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DE SÉCURITÉ SANITAIRE
DES ALIMENTS

AFSSA – Request no. 2008-SA-0270
Related requests nos. 2007-SA-0224 and 2007-SA-0385

Maisons-Alfort, 13 July 2009

THE DIRECTOR GENERAL

Scientific and Technical Support from the French Food Safety Agency regarding the entry into force of Regulation (EC) no. 396/2005 on MRLs of pesticides in foodstuffs

Context of the request:

In a letter dated 8 September 2008, the Directorate General for Health submitted a request to the French Food Safety Agency (AFSSA) for scientific and technical support related to the entry into force of Regulation (EC) no. 396/2005 on MRLs of pesticides in foodstuffs in order to:

- compare the applicable MRLs in European regulations with limits previously applied in France,
- describe potential consequences for consumers in terms of chronic risk related to dietary exposure.

Context:

Regulation (EC) no. 396/2005 on maximum residue levels of pesticides in or on food and feed of plant and animal origin entered into force on 1 September 2008.

This regulation concerns residues whose presence in food results from the current or former use of an active substance in plant protection products, in veterinary medicine or as a biocide.

It defines Maximum Residue Levels (MRLs) for 380 specific foods and groups of foods, the nomenclature of which is presented in Regulation (EC) no. 178/2006. It comprises several annexes:

- annexe II defines MRLs in the primary foodstuffs for substances that were already the subject of harmonised European MRLs,
- annexe III includes:
  - annexe IIIa, which defines MRLs for the other substances, whether or not they are listed in annexe I of Directive 91/414/EEC, which have not already been the subject of harmonised European MRLs. In accordance with article 12 of the regulation, these MRLs must be reviewed in the year following the decision to include or not include the active substance in annexe I of Directive 91/414/EEC,
  - annexe IIIb, which defines MRLs for the substances in annexe II but in foodstuffs that were hitherto not covered by European MRLs,
- annexe IV gives a list of substances for which an MRL does not need to be set,
- annexe V defines the default limits to be used when substances have no MRL and the limit of 0.01 mg/kg cannot be applied.

The MRLs in these annexes are reviewed every ten years during the ten-year reappraisal of active substances.

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The annexes of Regulation (EC) no. 396/2005 are defined and updated regularly with the publication of new regulations. To date, regulations (EC) no. 149/2008 and 839/2008 list 52 compounds for which an MRL does not need to be set (annexe IV). Annexes II and III also set 152,330 MRLs for a total of 443 compounds (206 not listed in annexe I of Directive 91/414/EEC and 237 listed or under assessment)[1].

The process to harmonise MRLs that had not yet been harmonised was undertaken by a national expert group under the aegis of the Directorate General for Health and Consumer Affairs (DG Sanco). It was validated by the European Food Safety Authority (EFSA).

The process first consisted in:

- making an inventory of existing MRLs applied by the 27 Member States,
- selecting, for each combination [pesticide x food product], the MRL covering the most critical application authorised in the European Union (EU),
- ensuring that this limit protects European consumers, in terms of both chronic and acute exposure.

This stage, which involved 62,068 MRLs representing 236 active substances (71 not listed and 165 under assessment), was the subject of an EFSA opinion published on 15 March 2007 (EFSA, 2007). EFSA concluded that 110 active substances needed to be reconsidered regarding the risk of chronic exposure, as well as some 2,570 MRLs that were problematic regarding the risk of acute exposure.

The assessment was then refined during meetings of the expert group, on the basis of information on national marketing authorisations and the results of field trials. EFSA took part in these meetings but did not publish an opinion of this stage.

The MRLs that had already been defined for Europe were adopted without undergoing a new assessment. It was stipulated that EFSA would henceforth validate them using a similar process, in accordance with article 12 of Regulation (EC) no. 396/2005. In this context, on 29 July 2008, AFSSA was requested to prepare the necessary information for this assessment.

The Agency had also received two other requests, on 23 July and 13 November 2007, to validate the model developed by EFSA to verify that the MRLs were such that they would protect French consumers, anticipating its replacement of national models for setting any new MRLs falling under Regulation (EC) no. 396/2005.

AFSSA issued a first statement on 21 March 2008 in favour of the principle of adopting a common European model. AFSSA first insisted on the importance of having a dynamic and interactive system between EFSA and national structures, in order to continually upgrade the European predictive model by integrating new knowledge and technologies to assess population exposure. In particular, for the prediction of chronic exposure, it suggested considering intake related to drinking water and “baby food”, even though they were the subject of separate regulations on “pesticide” MRLs. Moreover, it sent EFSA an updated description of French consumption patterns to be used in the European model (AFSSA, 2008a).

This statement was focused on chronic exposure. On 5 June 2008, AFSSA issued a second statement concerning prediction of acute exposure with the European model. Since there was no national model for predicting acute exposure – the Department of plants and the environment used the British model – AFSSA suggested inserting critical data on French consumption into the European model. It also contributed to European deliberations on equations to be used for acute intake prediction (AFSSA, 2008b).

Expert assessment method:

[1] According to the 18 February 2009 updated version of the European MRL database, accessible at the following address: http://ec.europa.eu/sanco_pesticides/public/index.cfm?event=substance.selection&ch=1

The method was developed by AFSSA's Chemical exposure and quantitative risk assessment unit (DERNS) and its Residues and Consumer Safety unit (DiVE). It was presented to the scientific panel on 'Crop protection products: chemical compounds and preparations', which met on 28 and 29 May 2009.

Notations:

In the rest of this document, active substances are indicated by their name together with the superscript:

- ***** to indicate that the substance is not listed in annexe I of Directive 91/414/EEC. The residue in the food is therefore the result either of environmental contamination, of use for purposes other than plant protection, or of plant protection use outside of the European Union.

- [1] to indicate that the substance is listed in annexe I of Directive 91/414/EEC. The residue in the food is the result either of plant protection use in or outside of the European Union, of environmental contamination, or of use for purposes other than plant protection.

If there is no superscript, this means that the compound is under assessment.

Discussion:

1. Comparison of MRLs

The yardsticks below were defined on the basis of information contained in the MRL databases of the French Ministry of Agriculture and the European Commission[2], cross-checked with texts published in the Official Journals of the French Republic and the European Union.

1.1 Substances with MRLs

Table 1 describes the typology of substances according to legal support for their MRLs. The substances are listed in detail in annexe 1.

Table 1: Typology of substances according to legislation specifying their MRLs

Typology	Number
Substances listed in annexes II and III of Regulation (EC) no. 396/2005	443
Regulated substances in Europe[a]	238
Regulated substances in France	129
Non-regulated substances in France	76
Substances not listed in annexes II and III of Regulation (EC) no. 396/2005	37
Substances with synergistic or plant protection properties or additives	*8*
Active "pesticide" substances regulated in Europe[a]	*3*
Active "pesticide" substances regulated in France	*26*

[a] *: until Regulation (EC) no. 396/2005 entered into force, European MRLs were published in directives transposed into French law.*

The table shows that 37 substances with MRLs were not listed anew in annexes II and III of Regulation (EC) no. 396/2005. In particular, as eight of them did not correspond to "pesticides" in the sense attributed by Directive 91/414/EEC, they were not harmonised. For the other 29

[2] Note that the administrators of the databases used accept no liability for any errors that these databases may contain.

compounds, article 18(1)(b) of Regulation (EC) no. 396/2005 applies: the "pesticide" residue level must not exceed 0.01 mg/kg regardless of the commodity. Likewise, Regulation (EC) no. 396/2005 defined MRLs for 76 active substances that hitherto had no MRL in France. The European MRLs of 238 compounds were listed anew 'as is' in annexe II.

The detailed comparison is therefore relevant only for active "pesticide" substances which have formerly been regulated in France, i.e. 155 compounds (129 listed in annexes II and III of Regulation (EC) no. 396/2005 and 26 to which article 18(1)(b) applies).

1.2 Comparison difficulties

The official list of foodstuffs to which MRLs apply has changed over time. There were 223 foodstuffs or groups of foodstuffs for which the limits previously applied in France, whereas Regulation (EC) no. 396/2005 now lists 380 foodstuffs or groups of foodstuffs. In general, the trend has been to include a larger number of individual foodstuffs. For example, in the past, only one MRL was set for all spices, whereas today, potentially 43 different MRLs are defined for spices. But some foodstuffs have also been grouped together over time: for example, late potatoes are no longer separated from early potatoes, and sunflower seeds with shells are no longer separated from sunflower seeds without shells.

Regulation (EC) no. 396/2005 also defined the concept of default limits, which did not exist previously and which caused the number of MRLs to rise significantly. Out of the 152,330 MRLs currently in force in Europe, 86.5% of them correspond either to the default limit of 0.01 mg/kg or, when analytical methods cannot reach this level, to another limit of quantification (LOQ).

These regulatory developments made it particularly difficult to compare the former French MRLs with the new MRLs.

1.3 Comparison

The comparison concerned the 155 compounds (92 not listed in annexe I of Directive 91/414/EEC and 63 listed or under assessment) that had strictly national MRLs before Regulation (EC) no. 396/2005 entered into force. For comparison purposes, some of these MRLs were translated into the new European nomenclature, which brought us to an equivalent of 4,240 MRLs defined for 316 foodstuffs or groups of foodstuffs. With the exception of Chlordecone*, these MRLs apply only to foods of plant origin.

According to Table 2, 34.1% of the European MRLs that have been in force since 1 September 2008 are strictly lower than the former French MRLs. As a result, national authorisations have been withdrawn or instructions for use have been modified for 12 active substances. The European MRLs are strictly higher than the former French MRLs in 29.1% of cases and are equivalent in 36.9% of cases.

Only one substance has new MRLs that are 100 to 500 times higher than the former ones. This substance is Propamocarb[1] in cabbage, with MRLs (N=4) that rose from 0.05 to 10 mg/kg. These MRLs are to be reviewed this year in accordance with article 12(2) of Regulation (EC) no. 396/2005.

There are 32 substances (around 21%) with new MRLs that are 10 to 100 times higher than the old ones. For 30 of them, only one to six MRLs increased to this extent. Trifluralin* has 17 MRLs that are more than 10 times higher than the former ones and Pyridaben* has 15. As these latter two compounds have been resubmitted for inclusion in annexe I of Directive 91/414/EEC, all of their MRLs will be reviewed after a definitive decision is made, which is expected to occur towards the end of 2010.

