Informes/Documentos Técnicos [58]

Derivation of processing factors for pesticide residues in cold pressed lemon oil (CPLO) and dietary risk assessment from pesticide residue intake

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CAJA RURAL

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DERIVATION OF PROCESSING FACTORS FOR PESTICIDE RESIDUES IN COLD PRESSED LEMON OIL (CPLO) AND DIETARY RISK ASSESSMENT FROM PESTICIDE RESIDUE INTAKE

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Design and layout: Beatriz Martínez Belmonte

Print: Masquelibros

Legal Deposit: AL-1428-2018

Date of publication: July 2018

Printed in Spain

Índice

Acknowledgements / *Agradecimientos*

This study has been possible thanks to: / *Este estudio ha sido posible gracias a:*

- John Bean Technologies (JBT) | *Carlos Fernández, David del Castillo y Pepe Lorente*
- Zumofresh Levante, SLU
- Cítricos de Murcia, SA
- Citromil, SL
- Miguel Parra e Hijos, SA
- Frutas Apemar, SL
- Frutas Condiso, SL
- Laboratorios Ecosur, SA
- AGREXIS AG | *Dr. Sabine Lorenz*
- Agrupación Española de Servicios y Procesos Postcosecha (AGRUPOST) | *Javier Gómez*
- European Federation of Essential Oils (EFEO) | *Jorge Miralles*
- AILIMPO | *Raúl Alcázar*

and the collaboration of: / *Y la colaboración de:*

- Agencia Española de Consumo, Seguridad Alimentaria y Nutrición (AECOSAN) | *Victorio Teruel, César Casado y Alicia Yagüe*
- Consejería de Agua, Agricultura, Ganadería y Pesca de la Región de Murcia | *Francisco José González Zapater*
- Cajamar Caja Rural

AILIMPO

AILIMPO is the Spanish Lemon and Grapefruit Interbranch Association representing all economic activities related to the production, trade and processing of these citrus products in Spain with an average annual turnover of 700 million €.

Ailimpo was founded in 1998 and is officially recognised by the European Commission according to Regulation (EU) no 1308/2013, formerly Regulation (EC) no 2200/96 (OJ C 190/ 7.7.1999).

Ailimpo focuses on:

- *improving knowledge and the transparency of production and the market;*
- *helping to coordinate better the way the products are placed on the market, in particular by means of research and market studies;*
- *drawing up standard forms of contract compatible with Union rules;*
- *exploiting to a fuller extent the potential of the fruit and vegetables produced;*
- *providing the information and carrying out the research necessary to adjust production towards products more suited to market requirements and consumer tastes and expectations, in particular with regard to product quality and protection of the environment;*
- *seeking ways of restricting the use of plant-health products and other inputs and ensuring product quality and soil and water conservation;*
- *developing methods and instruments for improving product quality at all stages of production and marketing;*
- *exploiting the potential of organic farming and protecting and promoting such farming as well as designations of origin, quality labels and geographical indications;*
- *promoting integrated production or other environmentally sound production methods.*

Summary / *Resumen*

The Spanish lemon processing industry produces cold pressed lemon oil (CPLO) from fresh lemons as raw material. Considering that CPLO is obtained from the oil glands located in the very external peel of fresh lemons, a higher concentration of pesticide residues is expected in the final product.

CPLO is not consumed directly as it is an ingredient used in a very low quantities in the composition of other food products, mainly soft drinks and beverages. For this reason, in pesticide presence terms, the impact on the final product for consumer is very limited.

MRLs are set in accordance with Regulation (EC) 396/2005 for pesticide residues in raw agricultural commodities (RAC) but no MRLs have been set for processed commodities although they are part of the scope of the Regulation. However, according to Article 20 (Reg (EC) 396/2005) «where MRLs are not set out in Annexes II or III for processed and/or composite food or feed, the MRLs applicable shall be those provided in Article 18(1) for the relevant product covered by Annex I, taking into account changes in the levels of pesticide residues caused by processing and/or mixing. Specific concentration or dilution factors for certain processing and/or mixing operations or for certain processed and/or composite products may be included in the list in Annex VI».

Unfortunately such processing factors are still not available for lemon oil, leaving the industry with considerable uncertainty as to the quality and consumer safety of the lemon oil product, even if legal compliance can be shown for pesticide residues in the raw commodity.

Since 2015, Ailimpo has been conducting a study and research program in order to assess the concentrations of 14 active substances residues in lemon oil obtaining a good collection of data. Based on this output, a chronic and acute consumer risk assessment has been done, concluding that residue intake from the consumption of lemon oil via soft drinks for the 14 active substances under investigation poses no unacceptable chronic or acute consumer risk to adults and children.

Furthermore, an approach has been done to calculate processing factors for lemon oil, based on processing factors obtained on the AILIMPO study and the potential correlation with the oil/water partition coefficient (log Pow). Log Pow was concluded to be a good predictor

of the PF for lemon oil for all substances with a log Pow ≥ 3 using the regression equation ($y = 40.66x – 81.04$) ($r^2 = 0.75$). For substances with a log Pow < 3 the prediction seems less accurate and residues in lemon oil may be overestimated. It is therefore proposed for all substances with a log Pow < 3 to use instead experimentally determined PF where available. A generic lemon oil PF of 2 is proposed to be used where no experimental data exist.

These processing factors for lemon oil are demanded to ensure harmonized interpretation of safety of product across MS´s avoiding distortions of the internal market, to support international trade, and to eliminate uncertainty and B2B disputes.

The Standing Committee on Plants, Animals, Food and Feed (SCoPAFF), Section Phytopharmaceuticals – Residues, met in Brussels on the 26-27 February 2018 with the participation of representants of the European and Commission and the Member States reviewed the AILIMPO study presented by the Spanish authorities. The proposal was discussed under point A30 of the agenda, concluding that according to the data provided, processing factors for 11 active substances could be taken into account. The summary report of the meeting makes the following statement:

- Processing factors in cold pressed lemon oil

  The point was added to the agenda by the chair on request of Spain.

  New studies have been submitted by a national association of producers of cold pressed lemon oil which demonstrate the safe application of certain processing factors for 11 substances. Spain, who had received the studies, suggested that those processing factors should be taken into consideration also by other national authorities. The Commission invited the other Member States to take those studies into account if considered appropriate.

The complete summary report of the meeting can be found here:

On the 25th April 2018, AECOSAN the Spanish Agency for Consumer Affairs, Food Safety and Nutrition depending from the Ministry of Health, Social Services and Equality, published an informative note on its webpage with the detailed processing factors applicable to Cold Pressed Lemon Oil.

The complete informative note from AECOSAN can be found here:

The details for the 11 substances can be found in this table: Active Substance, Processing Factor, MRL for Fresh Lemons, and the resulting MRL for CPLO:

	Mean PF AILIMPO data	EU MRL (lemon RAC) mg/kg	MRL_{det} lemon oil mg/kg
Chlorpyrifos	161,0	0,2	32,0
Chlorpyrifos-methyl	58,0	0,3	17,0
2-Phenylphenol	71,4	5,0	357,0
Pyriproxyfen	121,7	0,6	73,0
Pyrimethanil	56,0	10,0	560,0
Propiconazole	58,4	6,0	350,0
Imazalil	2,6	5,0	13,0
Prochloraz	31,9	10,0	319,0
Thiabendazole	0,8	5,0	4,0
Hexythiazox	34,0	1,0	34,0
Metalaxyl/Metalaxyl-M	4,5	0,5	2,0

*El sector de transformación de limón de España produce aceite de limón esencial (*Cold Pressed Lemon Oil-CPLO*) a partir de limones frescos como materia prima. Si se tiene en cuenta que el CPLO se obtiene de las glándulas oleosas que se encuentran en la piel externa de los limones frescos, se espera que haya una concentración alta de residuos de pesticidas en el producto final.*

El CPLO no se consume directamente, ya que es un ingrediente que se usa en cantidades muy pequeñas en la composición de otros productos alimentarios, como refrescos y bebidas. Por este motivo, en lo que respecta a la presencia de pesticidas, el impacto en el producto final para el consumidor es muy reducido.

Los límites máximos de residuos (LMR) vienen fijados conforme al Reglamento (CE) 396/2005 para residuos de pesticidas para materias primas agrícolas (RAC), pero no se ha establecido ningún LMR para los productos procesados, aunque forman parte del ámbito del reglamento. No obstante, según el artículo 20 (Reglamento [CE] 396/2005) «donde no se hayan estipulado los MRL en los Anexos II o III para comida o alimentos procesados o compuestos, los MRL aplicables serán los indicados en el artículo 18(1) del producto correspondiente tratado en el Anexo I, teniendo en cuenta los cambios en los niveles de residuos de pesticidas debidos al procesamiento o la mezcla. Los factores de concentración o disolución específicos para determinadas operaciones de procesamiento o mezcla, o para determinados productos procesados o compuestos, pueden estar incluidos en la lista del Anexo VI».

Lamentablemente, dichos factores de transferencia siguen sin estar disponibles para el aceite esencial de limón, lo que provoca un alto nivel de incertidumbre, incluso a pesar de que exista cumplimiento legal en cuanto a residuos de pesticidas en la materia prima utilizada (limones frescos).

Desde 2015 Ailimpo ha llevado a cabo un programa de estudio e investigación para evaluar las concentraciones de 14 residuos de sustancias activas en el aceite esencial de limón, lo que le ha permitido disponer de una buena base de datos. A partir de estos resultados, se ha efectuado una evaluación del riesgo crónico y agudo para el consumidor llegando a la conclusión de que la ingesta de residuos de pesticidas por el consumo de aceite esencial de limón en refrescos, correspondiente a las 14 sustancias activas de la investigación no supone un riesgo crónico o agudo inaceptable para adultos y niños.

Además, se han calculado los factores de transferencia para aceite esencial de limón tomando como base los datos experimentales obtenidos en el estudio de AILIMPO, así como la posible correlación con el coeficiente de reparto de aceite/agua (log Pow). Se llegó a la conclusión de que este coeficiente constituye un indicador adecuado del factor de transferencia para aceite esencial de limón para todas las sustancias, con un coeficiente log Pow ≥ 3 mediante la ecuación de regresión *(y = 40,66x-81,04) (r^2 = 0,75). En el caso de las sustancias con un coeficiente log Pow <3, la predicción a través de esta ecuación parece menos precisa y se podría llegar a hacer una sobrevaloración de los residuos en el aceite de limón. Por lo tanto, se propone que se use para todas las sustancias con un coeficiente log Pow < 3 en vez del PF determinado experimentalmente donde esté disponible. Finalmente, se propone que se use un factor de transferencia genérico de 2 para aquellos casos en los que no estén disponibles datos experimentales.*

El objetivo de este trabajo y de sus conclusiones es garantizar una interpretación armonizada de la seguridad del producto en los diferentes Estados miembro de la UE para evitar distorsiones del mercado interno, respaldar el comercio internacional y eliminar la incertidumbre y las disputas en el ámbito B2B.

El Comité Permanente de Plantas, Animales, Alimentos y Piensos (SCoPAFF), Sección Fitofármacos y Residuos, reunido en Bruselas el 26 y 27 de febrero de 2018 con la participación de representantes de la Comisión europea y de los Estados miembro, analizó el estudio de AILIMPO presentado por las autoridades españolas. La propuesta se debatió en el punto A30 del orden del día, concluyendo que, de acuerdo con los datos aportados pueden considerarse factores de transferencia para 11 materias activas.

- *Factores de transferencia en CPLO - Aceite Esencial de limón prensado en frío.*

  El punto se incluyó en el orden del día por el presidente a petición de España.

  Los nuevos estudios aportados por una asociación nacional de productores de aceite esencial de limón prensado en frío, han probado la aplicación segura de factores de transferencia para 11 materias activas. España, que ha recibido estos estudios, propuso que estos factores de transferencia se tomasen en consideración también por el resto de autoridades nacionales. La Comisión invitó a los Estados miembro a tener en cuenta estos estudios si lo consideraban adecuado.

El informe completo de la reunión del Comité Permanente puede consultarse aquí:

El 25 de abril de 2018, AECOSAN, la Agencia Española de Consumo, Seguridad Alimentaria y Nutrición (AECOSAN), dependiente del Ministerio de Sanidad, Servicios Sociales e Igualdad, publicó una nota informativa en su página web con el detalle de los factores de transferencia aplicables a aceite esencial de limón prensado en frío (CPLO).

La nota informativa completa puede consultarse aquí:

Los valores aplicables para las 11 materias activas puede encontrarse en la siguiente tabla, con el detalle para cada materia activa del LMR aplicable para limón fresco, el factor de transferencia y el resultante LMR para CPLO:

	Factor transferencia promedio. Dato estudio AILIMPO	LMR UE (limón fresco) mg/kg	LMR_{det} aceite de limón mg/kg
Chlorpyrifos	161,0	0,2	32,0
Chlorpyrifos-methyl	58,0	0,3	17,0
2-Phenylphenol	71,4	5,0	357,0
Pyriproxyfen	121,7	0,6	73,0
Pyrimethanil	56,0	10,0	560,0
Propiconazole	58,4	6,0	350,0
Imazalil	2,6	5,0	13,0
Prochloraz	31,9	10,0	319,0
Thiabendazole	0,8	5,0	4,0
Hexythiazox	34,0	1,0	34,0
Metalaxyl/Metalaxyl-M	4,5	0,5	2,0

EUROPEAN COMMISSION

Health and Food Safety Directorate General

sante.ddg2.g.5(2018)1450427

Standing Committee on Plants, Animals, Food and Feed
Section *Phytopharmaceuticals - Residues*
26-27 February 2018

SUMMARY REPORT

A.30 AOB

- Processing factors in cold pressed lemon oil

  The point was added to the agenda by the chair on request of Spain.

  New studies have been submitted by a national association of producers of cold pressed lemon oil which demonstrate the safe application of certain processing factors for 11 substances. Spain, who had received the studies, suggested that those processing factors should be taken into consideration also by other national authorities. The Commission invited the other Member States to take those studies into account if considered appropriate.

MINISTERIO
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FACTORES DE TRANSFORMACIÓN PARA ACEITE DE LIMÓN PRENSADO EN FRÍO

25 de abril de 2018

El Reglamento (CE) Nº 396/2005, del Parlamento Europeo y del Consejo relativo a los límites de residuos de plaguicidas (LMR) en alimentos y piensos de origen animal y vegetal y que modifica la Directiva 91/414/CEE del Consejo (Diario Oficial de la Unión Europea serie L70 del 16.03.05), en su Anexo I incluye aquellas materias primas sin transformar sobre las que se fijan los LMRs, por ello es necesario aplicar factores de transformación (concentración, dilución…etc.) sobre el LMR del producto inicial, según se establece en el artículo 20.1 del Reglamento anteriormente mencionado.

Actualmente no existen factores de transformación armonizados en la UE, algo que en ocasiones supone problemas en la interpretación de resultados cuando se analizan productos procesados y, en ocasiones, problemas comerciales.

