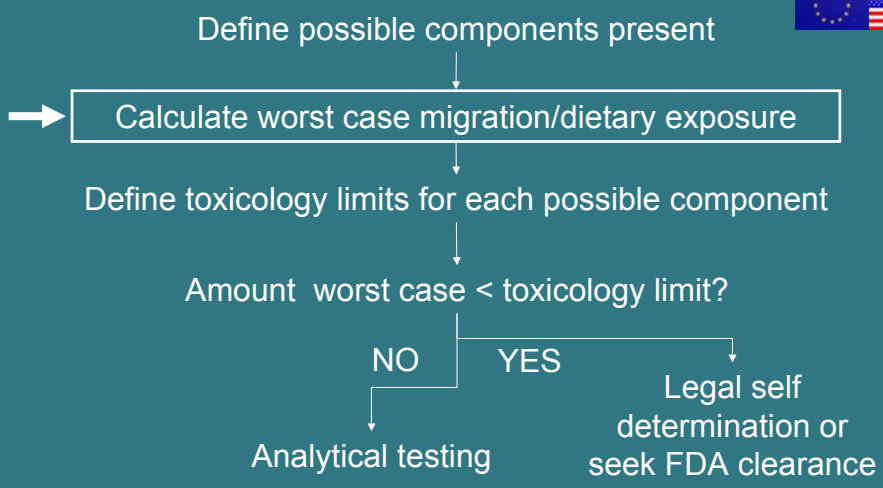


Overview of possible reactions



**Identity might be determined theoretically or experimentally identified*

Keller & Heckman approach



Example

- Package 2dm^2 holds 200g of food
- Package is printed paper (polymer coated) intended for fatty foodstuff
- 4 g of ink is applied per m^2
- To the ink 1% of UV initiator is added
- In UV initiator 1% impurity X is present
- During the radiation 90% of the UV initiator is initiated and Y is formed as byproduct

Example; worst case calculation

	Max available in ink after curing	*Max if all migrates to food (2 dm² in contact with 200g)*
Impurity in UV initiator	0.4 mg/m² (1% of the ink, 1% impurity, 4 g ink/m²)	0.04 mg/kg
UV initiator	4 mg/m² (1% of the ink, 90% radiated, 4 g ink/m²)	0.4 mg/kg
UV initiator-imbedded in polymer	Max 36 mg/m² (1% of the ink, 90% radiated, 4 g ink/m²)	Will not migrate, too large
Reaction product	Max 36 mg/m² (1% of the ink, 90% radiated, 4 g ink/m²)	3.6 mg/kg
By-product	Max 36 mg/m² (1% of the ink, 90% radiated, 4 g ink/m²)	3.6 mg/kg

Converting migration to diet

- Correction for use of material (CF)
  - Example polymer coated paper CF=0.2
- Correction for food-type distribution (f_T)
  - Example fatty foodstuff in polymer coated paper f_T=0.4

Diet calculated from a polymer coated paper in contact with fatty foodstuff

Diet = $(M_{water} \times f_{Twater} + M_{alcoholic} \times f_{Talcoholic} + M_{fat} \times f_{Tfat}) \times CF =$

$= (0 + 0 + M_{fat} \times 0.4) \times 0.2 = 0.08\ M_{fat}$

Day = 3 kg foodstuff x 0.08 M_{fat} =0.24 M_{fat}

Example; worst case calculation

	Max migration to food	*Max dietary exposure (using 3kg food/day, CF = 0.2, f_T= 0.4)*
Impurity in UV initiator	0.04 mg/kg	0.0096 mg/day
UV initiator	0.4 mg/kg	0. 096 mg/day
UV initiator-imbedded in polymer	Will not migrate, too large	Will not migrate, too large
Reaction product	3.6 mg/kg	0.864 mg/day
By-product	3.6 mg/kg	0.864 mg/day