Table 2: Comparison of MRLs

Situation	Number of MRLs (%)	Number of substances (%)
$MRL_{eu} < MRL_{fr}$	1445 (34.1%)	65 (42%)
$MRL_{eu} = MRL_{fr}$	1563 (36.9%)	82 (53%)
$MRL_{eu} > MRL_{fr}$ of which:	1232 (29.1%)	97 (63%)
Up to 5 times	*882 (20.8%)*	*83 (54%)*
More than 5 times and up to 10 times	*243 (5.7%)*	*40 (26%)*
More than 10 times and up to 100 times	*102 (2.4%)*	*32 (21%)*
More than 100 times and up to 500 times	*4 (0.1%)*	*1 (1%)*
Total	**4240**	**155**

Notations:

MRL_{fr}: French MRL or equivalent in force before 1 September 2008

MRL_{eu}: European MRL in force since 1 September 2008

Comment: since a substance generally has several MRLs, it may fall under various situations (e.g sometimes $MRL_{fr} < MRL_{eu}$ and sometimes $MRL_{fr} \geq MRL_{eu}$).

Eighty-six types of foodstuffs were affected by this increase, and in 77 of them the MRL rose only one to two times. It increased 6 times for barley, 5 times for dry peas and oats, 4 times for wheat and shelled peas, 3 times for colza seeds and buckwheat, and twice for cauliflower and apples.

This strict comparison of MRLs does not however allow us to draw a conclusion as to whether the level of protection associated with MRLs has increased or decreased. Such a conclusion requires a risk characterisation related to chronic and acute exposure of the population.

2. Level of protection against chronic risk associated with MRLs

2.1 General considerations concerning the methods for setting MRLs

When MRLs are set, the level of protection associated with the MRLs is estimated using models that predict consumer exposure.

The model for predicting the chronic exposure of French consumers that was previously used in France was based on the calculation of theoretical total intake. This factored in mean intakes of all food groups as well as the two food groups with the highest 97.5th percentile intakes. The model considered three diets: 'general population', 'toddler' and 'infant'. The consumption data for the 'general population' diet came from the 1997 Sécodip purchasing panel survey, which was conducted not among individuals but in French households. They were adjusted to account for the French population's self-production habits and consumption outside of the home (Nichèle *et al.,* 2005). The consumption data for the 'infant' and 'toddler' diets were taken from the 1997 Alliance 7 survey of infants and young children under the age of 3 on the basis of 3-day consumption records (Boggio *et al.*, 1999).

The European model has been used in France since it was validated (AFSSA, 2008a). This model is based on the Theoretical Maximum Daily Intake (TMDI) (EFSA, 2007, WHO, 1997) calculated simultaneously for 27 average diets from 13 Member States, 5 of which correspond to the WHO/FAO European diets (4 GEMS/Food Cluster Diets and 1 Regional Diet). It distinguishes between various age brackets and specific population groups: the general population (10/27), adults (6/27), children (9/27), high-level consumers (1/27) and vegetarians (1/27). With the exception of the Swedish 'high-level consumer' diet, which corresponds to the 90th consumption percentile, the other diets correspond to average or equivalent intakes. The French population is taken into consideration through three diets: 'general population', 'toddler' and 'infant', which correspond to the diets previously described in the national model. A revised European model, including, among other things, more recent data on French consumption supplied following the validation of this model, is pending.

In both of these models, the first stage involves estimating consumed foods that are systematically contaminated at the MRL. When the Acceptable Daily Intake[3] (ADI) is theoretically exceeded, the estimated exposure level is then refined, using the Supervised Trials Median Residue (STMR).

As a result, the models used to assess MRL protection level evolve over time. This is true both for their principle and for the consumption data used to describe diets. In order to avoid this methodological bias, a similar approach, based on the calculation of the TMDI using data from the individual and national study of food consumption (INCA), was used to describe trends relating to the protection level associated with MRLs.

As the median residue level for each crop was not available for all substances, and particularly for those under assessment and those that are not used in France, only the theoretical approach based on MRLs was applied in the framework of this request. As a result, the cases associated with ADI overrun should not be considered as at-risk situations for consumers, but as indicators enabling a comparison of two situations (before and after harmonisation of MRLs) and a classification of substances.

The entry into force of Regulation (EC) no. 396/2005 entailed not only the harmonisation of some MRLs that were hitherto national, but also a change in the official nomenclature of foodstuffs, and the systematic application of a default limit. Consequently, the protection level associated with MRLs may have been modified, both for substances that were harmonised for the first time, and for substances that had already been harmonised. Situations before and after harmonisation were therefore compared for all of the substances (443) with MRLs.

2.2 Calculation of TMDIs

- ✓ Principle

TMDIs were calculated for individuals and were used to obtain, in the population under study, a distribution of theoretical maximum daily exposure. The mean and 95th percentile exposure levels were compared to the ADI. The probability of exceeding the ADI was also estimated as the percentage of individuals likely to have an intake exceeding the ADI. This method made it possible to identify those compounds that potentially present a risk, i.e. compounds for which total theoretical maximum intakes exceed the ADI.

TMDIs were calculated in two ways:

- considering all foods consumed at the maximum residue level,

[3] ADI: The Acceptable Daily Intake (ADI) of a chemical product is the estimated quantity of an active substance in food or drinking water that can be ingested every day over a lifetime, without an appreciable consumer health risk based on all known factors at the time of assessment. It is expressed in milligrams of chemical substance per kilogram body weight (WHO, 1997).

- considering a zero residue level for consumed foods with an MRL that corresponded to the default limit of 0.01 mg/kg or a limit of quantification, and to the MRL for other consumed foods.

The TMDIs obtained using this method were compared to the TMDIs updated in late 2007, i.e. before Regulation (EC) no. 396/2005 entered into force. The TMDIs obtained with the new and old MRLs were compared overall and for each substance. The differences were interpreted with regard to the ADI used, the greater number of foods with MRLs and changes in MRLs.

✓ Population under study

This analysis was conducted in the general population of mainland France's, whose consumption habits were described in the INCA1 survey (Volatier, 2000). The survey was undertaken in France from August 1998 to June 1999 – so that seasonal effects were taken into consideration – among 3,003 children and adults who were representative of the French population. Stratification was used to ensure national representativeness (age, sex, individual socio-professional category and household size). The calculations concerned only non-under-reporters, with 1,474 adults over the age of 15 and 1,018 children between the ages of 3 and 14.

This survey referred to the individuals' consumption records to determine their dietary intakes. The 895 foods as consumed in the INCA survey were broken down into 153 "raw agricultural commodities" for which "pesticide" MRLs were set. This was done by using a table containing 402 recipes that took into account the wide variety of industrial processes and domestic food preparation habits.

Calculations were performed separately for adults over the age of 15 and children between the ages of 3 and 14 and over a lifetime[4].

✓ Maximum Residue Levels (MRLs)

The MRLs defined in Regulation (EC) no. 396/2005 were combined with water quality limits, as defined by Directive 1998/83/EC on the quality of water intended for human consumption.

The MRLs in wine grapes were corrected by an estimated grape-to-wine transfer level, which was 30% on average, according to the DGAL's work (Cugier and Bruchet, 2005).

When the compound is lipophilic[5], MRLs in foods of animal origin vary according to the food's fat content. The MRLs were consequently corrected to reflect the average fat content of consumed foods, in accordance with the instructions set forth in Regulation (EC) no. 178/2006.

✓ Acceptable Daily Intake (ADI)

ADIs were taken from a compilation put together by the European Food Safety Authority (EFSA) which was combined, when needed, with the Toxicological Reference Values (TRVs) proposed by other risk assessment bodies. In situations where several reference values were available for a same active substance, the order of priority when selecting the TRV was as follows:

- European level (EFSA, European Commission),
- international level (JMPR[6], JECFA[7]),

[4] The lifetime calculation consisted of a weighted average of the mean 'child' and 'adult' TMDIs according to the number of years in each age bracket (15 years for children and 60 years for adults).
[5] The criterion used is the indication of an "F" (Fat soluble) in the European Commission's database.
[6] Joint FAO/WHO Meeting on Pesticide Residues
[7] Joint Expert Committee on Food Additives

- national level (Member States, values proposed in the draft monographs of the rapporteur Member State in the framework of Directive 91/414/EEC, American and Australian authorities).

It should be noted that for some substances, this order of priority was not followed, particularly when European and international values were set well before a national value. For example, for Propargite*, an ADI of 0.007 mg/kg b.w/day proposed in a 2007 draft assessment report was used instead of the ADI of 0.01 mg/kg b.w./day proposed by the JMPR in 1999.

Moreover, when the MRL was defined for a group of compounds, if there was no ADI for the corresponding group of compounds, the ADI used for risk characterisation corresponded to the lowest ADI in the group, as shown in Table 3.

Table 3: ADIs used for groups of compounds

Group
Clethodim and Sethoxydim: ADI of Sethoxydim
Group of Dithiocarbamates: ADI of Ziram
Dimethoate and Omethoate: ADI of Omethoate
Fenvalerate and Esfenvalerate RR&SS: ADI of Fenvalerate
Fenvalerate and Esfenvalerate RS&SR: ADI of Fenvalerate
MCPA and MCPB: ADI of MCPB
Thiodicarb and Methomyl: ADI of Methomyl
Triadimenol and Triadimefon: ADI of Triadimefon

Furthermore, it should be emphasised that the TRV used for substances not included in annexe I of Directive 91/414/EEC is potentially subject to greater uncertainty than that of the substances included in annexe I, either because these substances are old and have not undergone a risk assessment according to the current guidelines, or because toxicity uncertainties identified during the assessment led to the substance not being included in annexe I of Directive 91/414/EEC.

All of the values used in the framework of this scientific and technical support are presented in annexe 2. TMDIs were calculated only for 424 substances out of the 443 that have European MRLs. It was not possible to determine an ADI for 19 substances with European MRLs for the following reasons:

- ADI not necessary or not proposed following the assessment of 8 substances,
- ADI not established because of inadequate data for 3 substances (none of which are included in annexe I of Directive 91/414/EEC),
- information not found for 9 substances (none of which are included in annexe I of Directive 91/414/EEC).

2.3 Results

✓ TMDIs

Adult, child and lifetime TMDIs were calculated. The detailed results by substance are presented in annexe 3. Table 5 presents a summary of the results for each population sub-group according to substance status.