La inclusión de factores de transformación armonizados en el anexo VI del Reglamento 396/2005 (aún no publicado), permitiría poner fin a los problemas mencionados, sin embargo teniendo en cuenta la complejidad de los productos procesados y la gran variabilidad, es un trabajo que aún está pendiente.

Para conocer la situación actual y cómo se aplican los LMR a productos transformados puede consultar la siguiente nota web:
http://www.aecosan.msssi.gob.es/AECOSAN/docs/documentos/seguridad_alimentaria/gestion_riesgos/contenido_extra_5_LMR_en_transformados.pdf

Mientras tanto, a la espera de la publicación del anexo VI del Reglamento 396/2005, es responsabilidad del operador demostrar la solidez de los factores de procesamiento a aplicar en su producción. Es por ello, que aparte del trabajo que se hace desde las autoridades oficiales, en algunos sectores industriales se realicen estudios para establecer factores de transformación y así poder aplicar los LMRs de forma adecuada a sus productos. Ese es el caso de la Asociación Interprofesional del Limón y Pomelo (AILIMPO) que recientemente ha presentado un completo estudio para el establecimiento de factores de concentración en aceite de limón prensado en frío que permite establecer dichos factores para 11 sustancias en ese producto en particular. Los valores de referencia obtenidos pueden consultarse en el siguiente cuadro:

	Mean PF AILIMPO data	EU MRL (lemon RAC) mg/kg	MRL_{det} lemon oil[(1)] mg/kg
Chlorpyrifos	161	0.2	32
Chlorpyrifos-methyl	**58**	0.3	17
2-Phenylphenol	**71.4**	5	357
Pyriproxyfen	**121.7**	0.6	73
Pyrimethanil	**56**	10	560
Propiconazole	**58.4**	6	350
Imazalil	**2.6**	5	13
Prochloraz	**31.9**	10	319
Thiabendazole	**0.8**	5	4
Hexythiazox	**34**	1	34
Metalaxyl/Metalaxyl-M	**4.5**	0.5	2

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Desde AECOSAN se apoya la iniciativa de AILIMPO, considerando de gran utilidad las conclusiones alcanzadas ante la ausencia de factores de transformación, y sobre unos productos en los que la concentración de las materias activas es notable y están sometidos a un intenso tráfico comercial. Por todo ello, los resultados de los estudios mencionados fueron presentados por AECOSAN ante la Comisión, EFSA y los 28 países de la UE en el Comité Permanente de Vegetales, Animales, Alimentos y Piensos – Sección « residuos de plaguicidas en alimentos» (reunión de 26-27 de febrero de 2018) con el fin de que fueran tomados en consideración por otras autoridades nacionales. La Comisión invitó a los demás Estados miembros a tener en cuenta esos estudios.

Se puede consultar el resumen de la reunión de CPVAAP de febrero en el que se incluyó en el Punto A.30-AOB en el siguiente enlace:
https://ec.europa.eu/food/sites/food/files/plant/docs/sc_phyto_20180226_ppr_sum.pdf

1. Background

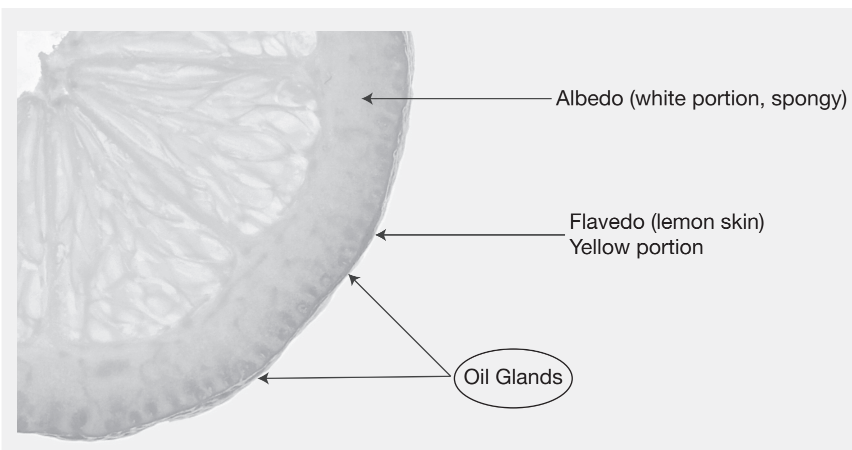
1. In the EU, MRLs (Maximum Residue Limits) are set in accordance with Regulation (EC) 396/2005 for pesticide residues in raw agricultural commodities (RAC). No MRLs have been set for processed commodities although they are part of the scope of the Regulation. However, according to Article 20 (Reg (EC) 396/2005 «where MRLs are not set out in Annexes II or III for processed and/or composite food or feed, the MRLs applicable shall be those provided in Article 18(1) for the relevant product covered by Annex I, taking into account changes in the levels of pesticide residues caused by processing and/or mixing. Specific concentration or dilution factors for certain processing and/or mixing operations or for certain processed and/or composite products may be included in the list in Annex VI».
2. To-date, such processing factors are still not available for lemon oil, leaving the industry with considerable uncertainty as to the quality and consumer safety of the lemon oil product, even if legal compliance can be shown for pesticide residues in the raw commodity.
3. Considering that CPLO is obtained from the oil glands located in the very external peel of fresh lemons, a higher concentration of pesticide residues is expected in the final product.
4. Absence of clear regulation means a potential risk (eg Different Member States applying different PF). In addition, a Grey / Black area around pesticide residues in B2B contract specifications has been developed and as a result clients demand for compliance but there is no legal nor clear reference to comply. A practical approach to solve this situation leads to a demand from clients to apply USA Regulation due to lack of EU Regulations or simply to demand for 0 mg/kg residues on CP Lemon Oil.
5. The result is that EU CP Lemon Oil Producers must prove legal compliance of their products but at this stage only raw material (fresh lemons) compliance with Regulation (EC) 396/2005 can be proved.
6. In 2015 AILIMPO conducted a study in order to assess the concentrations of 15 commonly found active substances or their

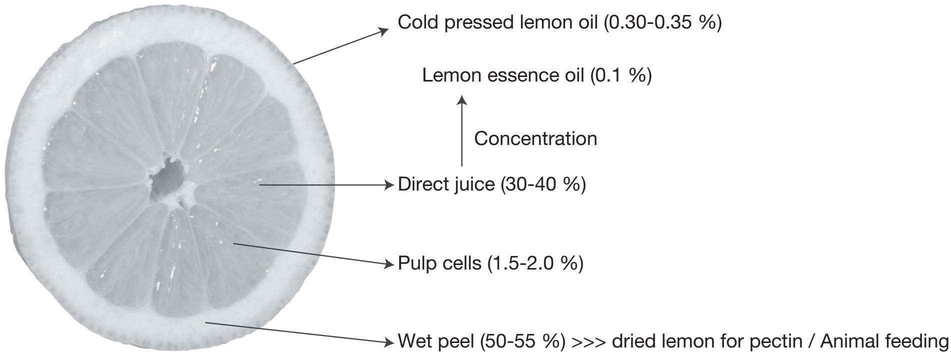
metabolites in fresh lemons (whole fruit) and CPLO, obtaining a good collection of data.

7. This report describes in detail the AILIMPO study and the results obtained. Based on this output, a chronic and acute consumer risk assessment has been done.
8. Finally, an approach is explored to estimate processing factors for lemon oil, based on processing factors obtained on the AILIMPO study and the potential correlation with the oil/water partition coefficient (log Pow). Setting of MRL´s following this procedure would ensure harmonized interpretation of safety of product across MS´s avoiding distortions of the internal market, to support international trade, and to eliminate uncertainty and B2B disputes.
9. Also, an overview about how this topic is addressed in the USA and Canada is enclosed.

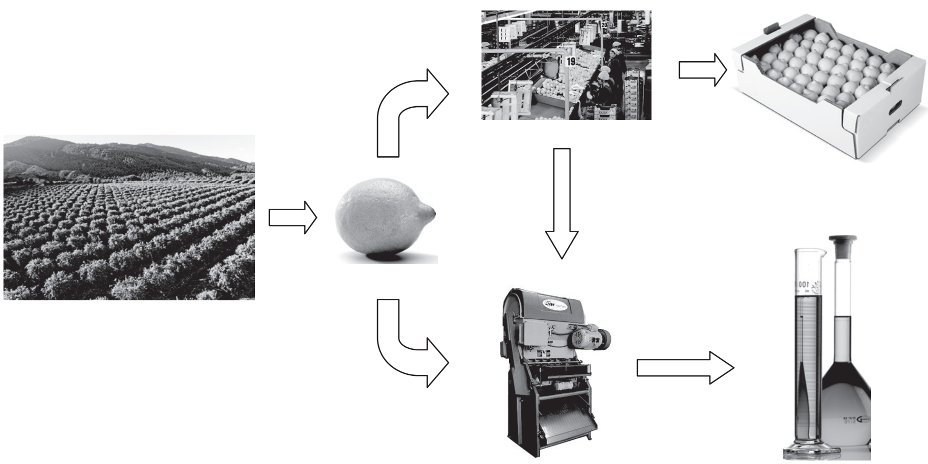
2. About cold pressed lemon oil

10. The following products are obtained processing fresh lemons. We obtain from the oil glands about 0.30-0.35 % of cold pressed oil, which is extracted from the skin with no thermal treatment and has the golden yellow colour of the lemon.

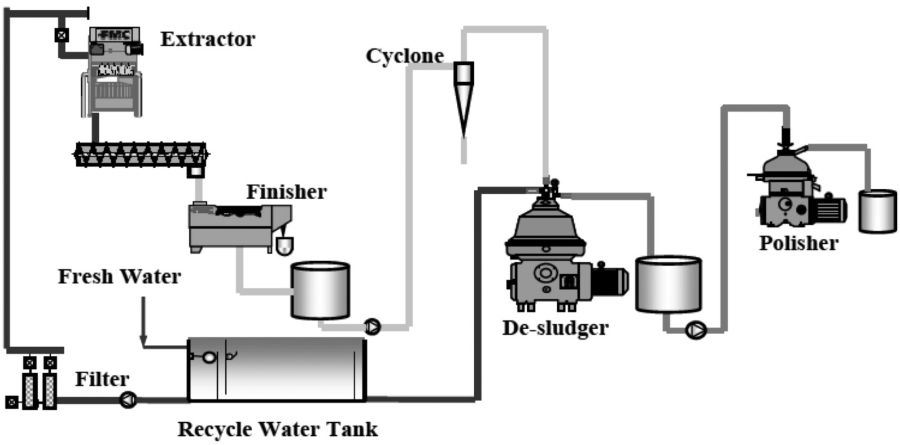




11. Lemon fruit sent to processing may come both from a packing house or directly from the orchard.



12. How is the extraction? The European lemon processing industry produces cold pressed lemon oil (CPLO) from fresh lemons as raw material using common technology based on JBT Food Tech extraction systems. Flow diagram of a typical CPLO manufacturing plant (JBT oil Recovery System):



13. What is used for? CPLO is mainly used in the Food Industry as an ingredient (eg Soft Drinks, Juices…). It is also used in Perfumery and cosmetic industry. As CP Lemon Oil is not consumed directly, it is an ingredient used in a very low proportion in the formulation of other food products. Thus, in pesticides presence terms, impact on the final product is very limited as quantity of CP Lemon Oil added is quite small.

3. Determination of pesticides residues in RAC and processed cplo samples. AILIMPO experimental study

14. Target. Target of the study was to quantify residue levels on lemons (RAC) and CP lemon oil obtained after processing them. The following processing companies were directly involved in the design of the AILIMPO study:

- Cítricos de Murcia, SA.
- Citromil, SL.
- Miguel Parra e Hijos, SA.

15. Fresh fruit. The following companies based on Murcia provided fresh fruit:

- Apemar, SL.
- Frutas Condiso, SL.

16. Processing. Processing of lemons was carried out as follows:

- Using 100 % JBT Technology.
- Study at a real industrial scale, not a laboratory scale.
- Trials carried out in an industrial operative plant. Zumofresh in Murcia.

  → 3 trials were carried out: Trial 1 – Trial 2 – Trial 3.

  → 3.000 kilos of fresh lemons were processed per trial considering the 2 main lemon varieties cultivated in Spain [Fino (2 trials) and Verna (1 trial)] representing the distribution of Spanish lemon crop (70 % fino / 30 % verna). 4 pallets of 36 boxes each trial.

  → Representative Samples taken by Laboratorios Ecosur (1 unit per box in each trial).

  → Processing data taken by JBT Experts.

Industrial plant where trials were done

17. Sampling. Samples taken:
    - Fresh Fruit (Whole Fruit).
    - CP Lemon Oil (Samples taken after centrifuge).

Trial	Variety	RAC processed (kg)	Washing	Analysed matrices	
				RAC (kg)	Oil (ml)
1	Fino	3,000	No	25	75
			Yes	25	
2	Fino	3,000	No	25	50
			Yes	25	
3	Verna	3,000	No	25	50
			Yes	25	

18. Laboratory Analysis. Laboratory certifications approvals and titles:
    - Laboratorios Ecosur has implemented UNE-EN ISO/IEC 17025 certified quality system. It currently holds certification numbers 354/LE709 and 354/LE976, issued by Entidad Nacional de Acreditación (ENAC). See Annex A.
    - Holds UNE-EN-ISO-9.001 certification number ESO6/2209.
    - Active member of Spanish Association of Independent Laboratories (AELI).
    - Active member of Union Internationale des Laboratoires Indépendants (UILI).
    - Member of Bureau Interprofessionnel des Etudes Analytiques (BIPEA- International Bureau for Analytical Studies).
    - Laboratorios Ecosur is certified to carry out QS tests. QS Facesellschaft Obst-Gemüse-Kartoffeln Gmbh.

19. Residue pesticide analysis techniques**.** Analytical work based on QuEChERS (Quick, Easy, Cheap, Effective, Rugged, and Safe) method with extraction method (extraction and clean-up) first. The identification and quantification of pesticides were by gas chromatography mass spectrometry, in mass-mass mode, and liquid chromatography mass spectrometry, in mass-mass mode. Analysis using Gas Chromatographic (GC)/MS SCION Bruker

system: autosampler column oven and triple quadrupole detector and Ultra Performance Liquid Chromatography (UPLC)/MS, EVOQ Bruker system: UPLC pump, autosampler and triple quadrupole detector.