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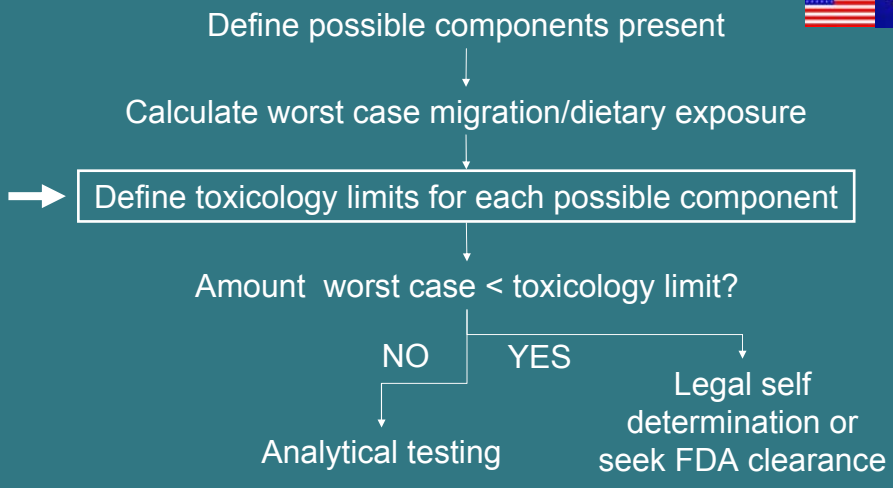


Obtaining limits; related EU Legislation

- Plastics (2002/72/EC and amendments)
  - Include multilayers of plastic (with or without adhesive)
  - Monomers completely harmonized
  - Additive list incomplete. Will be considered complete soon (1/1/2010?)
  - Catalysts and aid to polymerization and polymerization production aids not harmonized by EU
  - Some member states do have additional national legislation
  - Barrier concept (10ppb)
  - Requirements on composition, migration and purity
- Coatings (Regulation (EC) 1895/2005)
  - Only EU legislation is available concerning the use of BADGE
  - Legislation present in some member states

But a product must always comply with Article 3 of Framework Regulation (EC) 1935/2004!!!!

Obtaining limits; non-legal ink documents

Council of Europe Resolution (2005)2

- Must meet organoleptic characteristics
- Must meet SML and residual limits
- Inks may not be in direct food contact
- Ink suppliers are responsible for traceability
- No, or negligible, visible set-off or migration from printed or vanished non-food contact layer to food surface
- Has an unpublished list of requirements
- Has an unpublished inventory list of components

Obtaining limits; non-legal ink documents

Exclusion list for printing inks (EuPIA)

- Do not use substances that are
  - Carcinogenic, mutagenic and toxic for reproduction substances and preparations classified and labeled as toxic (T) according to the Dangerous Substances Directive 67/548/EEC with risk phrases R 45, R 46, R 49, R 60, R 61 2.
  - Substances and preparations classified and labeled as very toxic (T+) or toxic (T) according to the Dangerous Substances Directive 67/548/EEC with risk phrases R 23, R 24, R 25, R 26, R 27, R 28, R 39, R 48 2.

Obtaining limits; non-legal ink documents

Migration limits for components from printing inks according EuPIA

- 10 ppb, in case of insufficient toxicological data
- 50 ppb if three negative mutagenicity tests requested by EFSA
- above 50 ppb, if supported by favorable toxicological data and/or evaluation done in accordance with the EFSA Guidelines.

Obtaining limits; non-legal documents on dietary exposure limits

ILSI

- Compounds with structural alerts for genotoxicity: 0.15 µg/day (1 kg food day results in 0.15 ppb)
- All non-genotoxicity components 1.5 µg/day (1 kg food day results in 1.5 ppb)
- Organophosphates: 18 µg/day (1 kg food day results in 18 ppb)
- Others (depending on structure): 90 – 1800 µg/day (1 kg food day results in 90 ppb – 1800 ppb)

Conclusion on toxicological limits

- For listed components in EU plastic directive:
  - Use SML/QM(A) mentioned
- Unlisted components in EU & FDA
  - Situation is complicated
  - Some guidance available from legislative and non-legislative documents
  - Toxicological expertise needed
  - A case-by-case decision needs to be made

Keller & Heckman approach

Define possible components present

↓

Calculate worst case migration/dietary exposure

↓

Define toxicology limits for each possible component

↓

Amount worst case < toxicology limit?