Table 5: TMDI results by population sub-group

Status of the active substance and *presence in plant protection preparations in France*	N	Child			Adult			Lifetime
		$TMDI_{av}$ > ADI *(%)*	$TMDI_{95}$ > ADI *(%)*	Pc > 0 *(%)*	$TMDI_{av}$ > ADI *(%)*	$TMDI_{95}$ > ADI *(%)*	Pc > 0 *(%)*	$TMDI_{av}$ > ADI *(%)*
Annexe I	192	14 *(7.3)*	28 *(14.6)*	54 *(28.1)*	4 *(2.1)*	15 *(7.8)*	33 *(17.2)*	5 *(2.6)*
Present in France	*170*	*14 (8.2)*	*28 (16.5)*	*52 (30.6)*	*4 (2.4)*	*15 (8.8)*	*32 (18.8)*	*5 (2.9)*
Not present in France	*22*	*0 (0.0)*	*0 (0.0)*	*2 (9.1)*	*0 (0.0)*	*0 (0.0)*	*1 (4.5)*	*0 (0.0)*
Under assessment	47	2 *(4.3)*	7 *(14.9)*	14 *(29.8)*	2 *(4.3)*	2 *(4.3)*	8 *(17.0)*	2 *(4.3)*
Present in France	*21*	*1 (4.8)*	*5 (23.8)*	*10 (47.6)*	*1 (4.8)*	*1 (4.8)*	*6 (28.6)*	*1 (4.8)*
Not present in France	*26*	*1 (3.8)*	*2 (7.7)*	*4 (15.4)*	*1 (3.8)*	*1 (3.8)*	*2 (7.7)*	*1 (3.8)*
Not listed in annexe I	185	40 *(21.6)*	68 *(36.8)*	94 *(50.8)*	26 *(14.1)*	41 *(22.2)*	55 *(29.7)*	27 *(14.6)*
Total	**424**	**56 *(13.2)***	**103 *(24.3)***	**162 *(38.2)***	**32 *(7.5)***	**58 *(13.7)***	**96 *(22.6)***	**34 *(8.0)***

Key:
N = total number of substances
$TMDI_{av}$ > ADI (%) = number (percentage) of substances whose average TMDI is higher than the ADI,
$TMDI_{95}$ > ADI (%) = number (percentage) of substances whose 95th TMDI percentile is higher than the ADI, i.e. 5% of the population has a TMDI that exceeds the ADI,
Pc > 0 (%) = number (percentage) of substances with a non-null probability that the TMDI is greater than the ADI. This probability is estimated to be non-null if the lower boundary of the 95% confidence interval for the exceeded ADI percentage (percentage of individuals in each group with a TMDI greater than the ADI) is strictly greater than 0.

Comment: the substance's status (annexe I, under analysis, not listed in annexe I) refers to Directive 91/414/EEC.

Table 6 shows the influence of the refined calculation, which does not take into account MRLs set at the default value or at another limit of quantification and which considers the population sub-group with the highest TMDI for each substance.

If all of the various sub-groups are considered (adult, child, lifetime), a total of 57/424 (13.4%) different compounds have a $TMDI_{av}$ that exceeds the ADI.

Almost three-fourths (41/57) of these correspond to compounds not listed in annexe I of Directive 91/414/EEC, 7 of which (Fentin Acetate and Hydroxide*, Pyrazophos*, Dioxathion*, Mecarbam*, Mevinphos* and Quinalphos*) have all of their MRLs set at the LOQ. Further analysis would be necessary to lower their LOQs. When MRLs set at the LOQ or the default limit are not taken into account, the TMDI remains greater than the ADI for 22 compounds, including:

Table 6: Results of adjusted TMDIs

Status of the active substance and *presence in plant protection preparations in France*	$TMDI_{av}$ > ADI	$TMDI_{refined\ av}$ > ADI *(%)*	$TMDI_{95}$ > ADI	$TMDI_{refined\ 95}$ > ADI *(%)*	Pc > 0	Pc $_{refined}$ > 0 *(%)*
Annexe 1	14	8 *(57.1)*	28	25 *(89.3)*	54	40 *(74.1)*

Present in France	*14*	*8 (57.1)*	*28*	*25 (89.3)*	*52*	*39 (75.0)*
Not present in France	*0*	*0*	*0*	*0*	*2*	*1 (50.0)*
Under analysis	2	1 *(50.0)*	7	5 *(71.4)*	14	13 *(92.9)*
Present in France	*1*	*1 (100.0)*	*5*	*3 (60.0)*	*10*	*10 (100.0)*
Not present in France	*1*	*0 (0.0)*	*2*	*2 (100.0)*	*4*	*3 (75.0)*
Not listed in annexe I	41	22 *(53.7)*	70	45 *(64.3)*	94	60 *(63.8)*
Total	**57**	**31 *(54.4)***	**105**	**75 *(71.4)***	**162**	**113 *(69.8)***

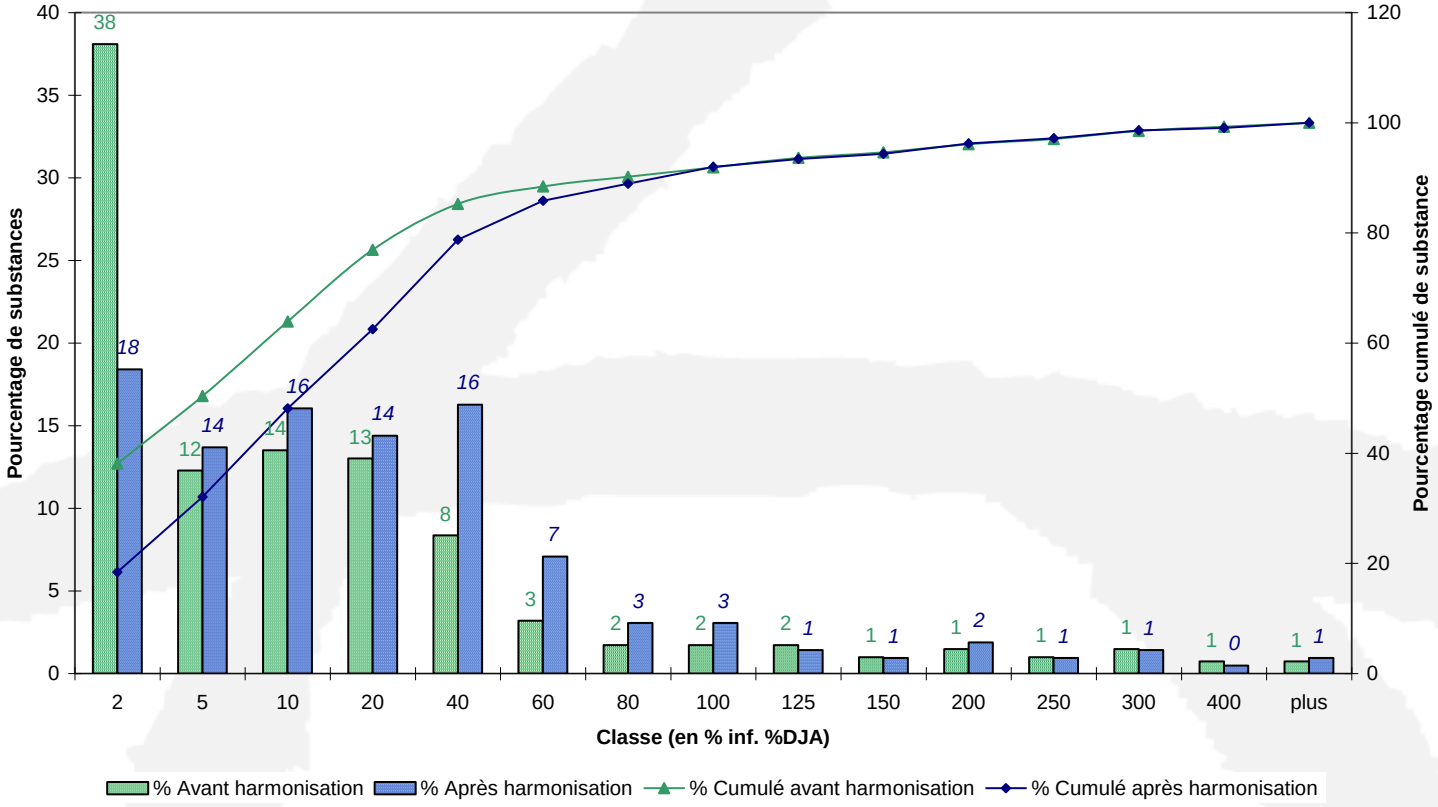
- Nine have been resubmitted and will be reappraised for a final decision: Acrinathrin*, Carbofuran*, Fluazifop-P-Butyl*, Fluquinconazole*, Guazatine*, Haloxyfop*, Malathion*, Prochloraz*, Propargite*,
- Two were recently the subject of an EFSA opinion that recommended lowering the MRLs: Procymidone* (EFSA, 2009) and Vinclozolin* (EFSA, 2008c). Considering the MRLs proposed by EFSA:
    - for Procymidone*, the $TMDI_{av}$ no longer exceeds the ADI regardless of the population sub-group,
    - for Vinclozolin*, the $TMDI_{av}$ still exceeds the ADI for the adult population, due to an MRL in wine grapes maintained at 5 mg/kg. Lowering this MRL to the limit of quantification of 0.05 mg/kg would give a $TMDI_{av}$ below the ADI.
- Ten are definitively not included in annexe I: Chlordecone*, Cyanides*, Diazinon*, Dieldrin*, Disulfoton*, Fenthion*, Furfural*, Heptachlor*, Methidathion* and Trichlorfon*. For these compounds, the degree of protection afforded by their MRLs should be assessed in the light of actual population exposure, which is what AFSSA did in 2007 for Chlordecone* (AFSSA, 2007). With the exception of Furfural* and Cyanides*, all of these compounds are included in the surveillance and control programmes, which makes this assessment possible. It should be noted that while Furfural* is no longer used in agriculture, it is however used as a food additive and is naturally produced by some plants such as maize.
- the MRLs for Dicofol* are being reappraised under article 12 of Regulation (EC) no. 396/2005.

It should be emphasised that only 8 of these 22 substances did not have harmonised MRLs before Regulation (EC) no. 396/2005 entered into force: Acrinathrin*, Fluazifop-P-Butyl*, Fluquinconazole*, Guazatine*, Propargite*, Chlordecone*, Cyanides* and Furfural*.

The other compounds (16/57) are listed in annexe I or are currently being assessed, and all of these, except for one, have been authorised for use in France: Chlorpyrifos-methyl[1], Copper compounds, Deltamethrin[1], Dimethoate[1], Diquat[1], Ethoprophos[1], Fenamiphos[1], Fenpropimorph[1], Fipronil[1], Fluorides (not authorised), Hydrogen phosphide[1], Phosmet[1], Pirimiphos-methyl[1], Propineb[1], Sulcotrione[1] and Thiram[1]. Nine substances still have a TMDI that exceeds the ADI when MRLs set at the limit of quantification or the default limit are not taken into account. The MRLs for Copper compounds and Fluorides will be reappraised after their present analysis. The MRLs for the other compounds are currently being reappraised, pursuant to articles 12(1) and 12(2) of Regulation (EC) no. 396/2005.