20. Results. Detailed report of each analysis carried on Trials 1 & 2 & 3 is enclosed in Annex B.

21. Processing factors for CPLO/FL. Residue levels were taken without washing for trials 1 and 2 and with washing for trial 3. PF were calculated for each trial (1, 2 and 3 are indicated on the next table in the same order) and then the mean value was obtained:

Active substance	Fresh Lemons (FL) mg/kg	Cold Pressed Lemon Oil (CPLO) mg/kg	Processing Factor Lemon Oil (CPLO/FL)
2, 4, 6 - Trichlorophenol[a]	0.870	26.480	30.4
	0.700	19.670	28.1
	0.060	7.130	118.8
Mean	0.540	17.760	59.1
Chlorpyrifos	0.030	3.140	104.7
	0.020	4.030	201.5
	0.006	1.060	176.7
Mean	0.019	2.740	160.9
Chlorpyrifos-methyl	nd	0.080	N/A
	nd	0.070	N/A
	0.005	0.290	58.0
Mean	0.005	0.150	58.0
Dicofol	nd	0.090	N/A
	nd	nd	N/A
	nd	nd	N/A
Mean	nd	0.090	N/A
2 - Phenylphenol	0.580	36.420	62.8
	1.550	80.740	52.1
	0.800	79.390	99.2
Mean	0.980	65.520	71.4

Active substance	Fresh Lemons (FL) mg/kg	Cold Pressed Lemon Oil (CPLO) mg/kg	Processing Factor Lemon Oil (CPLO/FL)
Pyriproxyfen	0.040	5.540	138.5
	0.040	5.220	130.5
	0.020	1.920	96.0
Mean	0.030	4.230	121.7
Pyrimethanil	0.010	0.860	86.0
	0.120	4.420	36.8
	0.440	19.940	45.3
Mean	0.190	8.410	56.0
Propiconazole	0.010	0.560	56.0
	0.006	0.460	76.7
	0.004	0.170	42.5
Mean	0.007	0.400	58.4
Propyzamide	nd	0.190	N/A
	nd	0.160	N/A
	nd	0.040	N/A
Mean	nd	0.130	N/A
Tebufenpyrad	nd	0.400	N/A
	nd	0.200	N/A
	nd	0.140	N/A
Mean	nd	0.250	N/A
Imazalil	1.190	0.970	0.8
	1.230	5.450	4.4
	1.390	3.700	2.7
Mean	1.270	3.370	2.6
Prochloraz	2.110	49.670	23.5
	2.260	90.740	40.2
	nd	9.830	N/A
Mean	2.190	50.080	31.8
Thiabendazole	1.270	0.410	0.3
	3.000	3.90	1.3
	nd	nd	N/A
Mean	2.140	2.160	0.8

Active substance	Fresh Lemons (FL) mg/kg	Cold Pressed Lemon Oil (CPLO) mg/kg	Processing Factor Lemon Oil (CPLO/FL)
Hexythiazox	nd	0.280	N/A
	0.005	0.180	36.0
	0.010	0.320	32.0
Mean	0.008	0.260	34.0
Metalaxyl / Metalaxyl-M	nd	nd	N/A
	nd	nd	N/A
	0.020	0.090	4.5
Mean	0.020	0.090	4.5

[a] Metabolite of prochloraz. Residue definition: sum of prochloraz and its metabolites containing the 2,4,6-Trichlorophenol moiety expressed as prochloraz.

nd = not detected.

N/A = not applicable.

4. Consumer risk assessment

22. A Consumer Risk Assessment for Pesticide Residue Intake from Lemon Oil was commissioned and carried out in 2017 by the swiss consulting company AGREXIS AG based in Basel – Switzerland. AGREXIS is an independent company offering scientific and regulatory consulting services to the Agrochemical and Biocidal industry.
23. Full AGREXIS AG report «Derivation of processing factors for pesticide residues in lemon oil and dietary risk assessment from pesticide residue intake» is enclosed in Annex C.
24. An extract from the AGREXIS report considering only the AILIMPO generated data is descripted as follows (please note that AGREXIS report is including additional scenarios).
25. In a further step, theoretical lemon oil MRLs were calculated for 14 substances (2,4,6-trichlorophenol was not included since it is not an active substance) based on PF from the AILIMPO study and using EU MRLs for lemon (RAC). The MRL_{det} was obtained by multiplying mean PF as determined in the AILIMPO study with EU MRLs for lemon (RAC):

	Mean PF AILIMPO data	EU MRL (lemon RAC) mg/kg	MRL_{det} lemon oil[a] mg/kg
Chlorpyrifos	161.00	0.20	32
Chlorpyrifos-methyl	58.00	0.30	17
Dicofol	-	0.02	0
2-Phenylphenol	71.40	5.00	357
Pyriproxyfen	121.70	0.60	73
Pyrimethanil	56.00	10.00	560
Propiconazole	58.40	6.00	350
Propyzamide	-	0.01	0
Tebufenpyrad	-	0.50	0
Imazalil	2.60	5.00	13
Prochloraz	31.90	10.00	319
Thiabendazole	0.80	5.00	4
Hexythiazox	34.00	1.00	34
Metalaxyl/Metalaxyl-M	4.50	0.50	2

[a] calculated by multiplying measured PF with EU MRL (lemon RAC).

26. A consumer risk assessment was done for adults and children using the following parameters / assumptions:

a) Using theoretical MRL_{det}.
b) ADI (Acceptable Daily Intake) for chronic and ARfD (Acute Reference Dose) for acute risk assessment, as published on EU Pesticide Database.
c) Body weights for child (16.15 kg) and adult (68.5 kg) according to EFSA PRIMo Rev.2 model.
d) Intake of lemon oil is assumed to be exclusively via soft drinks that contain 0.03% lemon oil.

e) Consumption data for acute intake assume that all liquid intake is via soft drink. According to WHO (2008), the default assumption for water intake is 2 L per day for adults and 1 L for children (10 kg bw). The liquid intake for children was adjusted here to 1.6 L per day to account for the greater body weight as compared to the WHO assumption.

f) Consumption data for chronic intake via soft drink were assumed to be 50% of standard liquid intake (1 L per day for adults, 0.8 L per day for children); for acute intake via soft drink assumptions were 2.5 L per day for adults and 2 L per day for children.

g) For the chronic risk assessment, usually all commodities that may be treated with the active substance and for which MRLs exist are included in the risk assessment. This is not feasible here since consumption and MRLs for fresh commodities include intake from processed foods already, and no separate intakes for processed foods are considered in the risk assessment models. Replacing existing MRLs for the RAC lemon (or citrus) with the «virtual» MRLs for citrus oil would overestimate intake. Only residue intake from lemon oil is therefore considered in the chronic risk assessment done here.

h) For the acute risk assessment, only substances are considered for which an ARfD has been set, i.e. for which acute toxicity has been shown. Where there is no acute toxicity and therefore no ARfD, an acute risk assessment is not necessary and not carried out.

27. The results of the consumer risk assessment using MRL_{det} are shown in table below.

Chronic and acute consumer risk assessment for children (16.15 kg bw) and adults (68.5 kg bw) for 14 pesticide active substances from consumption of lemon oil in soft drink – based on theoretical $MRLs_{det}$ for lemon oil

		Chronic risk assessment					Acute risk assessment				
			Child (16.5 kg bw)		Adult (68.5 kg bw)			Child (16.5 kg bw)		Adult (68.5 kg bw)	
Active substance	MRLdet lemon oil mg/kg	ADI mg/ kg bw	Max residue intake mg/ kg bw[a]	Max intake % ADI	Max residue intake mg/kg bw[b]	Max intake % ADI	ARfD mg/kg bw	Max residue intake mg/kg bw[c]	Max intake % ARfD	Max residue intake mg/kg bw[d]	Max intake % ADI
Chlorpyrifos	32	0.010	0.0005	4.8	0.0001	1.4	0.100	0.0012	1.2	0.0004	0.4
Chlorpyrifos-methyl	17	0.001	0.0003	25.9	0.0001	7.6	0.005	0.0006	12.9	0.0002	3.8
Dicofol	0	0.002	0.0000		0.0000		-	-	-	-	-
2 - Phenylphenol	357	0.400	0.0053	1.3	0.0016	0.4	-	-	-	-	-
Pyriproxyfen	73	0.100	0.0011	1.1	0.0003	0.3	-	-	-	-	-
Pyrimethanil	560	0.170	0.0083	4.9	0.0025	1.4	-	-	-	-	-
Propiconazole	350	0.040	0.0052	13.0	0.0015	3.8	0.300	0.0130	4.3	0.0038	1.3
Propyzamide	0	0.020	0.0000		0.0000		-	-	-	-	-
Tebufenpyrad	0	0.010	0.0000		0.0000		0.020	0.0000		0.0000	
Imazalil	13	0.025	0.0002	0.8	0.0001	0.2	0.050	0.0005	1.0	0.0001	0.3
Prochloraz	319	0.010	0.0047	47.4	0.0014	14.0	0.025	0.0119	47.4	0.0035	14.0
Thiabendazole	4	0.100	0.0001	0.1	0.0000	0.0	0.100	0.0001	0.1	0.0000	0.0
Hexythiazox	34	0.030	0.0005	1.7	0.0001	0.5	-	-	-	-	-
Metalaxyl/Metalaxyl-M	2	0.080	0.0000	0.0	0.0000	0.0	0.500	0.0001	0.0	0.0000	0.0

[a] Assumption: 800 mL soft drink per day containing 0.03 % citrus oil (=0.24 g).

[b] Assumption: 1 L soft drink per day containing 0.03 % citrus oil (=0.30 g).

[c] Assumption: 2 L soft drink containing 0.03 % citrus oil (=0.60 g).

[d] Assumption: 2.5 L soft drink containing 0.03 % citrus oil (=0.75 g).

NA: not applicable - no ARfD.

28. Chronic and acute intakes of residues from lemon oil are all below the toxicological reference values, with a considerable margin of safety for most active substances (marked green in the table).

29. With regard to the approach to chronic risk assessment, it may be argued that residue intakes from other commodities than lemon oil should also be considered. However, current MRLs for lemon (RAC) would already be based on residue intake from all sources and commodities, i. e. also including soft drink-based intakes. In addition, the assessment provides an overestimation of real intakes because it is assumed that, over the lifetime of a consumer, residues are always present at the MRL (when in reality residues are usually much lower) and that all commodities that may be treated with an active substance have been treated with it (despite the fact that no pesticide product has a market share of 100%). In a refined risk assessment therefore, the Supervised Trials Median Residue values (STMRs) would be used, which is always considerably lower than the MRL. STMRs would be available from EFSA opinions for a number of the active substances under consideration.

    Additionally, it could be considered to do a full chronic risk assessment. We would envisage an approach in which MRLs (or STMRs, where relevant and available) for all registered uses would be entered into the PRIMo model and the total intake (as % ADI) then be added to the intakes from citrus oil. This approach would, however, mean that intakes from lemon are somewhat overestimated, since the MRLs for RAC lemon should already include intake from processed commodities (such as citrus oil).

30. For acute risk assessment, commodities are always considered individually. That is, in common risk assessment models, the RAC lemon fruit would be assessed on its own, and some processed commodities are also considered. A proportion of total lemon fruit consumption is assumed to be from lemon oil, but the size of this proportion is not known since lemon oil is not included in any of the models. Since the calculated intakes are generally below 50 % of the ARfD, however, there seems to be a large enough margin to allow for residue intake from other lemon sources, e. g. as juice.

31. In addition, also in this acute assessment the use of MRLs gives an exaggerated result with regard to the possible peak intake of pesticide residues from citrus oil. This is because citrus oil in commercial processing operations involves a large number of fruit and considerable mixing, so that residues at the MRL are highly unlikely to be present in the resulting citrus oil product. Risk assessment models (e.g. EFSA PRIMo, WHO IESTI) use STMRs for commodities, which are bulked or blended (obtained by multiplying the STMR of the raw commodity by the PF) to obtain a more realistic result. In the absence of STMR data, a refinement of the acute risk assessment would currently not be possible.
32. Overall, it can be concluded that residue intake from the consumption of lemon oil via soft drinks for the 14 active substances under investigation poses no unacceptable chronic or acute consumer risk to adults and children.

5. A practical approach for setting mrl´s taking into account processing factors based on octanol/water partition coefficient (log Pow)

33. The octanol/water partition coefficient (log Pow) is defined as the ratio of a chemical's concentration in the octanol phase to its concentration in the aqueous phase of a two-phase octanol/water system.
34. A study to evaluate a potential correlation between lemon oil processing factor and log Pow was commissioned and carried out in 2017 by the swiss consulting company AGREXIS AG based in Basel – Switzerland. AGREXIS is an independent company offering scientific and regulatory consulting services to the Agrochemical and Biocidal industry.
35. Full AGREXIS AG report «Derivation of processing factors for pesticide residues in lemon oil and dietary risk assessment from pesticide residue intake» is enclosed in Annex C.
36. An extract from the AGREXIS report is descripted as follows (please note that AGREXIS report is including additional compiled information and calculations including processing factors searched in the literature and databases like BfR).

37. Facing the lack of reliable processing factors, the oil/water partition coefficient (log Pow) has been suggested as a predictor of pesticide residues in processed commodities. Fernandez-Alba (2009) found that log Pow correlated with the residue of 19 pesticides in citrus juice, apple juice and wine, but not in olive oil. In contrast, Li *et al.* (2012) found no relationship between log Pow and pesticide concentration in apple juice, however, they suggested a possible relationship between log Pow and residue in citrus oil.

38. In the following, an approach is explored to calculate generic processing factors for lemon oil, based on processing factors obtained from a processing study commissioned by AILIMPO and on log Pow of the pesticides.

39. Mean citrus oil PF AILIMPO study (lemon oil only) were then used further to assess the correlation between PF and the oil/water partition coefficient (log Pow). Log Pow values for each pesticide are based on data published in EU assessments as follows:

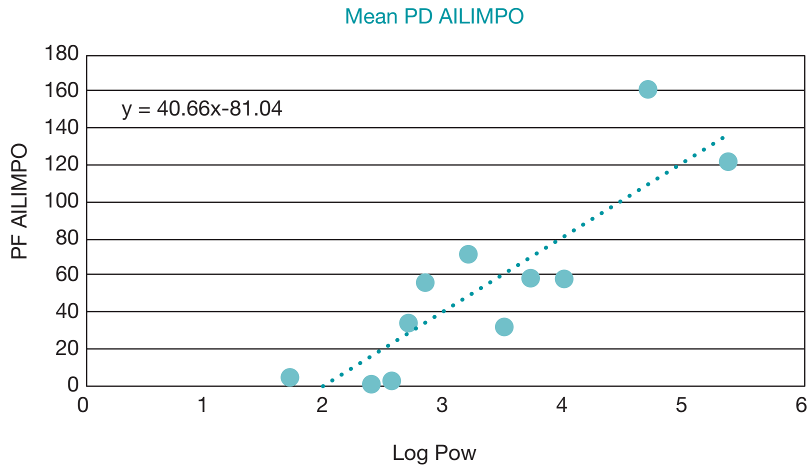
Active substance	log Pow	Source of log Pow
Chlorpyrifos	4.70	EU Review Report, Jan. 2005
Chlorpyrifos-methyl	4.00	EU Review Report, June 2015
Dicofol	-[a]	-[a]
2-Phenylphenol	3.20	Draft Assessment Report, May 2007
Pyriproxyfen	5.37	Draft Assessment Report, Nov. 2005
Pyrimethanil	2.84	Draft Assessment Report, April 2004
Propiconazole	3.72	Renewal Assessment Report, June 2016
Propyzamid	3.72	Renewal Assessment Report, July 2015
Tebufenpyrad	4.93	Draft Assessment Report, Nov. 2007
Imazalil	2.56	Draft Assessment Report, June 2009
Prochloraz	3.50	Draft Assessment Report, July 2010
Thiabendazole	2.39	Renewal Assessment Report, May 2013
Hexythiazox	2.70	Draft Assessment Report, June 2006
Metalaxyl / Metalaxyl-M	1.71	Renewal Assessment Report, Nov. 2013

[a] Not registered in the EU, therefore no log Pow published.

