AGENCE FRANÇAISE
DE SÉCURITÉ SANITAIRE
DES ALIMENTS

LA DIRECTRICE GENERALE

**Afssa – Mandate n° 2004-SA-0209**

Maisons-Alfort, 6 February 06

# OPINION *

## of the French Food Safety Agency (Afssa) on the constitution of health risk assessment dossiers related to the use of plastic materials treated by ionising radiation and intended for contact with foodstuffs:

## Guidelines

Afssa's assessment of registrations requesting authorisation of use of irradiated plastic materials intended for contact with foodstuffs demonstrated that certain registrations did not contain all the elements required for assessment. As a result, Afssa has been prompted, through self-tasking, to specify the information that needs to be provided by the petitioner.

After consultation with the specialist expert committee "Food Contact Materials", Afssa is updating the recommendations of 31 May 2001 and issuing the following guidelines for constituting dossiers requesting authorisation of use of plastic materials treated by ionising radiation and intended for contact with foodstuffs:

Afssa considers that an authorisation request concerning irradiated materials should contain the information described in this opinion:

REGULATORY FRAMEWORK

*All regulatory references are those in force at the time of the opinion's publication. The authorisation request shall refer to the most recent regulations which may be verified by office C2 of the DGCCRF [1].*

**Any disparity in relation to the information required must be justified scientifically, for example by including exposure data.**

FORMAL FRAMEWORK

*1/ An electronic version of the overview containing the tables of points 4.1, 4.4, 4.5 and 5.2 shall be submitted along with the authorisation request. The request must be in Word format, but the annexes may be in other computer formats.*

*2/ The dossier shall be drafted in French on the basis of the guidelines. The test and study reports and certificates relative to monomers and additives shall be submitted in French or, failing that, English.*

*3/ On each page of the report and each dossier element, the trade and/or chemical name of the material in question in the authorisation request shall be clearly stated.*

*4/ Assessment concerns a material of composition, of ionising treatment and well defined conditions for use of the finished object. Any change in these parameters or parameters likely to influence the risk assessment shall be dealt with in a new assessment request. The dossier of this request may be based on the initial dossier with identification of modifications. Inertia of the new material must be ensured (cf. 5.).*

* Cancels and replaces the recommendations of 31 May 2001.

[1] Office C2 of the General Directorate for Fair Trading, Consumer Affairs and Fraud Control – Ministry for the Economy, Finance and Industry.

**Preamble,**

Specify:

- the subject of the request, name of the irradiated material and maximum conditions for use (food intended to be packaged, contact temperatures and timeframes),
- the type of packaging (thermal shrink packaging, vacuum cooking, *etc.*).

## 1. Description and certificates of periodic verifications of the installation

Each certificate should state the name of the company conducting the ionising radiation and of the site where this took place. The periodicity of the verifications must be specified.

## 2. Information on the type, source, dose and dosimetry of ionising radiation applied

## 3. Technical justifications for the treatment

## 4. Material composition before treatment

All the additives and monomers making up the material must be authorised.
A material may comprise several layers, each made up of one or more polymers and additives. Each polymer is made up of monomer(s) and possibly additives.

### 4.1 General description of the material: polymers and layers (in the event of a multilayer)

| No. of layers | Trade name of polymers & other additives making up the layer | | Chemical name of polymers & other additives making up the layer | Thickness (µm) | % of mass |
|---|---|---|---|---|---|
| **1** | | | | 12 | 25 (% mass of material) |
| Polymers | 1a | Polymer a | Low density polyethylene | | 50 (% mass of layer 1) |
| | 1b | Polymer b | Ethylene copolymer/vinyl acetate | | 10 |
| | 1c | Polymer c | X | | 20 |
| Other additives added | 1d | Additive d | X | | 10 |
| | 1e | Additive e | X | | 10 |
| **2** | | | | X | (75) |
| Polymers | 2a | X | X | | X |
| | 2b | X | X | | X |
| Other additives added | 2c | X | X | | X |
| | 2d | X | X | | X |
| ***etc.*** | | | | | |
| TOTAL | | | | Material thickness | (/100% of material) |

X: box to be filled in

***Table 4.1: example of description of a material's layers***

For following up a dossier, the chemical name of the polymer and corresponding number (1a, 1b, *etc.*) will be used.