✓ Overall comparative analysis before and after harmonisation

Figure 1: Lifetime distribution of TMDIs before and after harmonisation



Pourcentage de substances	Percentage of substances
Pourcentage cumulé de substances	Cumulative percentage of substances
% Avant harmonisation	% Before harmonisation
% Après harmonisation	% After harmonisation
% Cumulé avant harmonisation	Cumulative % before harmonisation
% Cumulé après harmonisation	Cumulative% after harmonisation
Classe (en % inf. % DJA)	Class ratio TMDI / ADI

Figure 1 presents the lifetime distribution of TMDIs before and after harmonisation (the TMDIs calculated for the 'child' and 'adult' sub-groups are not shown). From 0 to 60% of the ADI, a right shift can be observed in the cumulative distribution of the new TMDIs, i.e. TMDIs are generally higher with the harmonised MRLs. However, this shift is no longer perceptible when the value gets close to or exceeds the ADI. Whether we consider the MRLs before or after harmonisation, 8.0% of all substances have a lifetime TMDI higher than their ADI. Although theoretical intakes increased for some substances, overall, the level of protection associated with MRLs was the same before and after harmonisation.

✓ Detailed comparative analysis

All of the individual compounds were compared for 329 substances for which a TMDI had been defined in 2007 by the Pesticide Residues Observatory. Out of the 424 investigated substances, 74 did not have MRLs that were applicable in France before 1 September 2008, 20 were incomplete in AFSSA's database (information lacking about the ADI or MRLs), and one compound – Chlordecone* – was not examined for the general population in mainland France, as it was not considered to involve any risk. Note that six of the compounds that were not compared

before and after harmonisation have a $TMDI_{av}$ that is greater than the ADI: Chlordecone*, Carboxin*, Sulcotrione[1], Guazatine*, Furfural* and Fluorides.

The highest $TMDI_{av.}$ values of the various substances were compared.

Table 7: Detailed comparison before and after harmonisation

Situation	All compounds (%)	Recently harmonised compounds (%)
Unchanged	297 (90.3%)	107 (91.4%)
$TMDI_{av}$ < ADI before and after harmonisation	268 (81.5%)	107 (91.4%
$TMDI_{av}$ > ADI before and after harmonisation	29 *(8.8%)*	0 (0%)
Changed	32 (9.7%)	10 (8.6%)
$TMDI_{av}$ ≥ ADI before and < ADI after harmonisation	11 (3.3%)	1 (0.9%)
$TMDI_{av}$ < ADI before and ≥ ADI after harmonisation	21 *(6.4%)*	9 (7.7%)
Total	**329**	**117**

Table 7 shows that for around 90% of all compounds, the situation (i.e. whether or not the ADI was exceeded) was the same before and after harmonisation. The situation changed for 32 molecules. For only one-third of these compounds (11/32), the level of protection associated with the MRLs increased, and for two-thirds, it decreased.

One hundred and seventeen of the 329 compounds previously studied had strictly national MRLs. The situation remained unchanged for 91.4% of all substances. Witness that for nine out of the ten compounds for which the situation changed, the level of protection decreased (before the data were refined).

The differences may be explained by:

- a change in the ADI used for evaluation,
- a change in the types of foods with MRLs,
- modified MRLs.

Effect of the ADI:

The ADI used for evaluation did indeed change for over half of the compounds concerned by a change of situation (18/32). The impact of this change was estimated by comparing:

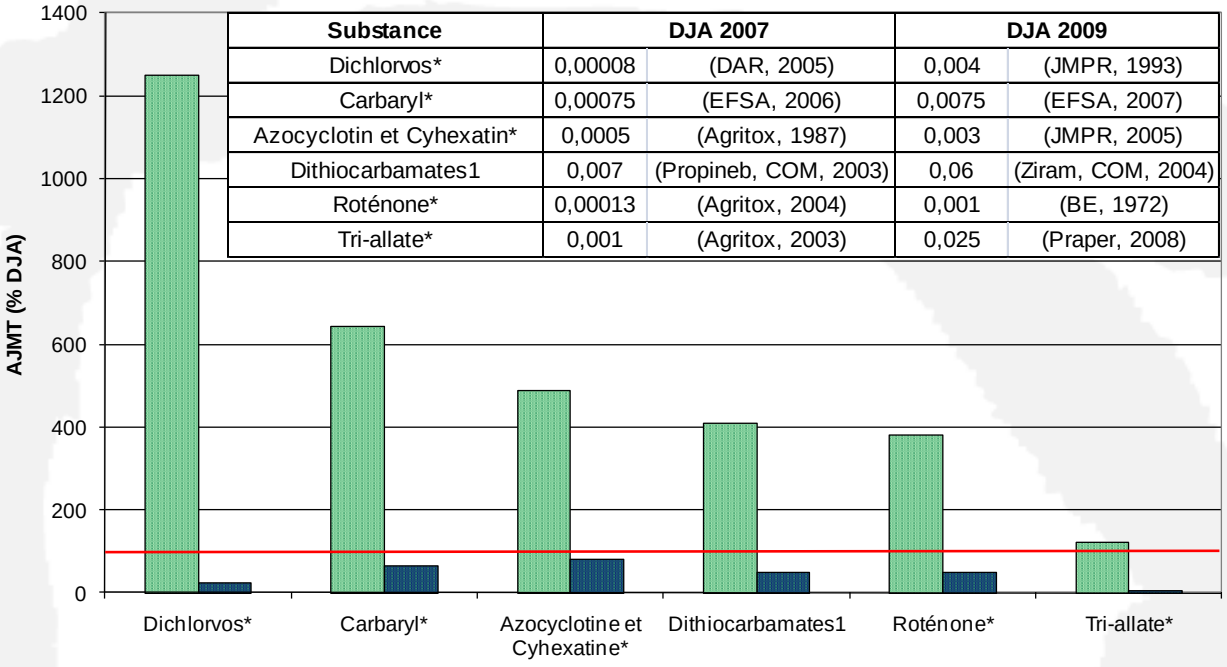
- the TMDI before and after harmonisation at the ADI adopted in 2007 for compounds with a TMDI ≥ ADI before and < ADI after harmonisation.
- the TMDI before and after harmonisation at the ADI adopted in 2009 for compounds with a TMDI < ADI before and ≥ ADI after harmonisation.

According to Figure 2, with the exception of Fluquinconazole*, the conclusion regarding the protection associated with MRLs changed not because of the change in MRLs but because of the change in ADIs used for evaluation. Among the compounds concerned:

- six have less stringent ADIs and a risk that is now acceptable whereas it was not in the past: Carbaryl*, Dichlorvos*, Azocyclotin and Cyhexatin*, Dithiocarbamates[1], Rotenone* and Triallate,
- eleven have more stringent ADIs and their previously acceptable risk is now a risk that requires further evaluation: Acrinathrin*, Copper compounds, Fenbuconazole*, Flufenoxuron*, Mecarbam*, Mevinphos*, Parathion*, Procymidone*, Propargite*, Pyrazophos* and Trichlorfon*.

Figure 2a. Compounds having a TMDI ≥ ADI before and < ADI after harmonisation

Substance	DJA 2007		DJA 2009	
Dichlorvos*	0,00008	(DAR, 2005)	0,004	(JMPR, 1993)
Carbaryl*	0,00075	(EFSA, 2006)	0,0075	(EFSA, 2007)
Azocyclotin et Cyhexatin*	0,0005	(Agritox, 1987)	0,003	(JMPR, 2005)
Dithiocarbamates1	0,007	(Propineb, COM, 2003)	0,06	(Ziram, COM, 2004)
Roténone*	0,00013	(Agritox, 2004)	0,001	(BE, 1972)
Tri-allate*	0,001	(Agritox, 2003)	0,025	(Praper, 2008)



Substance	DJA 2009 (mg /kg p. c./jour)		DJA 2007 (mg /kg p. c./jour)	
Trichlorfon*	0,002	(JMPR, 2003)	0,01	
Procymidone*	0,0028	(COM, 2007)	0,025	(Agritox, 2003)
Parathion*	0,0006	(ECCO, 2001)	0,004	(Agritox, 2000)
Propargite*	0,007	(DAR, 2007)	0,02	
Acrinathrine*	0,001	(DAR, 2007)	0,02	
Mecarbame*	0,0005	(SC, 2005)	0,002	(COM, 2000)
Cuivre	0,15	(EFSA, 2008)	0,5	(UE)
Fluquinconazole*	0,002	(PRAPER, 2006)	0,003	
Mevinphos*	0,00025	(BE, 2001)	0,0008	(COM, 2000)
Pyrazophos*	0,001	(ECCO, 1999)	0,004	(COM, 2000)
Flufenoxuron*	0,0035	(DAR, 2006)	0,01	
Fenbuconazole*	0,006	(PRAPER, 2004)	0,036	