40. Linear correlations between mean PF and log Pow were calculated for all 11 active substances for which data were available (chlorpyrifos, chlorpyrifos-methyl, 2-phenylphenol, pyriproxyfen, pyrimethanil, propiconazole, imazalil, prochloraz, thiabendazole, hexythiazox, metalaxyl /metalaxyl-m). No processing data were available for dicofol, propyzamide and tebufenpyrad, which were therefore excluded. Also, 2,4,6-trichlorophenol was not included since it is not an active substance (it is a metabolite of prochloraz) and a log Pow has not been published.

41. Data and results of the regression analysis as follows:

Active substance	Log Pow	Mean PF AILIMPO
Chlorpyrifos	4.70	161.0
Chlorpyrifos-methyl	4.00	58.0
2 - Phenylphenol	3.20	71.4
Pyriproxyfen	5.37	121.7
Pyrimethanil	2.84	56.0
Propiconazole	3.72	58.4
Imazalil	2.56	2.6
Prochloraz	3.50	31.9
Thiabendazole	2.39	0.8
Hexythiazox	2.70	34.0
Metalaxyl /Metalaxyl-M	1.71	4.5
Linear regression equation		y = 40.66x-81.04
Correlation coefficient r2		0.75
Significance / F-value		0.0006



42. A good correlation was obtained for the data from the AILIMPO study (y = 40.66x-81.04), with a close and highly significant relationship between log Pow and lemon oil PF (r^2 = 0.75, F=0.0006).

43. Based on the data from the AILIMPO study it is suggested that log Pow of a substance may be a good predictor of the PF for lemon oil.

6. Applicability in the EU of US and Canada approaches to MRLS for citrus oil USA and Canada

44. A study to evaluate the applicability in the EU of US and Canada approaches to MRLs for citrus oil was commissioned and carried out in 2017 by the swiss consulting company AGREXIS AG based in Basel – Switzerland. AGREXIS is an independent company offering scientific and regulatory consulting services to the Agrochemical and Biocidal industry.

45. Full AGREXIS AG report «*Applicability in the EU of US and Canada approaches to MRLs for citrus oil*» is enclosed in Annex D.

7. Comments

7.1. Consumer risk assesment

46. Theoretical MRLs for lemon oil were calculated by multiplying MRLs for lemon RAC with the lemon oil PF. Two different lemon oil MRLs were calculated and used for the risk assessment: MRL_{det} was based on PF from analytical data in the AILIMPO study. MRL_{calc} was calculated for all substances with a log Pow ≥3 from the linear regression equation using the Log Pow of the substance and lemon oil PF from the AILIMPO study. For substances with a log Pow <3, a generic PF of 2 was used to obtain MRL_{calc}. However, experimental data should preferentially be used for these more hydrophilic substances.

47. MRL_{det} was obtained for 11 active substances for which analytical data were available (chlorpyrifos, chlorpyrifos-methyl, 2-phenylphenol, pyriproxyfen, pyrimethanil, propiconazole, imazalil, prochloraz, thiabendazole, hexythiazox, metalaxyl/metalaxyl-M). MRLcalc was obtained for three further active substance where no analytical data had been available (dicofol, propyzamide and tebufenpyrad), in addition to the 11 substances above.

48. Acute and chronic risk assessments were carried out for the residue intake from lemon oil in soft drink, using either MRL_{det} or MRL_{calc}, and based on the EFSA PRIMo Rev. 2 model. Worst-case assumption was made regarding the amount of soft drink consumed and the concentration of lemon oil in soft drink.

49. With both approaches, acute and chronic intake from lemon oil was usually well below 50% of the toxicological threshold values (ADI or ARfD), with the exception of prochloraz, where ADI and ARfD exhaustion for children was > 90% when the assessment was based on MRL_{calc}. However, when using $\underline{MRL_{det}}$, intake of prochloraz from lemon oil was much lower (< 50% of ADI/ARfD). Since $\underline{MRL_{det}}$ can be considered to be more realistic than MRL_{calc} it should be used where it is available, i.e. also in the case of prochloraz.

50. However, for substances with log Pow ≥3 for which no measured PF is available and therefore no MRL_{det} can be derived, risk assessment is possible by using lemon oil PF that are derived from the linear correlation between log Pow of the substance.

7.2. A practical approach for setting MRL´S taking into account processing factors based on octanol/water partition coefficient (log pow)

51. Lemon oil PF were available for 12 active substances (2, 4, 6-trichlorophenol, chlorpyrifos, chlorpyrifos-methyl, 2-phenylphenol, pyriproxyfen, pyrimethanil, propiconazole, imazalil, prochloraz, thiabendazole, hexythiazox, metalaxyl/metalaxyl-M) from an AILIMPO processing study. No processing factors were available for dicofol, propyzamide and tebufenpyrad.

52. In order to determine whether log Pow can be used to predict the concentration of residues in lemon oil, linear correlations of mean citrus oil PF with the relevant log Pow of the substance were calculated in a further step. Data from 11 active substances were used for the analysis.

53. A good correlation was obtained with PF data from the AILIMPO study, showing a close and significant relationship between lemon oil PF and log Pow ($r^2 = 0.75$).

54. In a further step, theoretical lemon oil processing factors were calculated using the regression equation from the AILIMPO processing data study ($y = 40.66x - 81.04$). In addition to the 11 active substances above, lemon oil PF were also calculated for three substances, for which no processing data are available (dicofol, propyzamide and tebufenpyrad). There was generally good agreement between measured and calculated lemon oil PF. However, it appears, that at a log Pow between 2.56 and 2.7 and below, the calculation becomes less accurate.

55. Based on the data from AILIMPO study it was concluded that, for substances with a log Pow of 3 or greater, log Pow is a useful indicator of the expected concentration of pesticide residue in lemon oil. A log Pow of 3 rather than 2.7 was chosen since it is generally used as a cut-off point for determining lipophilicity of a substance.

56. For water soluble substances with a log Pow <3, the concentration of residue in lemon oil is generally small and cannot accurately be predicted via log Pow. To account for the fact that for these substances some concentration of residue may still occur,

it is proposed to use experimental data if available. Only if no experimental data are available, a generic PF of 2 may be used.

57. Overview of calculated lemon oil PF, EU MRLs for lemon and theoretical lemon oil MRL_{calc}.

	Calculated PF[a]	EU MRL (lemon RAC) mg/kg	MRL_{calc} lemon oil[b] mg/kg
Chlorpyrifos	110	0.20	22.0
Chlorpyrifos-methyl	82	0.30	24.0
Dicofol	123	0.02	2.0
2-Phenylphenol	49	5.00	245.0
Pyriproxyfen	137	0.60	82.0
Pyrimethanil	34	10.00	344.0
Propiconazole	70	6.00	421.0
Propyzamide	70	0.01	0.7
Tebufenpyrad	119	0.50	60.0
Imazalil	2[c]	5.00	10.0
Prochloraz	61	10.00	613.0
Thiabendazole	2[c]	5.00	10.0
Hexythiazox	2[c]	1.00	2.0
Metalaxyl/Metalaxyl-M	2[c]	0.50	1.0

[a] Calculated using equation y = 40.66x-81.04.

[b] Calculated by multiplying calculated PF with EU MRL (lemon RAC).

[c] For substances with a log Pow <3, log Pow cannot be used to calculate the PF. Instead a default PF of 2 was used here. Experimentally determined PF should normally be preferred for these substances.

In no case these calculated lemon oil PF could be considered as overestimated values, specially considering that the OECD guideline proposes a PF equal to 1.000. See *GUIDELINE FOR THE TESTING OF CHEMICALS. Magnitude of Residues in Processed Commodities.* http://www.oecd.org/chemicalsafety/testing/39736351.pdf; paragraphs 35-41.

7.3. Applicability in the EU of US and Canada approaches to MRLS for citrus oil USA and Canada

58. Whereas the Canadian approach to setting MRLs in processed commodities is not specified and therefore not discussed any further, the US approach was considered further with regard to its relevance for the EU.
59. Due to the absence of field residue data for lemon and processing factors for lemon oil, measured residues in citrus oil were used for an example calculation of residues in the edible food soft drink. Whereas residues in citrus oil often exceeded the MRL for lemon RAC, the calculated residue concentration in the consumable soft drink was always well below the MRLs for lemon RAC. From this calculation it can be concluded that, due to the great dilution of citrus oil in soft drink, no MRLs for citrus oil would have to be set in the EU if US criteria would apply.
60. In addition to the above considerations, the use of dilution factors may be an easy way to decide whether residues that were measured in citrus oil are compliant with current lemon/citrus MRLs.

8. Conclusions

8.1. Consumer risk assesment

61. The assessment has clearly shown that residue intake from the consumption of lemon oil via soft drinks for the 14 active substances under investigation poses no unacceptable chronic or acute consumer risk to adults and children. A large margin of safety was shown to exist despite the conservative approach that was taken.

8.2. A practical approach for setting mrl´s taking into account processing factors based on octanol/water partition coefficient (log pow)

62. Log Pow was shown to be a good predictor of the PF for lemon oil for all substances with a log Pow ≥ 3. A close linear relation-

ship exists between lemon oil PF from an AILIMPO study and the log Pow for the 11 active substances under investigation.

63. For substances with a log Pow < 3 the prediction seems less accurate and residues in lemon oil may be overestimated. It is therefore proposed for all substances with a log Pow < 3 to use instead experimentally determined PF where available. A generic lemon oil PF of 2 could be used where no experimental data exist.

8.3. Applicability in the EU of US and Canada approaches to MRLS for citrus oil USA and Canada

64. Direct transfer of MRLs that have been set in USA or Canada for citrus oil is not considered feasible since in many cases residue definitions differ between USA/Canada and the EU. MRLs for lemon/citrus fruit RAC also differ between USA/Canada and EU for many active substances.
65. The US approach to MRL setting in processed commodities (using dilution factors for processed commodities that are not eaten directly) may be useful for establishing whether specific MRLs for citrus oil are needed. However, field residue data and processing factors are nevertheless required.
66. In the absence of reliable processing factors for citrus oil, the use of dilution factors may be a practical way of assessing whether residues measured in citrus oil comply with existing MRLs for lemon/citrus RAC. However, it is uncertain whether this would be an approach that can be translated into EU policy.

ANNEXES

Annex A. Ecosur Lab. Schedule of accreditation by ENAC. UNE-EN ISO/IEC 17025: 2005. Tests in foods stuffs. 2017

Annex B. Ecosur Lab. Test reports. Trials 1 & 2 & 3. 2015

Annex C. Derivatión of processing factors for pesticide residues in lemon oil and dietary risk assessment from pesticide residue intake

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Table of contents

List of tables

List of figures

1. Introduction

Pesticide residues in food commodities may be concentrated as compared to the raw agricultural commodity (RAC), owing to the processing they undergo. Such concentration of residues is regularly observed for lemon oil, which often contains significant levels of pesticide residues, even when they are low or below detection in the unprocessed raw commodity.

Lemon oil is usually produced from cold-pressing of lemon peels and is a common ingredient in soft drinks and juices, albeit at a low concentration (about 0.03 %). Alternatively, lemon oil may be obtained by distillation with alcohol.

In the EU, MRLs (Maximum Residue Limits) are set in accordance with Regulation (EC) 396/2005 for pesticide residues in raw agricultural commodities (RAC). No MRLs have been set for processed commodities although they are part of the scope of the Regulation. However, according to Article 20 (Reg (EC) 396/2005 «*where MRLs are not set out in Annexes II or III for processed and/or composite food or feed, the MRLs applicable shall be those provided in Article 18*[1] *for the relevant product covered by Annex I, taking into account changes in the levels of pesticide residues caused by processing and/or mixing. Specific concentration or dilution factors for certain processing and/or mixing operations or for certain processed and/or composite products may be included in the list in Annex VI*».

To-date, such processing factors are still not available for lemon oil, leaving the industry with considerable uncertainty as to the quality and consumer safety of the lemon oil product, even if legal compliance can be shown for pesticide residues in the raw commodity.

Facing the lack of reliable processing factors, the oil/water partition coefficient (log Pow) has been suggested as a predictor of pesticide residues in processed commodities. Fernandez-Alba (2009) found that log Pow correlated with the residue of 19 pesticides in citrus juice, apple juice and wine, but not in olive oil[1]. In contrast, Li *et al.* (2012) found no relationship between log Pow and pesticide concentration in apple juice,

[1] Fernandez-Alba, A. R. (2009): *Discussion paper on the evaluation of distribution of pesticide residues after primary process in citrus fruit, pome fruit, oilseeds and wine grapes*. EU CRL, Bejing. In http://www.crl-pesticides.eu/library/docs/fv/Beijing2009.pdf.

however, they suggested a possible relationship between log Pow and residue in citrus oil[2].

In the following, an approach is explored to calculate generic processing factors for lemon oil, based on processing factors obtained from a processing study commissioned by AILIMPO and from publicly available sources, and on log Pow of the pesticides.

Calculated generic processing factors are then used to conduct a consumer risk assessment on 14 pesticide active substances.

Finally, recommendations are made for further steps that may be taken to achieve reliable lemon oil processing factors and therefore improve the risk assessment for pesticide residues in lemon oil.

2. Processing Factors for Lemon Oil

2.1. AILIMPO Processing Study

A study was commissioned by AILIMPO (Asociación Interprofesional de Limón y Pomelo) to assess the residue levels of 15 commonly found active substances or their metabolites in lemon whole fruits, and cold pressed lemon oil, and to derive processing factors (PF).

2.1.1. Materials and Methods (Brief Outline)

- Study done at industrial scale, not laboratory scale.
- Carried out in industrial operative plant Zumofresh (Murcia).
- Technology by JBT Tech.
- 3 trials carried out, 3t of fresh lemons used per trial.
- Representative samples taken and analysed by Laboratorios Ecosur (certified laboratory).
- Processing data taken by JBT.
- Pesticide analysis of 15 pesticide active substances using QuEChERS method and GC-MS or LC-MS/MS.
- Non-GLP.

[2] Li, Y.; Jiao, B.; Zhao, Q.; Wang, C.; Gong, Y.; Zhang, Y. and Chen W. (2012): «Effect of commercial processing on pesticide residues in orange products»; *European Food Research and Technology* 234(3); pp. 449-456. In https://link.springer.com/article/10.1007/s00217-011-1651-1.

2.1.2. Results

Details of analytical results and processing factors for lemon and cold-pressed lemon oil are shown in Table 2.1. An overview of mean, minimum and maximum PF obtained is given in Figure 2.1.