### 4.2 Description of the material manufacturing method

### 4.3 Properties of the material subject to treatment, particularly its thickness and weight

### 4.4 Type of monomer(s), with their most recent regulatory references (France and European Union), CAS and PM numbers[2].

Restrictions and/or specifications (Maximum permitted quantity of the **residual** substance in the material (QM), specific migration limits (SML), *etc.*) must be stated on suppliers' certificates (attach these certificates in the annexes).

| No. of layers * | Name of polymer | Monomers (trade and chemical name) | CAS No. | PM No. | Restrictions including QM(S), SML ** | | | Regulatory references |
|---|---|---|---|---|---|---|---|---|
| | | | | | QM(S) | SML | ** | |
| **1** | | | | | | | | |
| 1a | *e.g.*: Low density polyethylene | Monomer 1 | | | | | | |
| | | Monomer 2 | | | | | | |
| 1b | | | | | | | | |
| | | | | | | | | |
| *etc.* | | | | | | | | |
| **2** | | | | | | | | |
| 2a | | | | | | | | |
| Etc. | | | | | | | | |
| ***etc.*** | | | | | | | | |

* number attributed in Table 4.1 (1a, 1b, *etc.*)

** specify the possible restrictions for use (for example not for contact with fatty foods, SML, *etc.*); QM in mg/kg of material, QMS in mg/6dm² of material, SML in mg/kg of simulator or food

***Table 4.4: example of description of monomers of a material intended for ionising radiation***

### 4.5 Type of additive(s), with their most recent regulatory references (France and European Union), CAS and PM numbers[2]

The maximum additive contents must be specified for each:

- Additive of each polymer of each layer (if necessary, the information may be sent confidentially to the DGCCRF),
- Other additives (for example, added or used by the petitioner).

Restrictions and/or specifications (SML, *etc.*) must be specified.

Documents specifying the food composition and/or conformity must be attached in the annexes.

| No. of layers * | Chemical name of polymer | | Additives (trade name and chemical name) | CAS No. | PM No. | Concentration used (mg/kg polymer) | Restrictions incl. SML (mg/kg) ** | Regulatory reference |
|---|---|---|---|---|---|---|---|---|
| **1** | | | | | | | | |
| Additives of polymers | 1a | Polyethylene | Antioxydant 1 | | | | | |
| | | | Antioxydant 2 | | | | | |
| | | | Lubricant | | | | | |

[2] The PM/ref. No. is used in European directives and the synoptic document of the DG Sanco (General Directorate for Health and Consumer Protection).

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| of layer 1 | | | *etc.* | | | | | |
| | 1b | | | | | | | |
| | | | | | | | | |
| | | | | | | | | |
| | | | | | | | | |
| | | *etc.* | | | | | | |
| Other additives added in layer 1 | 1d | | Lubricant | | | | | |
| | 1e | | *etc.* | | | | | |
| **2** | | | | | | | | |
| *etc.* | | | | | | | | |

***Table 4.5: example of description of additives of a material intended for ionising radiation***

## 5. Study of the inertia of the material after treatment

**For all** elements in this chapter, **detailed study reports must be sent** with:

- the protocols,
- the elements of validation of the analytical methods:
  - chemical: detection and quantification limits, specifications, calibration data,
  - sensory: statistical signification of results,
- the chromatograms or possible spectra,
- the references to the standards used.

The migration conditions must comply with the conditions provided for by the most recent regulations in force (Directive 97/48/EC and 85/572/EC [3] or any other more recent directive) respectively laying down the basic rules necessary for checking the migration of material and fixing the list of simulants to use.

### 5.1 Global migration

The simulators must correspond to the foods listed in the preamble and this correspondence must be made explicit.

### 5.2 Specific migration of monomers and additives

Demonstration of the material's conformity to the restrictions and specifications specified in the positive lists of the most recent regulation (2002/72/EC[3]), particularly the conformity of substances mentioned in 4.4 and 4.5 to the specific migration limits.