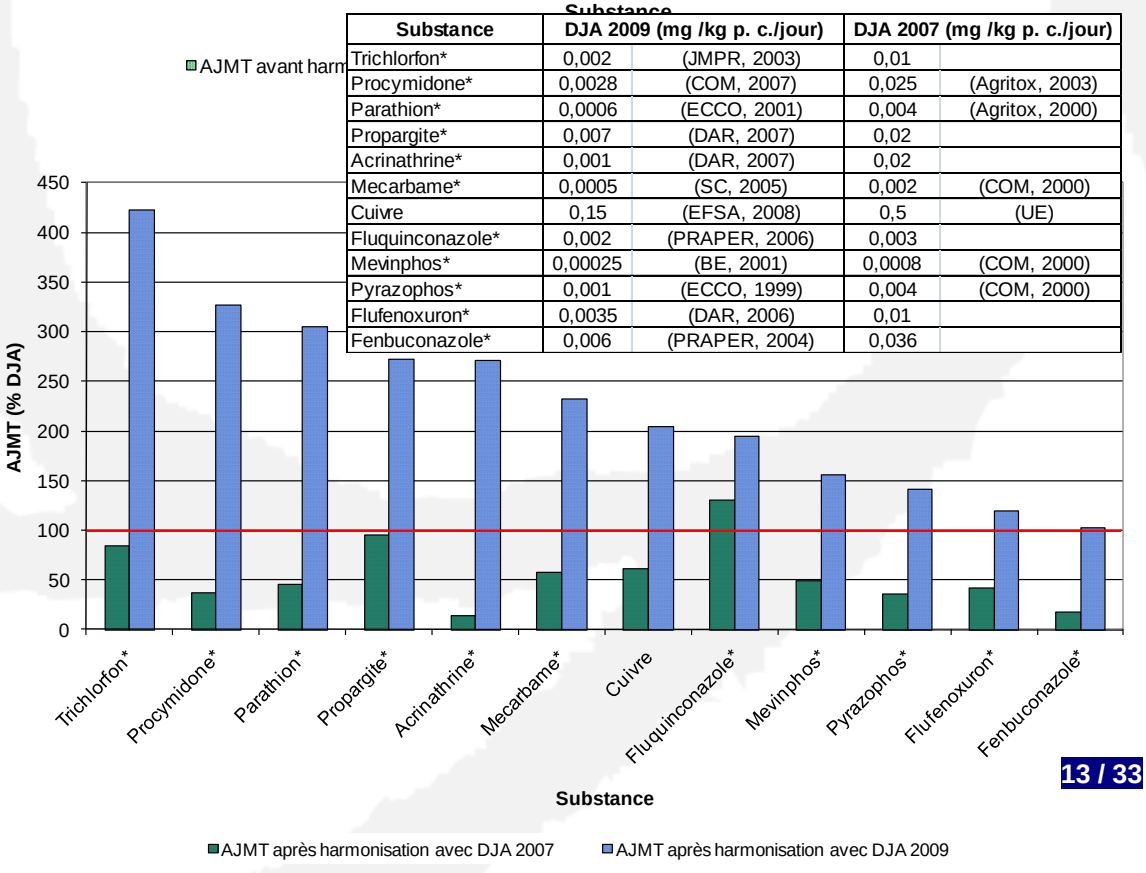


Figure 2b. Compounds having a TMDI < ADI before and ≥ ADI after harmonisation

Substance	Substance
DJA 2007	2007 ADI
DJA 2009	2009 ADI
Dichlorvos	Dichlorvos
Carbaryl	Carbaryl
Azocyclotin et Cyhexatin	Azocyclotin and Cyhexatin
Dithiocarbamates1	Dithiocarbamates1
Roténone	Rotenone
Tri-allate	Triallate
AJMT (% DJA)	TMDI (% ADI)
AJMT avant harmonisation avec DJA 2007	TMDI before harmonisation with 2007 ADI
AJMT avant harmonisation avec DJA 2009	TMDI before harmonisation with 2009 ADI

Substance	Substance
DJA 2009 (mg/kg p.c./jour)	2009 ADI (mg/kg b.w./day)
DJA 2007 (mg/kg p.c./jour)	2007 ADI (mg/kg b.w./day)
Trichlorfon	Trichlorfon
Procymidone	Procymidone
Parathion	Parathion
Propargite	Propargite
Acrinathrine	Acrinathrin
Mecarbame	Mecarbam
Cuivre	Copper
Fluquinconazole	Fluquinconazole
Mevinphos	Mevinphos
Pyrazophos	Pyrazophos
Flufenoxuron	Flufenoxuron

Effect of MRLs

The change in MRLs is likely to influence the population's protection level for 5% (15/329) of all of the investigated substances.

The impact of this change is illustrated by comparing the contribution of the various food categories to the theoretical total intake expressed in % of ADI: fruits, vegetables, cereals, other foodstuffs of plant origin (oilseeds, spices, tea and other plants for infusing, hops, etc.), wine, meat, other foodstuffs of animal origin (eggs, dairy products) and water.

Figure 3 shows that for 11 of the 15 substances studied (Monocrotophos*, Ethion*, Azinphos-methyl*, Phosalone*, Haloxyfop*, Fluquinconazole*, Fipronil[1], Ethoprophos[1], Dioxathion*, Carbon tetrachloride* and Fluazifop-P-Butyl*), there are now more food groups which explains the theoretical total intake after harmonisation, with a contribution ranging from 8.0% (Phosalone*) to 106.6% (Haloxfop*) of the ADI.

In particular, we can see that for Dioxathion* and Carbon tetrachloride*, the foodstuffs that contributed to total intake before harmonisation contribute to the same degree afterwards. The difference is due solely to the contribution of foods for which no MRL had previously been defined:

- cereals and other foods of plant origin, meats and other foods of animal origin for Dioxathion* which, before harmonisation, had MRLs only in fruits, vegetables, wine and water,
- fruits, vegetables and other foods of plant origin, wine, meats and other foods of animal origin for Carbon tetrachloride* which, before harmonisation, had MRLs only in cereals and water (as it was previously used only to treat cereals in storage).

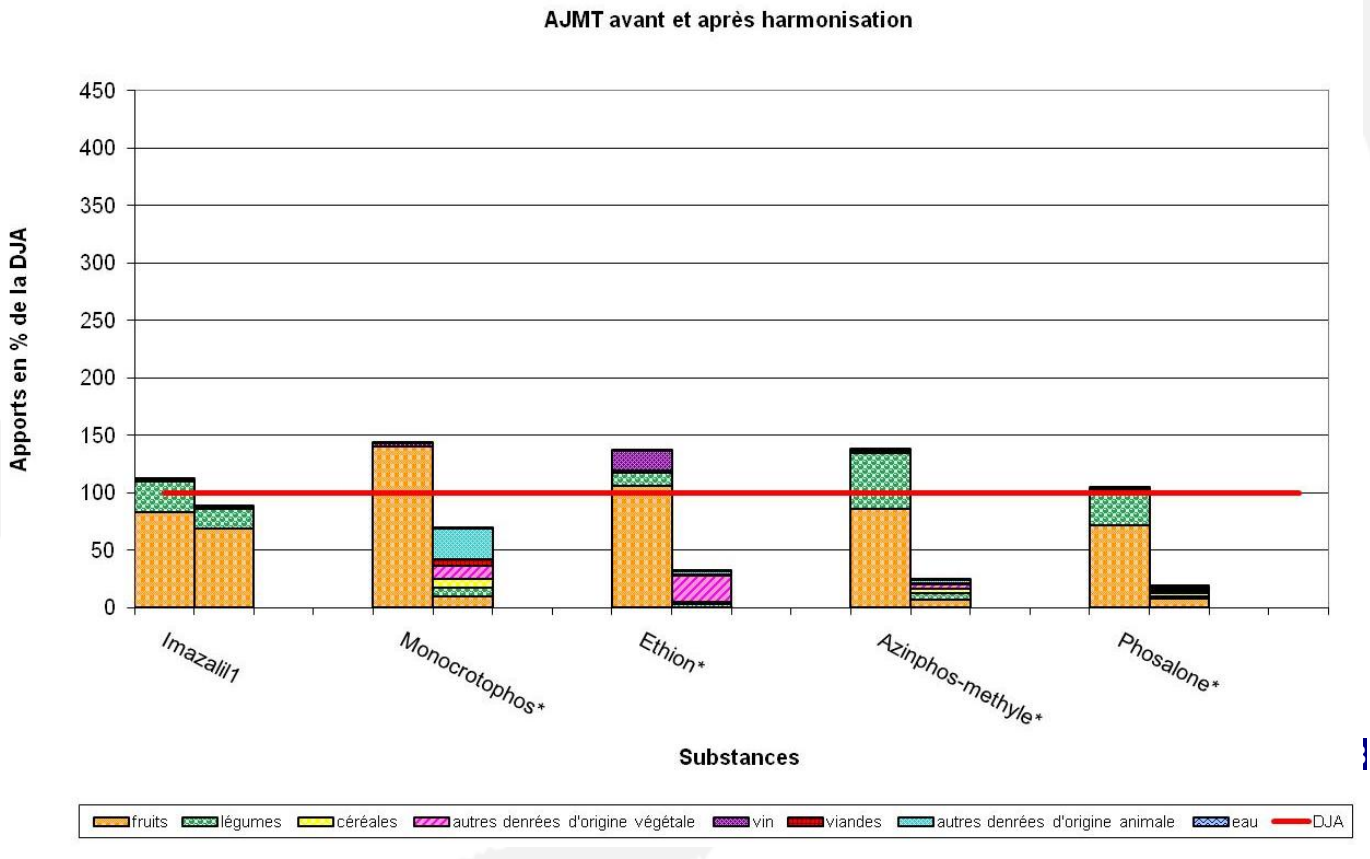
This observation can be explained, among other things, by the application of a default limit, given the lack of an *ad hoc* MRL for all of the foodstuffs in diets. If we look at the previous examples again, we can see that all of the MRLs for Dioxathion* are set at the LOQ whereas those for Carbon tetrachloride* are all at the default level, with the exception of cereals (0.1 mg/kg).

Figure 3 also shows that the contribution of some food groups changed considerably. Concerning:

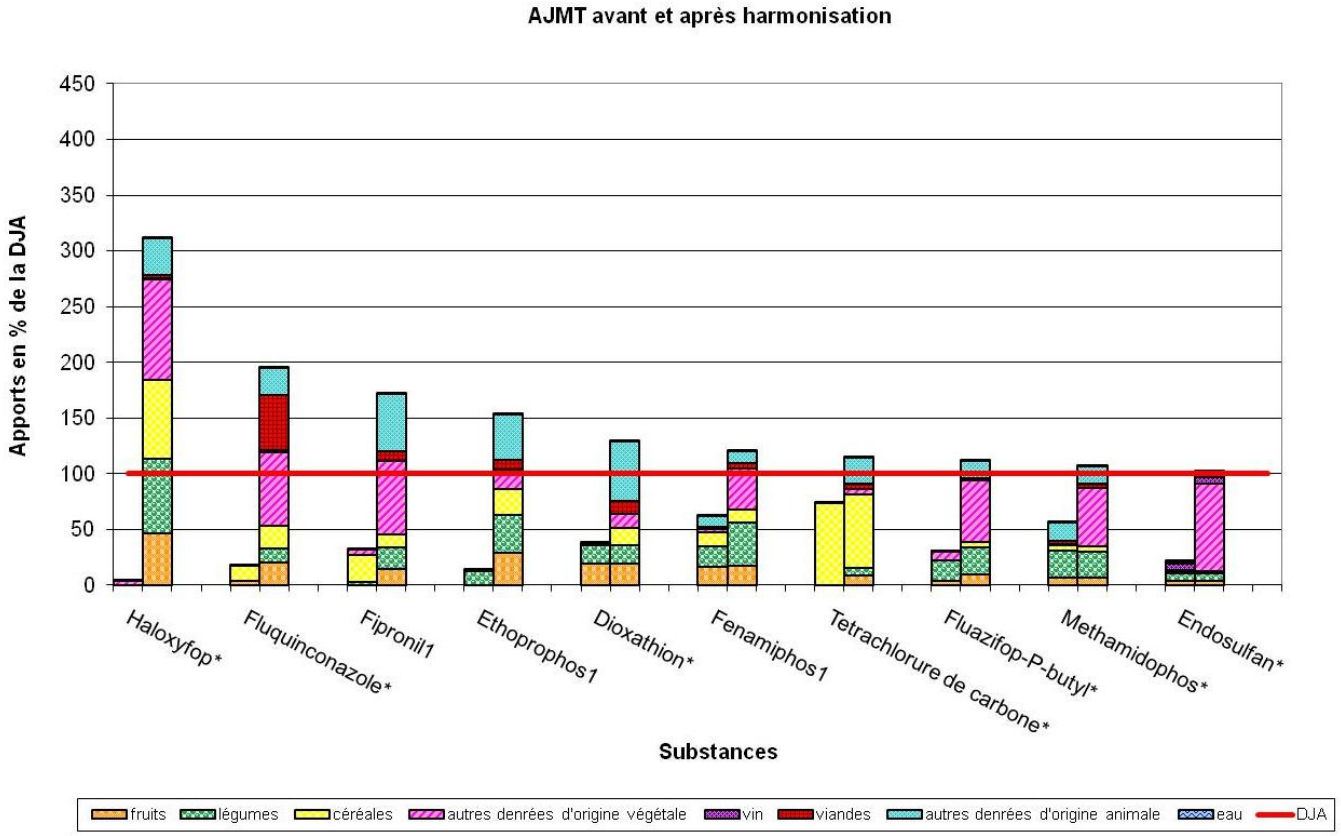
- cereals: intake increased from 0.9 to 23.0% of the ADI for Ethoprophos[1], as only maize had an MRL of 0.01 mg/kg before harmonisation, while presently all cereals have an MRL of 0.02 mg/kg,
- fruits: intake increased by a factor greater than 5 for Haloxyfop*, Fipronil[1], and Ethoprophos[1], due to the application of a default limit for all fruits that did not previously have MRLs – Ethoprophos[1] and Fipronil[1] had an MRL solely in bananas, Haloxyfop* in table and wine grapes – and MRLs that rose from 0.01 mg/kg to 0.02 and 0.05 mg/kg for Ethoprophos[1] and Haloxyfop* respectively. Conversely, intake decreased by a factor greater than 10 for Phosalone*, Azinphos-methyl*, Ethion* and Monocrotophos*. Some MRLs were in fact lowered to the limit of quantification, because these active substances are not listed in annexe I of Directive 91/414/EEC,
- vegetables: intake increased by a factor greater than 5 for Fipronil[1]. There was previously only one MRL for Fipronil[1], in sweet corn, which remained the same, but MRLs were defined in all vegetables and were sometimes different from the LOQ. Intake decreased by a factor greater than 10 for Phosalone* and Azinphos-methyl*, since the MRLs were lowered to the LOQ due to the non-inclusion of these substances in annexe I of Directive 91/414/EEC.

Figure 3 Effect of the change in MRLs

a. Compounds having a TMDI ≥ ADI before and < ADI after harmonisation



b. Compounds having a TMDI < ADI before and ≥ ADI after harmonisation



- other foodstuffs of plant origin: intake increased by a factor greater than 5 for Haloxyfop*, Dioxathion*, Fenamiphos[1], Fluazifop-P-Butyl*, Methamidophos* and Endosulfan*, mainly because a default limit was applied to many foodstuffs, few of which previously had an MRL, such as spices, aromatic plants, tea, etc.

AJMT avant et après harmonisation	TMDI before and after harmonisation
Apports en % de la DJA	Intakes in % of ADI
Imazalil 1	Imazalil 1
Monocrotophos	Monocrotophos
Ethion	Ethion
Azinphos-methyle	Azinphos-methyl
Phosalone	Phosalone
Substances	Substances
Fruits	Fruits
Légumes	Vegetables
Céréales	Cereals
Autres denrées d'origine végétale	Other foods of plant origin
Vin	Wine
Viandes	Meat
Autres denrées d'origine animale	Other foods of animal origin
Eau	Water
DJA	ADI

AJMT avant et après harmonisation	TMDI before and after harmonisation
Apports en % de la DJA	Intakes in % of ADI
Haloxyfop	Haloxyfop

Fluquinconazole	Fluquinconazole
Fipronil1	Fipronil1
Ethoprophos1	Ethoprophos1
Dioxathion	Dioxathion
Fenamiphos1	Fenamiphos
Tetrachlorure de carbone	Carbon tetrachloride
Fluazifop-P-butyl	Fluazifop-P-butyl
Methamidophos	Methamidophos
Endosulfan	Endosulfan
Substances	Substances
Fruits	Fruits
Légumes	Vegetables
Céréales	Cereals
Autres denrées d'origine végétale	Other foods of plant origin
Vin	Wine
Viandes	Meat
Autres denrées d'origine animale	Other foods of animal origin
Eau	Water
DJA	ADI

2.4 Conclusion

On the whole, protection offered by MRLs against the risk of chronic exposure was the same before and after harmonisation.

The application of a default limit for all foodstuffs generally led to a higher theoretical total intake due to a wider variety of contributing foodstuffs. This new rule alone explains why the ADI was exceeded for Haloxyfop*, and helps explain why the ADIs were exceeded for Fluquinconazole*, Fipronil[1], Ethoprophos[1], Dioxathion*, Carbon tetrachloride* and Fluazifop-P-Butyl* after harmonisation.

The comparison in the first section highlights changes made to some MRLs before and after harmonisation. However, these changes only had a slight impact on situations in which the ADI was exceeded: they do help to explain why the ADI was exceeded for Ethoprophos[1], Haloxyfop* and Fipronil[1], but this explanation is not that significant when compared with the increased number of foods with MRLs.

However, we can see that lowering the MRLs that had already been harmonised for Imazalil[1], Monocrotophos*, Ethion*, Azinphos-methyl* and Phosalone* generated a $TMDI_{av}$ below the ADI.

Furthermore, this comparative study illustrates the effect that the ADI has when evaluating protection: over half of all of the situations that changed before and after harmonisation were due to a new ADI.

3. Level of protection against acute risk associated with MRLs

3.1 General considerations

When evaluating the level of protection associated with MRLs, it is important to consider not only risk related to chronic exposure but also that related to acute exposure. During the MRL harmonisation procedure, the model used to predict acute exposure in Europe did not take the consumption habits of the French population into account. This model was based on a compilation of the highest identified consumption levels taken from data submitted by Belgium,

Germany, Denmark, Spain, Finland, Ireland, Italy, Lithuania, the Netherlands, Poland and the United Kingdom but not France. As a result, when it validated this model, AFSSA recommended that it incorporate French consumption data.

As the validation occurred subsequent to the harmonisation procedure, it was therefore necessary to describe to what extent the harmonised MRLs also protect against risk related to acute exposure in the French population. The first step towards such a description involves calculating the Estimated Short-Term Intake (ESTI).

As the methodology for calculating acute exposure was under development in both France and Europe, no comparisons were made with the situation before harmonisation.

3.2 ESTI calculation

- ✓ Principle

According to WHO's guidelines, the ESTI is calculated by estimating, for each food product, the daily intake related to consumption of a highly-contaminated large portion (WHO, 1997). The ESTI is based on various equations, depending on the food in question, as presented in detail in annexe 4.

As we currently lack structured information on the HR[8] and STMRp[9] levels associated with each combination [pesticide x food product], the MRL was used for a first approximation, following EFSA's example in the harmonisation process (EFSA, 2007). During a second phase, situations in which the ARfD[10] was exceeded were, insofar as possible, further examined using knowledge available in France of HR and STMRp levels.

The large portions used correspond to those defined in the STS 2007-SA-385 based on the food consumption habits of the general population aged over 3 in mainland France (INCA 1 study, Volatier, 2000) and those of infants and young children in mainland France, as described in the Alliance 7 study (Fantino and Gourmet, 2008). Using this method, an ESTI can be calculated for 161 types of foods.

The unit weight of the edible part of each food was estimated on the basis of the photo manual (Hercberg, 1994) used for INCA surveys to describe food quantities. If this was not possible, the unit weight proposed in the EFSA model was used (EFSA, 2007).

The parameters used for each food product are summarised in annexe 5.

The ESTIs were then compared with the ARfD.

- ✓ Acute Reference Dose (ARfD)

The ARfDs were selected in the same way as the ADIs. The ARfDs applied to groups of compounds are listed in Table 8. All of the values used in the framework of this scientific and technical support can be found in annexe 2.

The ESTI was calculated for only 239 of the 443 substances having European MRLs. It was not possible to determine an ARfD for 204 substances with European MRLs for the following reasons:

- ARfD not necessary or not proposed following the assessment of 130 substances,

[8] HR: highest residue levels

[9] STMRp: supervised trials median residues in processed foods

[10] ARfD: The Acute Reference Dose (ARfD) of a chemical product is the estimated quantity of a substance in food or drinking water, expressed according to body weight, that can be ingested over a short period, generally over the course of a meal or a day, without an appreciable consumer health risk based on all known factors at the time of the evaluation. It is expressed in milligrams of the chemical substance per kilogram body weight (WHO, 1997).

- ARfD not determined due to uncertainties surrounding four substances, none of which are included in annexe 1,
- Information lacking for 70 substances. It should be noted that the definition of Acute Reference Dose as part of the risk assessment procedure appeared only recently. As a result, many relatively old compounds do not have an ARfD.

Table 8: ARfDs used for groups of molecules

Group
Dichlorprop and Dichlorprop-P: ARfD of Dichlorprop-P
Clethodim and Sethoxydim: ARfD of Clethodim
MCPA and MCPB: ARfD of MCPB
Triadimenol and Triadimefon: ARfD of Triadimenol
Group of Dithiocarbamates: ARfD of Ziram
Dimethoate and Omethoate: ARfD of Omethoate
Thiodicarb and Methomyl: ARfD of Methomyl

3.3 Results

The calculation was performed on 28,202 combinations [food product x pesticide], taken from 239 substances and 161 food types, 223 (0.8%) of which had an ESTI that exceeded the ARfD. Table 9 shows the breakdown of substances affected by a problem related to acute exposure according to their status.

Table 9 ESTI results

Status of the active substance and *presence in plant protection preparations in France*	Number of combinations [pesticide x food product] studied	Number of combinations where ESTI > ARfD	Number of substances studied	Number of substances where at least one ESTI > ARfD
Annexe 1	12272	66	104	20 (19%)
Present in France	*10502*	*65*	*89*	*19 (21%)*
Not present in France	*1770*	*1*	*15*	*1 (7%)*
Under analysis	3304	2	28	2 (7%)
Present in France	*1534*	*2*	*13*	*2 (15%)*
Not present in France	*1770*	*0*	*15*	*0 (0%)*
Not listed in annexe I	12626	155	107	24 (22%)
Total	**28202**	**223**	**239**	**46 (19%)**

Whereas, in absolute terms, the ARfD was exceeded for fewer substances than the ADI, relative to the total number of substances studied, for nearly 20% of the substances studied, the ESTI, calculated on the basis of the MRLs, was greater than the ARfD.