NO → Analytical testing

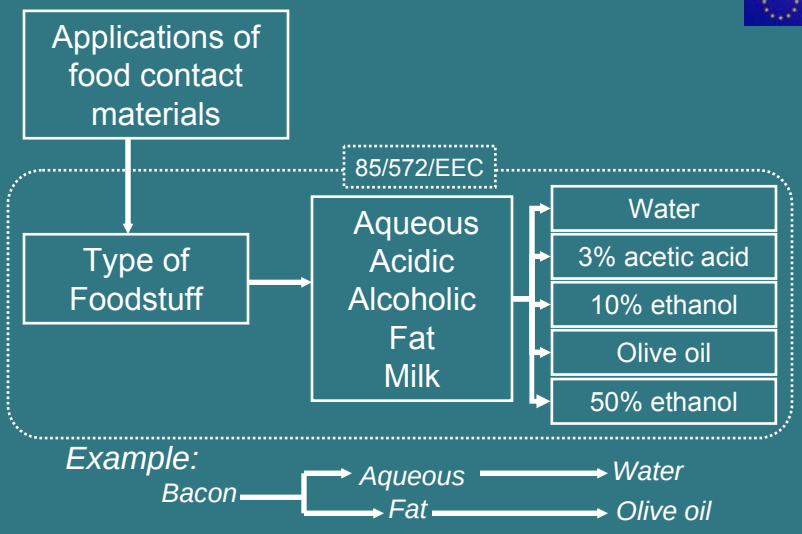
YES → Legal self determination or seek FDA clearance

Analytical testing

Choose for a residual amount (QM) or specific migration (SM)

- Demonstrate QM complies
- Obtain application of material
  - simulants
- Define test conditions
  - contact time
  - contact temperature
- Demonstrate SM complies

Selection of test simulants



Selection of test time & temperature

82/711/EEC and amendments

Contact time	*Test time*
< 5min	Actual use
5min-0.5h	0.5h
0.5h-1h	1h
1h-2h	2h
2h-4h	4h
4h-24h	24h
>24h	10d

Contact temp	Test temp
<5°C	5°C
5°C-20°C	20°C
20°C-40°C	40°C
40°C-70°C	70°C
70°C-100°C	100°C
100°C-121°C	121°C
121°C-130°C	130°C
130°C-150°C	150°C
>150°C	175°C

Example: Storage for 3 months at room temperature:
Test conditions: 10 days at 40°C

Selection of test simulants, test time & temperature

	10% ethanol	50% ethanol	Food oil	50%/95% ethanol
>100°C	121°C@2h +1d, 3d, 10d @40°C	71°C@2h +1d, 3d, 10d @40°C	121°C@2h +1d, 3d, 10d @40°C	121°C@2h +1d, 3d, 10d @40°C
Up to 100°C	100°C@2h +1d, 3d, 10d @40°C	71°C@2h +1d, 3d, 10d @40°C	100°C@2h +1d, 3d, 10d @40°C	100°C@2h +1d, 3d, 10d @40°C
Hot fill above 66°C	66°C @ 30min, cool to 40°C+1d, 3d, 10d @40°C	66°C @ 30min, cool to 40°C+1d, 3d, 10d @40°C	66°C @ 30min, cool to 40°C+1d, 3d, 10d @40°C	66°C @ 30min, cool to 40°C+1d, 3d, 10d @40°C
etc	etc	etc	etc	etc

Generic conditions!!!! Many exceptions do exist!!!!

Migration cell

Important for multilayers: single side contact

Determination of SM & QM

Sample

Bring into contact with simulant

Determine SM using

Extraction

Determine QM using

or other analytical equipment

QM = residual content
SM = specific migration

Conclusions

- EU directives and regulations applies to all EU member states
- Member states of the EU can have additional legislation
- FDA compliance ≠ EU compliance (and *visa versa*)
- EuPIA guidelines and Council of Europe resolutions have no legal status, but can be used as guidance
- The safe use of UV initiators can be demonstrated, but complicated
- A combination of chemical, toxicological, analytical and legislative expertise needed to come to justified decision!!!

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Thank you!

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