This conformity may be checked by calculation where necessary.
Hypothesis for calculating a total migration:

- 6 dm² of each layer are in contact with 1 kg of food,

[3] The authorisation request shall refer to the most recent regulations which may be verified by office C2 of the DGCCRF.

- the average density of the material (or polymer or layer) is considered to be equal to 1 ($dm^3$/kg), (real value between 0.94 and 1.5),
- the whole of the additive/monomer migrates.

Should the regulatory limits be exceeded with determination on the basis of the total migration hypothesis, the petitioner may use a scientifically recognised prediction model or conduct experimental tests.

Experimental migration studies may be conducted in the substitution conditions stipulated by Directive 97/48/EEC. Therefore, when specific migration in olive oil cannot be determined, migration studies in iso-octane **and** ethanol at 95% shall be performed.

| No. of layers * and thickness | Mass (kg) of layer (d=1) in contact 1 kg food | Polymers and other additives added to layer | | % in mass of polymers and additives per layer | Mass of polymers and additives in the layer (kg) | Substances (additives and monomers with SML) | Initial concentration of additives and residual conc. of monomers (mg/kg) | Measured or calculated migration (mg/kg food) *** | Restrictions incl. SML (mg/kg) * |
|---|---|---|---|---|---|---|---|---|---|
| **1** | | | | | | | | | |
| $12 .10^{-5}$ | 6 ($dm^2$) * $12.10^{-5}$ (dm) = $72.10^{-5}$ | Polymers (a,b,c) of layer 1 | 1a | 50 | $72.10^{-5} * 0.5 = 36.10^{-5}$ | Monomer 1 | | | |
| | | | | | | Antioxydant 1 | 1500 | 1500 * $36.10^{-5}$ = 0.54 | 30 |
| | | | | | | *etc.* | | | |
| | | | 1b | 10 | $72.10^{-5} * 0.1$ | | | | |
| | | | | | | | | | |
| | | | 1c | 20 | | *etc.* | | | |
| | | Other additives (d,e) added in layer 1 | 1d | 10 | | Lubricant | | | |
| | | | 1e | 10 | | *etc.* | | | |
| **2** | | | | | | | | | |
| *etc.* | | | | | | | | | |

*** specify whether measured or calculated migration applies

***Table 5.2: example of table grouping together specific migration data of monomers and additives subject to a restriction***

### 5.3 Possible products of degradation generated by the ionising radiation treatment

**5.3.1** **The formation of newly formed products must be reported**, for example by comparing analyses of the material (see 5.3.3) before and after treatment. The petitioner may not need to carry out these studies if he can produce scientific studies (for example literature publications) performed on similar materials.

**5.3.2** **If a newly formed substance (not specified in 4.4 and 4.5) is detected**, it must be identified (see 5.3.3) then researched if it has been assessed and/or authorised.

- If it is authorised (France, Europe) without SML, quote the references and provide the *ad hoc* documents,
- If it is authorised with a SML, quote the references and provide the *ad hoc* documents and prove, through an extraction study (similar calculation to those described in point 5.2) or a specific migration study, that this SML is compliant,
- If it has not been assessed, the petitioner shall provide a specific migration study (see 5.3.4) and toxicological information about the newly formed substance as indicated in paragraph 5.3.5.

**5.3.3** **Extraction, Identification and quantification in the material**

In the event of new products forming, the following procedure must be applied to volatile, semi-volatile and non-volatile products:

1. **Extraction**: the search for newly formed products shall be conducted using suitable extraction techniques.
   - Semi- and non-volatile products
     The use of suitable extraction solvents, for example dichloromethane for polyolefins and poly(ethylene terephtalate) is recommended.
   - Volatile products
     Extraction techniques by dynamic headspace gas chromatography coupled with universal detectors (for example mass spectrometry [MS], flame ionisation detector [FID]) are recommended.
2. **Identification**: all the necessary means should be implemented.
3. **Quantification**: the known newly formed products must be measured using suitable techniques.
   Should identification of the product be uncertain, all the available information must be supplied (chemical function, molecular mass, probability of identification).
   Structural similarities may be used for quantification where necessary.