The ARfD was exceeded 1 to 5 times for 33 of the 46 substances studied (70%). For 10 compounds, the ARfD was exceeded 6 to 15 times, and for 3 (Procymidone*, Chlorothalonil[1], Rotenone*) it was exceeded 18, 19 and 28 times respectively.

The ARfD was exceeded in 41 food types. The foods the most frequently involved (where the ARfD was exceeded more than 10 times) were citrus fruits (grapefruit, mandarins, oranges), pears, peaches, melons and table grapes. We can see that for half of these foods (avocados, lentils, strawberries, apricots, beans with pods, courgette, tea, wheat, cow's milk, artichokes, wine grapes, carrots, kiwis, tomatoes, potatoes, bananas, peaches, oranges, table grapes, apples), the large portion used in this assessment was bigger than the one used in the European model during the harmonisation process. As a result, over half (N = 128) of the combinations [food product x pesticide] with an ESTI higher than the ARfD may not have appeared as such during the harmonisation process.

The calculation was refined for 26/223 combinations [food product x pesticide] using the HR and transfer factors[11] leading to an $ESTI_{refined}$ below the ARfD for 24/26 combinations studied.

Table 10 lists the 223 combinations [food product x pesticide] with an ESTI above the ARfD:

- 42 combinations [food product x pesticide] corresponding to 6 substances - Omethoate and Dimethoate[1], Methamidophos*, Fenamiphos[1], Vinclozolin*, Methomyl*, Procymidone* - were also identified as having an ESTI > ARfD by EFSA, which recommended lowering the MRLs in question or undertaking further analysis when they were already at the limit of quantification (EFSA 2008a, 2008b, 2008c, 2008d, 2008e, 2008f, 2009). If all of EFSA's recommendations were followed in these situations, the ARfD would no longer be theoretically exceeded in the French population,
- 2 combinations [food product x pesticide] correspond to two substances under assessment: Cyromazine and Flonicamid. Their MRLs will be reappraised after the analysis,
- 51 combinations [food product x pesticide] corresponding to 13 substances listed in annexe I (Ioxynil[1], Glufosinate-ammonium[1], Fenpropimorph[1], Lambda-Cyhalothrin[1], Thiabendazole[1], Triadimefon and triadimenol[1], Pyraclostrobin[1], Tebuconazole[1], Deltamethrin[1], Dithiocarbamates[1], Imazalil[1], Chlorothalonil[1], Quizalofop isomers[1]) are currently being reappraised,
- 31 combinations [food product x pesticide] correspond to 8 substances that currently are not listed but are undergoing resubmission or reappraisal: 1-naphthylacetic acid*, Acrinathrin*, Carbofuran*, Dithianon*, Guazatine*, Propargite*, Prochloraz*, Bitertanol*. Their MRLs will be reappraised after a definitive decision has been made by the European Community (inclusion/non-inclusion),
- 5 combinations [food product x pesticides] corresponding to 4 substances listed in annexe I (Dinocap[1], Methiocarb[1], Pirimicarb[1] and Tebufenpyrad[1]) have an $ESTI_{refined}$ below the ARfD,
- 2 combinations [Pirimicarb[1] x apple] and [Formetanate[1] x courgette] corresponding to substances listed in annexe I would benefit from undergoing a refined assessment,
- 74 combinations [food product x pesticide] correspond to MRLs set at the limit of quantification for 7 substances, none of which are listed in annexe I: Amitraz*, Fentin Acetate and Hydroxide*, Pyrazophos*, Carbofuran*, Phorate* and Rotenone*. Further analysis is needed to lower the limits of quantification and the (very theoretical) levels of exposure,
- 16 combinations [food product x pesticide] correspond to 6 substances that are definitively not included in annexe I: Dodine*, Chlorfenapyr*, Endosulfan*, Fenthion*, Methidathion*, Fenpropathrin*. This raises the question of whether maintaining MRLs above the limits of quantification is relevant when the ARfD may be exceeded. The MRLs for Endosulfan* in grapes, Fenthion* and Fenpropathrin* are in the process of being revised.

[11] Factor that takes into account the concentration or reduction of residue levels in foods as they are consumed on the basis of the edible portion (for kiwis, bananas and avocados, for example), industrial processing or domestic preparations.

3.4 Conclusion

In terms of acute exposure, out of 28,202 combinations [food product x pesticide] of 239 substances and 161 food types, 223 combinations (0.8%) were identified as having a theoretical maximum acute exposure level above the toxicological reference value.

Out of the 223 MRLs that correspond to these combinations:

- 134 MRLs, related to 29 substances, have been, are being or will soon be reappraised,
- 82 MRLs, related to 13 substances that are no longer listed in the annexe, could be revised, either by improving the performance of analytical methods when the MRL is set at the LOQ, or by lowering them to the LOQ.
- 2 MRLs (Pirimicarb[1] in apples and Formetanate[1] in courgettes) would benefit from reappraisal in the light of actual field trial data and monitoring.

Table 10 Detailed ESTI results

Substance	Substance status (authorised preparation in France)	Foods in which the ARfD is exceeded (MRL in mg/kg)	Comments
Dinocap[1]	Annexe 1 (not authorised in France)	Wine grapes (1)	No risk of exceeding the ARfD when considering an STMRp of 0.03 mg/kg
Ioxynil[1]	Annexe 1 (authorised in France)	Leeks (3)	MRL under reappraisal (article 12-2) No risk of exceeding the ARfD when considering an HRp of 0.675 mg/kg
Formetanate[1]	Annexe 1 (authorised in France)	Courgettes (0.5)	
Glufosinate-ammonium[1]	Annexe 1 (authorised in France)	Dry lentils (3)	MRL under reappraisal (article 12-2)
Methiocarb[1]	Annexe 1 (authorised in France)	Melons (0.5)	No risk of exceeding the ARfD when considering an HRp of 0.05 mg/kg
Fenpropimorph[1]	Annexe 1 (authorised in France)	Bananas (2)	MRL under reappraisal (article 12-1) No risk of exceeding the ARfD when considering an HRp of 0.01 mg/kg
Lambda-Cyhalothrin[1]	Annexe 1 (authorised in France)	Peaches (0.2), table grapes (0.2)	MRL under reappraisal (article 12-2) No risk of exceeding the ARfD when considering an HR of 0.05 mg/kg
Thiabendazole[1]	Annexe 1 (authorised in France)	Potatoes (15), apples (5)	MRL under reappraisal (article 12-2)
Fenamiphos[1]	Annexe 1 (authorised in France)	Carrots (0.5), melons (0.05)	EFSA 15 September 2008 opinion recommending withdrawing import tolerances for carrots, revising critical agricultural practices for melons, and lowering the MRLs in these two foods to the limit of quantification of 0.02 mg/kg (EFSA, 2008a). No risk of exceeding the ARfD with an MRL at the LOQ for these foods.
Pirimicarb[1]	Annexe 1 (authorised in France)	Apples (2), artichokes (5)	No risk of exceeding the ARfD when considering an HR in artichokes of 2.8 mg/kg
Triadimefon and triadimenol[1]	Annexe 1 (authorised in France)	Pineapples (3), table grapes (2)	MRL for Triadimenol under reappraisal (article 12-1)
Tebufenpyrad[1]	Annexe 1 (authorised in France)	Melons (0.5), table grapes (0.5)	No risk of exceeding the ARfD when considering an HR in table grapes of 0.3 mg/kg and in melons of 0.01 mg/kg.

Substance	Substance status (authorised preparation in France)	Foods in which the ARfD is exceeded (MRL in mg/kg)	Comments
Pyraclostrobin[1]	Annexe 1 (authorised in France)	Oranges (1), table grapes (1)	MRL under reappraisal (article 12-2)
Tebuconazole[1]	Annexe 1 (authorised in France)	Apples (1), peaches (1), table grapes (2)	MRL under reappraisal (article 12-2)
Quizalofop[1]	Isomers listed in Annexe I	Melons (0.4)	MRL under reappraisal (article 12-1)
Deltamethrin[1]	Annexe 1 (authorised in France)	Tea (5), apples (0.2), melons (0.2), wheat (2)	MRL under reappraisal (article 12-2) No risk of exceeding the ARfD when considering an HR in apples of 0.07 mg/kg and in melons of 0.02 mg/kg. An HRp of 1.47 in wheat always causes the ARfD to be exceeded for the French population.
Dimethoate[1]	Annexe 1 (authorised in France)	Cauliflower (0.2), cherries (1), cabbage (1), lettuce (0.5), sugar beets (1), wheat (0.3)	EFSA 20 October 2008 opinion recommending lowering the MRLs in these foods to the LOQ of 0.02 mg/kg (EFSA, 2008f). No risk of exceeding the ARfD with an MRL at the LOQ for these foods.
Group of Dithiocarbamates[1]	Annexe 1 (authorised in France)	Apples (5), grapefruit (5), mandarins (5), oranges (5), pears (5), table grapes (5)	MRL under reappraisal (article 12-2)
Imazalil[1]	Annexe 1 (authorised in France)	Potatoes (3), apples (2), bananas (2), grapefruit (5), mandarins (5), melons (2), oranges (5)	MRL under reappraisal (article 12-2) No risk of exceeding the ARfD when considering an HR in potatoes of 0.08 and a transfer factor of 0.15 in bananas and 0.1 in citrus fruits.
Chlorothalonil[1]	Annexe 1 (authorised in France)	Strawberries (3), apples (1), aubergines (2), beans with pods (5), broccoli (3), carrots (1), cauliflower (3), celery (10), cucumber (1), cabbage (3), leeks (10), melons (1), peaches (1), pears (1), bell peppers (2), table grapes (1), tomatoes (2), watermelons (1), wine grapes (3)	MRL under reappraisal (article 12-2)
Cyromazine	Under appraisal (authorised in France)	Swiss chard (20)	MRL to be reappraised within two years

Substance	Substance status (authorised preparation in France)	Foods in which the ARfD is exceeded (MRL in mg/kg)	Comments
Flonicamid	Under appraisal (authorised in France)	Wheat (2)	No risk of exceeding the ARfD when considering an HR in wheat of 0.12 mg/kg
Acrinathrin*	Not listed	Bananas (0.5)	Substance under reappraisal No risk of exceeding the ARfD when considering an HR in bananas of 0.19 mg/kg
Dodine*	Not listed	Apples (5)	No risk of exceeding the ARfD when considering an HR in apples of 0.65 mg/kg
Dithianon*	Not listed	Apples (3), table grapes (3)	Substance withdrawn voluntarily but reappraisal anticipated. No risk of exceeding the ARfD when considering an HR in table grapes of 1.48 mg/kg. An HR of 1.89 mg/kg in apples always causes the ARfD to be exceeded.
Prochloraz*	Not listed	Grapefruit (10), mandarins (10), oranges (10)	Substance withdrawn voluntarily but reappraisal anticipated.
Bitertanol*	Not listed	Apples (2), apricots (1), bananas (3), peaches (1), pears (2), tomatoes (3)	Substance withdrawn voluntarily but reappraisal anticipated.
Carbofuran*	Not listed	Apples (0.02*), cow's milk (0.1*), grapefruit (0.3), lemons (0.3), mandarins (0.3), melons (0.02*), oranges (0.3), sugar beets (0.2)	Substance resubmitted: reappraisal anticipated. Some MRLs are set at the limit of quantification: further analysis required.
Propargite*	Not listed	Apples (3), apricots (4), grapefruit (3), mandarins (3), oranges (3), peaches (4), pears (3), table grapes (7), tomatoes (2), wine grapes (7)	Substance withdrawn voluntarily but reappraisal anticipated.
Methomyl and Thiodicarb*	Not listed	Apples (0.2), broccoli (0.2), grapefruit (0.5), lemons (1), mandarins (1), melons (0.05*), oranges (0.5), peaches (0.2), pears (0.2), tomatoes (0.2), wine grapes (1)	Methomyl resubmitted: reappraisal anticipated. EFSA 26 September 2008 opinion recommending lowering the MRLs in these foods to the LOQ of 0.02 mg/kg, and to 0.01 mg/kg in oranges and melons (EFSA, 2008e). No risk of exceeding the ARfD with an MRL of 0.02 mg/kg for these foods.