Table 2.1. Analytical results and processing factors of lemon and lemon oil; AILIMPO Processing Study

Active substance	Fresh Lemons (FL) mg/kg	Cold Pressed Lemon Oil (CPLO) mg/kg	Processing Factor Lemon Oil (CPLO/FL)
2, 4, 6 - Trichlorophenol[a]	0.870	26.480	30.4
	0.700	19.670	28.1
	0.060	7.130	118.8
Mean	0.540	17.760	59.1
Chlorpyrifos	0.030	3.140	104.7
	0.020	4.030	201.5
	0.006	1.060	176.7
Mean	0.019	2.740	160.9
Chlorpyrifos-methyl	nd	0.080	N/A
	nd	0.070	N/A
	0.005	0.290	58.0
Mean	0.005	0.150	58.0
Dicofol	nd	0.090	N/A
	nd	nd	N/A
	nd	nd	N/A
Mean	nd	0.090	N/A
2 - Phenylphenol	0.580	36.420	62.8
	1.550	80.740	52.1
	0.800	79.390	99.2
Mean	0.980	65.520	71.4
Pyriproxyfen	0.040	5.540	138.5
	0.040	5.220	130.5
	0.020	1.920	96.0
Mean	0.030	4.230	121.7

Table 2.1. (cont.) Analytical results and processing factors of lemon and lemon oil; AILIMPO Processing Study

Active substance	Fresh Lemons (FL) mg/kg	Cold Pressed Lemon Oil (CPLO) mg/kg	Processing Factor Lemon Oil (CPLO/FL)
Pyrimethanil	0.010	0.860	86.0
	0.120	4.420	36.8
	0.440	19.940	45.3
Mean	0.190	8.410	56.0
Propiconazole	0.010	0.560	56.0
	0.006	0.460	76.7
	0.004	0.170	42.5
Mean	0.007	0.400	58.4
Propyzamide	nd	0.190	N/A
	nd	0.160	N/A
	nd	0.040	N/A
Mean	nd	0.130	N/A
Tebufenpyrad	nd	0.400	N/A
	nd	0.200	N/A
	nd	0.140	N/A
Mean	nd	0.250	N/A
Imazalil	1.190	0.970	0.8
	1.230	5.450	4.4
	1.390	3.700	2.7
Mean	1.270	3.370	2.6
Prochloraz	2.110	49.670	23.5
	2.260	90.740	40.2
	nd	9.830	N/A
Mean	2.190	50.080	31.8
Thiabendazole	1.270	0.410	0.3
	3.000	3.90	1.3
	nd	nd	N/A
Mean	2.140	2.160	0.8

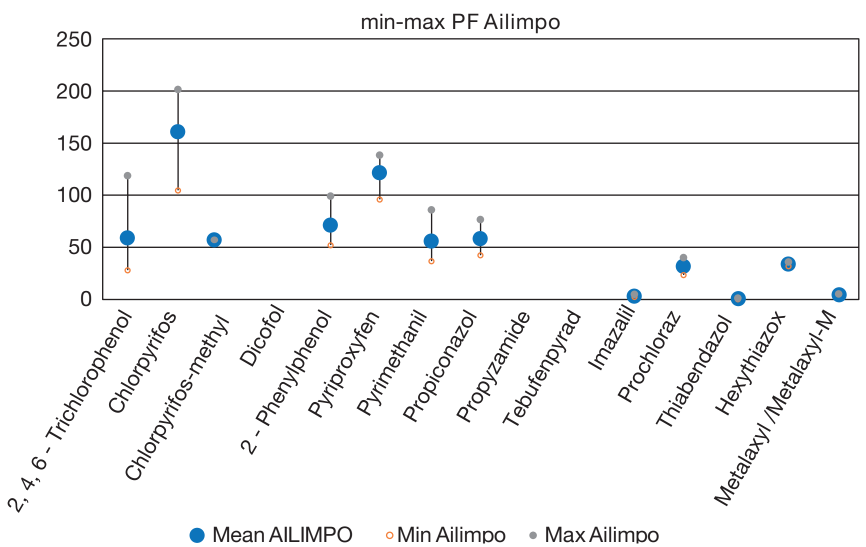
Table 2.1. (cont.) Analytical results and processing factors of lemon and lemon oil; AILIMPO Processing Study

Active substance	Fresh Lemons (FL) mg/kg	Cold Pressed Lemon Oil (CPLO) mg/kg	Processing Factor Lemon Oil (CPLO/FL)
Hexythiazox	nd	0.280	N/A
	0.005	0.180	36.0
	0.010	0.320	32.0
Mean	0.008	0.260	34.0
Metalaxyl / Metalaxyl-M	nd	nd	N/A
	nd	nd	N/A
	0.020	0.090	4.5
Mean	0.020	0.090	4.5

[a] Metabolite of prochloraz. Residue definition: sum of prochloraz and its metabolites containing the 2,4,6-Trichlorophenol moiety expressed as prochloraz.

nd = not detected; N/A = not applicable.

Figure 2.1. Lemon oil processing factors – min-max chart (AILIMPO study)



Most samples of fresh lemons contained residues of the 15 active substances that were monitored. Dicofol, propyzamide and tebufenpyrad were not detected in any of the trials. Chlorpyrifos-methyl, prochloraz, thiabendazole, hexythiazox, metalaxyl / metalaxyl-M were only detected in one or two of the three samples. Residues of all substances in all samples were below the EU MRLs (see Table 2.2).

No processing factors could be calculated for dicofol, propyzamide and tebufenpyrad due to the lack of residues in the RAC (fresh lemons). PF for the other substances varied greatly: the lowest PF (PF_{min}) was obtained for thiabendazole (0.3) and the highest for chlorpyrifos (202). Generally, a concentration of residues in lemon oil as compared to the RAC was seen, with the exception of thiabendazole, where the mean PF is around 1.

Table 2.2. Fresh lemon EU MRLs and maximum residues in AILIMPO study for 15 pesticide active substances

	EU MRL (lemon) mg/kg	Max. residue fresh lemon mg/kg
2,4,6-Trichlorophenol[a]	–	0.870
Chlorpyrifos	0.20	0.030
Chlorpyrifos-methyl	0.30	0.005
Dicofol	0.02	nd
2 - Phenylphenol	5.00	1.550
Pyriproxyfen	0.60	0.040
Pyrimethanil	10.00	0.440
Propiconazol	6.00	0.007
Propyzamide	0.01	nd
Tebufenpyrad	0.50	nd
Imazalil	5.00	1.390
Prochloraz	10.00	2.260
Thiabendazol	5.00	3.000
Hexythiazox	1.00	0.008
Metalaxyl	0.50	0.020

[a] Metabolite of prochloraz. No MRL has been assigned.

nd = not detected.

For individual substances, most PF were relatively consistent between the three different trials. Largest variations between PF were seen for 2,4,6-trichlorophenol, thiabendazole and imazalil, where the highest PF (PF_{max}) was between 4.2 and 5.5 times higher than the lowest PF (PF_{min}) (see Table 2.4).

2.2. Lemon processing factors from published sources

2.2.1. Materials and methods

For the 15 pesticides used in the AILIMPO study (2, 4, 6 - trichlorphenol, chlorpyrifos, chlorpyrifos-methyl, dicofol, 2 - phenylphenol, pyriproxyfen, pyrimethanil, propiconazole, propyzamide, tebufenpyrad, imazalil, prochloraz, thiabendazole, hexythiazox, metalaxyl/metalaxyl-M), the following sources were searched for published processing factors on lemon oil:

- EU Draft Assessment Reports / Renewal Assessment Reports[3].
- EFSA Conclusions[4].
- EFSA MRL Reviews[5].
- JMPR dossiers[6].
- BfR (Bundesinstitut für Risikoabschätzung) Compilation of Processing Factors[7].

To increase the number of available data, processing factors obtained from citrus fruit other than lemon were also considered (orange, grapefruit, tangelo). According to OECD guidance[8] *«for commodities belonging to the same commodity type and undergoing the same processing procedure it is assumed that the results from studies from one commodity can be extrapolated to the other commodities of this type, including all similar processed commodities within the procedure.»* Grouping all cit-

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3 http://www.efsa.europa.eu or http://dar.efsa.europa.eu/dar-web/provision.

4 http://www.efsa.europa.eu.

5 http://www.efsa.europa.eu.

6 http://apps.who.int/pesticide-residues-jmpr-database.

7 http://www.bfr.bund.de/cm/349/bfr-compilation-of-processing-factors.xlsx.

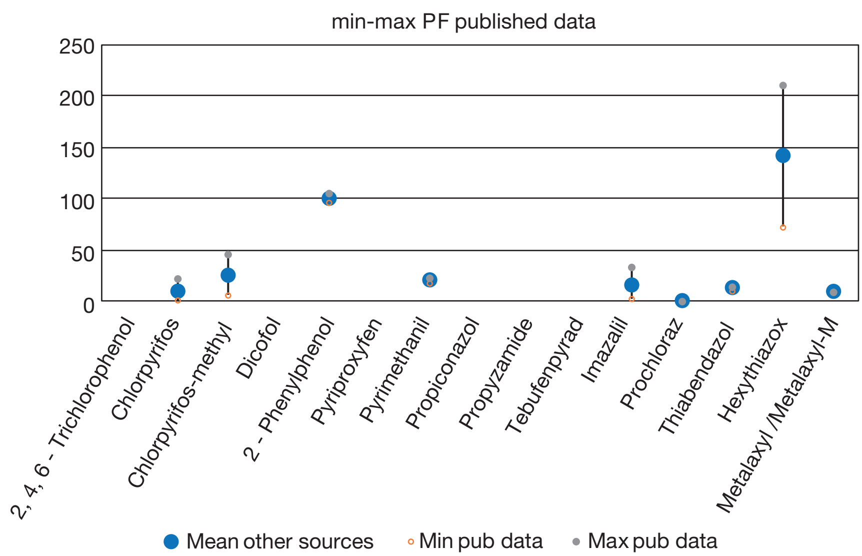
8 OCED Guidance Document on Magnitude of Pesticide Residues in Processed Commodities; Series on Testing and Assessment No. 96; NV/JM/MONO(2008)23; 29 July 2008.

rus fruit in this case therefore seems justified, since citrus fruit matrices are similar and the processing procedures of citrus oil comparable. The range of available PF obtained for the different citrus sources showed no systematic differences between lemon and other citrus sources.

2.2.2. Results

Results of the literature search on processing factors for citrus oil in 15 active substances are shown in Table 2.3. An overview of mean, minimum and maximum PF obtained is given in Figure 2.2.

Figure 2.2. Citrus oil processing factors – min-max chart (published data)



No processing factors were found for 2,4,6-Trichlorophenol (as a metabolite of prochloraz), dicofol, propiconazole, pyriproxyfen, propyzamide, prochloraz and tebufenpyrad.

For each of the remaining 8 substances, between 1 and 7 citrus oil PF were found in the literature.

As for the AILIMPO study, PF varied widely between substances, with the lowest PF for chlorpyrifos (1.2) and the greatest PF for hexythiathox (210).

Table 2.3. Citrus oil processing factors for 15 pesticide active substances from published sources

Active substance	RAR/DAR/EFSA		JMPR		BfR
	Year of evaluation	PF	Year of evaluation	PF	PF
2, 4, 6 - Trichlorphenol[a]	no DAR/EFSA	no data	no data		no data
Chlorpyrifos	EFSA MRL Review 2015	no data	2000	22 (grapefruit) 3.2 (lemon) 6.4 (orange) 13 (tangelo)	1.17 (orange)
Chlorpyrifos-methyl	EFSA MRL review 2017	no data	2009	40.2 (orange, 2 trials)	5.91 (lemon) 6.55 (lemon) 9.41 (lemon) 45.7 (lemon) 40.7 (lemon) 24.4 (lemon)
Dicofol	no DAR	not approved/ no data	2005	no data	no data
2-Phenylphenol	DAR 2007	96 (orange)	1994	97 (orange) 105 (orange)	no data
Pyriproxyfen	DAR 2005	no data	2000	no data	no data
Pyrimethanil	DAR 2005	no data	2007	22.7 (citrus) 17.6 (citrus)	no data
Propiconazole	RAR 2016	no data	2005/2007	no data	no data
Propyzamide	RAR 2015	no data	no	no data	no data
Tebufenpyrad	DAR 2007	no data	no	no data	no data
Imazalil	EFSA Conclusion 2010	13.3 (Citrus, 3 trials)	1994	no data	2.51 (lemon) 4.12 (lemon) 23.7 (orange) 33.2 (orange) 11.63 (grapefruit) 18 (grapefruit)
Prochloraz	DAR 2007/2010	no data	2004	no data	no data
Thiabendazole	RAR 2013	14 (orange) 10 (grapefruit)	1997, (2000)	12.7 (orange) 14 (grapefruit)	no data
Hexythiazox	DAR 2006	no data	2009	72 (orange) 210 (orange)	no data
(Metalaxyl) / Metalaxyl-M	RAR 2013	no data	2004	Met-M: citrus 9 (mean of 4 trials)	no data

[a] Metabolite of prochloraz. Residue definition: sum of prochloraz and its metabolites containing the 2,4,6-Trichlorophenol moiety expressed as prochloraz.

For individual substances, PF also often varied widely. The range of PF was greatest for chlorpyrifos (PF_{max} approx 18 x PF_{min}), chlorpyrifos-methyl (PF_{max} / PF_{min} = 7.7), imazalil (PF_{max} / PF_{min} = 13) and hexythiazox (PF_{max} / PF_{min} = 3). The PF for 2-phenylphenol, pyrimethanil and thiabendazole were quite consistent (see Table 2.4).

2.3. Compilation of mean processing factors

An overview of mean, minimum and maximum processing factors for lemon and other citrus oil from AILIMPO and from published sources, and for the combined data, is given in Table 2.4. An overview of mean, minimum and maximum PF obtained is given in Figure 2.3.

When combining all available PF, the range of PF obtained for each active substance was greater than within the datasets of the AILIMPO study or published data alone. For chlorpyrifos in particular, the range was extremely large, with the combined PF ranging from 1.2 to 202 (PF_{max} / PF_{min} = 168). Large variability also exists for thiabendazole (PF_{max} / PF_{min} = 47) imazalil (PF_{max} / PF_{min} = 42) and chlorpyrifos-methyl (PF_{max} / PF_{min} = 10).