**5.3.4** **Migration in simulators**

Migration may be estimated or measured as specified in point 5.2.

**5.3.5** **Toxicological information**

The type of toxicological dossier to be submitted for assessing the substance depends on the theoretical exposure level (NET).

In the absence of a relevant assessment of the real exposure level of the substance to consumers, this level is calculated on the basis of specific migrations of the substance by using the following formula:

$NET = 0.8 \times [(M_A + M_B + M_C) / 3] + 0.2 \times M_D$

*($M_A$, $M_B$, $M_C$, $M_D$: specific migration of the pigment in water, alcohol, acid and fat simulating liquids respectively).*

If one of the water simulators is not used, the formula must be adapted. Accordingly, in the event that only tests B and C are practised, the calculation becomes: $NET = 0.8 \times [(M_B + M_C) / 2] + 0.2 \times M_D$.

**NET less than 0.5 µg/person/day:**

When the theoretical exposure level is less than 0.5 µg/person/day, the substances for which elements enabling the characterisation of the absence of genotoxic potential may be introduced may not be necessary in the genotoxicity tests. The petitioner must develop his arguments in a specific dossier. In view of the scientific justifications given, the standard dossier may nevertheless be required.

**NET between 0.5 and 50 µg/person/day:**

- 3 genotoxicity tests *in vitro*[4] :
  - a gene mutation test on bacteria,
  - a gene mutation test on mammal cell culture,
  - a chromosomal abnormality test on mammal cell culture.

**NET between 50 and 5000 µg/person/day:**

- 3 genotoxicity tests *in vitro* :
  - a gene mutation test on bacteria,
  - a gene mutation test on mammal cell culture,
  - a chromosomal abnormality test on mammal cell culture;
- a subchronic oral toxicity study, with reversibility (such as a 90 day study in rats);
- data showing the absence of accumulation potential in humans, such as the octanol/water partition coefficient.

**NET higher than 5000 µg/person/day:**

- 3 genotoxicity tests *in vitro (see above)*;
- a subchronic oral toxicity study, with reversibility (such as a 90 day study in rats);
- a study on absorption, distribution, metabolism and excretion;
- studies on the reproduction of a species and toxicity on the development of normally two species;
- a long-term toxicity/cancerogenesis study, normally on two species;
- If data exists on sensitisation, eye and skin irritation or respiratory toxicity, their results must be included along with any comments made on the health of people exposed to the molecule.

In all cases, other studies may be necessary if the data indicates effects on neurotoxicity, immunotoxicity, endocrinal effects or peroxysomal proliferation.

Irrespective of the theoretical exposure level value, **when the result of a genotoxicity test is positive or ambiguous**, other genotoxicity tests including *in vivo* may be required to reveal the genotoxic potential of the substance. The supplementary test choice is made on a case-by-case basis, according to the results obtained and other information available.

Toxicological tests must be carried out on the basis of European Community methods, OECD guidelines or equivalent methods, in facilities accredited with 'Good laboratory practices' or, failing this, in compliance with a quality assurance system.

[4] Discussions on the number and type of genotoxicity tests were being held at the time of publication of these guidelines. They will be updated if additional information is likely to modify them.

### 5.4 Organoleptic effects

Tests of the possible transfers of odour to foodstuffs will be conducted in accordance with the standards in force (for example standard NF V09/009).

Any odours detected following ionising radiation treatment shall be described by specifying if the origin of these odours is known (for example, odour of acetic acid after vinyl polyacetate ionising radiation, etc.).

## 6. Other information

The dossier may also contain any other specific information concerning the request and which is useful for the health assessment.

**Pascale BRIAND**

27-31, avenue
du Général Leclerc
BP 19, 94701
Maisons-Alfort cedex
Tel 01 49 77 13 50
Fax 01 49 77 26 13
www.afssa.fr

REPUBLIQUE
FRANÇAISE