Substance	Substance status (authorised preparation in France)	Foods in which the ARfD is exceeded (MRL in mg/kg)	Comments
Rotenone*	Not listed	Potatoes (0.01*), endives (0.01*), apples (0.01*), avocadoes (0.01*), bananas (0.01*), broccoli (0.01*), carrots (0.01*), cauliflower (0.01*), celery (0.01*), cow's milk (0.01*), courgettes (0.01*), cucumber (0.01*), artichokes (0.01*), grapefruit (0.01*), cabbage (0.01*), kiwis (0.01*), leeks (0.01*), mandarins (0.01*), melons (0.01*), onions (0.01*), oranges (0.01*), peaches (0.01*), pears (0.01*), pineapples (0.01*), sugar beets (0.01*), table grapes (0.01*), tomatoes (0.01*), watermelons (0.01*)	All of the MRLs are set at the limit of quantification. Further analysis required.
Amitraz*	Not listed	Apples (0.05*)	The MRL is set at the limit of quantification. Further analysis required.
Methamidophos*	Not listed	Beans with pods (0.5)	EFSA 15 September 2008 opinion recommending lowering the MRL in this food to the LOQ of 0.01 mg/kg after the substance was withdrawn from use (EFSA, 2008b). No risk of exceeding the ARfD with an MRL of 0.01 for this food.
Phorate*	Not listed	Apples (0.05*)	The MRL is set at the limit of quantification. Further analysis required.
1-naphthylacetic acid*	Not listed	Apples (1)	The substance is to be reappraised.
Chlorfenapyr*	Not listed	Tea (50)	
Endosulfan*	Not listed	Tea (30), table grapes (0.5)	Revision of the MRL in grapes in progress.
Guazatine*	Not listed	Grapefruit (5), mandarins (5), oranges (5)	The substance is to be reappraised.
Fenthion*	Not listed	Grapefruit (3), lemons (3), mandarins (3), oranges (3)	Revision of MRLs in progress.

Substance	Substance status (authorised preparation in France)	Foods in which the ARfD is exceeded (MRL in mg/kg)	Comments
Vinclozolin*	Not listed	Endives (2), apples (1), kiwis (10), table grapes (5)	EFSA 16 September 2008 opinion recommending lowering the MRL to the limit of quantification of 0.05 due to repealed usages for apples, table grapes and endives but maintaining the MRL at 10 mg/kg in kiwis due to the lack of acute risk (EFSA, 2008d). No risk of exceeding the ARfD with an MRL of 0.05 in all of these 4 foods (including kiwis).
Methidathion*	Not listed	Grapefruit (5), lemons (5), mandarins (5), oranges (5)	
Fenpropathrin*	Not listed	Grapefruit (3), mandarins (3), melons (1), oranges (2)	Revision of MRLs in citrus fruits in progress.
Pyrazophos*	Not listed	Potatoes (0.05*), endives (0.05*), apples (0.05*), bananas (0.05*), carrots (0.05*), artichokes (0.05*), kiwis (0.05*), melons (0.05*), oranges (0.05*), peaches (0.05*), pears (0.05*), table grapes (0.05*), watermelons (0.05*)	All of the MRLs are set at the limit of quantification. Further analysis required.
Fentin Acetate and Hydroxide*	Not listed	Potatoes (0.05*), endives (0.05*), apples (0.05*), bananas (0.05*), carrots (0.05*), cow's milk (0.05*), artichokes (0.05*), kiwis (0.05*), melons (0.05*), oranges (0.05*), peaches (0.05*), pears (0.05*), table grapes (0.05*), watermelons (0.05*)	All of the MRLs are set at the limit of quantification. Further analysis required.
Procymidone*	Not listed	Strawberries (5), endives (2), apricots (2), aubergines (2), beans with pods (2), courgettes (1), cucumbers (1), kiwis (5), lettuce (5), melons (1), peaches (2), pears (1), bell peppers (2), raspberries (10), table grapes (5), tomatoes (2), watermelons (1), wine grapes (5)	EFSA 15 September 2008 and 21 January 2009 opinions recommending lowering the MRL to the limit of quantification of 0.02 because the substance was no longer authorised in Europe and the ARfD had been lowered (EFSA, 2008c, EFSA, 2009). No risk of exceeding the ARfD with an MRL of 0.02 in all of these foods (including wine grapes).

Conclusion and recommendations

The entry into force of Regulation (EC) no. 396/2005 replaced the strictly national MRLs for active substances falling within the scope of Directive 91/414/EEC and included a new system for setting MRLs to protect European consumers from risk related to chronic or acute exposure to pesticide residues.

The primary change concerned the 155 substances that previously had only strictly French MRLs. The comparison of these MRLs before and after harmonisation showed an increase in 29.1% of cases and a decrease in 34.1% of cases. The entry into force of Regulation (EC) no. 396/2005 also entailed the systematic application of a default value of 0.01 mg/kg. All of these changes only slightly impacted overall protection as estimated through the calculation of the Theoretical Maximum Daily Intake. Both before and after harmonisation, around 92% of the 424 substances that were studied had a lifetime TMDI lower than their respective ADI.

As for situations in which Toxicological Reference Values were theoretically exceeded, related to chronic or acute exposure in the population, some of them should promptly be taken into account:

- either because they have already been the subject of EFSA opinions,
- or because they will be examined after current or upcoming appraisals aiming to include certain active substances in annexe I of Directive 91/414/EEC,
- or because they are currently being examined as part of the reappraisal of all of the MRLs that had been kept 'as is' in Regulation (EC) no. 396/2005.

However, AFSSA would like to draw attention to the situation of:

- substances that are definitively not listed in annexe I for which the refined TMDI is greater than the ADI (Cyanides*, Diazinon*, Dieldrin*, Disulfoton*, Fenthion*, Furfural*, Heptachlor*, Methidathion*, Trichlorfon*). The protection level related to MRLs should be evaluated based on actual contamination levels in foods and the MRLs should be adjusted accordingly if necessary. As for Vinclozoline*, EFSA recommended lowering the MRLs and this could be extended to wine grapes.
- substances definitively not included in annexe I and having MRLs that cause the ARfD to be exceeded (Amitraz*, Bitertanol*, Chlorfenapyr*, Dodine*, Endosulfan*, Fenpropathrin*, Fentin Acetate and Hydroxide*, Methidathion*, Phorate*, Pyrazophos* and Rotenone*). The MRLs in question should be revised downward, if necessary, by making analytical improvements.
- substances included in annexe I for which the ARfD was exceeded (Pirimicarb[1] and Formetanate[1]) whereas no reappraisal of the MRL is planned over the short term. A refined assessment of acute risk to consumers related to the presence of Pirimicarb[1] in apples and Formetanate[1] in courgettes, based on more precise data on levels observed during field trials or monitoring, is recommended.

Moreover, it should be noted that some of these situations occurred because the European model did not take into account AFSSA's recommendations in response to the requests 2007-SA-224

and 2007-SA-385, particularly as regarding data on the French population's dietary consumption. AFSSA therefore recommends rapidly updating the European model used for setting MRLs.

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Annexe 1: list of substances according to legislation specifying their MRLs (updated in February 2009)

Annexe 2: comprehensive list of values used for this Scientific and Technical Support (updated in February 2009)

Annexe 3: results of detailed adult, child and lifetime TMDI calculations by substance

Annexe 5: parameters used to estimate individuals' consumption in the INCA survey for each food product

These four appendices are in separate PDF files.

Annexe 4 is below.

Annexe 4: ESTI calculation equations

The ESTI value is determined using various equations depending on the food product:

Case 1: U<25g, U being the unit weight. For example, for rice, it is the weight of a grain of rice:

$$IESTI = \frac{LP \times (HR\,ou\,HR - P)}{bw}$$

This case applies to small fruits and vegetables and to products of animal origin, with the exception of milk and cereals, oilseeds and dry vegetables when the HR or HR-P is based on a post-harvest treatment.

Case 2: U>25g

Case 2a: U<LP (e.g. apples)	**Case 2b**: U>LP (e.g. watermelon)
$IESTI = \frac{U \times (HR\,ou\,HR - P) \times v + (LP - U) \times (}{bw}$	$IESTI = \frac{LP \times (HR\,ou\,HR - P) \times v}{bw}$
This equation may be worded as follows: we consider that the first unit weight consumed (e.g. a fruit or a vegetable) has a maximum contamination level (HR * v) given the variability of levels in a sample, while the following unit weights have a level that equals the maximum level observed during field trials (HR).	We take the heterogeneity or variability factor into account for the entire LP.

Case 3: Processed foodstuffs, as well as milk and cereals, oilseeds and dry vegetables when the STMR or the STMR-P is based on a pre-harvest treatment.

$$IESTI = \frac{LP \times STMR - P}{bw}$$

Where:

LP	Highest large portion provided (97.5th percentile of eaters) over one day (kg/person/day),
HR	highest residue level (mg/kg) found in a composite sample from the edible portion of a food during field trials,
HR-P	equivalent of the HR (mg/kg) for processed commodities,
bw	body weight (kg),
v	variability factor,
U	weight of the food's reference unit (kg),
STMR	supervised trials median residue (mg/kg),