Figure 2.3. Lemon/citrus oil processing factors – min-max chart (combined data)

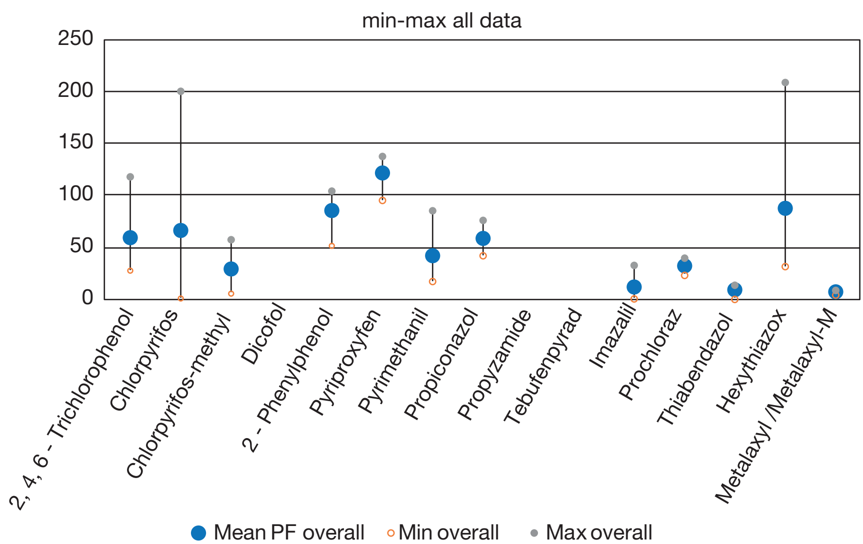


Table 2.4. Overview of lemon and other citrus oil PF obtained from AILIMPO study and from published data, and for all data combined

Active substance	ALIMPO PF (lemon oil)					Published data PF (citrus oil)					All data PF (lemon/citrus oil)				
	Min.	Max.	Mean	Ratio Max/Min	n	Min.	Max.	Mean	Ratio Max/Min	n	Min.	Max.	Mean	Ratio Max/Min	n
2, 4, 6 - Trichloro-phenol	28.1	118.8	59.1	4.2	3	-	-	-		-	28.1	118.8	59.1	4.2	3
Chlorpyrifos	104.7	201.5	161.0	1.9	3	1.2	22.0	9.2	18.0	5	1.2	201.5	66.1	168.0	8
Chlorpyrifos-methyl	58.0	58.0	58.0	1.0	1	5.9	45.7	24.7	7.7	7	5.9	58.0	28.9	9.8	8
Dicofol	-	-	-		-	-	-	-		-	-	-	-		-
2-Phenylphenol	52.1	99.2	71.4	1.9	3	96.0	105.0	99.3	1.1	3	52.1	105.0	85.4	2.0	6
Pyriproxyfen	96.0	138.5	121.7	1.4	3	-	-	-		-	96.0	138.5	121.7	1.4	3
Pyrimethanil	36.8	86.0	56.0	2.3	3	17.6	22.7	20.2	1.3	2	17.6	86.0	41.7	4.9	5
Propiconazole	42.5	76.7	58.4	1.8	3	-	-	-		-	42.5	76.7	58.4	1.8	3
Propyzamide	-	-	-		-	-	-	-		-	-	-	-		-
Tebufenpyrad	-	-	-		-	-	-	-		-	-	-	-		-
Imazalil	0.8	4.4	2.6	5.5	3	2.5	33.2	15.2	13	7	0.8	33.2	11.4	42	10
Prochloraz	23.5	40.2	31.9	1.7	2	-	-	-		-	23.5	40.2	31.9	1.7	2
Thiabendazole	0.3	1.3	0.8	4.3	2	10.0	14.0	12.7	1.4	4	0.3	14.0	8.7	47	6
Hexythiazox	32.0	36.0	34.0	1.1	2	72.0	210.0	141.0	2.9	2	32.0	210.0	87.5	6.6	4
Metalaxyl /Metalaxyl-M	4.5	4.5	4.5	1.0	1	9.0	9.0	9.0	1.0	1	4.5	9.0	6.8	2.0	2

These large deviations may be a result of differences in the processing procedure (cold pressing *vs.* distillation), which are known to yield different PF. However, the published data often contain no information on the employed procedure for obtaining citrus oil.

2.4. Correlation between lemon / citrus oil pf and oil / water partition coefficient

As was shown above, lemon/citrus oil PF vary widely not just for each substance, but also greatly between active substances. Despite the variability, mean citrus oil PF were calculated from all data, since no information was available to justify excluding any extreme data.

Mean citrus oil PF were then used further to assess the correlation between PF and the oil/water partition coefficient (log Pow). Log Pow values for each pesticide are based on data published in EU assessments as indicated (see Table 2.5).

Table 2.5. Oil/water partition coefficients (log Pow) from EU published sources for 15 pesticide active substances

Active substance	log Pow	Source of log Pow
Chlorpyrifos	4.70	EU Review Report, January 2005
Chlorpyrifos-methyl	4.00	EU Review Report, June 2015
Dicofol	–[a]	–[a]
2-Phenylphenol	3.20	Draft Assessment Report, May 2007
Pyriproxyfen	5.37	Draft Assessment Report, November 2005
Pyrimethanil	2.84	Draft Assessment Report, April 2004
Propiconazole	3.72	Renewal Assessment Report, June 2016
Propyzamid	3.72	Renewal Assessment Report, July 2015
Tebufenpyrad	4.93	Draft Assessment Report, November 2007
Imazalil	2.56	Draft Assessment Report, June 2009
Prochloraz	3.50	Draft Assessment Report, July 2010
Thiabendazole	2.39	Renewal Assessment Report, May 2013
Hexythiazox	2.70	Draft Assessment Report, June 2006
Metalaxyl / Metalaxyl-M	1.71	Renewal Assessment Report, November 2013

[a] Not registered in the EU, therefore no log Pow published.

Linear correlations between mean PF and log Pow were calculated for all 11 active substances for which data were available (chlorpyrifos, chlorpyrifos-methyl, 2-phenylphenol, pyriproxyfen, pyrimethanil, propiconazole, imazalil, prochloraz, thiabendazole, hexythiazox, metalaxyl / metalaxyl-m). No processing data were available for dicofol, propyzamide and tebufenpyrad, which were therefore excluded. Also, 2,4,6-trichlorophenol was not included since it is not an active substance and a log Pow has not been published.

Three data sets were assessed separately:

(a) AILIMPO study (lemon oil only).

(b) Published data (various citrus fruit).

(c) AILIMPO and published data combined (overall data).

Data and results of the regression analysis are shown in Table 2.6. An illustration of the linear relationships between PF and log Pow is given in the charts (Figure 2.4 to Figure 2.6).

Table 2.6. Input values and results of linear regression analysis for lemon / citrus oil PF

	Log Pow	Mean PF AILIMPO	Mean PF published data	Mean PF combined data
Chlorpyrifos	4.70	161.0	9.2	66.1
Chlorpyrifos-methyl	4.00	58.0	24.7	28.9
2-Phenylphenol	3.20	71.4	99.3	85.4
Pyriproxyfen	5.37	121.7	–	121.7
Pyrimethanil	2.84	56.0	20.2	41.7
Propiconazole	3.72	58.4	–	58.4
Imazalil	2.56	2.6	15.2	11.4
Prochloraz	3.50	31.9	–	31.9
Thiabendazole	2.39	0.8	12.7	8.7
Hexythiazox	2.70	34.0	141.0	87.5
Metalaxyl /Metalaxyl-M	1.71	4.5	9.0	6.8
Linear regression equation		$y = 40.66x - 81.04$	$y = -2.473x + 48.864$	$y = 23.53x - 28.61$
Correlation coefficient r^2		0.75	0.002	0.45
Significance / F-value		0.0006	0.913	0.023

Figure 2.4. Linear relationship between mean PF AILIMPO and log Pow (data from AILIMPO study)

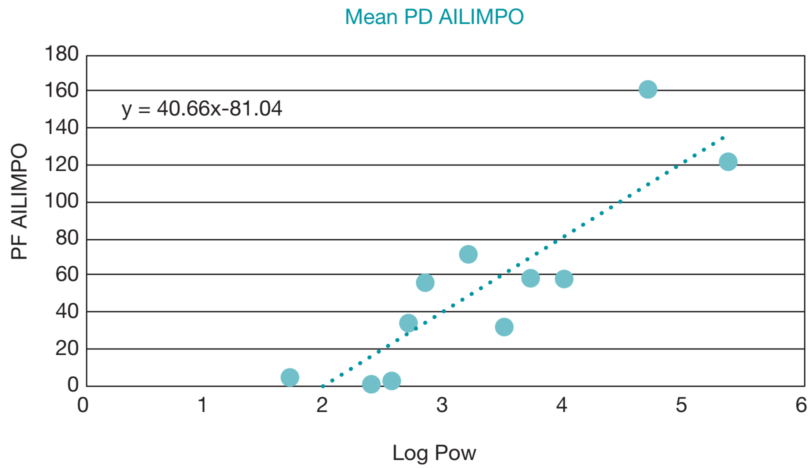
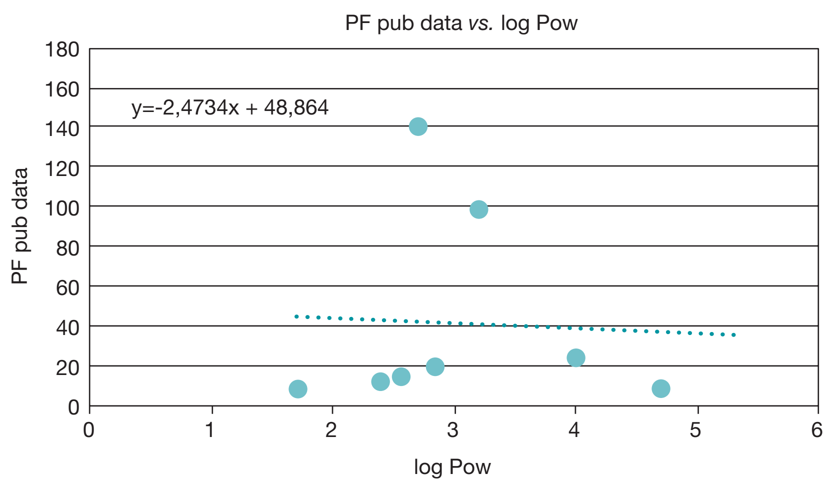


Figure 2.5. Linear relationship between mean citrus oil PF and log Pow (published data)

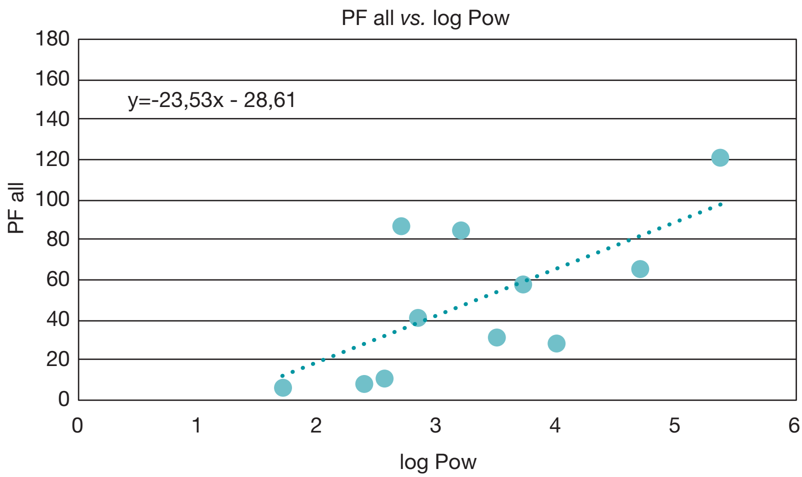


The best linear correlation was obtained for the data from the AILIMPO study, with a close and highly significant relationship between log Pow and lemon oil PF ($r^2 = 0.75$, F=0.0006).

In contrast, regression analysis of published data and combined data gave no or only weak relationships between the two variables.

Based on the data from the AILIMPO study it is suggested that log Pow of a substance may be a good predictor of the PF for lemon oil.

Figure 2.6. Linear relationship between mean lemon / citrus oil PF and log Pow (combined AILIMPO and published data)



2.5. Calculation of Theoretical PF in Lemon Oil

Theoretical lemon oil processing factors were calculated using the regression equation based on the AILIMPO data (y = 40.66x - 81.04; see Table 2.6), which resulted in the best fit between PF and Log Pow. Fourteen pesticides were used in the calculation: in addition to the 11 active substances above (see Point 2.4), also dicofol, propyzamide and tebufenpyrad were included for which no processing data are available. There are no ADI, ARfD or MRL data available for 2,4,6-trichlorophenol, which is a metabolite of prochloraz and as such expressed as (a proportion of total) prochloraz. It was therefore excluded from further assessment.

Lemon oil PF for the 14 active substances varied between -12 and 137 (Table 2.7). Greatest deviation between measured and calculated PF was obtained for imazalil and thiabendazole, where the calculated PF was between 8.8 and 20 times greater than the measured PF, and for metalaxyl/metalaxyl-M, where the calculated PF was 2.7 times *lower* than the measured PF and even negative. Imazalil, thiabendazole and metalaxyl/metalaxyl-M are the three substances with the lowest log Pow values

(2.56, 2.39, 1.71). For all other substances, calculated and measured PFs deviated no more than 1.9 fold from each other. Good agreement was also obtained for two substances with a log Pow of 2.84 (pyrimethanil) and 2.7 (hexythiathox), respectively, so that it appears that at a cut-off point somewhere between log Pow 2.56 and 2.7 the calculation becomes less accurate. At a log Pow <2.0 the calculated PF becomes negative.

Table 2.7. Overview of mean (AILIMPO) and calculated lemon oil PF, ratio of actual/calculated PF, and log Pow

	Mean PF AILIMPO data	Calculated PF[a]	Ratio calculated PF/mean PF	log Pow
Chlorpyrifos	161.0	110	0.7	4.70
Chlorpyrifos-methyl	58.0	82	1.4	4.00
Dicofol	–	123	–	5.02
2-Phenylphenol	71.4	49	0.7	3.20
Pyriproxyfen	121.7	137	1.1	5.37
Pyrimethanil	56	34	0.6	2.84
Propiconazole	58.4	70	1.2	3.72
Propyzamide	–	70	–	3.72
Tebufenpyrad	–	119	–	4.93
Imazalil	2.6	23	8.8	2.56
Prochloraz	31.9	61	1.9	3.50
Thiabendazole	0.8	16	20.0	2.39
Hexythiazox	34	29	0.9	2.70
Metalaxyl/Metalaxyl-M	4.5	-12	-2.7	1.71

[a] Calculated using equation $y = 40.66x - 81.04$ (see Table 2.6).

2.6. Discussion - Lemon Oil Processing Factors

Lemon oil PF were available for 12 active substances (2,4,6-trichlorophenol, chlorpyrifos, chlorpyrifos-methyl, 2-phenylphenol, pyriproxyfen, pyrimethanil, propiconazole, imazalil, prochloraz, thiabendazole, hexythiazox, metalaxyl/metalaxyl-M) from an AILIMPO processing study and from published sources. No processing factors were available for dicofol, propyzamide and tebufenpyrad.

Lemon oil PFs differed in some cases more than a 100 fold between substances. Processing factors from different studies on the same substances also varied, but less for data from the AILIMPO study as compared to PF from published sources. However, since no information was available to justify excluding any extreme data and may also be a result of differences in processing procedures, all available data were used for further analysis.

In order to determine whether log Pow can be used to predict the concentration of residues in lemon oil, linear correlations of mean lemon/citrus oil PF with the relevant log Pow of the substance were calculated in a further step. Data from 11 active substances (as listed above but excluding 2,4,6-trichlorophenol, which is a metabolite of prochloraz) were used for the analysis.

The best correlation was obtained with PF data from the AILIMPO study, showing a close and significant relationship between lemon oil PF and log Pow (r^2 = 0.75). In contrast, no correlation was obtained for the published citrus oil PF data, and only a weak correlation existed for the combined AILIMPO/published data set.

Poor results for the published data may be explained by the fact that, in contrast to the AILIMPO study, different processing procedures and citrus fruits had been used. This highlights the importance of comparable processing conditions in order to arrive at meaningful data.

In a further step, theoretical lemon oil processing factors were calculated using the regression equation from the AILIMPO processing data. In addition to the 11 active substances above, lemon oil PF were also calculated for three substances, for which no processing data are available (dicofol, propyzamide and tebufenpyrad). There was generally good agreement between measured and calculated lemon oil PF. However, it appears, that at a log Pow between 2.56 and 2.7 and below, the calculation becomes less accurate.

Based on the data from AILIMPO study it was concluded that, for substances with a log Pow of 3 or greater, log Pow is a useful indicator of the expected concentration of pesticide residue in lemon oil. A log Pow of 3 rather than 2.7 was chosen since it is generally used as a cut-off point for determining lipophilicity of a substance.

For water soluble substances with a log Pow <3, the concentration of residue in lemon oil is generally small and cannot accurately be predicted via log Pow. To account for the fact that for these substances some concentration of residue may still occur, it is proposed to use experimental data if available. Only if no experimental data are available, a generic PF of 2 may be used.

3. Consumer risk assessment for pesticide residue intake from lemon oil

In a further step, theoretical lemon oil MRLs were calculated for 14 substances (see Point 2.5), based on PF from the Ailimpo study or on calculated PF as shown in Table 27, and using EU MRLs for lemon (RAC). The MRL_{det} was obtained by multiplying mean PF as determined in the AILIMPO study with EU MRLs for lemon (RAC). MRL_{calc} was obtained by using the calculated PF instead of the measured PF. Results are shown in Table 3.1 and Table 3.2; Table 2.7.

Table 3.1. Overview of mean lemon oil PF (AILIMPO study), EU MRLs for lemon RAC and theoretical lemon oil MRL_{det}

	Mean PF AILIMPO data	EU MRL (lemon RAC) mg/kg	MRLdet lemon oil[a] mg/kg
Chlorpyrifos	161.0	0.20	32
Chlorpyrifos-methyl	58.0	0.30	17
Dicofol	-	0.02	0
2-Phenylphenol	71.4	5.00	357
Pyriproxyfen	121.7	0.60	73
Pyrimethanil	56.0	10.00	560
Propiconazole	58.4	6.00	350
Propyzamide	-	0.01	0
Tebufenpyrad	-	0.50	0
Imazalil	2.6	5.00	13
Prochloraz	31.9	10.00	319
Thiabendazole	0.8	5.00	4
Hexythiazox	34.0	1.00	34
Metalaxyl/Metalaxyl-M	4.5	0.50	2

[a] calculated by multiplying measured PF with EU MRL (lemon RAC).

Table 3.2. Overview of calculated lemon oil PF, EU MRLs for lemon and theoretical lemon oil MRL_{calc}

	Calculated PF[a]	EU MRL (lemon RAC) mg/kg	MRLcalc lemon oil[b] mg/kg
Chlorpyrifos	110	0.20	22.0
Chlorpyrifos-methyl	82	0.30	24.0
Dicofol	123	0.02	2.0
2-Phenylphenol	49	5.00	245.0
Pyriproxyfen	137	0.60	82.0
Pyrimethanil	34	10.00	344.0
Propiconazole	70	6.00	421.0
Propyzamide	70	0.01	0.7
Tebufenpyrad	119	0.50	60.0
Imazalil	2[c]	5.00	10.0
Prochloraz	61	10.00	613.0
Thiabendazole	2[c]	5.00	10.0
Hexythiazox	2[c]	1.00	2.0
Metalaxyl/Metalaxyl-M	2[c]	0.50	1.0

[a] Calculated using equation y = 40.66x - 81.04 (see Table 2.6).

[b] Calculated by multiplying calculated PF with EU MRL (lemon RAC).

[c] For substances with a log Pow <3, log Pow cannot be used to calculate the PF. Instead a default PF of 2 was used here. Experimentally determined PF should normally be preferred for these substances. See justification Point 2.6.

3.1. Consumer risk assessment for lemon oil

A consumer risk assessment was done for adults and children using the following parameters / assumptions:

- Using theoretical MRL_{det} (see Table 3.1) or MRL_{calc} for lemon oil (see Table 3.2).
- ADI (Acceptable Daily Intake) for chronic and ARfD (Acute Reference Dose) for acute risk assessment, as published on EU Pesticide Database[9].

[9] http://ec.europa.eu/food/plant/pesticides/eu-pesticides-database/public/?event=homepage&language=EN.

- Body weights for child (16.15 kg) and adult (68.5 kg) according to EFSA PRIMo Rev. 2 model[10].
- Intake of lemon oil is assumed to be exclusively via soft drinks that contain 0.03 % lemon oil.
- Consumption data for acute intake assume that all liquid intake is via soft drink. According to WHO (2008)[11], the default assumption for water intake is 2 L per day for adults and 1 L for children (10 kg bw). The liquid intake for children was adjusted here to 1.6 L per day to account for the greater body weight as compared to the WHO assumption.
- Consumption data for chronic intake via soft drink were assumed to be 50% of standard liquid intake (1 L per day for adults, 0.8 L per day for children); for acute intake via soft drink assumptions were 2.5 L per day for adults and 2 L per day for children.
- For the chronic risk assessment, usually all commodities that may be treated with the active substance and for which MRLs exist are included in the risk assessment. This is not feasible here since consumption and MRLs for fresh commodities include intake from processed foods already, and no separate intakes for processed foods are considered in the risk assessment models. Replacing existing MRLs for the RAC lemon (or citrus) with the «virtual» MRLs for citrus oil would overestimate intake. Only residue intake from lemon oil is therefore considered in the chronic risk assessment done here.
- For the acute risk assessment, only substances are considered for which an ARfD has been set, i.e. for which acute toxicity has been shown. Where there is no acute toxicity and therefore no ARfD, an acute risk assessment is not necessary and not carried out.

The results of the consumer risk assessment using MRL_{det} are shown in Table 3.3 below, and the results for MRL_{calc} are shown in Table 3.4.

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10 https://www.efsa.europa.eu/de/applications/pesticides/tools.

11 WHO (2008): Guidelines for Drinking Water Quality, Vol. 1, 3rd ed. http://www.who.int/water_sanitation_health/dwq/fulltext.pdf.

Chronic and acute intakes of residues from lemon oil are all below the toxicological reference values, with a considerable margin of safety for most active substances (marked green in the tables). This applies generally to both assessments, regardless of whether MRLs based on analytically determined or on calculated PF were used. The only exception is prochloraz, where both, chronic and acute intakes by children are close to the toxicological thresholds when using MRL_{calc}. However, for prochloraz the chronic and acute intakes by children are below 50 % of ADI/ARfD when the MRL_{det} is used instead (see Table 3.3). Since the latter is based on PF obtained from analytically determined data rather than from regression calculation, these results are considered the more relevant. Generally, the MRL_{calc} assessment would only seem reasonable where no assessment based on MRL_{det} is possible, i. e. in this case for dicofol, propyzamide and tebufenpyrad. For all other substances, the assessment using MRL_{det} is likely to be more realistic.

With regard to the approach to *chronic risk assessment*, it may be argued that residue intakes from other commodities than lemon oil should also be considered. However, current MRLs for lemon (RAC) would already be based on residue intake from all sources and commodities, i.e. also including soft drink-based intakes. In addition, the assessment provides an overestimation of real intakes because it is assumed that, over the lifetime of a consumer, residues are always present at the MRL (when in reality residues are usually much lower) and that all commodities that may be treated with an active substance have been treated with it (despite the fact that no pesticide product has a market share of 100%). In a refined risk assessment therefore, the Supervised Trials Median Residue values (STMRs) would be used, which is always considerably lower than the MRL. STMRs would be available from EFSA opinions for a number of the active substances under consideration.

Additionally, it could be considered to do a full chronic risk assessment. We would envisage an approach in which MRLs (or STMRs, where relevant and available) for all registered uses would be entered into the PRIMo model and the total intake (as %ADI) then be added to the intakes from citrus oil. This approach would, however, mean that intakes from lemon are somewhat overestimated, since the MRLs for RAC lemon should already include intake from processed commodities (such as citrus oil).

For *acute risk assessment,* commodities are always considered individually. That is, in common risk assessment models, the RAC lemon fruit would be assessed on its own, and some processed commodities are also considered. A proportion of total lemon fruit consumption is assumed to be from lemon oil, but the size of this proportion is not known since lemon oil is not included in any of the models. Since the calculated intakes are generally below 50% of the ARfD, however, there seems to be a large enough margin to allow for residue intake from other lemon sources, e.g. as juice.

In addition, also in this acute assessment the use of MRLs gives an exaggerated result with regard to the possible peak intake of pesticide residues from lemon oil. This is because lemon oil in commercial processing operations involves a large number of fruit and considerable mixing, so that residues at the MRL are highly unlikely to be present in the resulting lemon oil product. Risk assessment models (e.g. EFSA PRIMo, WHO IESTI) use STMRs for commodities which are bulked or blended (obtained by multiplying the STMR of the raw commodity by the PF) to obtain a more realistic result. In the absence of STMR data, a refinement of the acute risk assessment would currently not be possible.

Overall, it can be concluded that residue intake from the consumption of lemon oil via soft drinks for the 14 active substances under investigation poses no unacceptable chronic or acute consumer risk to adults and children.

Table 3.3. Chronic and acute consumer risk assessment for children (16.15 kg bw) and adults (68.5 kg bw) for 14 pesticide active substances from consumption of lemon oil in soft drink-based on theoretical $MRLs_{det}$ for lemon oil

Active substance	MRLdet lemon oil mg/kg	Chronic risk assessment					Acute risk assessment				
		ADI mg/kg bw	Child (16.5 kg bw)		Adult (68.5 kg bw)		ARfD mg/kg bw	Child (16.5 kg bw)		Adult (68.5 kg bw)	
			Max residue intake mg/kg bw[a]	Max intake %ADI	Max residue intake mg/kg bw[b]	Max intake %ADI		Max residue intake mg/kg bw[c]	Max intake %ARfD	Max residue intake mg/kg bw[d]	Max intake %ADI
Chlorpyrifos	32	0.010	0.0005	4.8	0.0001	1.4	0.100	0.0012	1.2	0.0004	0.4
Chlorpyrifos-methyl	17	0.001	0.0003	25.9	0.0001	7.6	0.005	0.0006	12.9	0.0002	3.8
Dicofol	0	0.002	0.0000		0.0000		-	-	-	-	-
2-Phenylphenol	357	0.400	0.0053	1.3	0.0016	0.4	-	-	-	-	-
Pyriproxyfen	73	0.100	0.0011	1.1	0.0003	0.3	-	-	-	-	-
Pyrimethanil	560	0.170	0.0083	4.9	0.0025	1.4	-	-	-	-	-
Propiconazole	350	0.040	0.0052	13.0	0.0015	3.8	0.300	0.0130	4.3	0.0038	1.3
Propyzamide	0	0.020	0.0000		0.0000		-	-	-	-	-
Tebufenpyrad	0	0.010	0.0000		0.0000		0.020	0.0000		0.0000	
Imazalil	13	0.025	0.0002	0.8	0.0001	0.2	0.050	0.0005	1.0	0.0001	0.3
Prochloraz	319	0.010	0.0047	47.4	0.0014	14.0	0.025	0.0119	47.4	0.0035	14.0
Thiabendazole	4	0.100	0.0001	0.1	0.0000	0.0	0.100	0.0001	0.1	0.0000	0.0
Hexythiazox	34	0.030	0.0005	1.7	0.0001	0.5	-	-	-	-	-
Metalaxyl/Metalaxyl-M	2	0.080	0.0000	0.0	0.0000	0.0	0.500	0.0001	0.0	0.0000	0.0

[a] Assumption: 800mL soft drink per day containing 0.03% lemon oil (=0.24 g).
[b] Assumption: 1L soft drink per day containing 0.03% lemon oil (=0.3 g).
[c] Assumption: 2L soft drink containing 0.03% lemon oil (=0.6 g).
[d] Assumption: 2.5L soft drink containing 0.03% lemon oil (=0.75 g).
N/A: not applicable – no ARfD.

Table 3.4. Chronic and acute consumer risk assessment for children (16.15 kg bw) and adults (68.5 kg bw) for 14 pesticide active substances from consumption of lemon oil in soft drink – based on theoretical MRLs$_{calc}$ for lemon oil

Active substance	MRLcalc lemon oil mg/kg	Chronic risk assessment					Acute risk assessment				
		ADI mg/kg bw	Child (16.5 kg bw)		Adult (68.5 kg bw)		ARfD mg/kg bw	Child (16.5 kg bw)		Adult (68.5 kg bw)	
			Max residue intake mg/kg bw[a]	Max intake %ADI	Max residue intake mg/kg bw[b]	Max intake %ADI		Max residue intake mg/kg bw[c]	Max intake %ARfD	Max residue intake mg/kg bw[d]	Max intake %ADI
Chlorpyrifos	22	0.010	0.0003	3.3	0.0001	1.0	0.100	0.0008	0.8	0.0002	0.2
Chlorpyrifos-methyl	24	0.001	0.0004	36.4	0.0001	10.7	0.005	0.0009	18.2	0.0003	5.4
Dicofol	2	0.002	0.0000	1.8	0.0000	0.5	-	-	-	-	-
2-Phenylphenol	245	0.400	0.0036	0.9	0.0011	0.3	-	-	-	-	-
Pyriproxyfen	82	0.100	0.0012	1.2	0.0004	0.4	-	-	-	-	-
Pyrimethanil	344	0.170	0.0051	3.0	0.0015	0.9	-	-	-	-	-
Propiconazole	421	0.040	0.0063	15.7	0.0018	4.6	0.300	0.0157	5.2	0.0046	1.5
Propyzamide	0.70	0.020	0.0000	0.05	0.0000	0.0	-	-	-	-	-
Tebufenpyrad	60	0.010	0.0009	8.9	0.0003	2.6	0.020	0.0022	11.1	0.0007	3.3
Imazalil	10	0.025	0.0001	0.6	0.0000	0.2	0.050	0.0004	0.7	0.0001	0.2
Prochloraz	613	0.010	0.0091	91.1	0.0027	26.8	0.025	0.0228	91.1	0.0067	26.8
Thiabendazole	10	0.100	0.0001	0.1	0.0000	0.0	0.100	0.0004	0.4	0.0001	0.1
Hexythiazox	2	0.030	0.0000	0.1	0.0000	0.0					
Metalaxyl/Metalaxyl-M	1	0.080	0.0000	0.0	0.0000	0.0	0.500	0.0000	0.0	0.0000	0.0

[a] Assumption: 800mL soft drink per day containing 0.03% lemon oil (=0.24 g).

[b] Assumption: 1L soft drink per day containing 0.03% lemon oil (=0.3 g).

[c] Assumption: 2L soft drink containing 0.03% lemon oil (=0.6 g).

[d] Assumption: 2.5L soft drink containing 0.03% lemon oil (=0.75 g).

3.2. Discussion - consumer risk assessment

Theoretical MRLs for lemon oil were calculated by multiplying MRLs for lemon RAC with the lemon oil PF. Two different lemon oil MRLs were calculated and used for the risk assessment: MRL_{det} was based on PF from analytical data in the AILIMPO study. MRL_{calc} was calculated for all substances with a log Pow ≥3 from the linear regression equation using the Log Pow of the substance and lemon oil PF from the AILIMPO study. For substances with a log Pow <3, a generic PF of 2 was used to obtain MRL_{calc}. However, experimental data should preferentially be used for these more hydrophilic substances.

MRL_{det} was obtained for 11 active substances for which analytical data were available (chlorpyrifos, chlorpyrifos-methyl, 2-phenylphenol, pyriproxyfen, pyrimethanil, propiconazole, imazalil, prochloraz, thiabendazole, hexythiazox, metalaxyl/metalaxyl-M). MRL_{calc} was obtained for three further active substance where no analytical data had been available (dicofol, propyzamide and tebufenpyrad), in addition to the 11 substances above.

Acute and chronic risk assessments were carried out for the residue intake from lemon oil in soft drink, using either MRL_{det} or $MRL_{calc,}$ and based on the EFSA PRIMo Rev. 2 model. Worst-case assumption were made regarding the amount of soft drink consumed and the concentration of lemon oil in soft drink.

With both approaches, acute and chronic intake from lemon oil was usually well below 50% of the toxicological threshold values (ADI or ARfD), with the exception of prochloraz, where ADI and ARfD exhaustion for children was >90% when the assessment was based on MRL_{calc}. However, when using MRL_{det}, intake of prochloraz from lemon oil was much lower (<50 % of ADI/ARfD). Since MRL_{det} can be considered to be more realistic than MRL_{calc} it should be used where it is available, i.e. also in the case of prochloraz.

However, for substances with log Pow ≥3 for which no measured PF is available and therefore no MRL_{det} can be derived, risk assessment is possible by using lemon oil PF that are derived from the linear correlation between log Pow of the substance.

The assessment has clearly shown that residue intake from the consumption of lemon oil via soft drinks for the 14 active substances under investigation poses no unacceptable chronic or acute consumer risk to adults and children. A large margin of safety was shown to exist despite the conservative approach that was taken.

4. Overall Conclusion and Recommendations

The following conclusions are drawn:

- Lemon oil PF available from an AILIMPO study and published data vary widely between active substances. It is therefore not considered feasible to derive a single lemon oil PF for all pesticide active substances.
- Log Pow was shown to be a good predictor of the PF for lemon oil for all substances with a log Pow ≥3. A close linear relationship exists between lemon oil PF from an AILIMPO study and the log Pow for the 11 active substances under investigation.
- For substances with a log Pow <3 the prediction seems less accurate and residues in lemon oil may be overestimated. It is therefore proposed for all substances with a log Pow <3 to use instead experimentally determined PF where available. A generic lemon oil PF of 2 could be used where no experimental data exist.

The following recommendations are made:

- The presented AILIMPO study was done to a good standard, however, it was not done according to GLP and OECD guidelines. In addition, for several substances PF data could only be obtained for 1 or 2 of the 3 replicate trials. It would be desirable to add more experimental data to the existing data set to confirm and refine the correlation between log Pow and lemon oil PF. These new data should be produced under GLP and according to current OECD guidelines.
- In order to refine the consumer risk assessment as part of standard quality checks of RAC lemons, the calculated PF may be multiplied by the measured residue in the raw commodity (rather than the EU MRL for lemon) as input value to the risk assessment.

Annex D. Applicability in the EU of US and Canada approaches to MRLs for citrus oil

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Table of Contents

List of Tables

1. Introduction

Pesticide residues in food commodities may be concentrated as compared to the raw agricultural commodity (RAC), owing to the processing they undergo. Such concentration of residues is regularly observed for citrus oil, which often contains significant levels of pesticide residues, even when they are low or below detection in the unprocessed raw commodity.

Citrus oil is usually produced from cold-pressing of lemon peels. Alternatively, citrus oil may be obtained by distillation with alcohol. It is not consumed directly but is a common ingredient in soft drinks and juices, albeit at a low concentration (about 0.03%).

In the EU, MRLs (Maximum Residue Limits) are set in accordance with Regulation (EC) 396/2005 for pesticide residues in raw agricultural commodities (RAC). No MRLs have been set for processed commodities although they are part of the scope of the Regulation. However, according to Article 20 (Reg (EC) 396/2005 «*where MRLs are not set out in Annexes II or III for processed and/or composite food or feed, the MRLs applicable shall be those provided in Article 18(1) for the relevant product covered by Annex I, taking into account changes in the levels of pesticide residues caused by processing and/or mixing. Specific concentration or dilution factors for certain processing and/or mixing operations or for certain processed and/or composite products may be included in the list in Annex VI*».

To-date, such processing factors are still not available for citrus oil, leaving the industry with considerable uncertainty as to the quality and consumer safety of the citrus oil product, even if legal compliance can be shown for pesticide residues in the raw commodity.

In both, USA and Canada, MRLs have already been set for processed commodities such as citrus oil for a number of active substances..

Facing the lack of reliable processing factors or MRLs for citrus oil in the EU, it is investigated (1) whether US or Canada MRLs for citrus oil may be used for EU purposes directly and (2) whether US or Canada approaches to setting MRLs for citrus oil may be applicable to the EU.

The assessment was limited to 14 commonly found active substances. A 15th compound, 2,4,6-Trichlorophenol, was excluded from further investigation, since it is a metabolite of prochloraz and MRLs do not apply.

2. Use of Canadian or US MRLs for citrus oil in the EU

2.1. Residue definitions

2.1.1. Comparison of residue definitions for 14 pesticides in the EU, USA and Canada

In order to be able to apply MRLs set in the USA and Canada in the EU, it is important to establish whether the relevant residue is the same in the EU as in Canada/USA.

Residue definitions (RD) for 14 selected active substances were therefore compared for USA and Canada on the one hand, and the EU on the other. Current residue definitions were extracted from published sources, as indicated and are shown in Table 21.

The results are summarized as follows:

- There are no RD available from Canada for 2 of 14 active substances (prochloraz and chlorpyrifos-methyl), and from USA for 4 of 14 active substances (prochloraz and chlorpyrifos-methyl, propyzamide and tebufenpyrad).
- For a number of active substances in the EU and the USA, different RD have been set for risk assessment and enforcement. This is not the case in Canada, where only one RD exists for each active substance.
- Substances with different RD for risk assessment and enforcement differ between EU and USA. Since only enforcement RD are relevant with respect to MRLs, only the latter are considered further.
- RD often differ between EU and USA, and between EU and Canada.
- Enforcement RD agree between EU and USA for 4 of the 10 active substances for which RD are available for USA (chlorpyrifos, dicofol, pyriproxyfen, pyrimethanil).
- Between EU and Canada, enforcement RD agree for 7 of the 12 active substances (pyriproxyfen, pyrimethanil, propiconazole, tebufenpyrad, imazalil, thiabendazole and hexythiathox) for which RD are available in Canada.

Table 2.1. Residue definitions in USA and Canada compared to EU residue definitions for 14 pesticide active substances

	EU		USA[a]	Canada[b]	Residue definitions same for USA/ Canada and EU?
	Residue definition for risk assessment (RA)	Residue definition for enforcement (E)			
Chlorpyrifos	Two separate residue definitions: 1) Chlorpyrifos; 2) Sum of 3,5,6-trichloropyridinol (TCP) and its conjugates expressed as TCP[c]	Chlorpyrifos (O,O-diethyl-O-(3,5,6-trichloro-2-pyridyl) phosphorothioate)[c]	Residues of pesticide chlorpyrifos per se (O,O-diethyl-O-(3,5,6-trichloro-2-pyridyl) phosphorothioate)	Chlorpyrifos: O,O-diethyl-O-(3,5,6- trichloro-2-pyridyl) phosphorothioate, including the metabolite 3,5,6-trichloro-2-pyridinol	USA: Yes (E); No (RA) CAN: No (E); Yes (RA)
Chlorpyrifos-methyl	Two separate residue definitions: 1) Chlorpyrifos-methyl; 2) Sum 3,5,6-trichloropyridinol (TCP) and its conjugates expressed as TCP[d]	Chlorpyrifos-methyl[d]	No data	No data	Not applicable
Dicofol	Not applicable (not approved in EU)	Dicofol as the sum of its p,p-dicofol and o,p-dicofol isomers: 4-chloro-α-(4-chlorophenyl)-α-(trichloromethyl) benzenemethanol and 2-chloro-α-(4-chlorophenyl)-α-(trichloromethyl)benzenemethanol[e]	Residues of the insecticide dicofol, including its metabolites and degradates. Compliance by measuring only dicofol as the sum of its p,p-dicofol and o,p-dicofol isomers: 4-chloro-α-(4-chlorophenyl)-α-(trichloromethyl) benzenemethanol and 2-chloro-α-(4-chlorophenyl)-α-(trichloromethyl) benzenemethanol	4-chloro-α-(4-chlorophenyl)-α-(trichloromethyl)benzenemethanol	USA: Yes (E) CAN: No (E)
2-Phenylphenol	Sum of orthophenylphenol and 2-phenylhydroquinone and their conjugates, expressed as orthophenylphenol[f]	Sum of orthophenylphenol and 2-phenylhydroquinone and their conjugates, expressed as orthophenylphenol[f]	Combined residues of the fungicide o-phenylphenol and sodium o-phenylphenate, each expressed as o-phenylphenol, from postharvest application	Sodium orthophenyl phenate: σ-phenylphenol, sodium salt (calculated as orthophenylphenol)	USA: No (E and RA) CAN: No (E and RA)

Table 2.1. (cont.) Residue definitions in USA and Canada compared to EU residue definitions for 14 pesticide active substances

	EU		USA[a]	Canada[b]	Residue definitions same for USA/ Canada and EU?
	Residue definition for risk assessment (RA)	Residue definition for enforcement (E)			
Pyriproxyfen	Pyriproxyfen: 2-[1-methyl-2-(4-phenoxyphenoxy) ethoxy]pyridine[g]	Pyriproxyfen: 2-[1-methyl-2-(4-phenoxyphenoxy) ethoxy]pyridine[g]	Residues of pyriproxyfen, including its metabolites and degradates. Compliance by measuring only pyriproxyfen, 2-[1-methyl-2-(4-phenoxy-phenoxy) ethoxy]pyridine	Pyriproxyfen: 2-[1-methyl-2-(4-phenoxyphenoxy) ethoxy]pyridine	USA: Yes (E); No (RA) CAN: Yes (E and RA)
Pyrimethanil	Pyrimethanil (4,6-dimethyl-N-phenyl-2-pyrimidinamine)[h]	Pyrimethanil (4,6-dimethyl-N-phenyl-2-pyrimidinamine)[h]	Residues of the fungicide pyrimethanil, including its metabolites and degradates. Compliance by measuring only pyrimethanil (4,6-dimethyl-N-phenyl-2-pyrimidinamine)	Pyrimethanil (4,6-dimethyl-N-phenyl-2-pyrimidinamine)	USA: Yes (E); No (RA) CAN: Yes (E and RA)
Propiconazole	1. 'Total propiconazole' i.e. sum of all metabolites, which yield 2,4-dichlorobenzoic acid (DCBA) in a common moiety assay expressed as propiconazole equivalents. 2. A separate RD-RA definition for Triazole Derivative Metabolites is comprised of: 1,2,4-triazole Triazole alanine Triazole acetic acid Triazole lactic acid[i]	Propiconazole: 1-[[2-(2,4-dichlorophenyl)-4-propyl-1,3-dioxolan-2-yl] methyl]-1H-1,2,4-triazole[i]	Compliance for only those propiconazole residues convertible to 2,4-dichlorobenzoic acid (2,4-DCBA)	Propiconazole: 1-[[2-(2,4-dichlorophenyl)-4-propyl-1,3-dioxolan-2-yl] methyl]-1H-1,2,4-triazole	USA: No (E); Yes (RA 1); No (RA 2) CAN: Yes (E); No (RA)

Table 2.1. (cont.) Residue definitions in USA and Canada compared to EU residue definitions for 14 pesticide active substances

	EU		USA[a]	Canada[b]	Residue definitions same for USA/ Canada and EU?
	Residue definition for risk assessment (RA)	Residue definition for enforcement (E)			
Propyzamide	Propyzamide and all metabolites (and their conjugates) bearing the 3,5-dichloroben-zoic acid (DCBA) moiety, expressed as propyza-mide; following foliar application[j]	Propyzamide, 3,5-dichloro-N-(1,1-dimethyl-2-propyn-1-yl)benzamide[j]	No data	Propyzamide (3,5-dichloro-N-(1,1-dimethyl-2-propyn-1-yl)benzamide) including metabolites containing the 3,5-dichlorobenzoate moiety	USA: Not applicable CAN: No (E); Yes (RA)
Tebufenpyrad	Tebufenpyrad: 4-chloro-N-[[4-(1,1-dimethylethyl) phenyl]methyl]-3-ethyl-1-methyl-1H-pyrazole-5-carboxamide[k]	Tebufenpyrad: 4-chloro-N-[[4-(1,1-dimethylethyl)phenyl] methyl]-3-ethyl-1-methyl-1H-pyrazole-5-carboxamide[k]	No data	Tebufenpyrad: 4-chloro-N-[[4-(1,1-dimethylethyl)phenyl] methyl]-3-ethyl-1-methyl-1H-pyrazole-5-carboxamide	USA: Not applicable CAN: Yes (E and RA)
Imazalil	Imazalil: 1-[2-(2,4-dichlorophenyl)-2-(2-propenyloxy) ethyl]-1H-imidazole, and its metabolite, 1-(2,4-dichlorophenyl)-2-(1H-imidazole-1-yl)-1-ethanol[l]	Imazalil: 1-[2-(2,4-dichlorophenyl)-2-(2-propenyloxy)ethyl]-1H-imidazole[l]	Combined residues of the fungicide imazalil, 1-[2-(2,4-dichlorophenyl)-2-(2-propenyloxy)ethyl]-1H-imidazole, and its metabolite, 1-(2,4-dichlorophenyl)-2-(1H-imidazole-1-yl)-1-ethanol.	Imazalil:1-[2-(2,4-dichlorophenyl)-2-(2-propen-1-yloxy)ethyl]-1H-imidazole	USA: No (E); Yes (RA) CAN: Yes (E); No (RA)
Prochloraz	Sum of prochloraz and its metabolites contain-ing the 2,4,6-Trichloro-phenol moiety expressed as prochloraz[m]	Sum of prochloraz, BTS 44595 (N-propyl-N-[2-(2,4,6-trichlorophenoxy)ethyl]urea), and BTS 44596 (N-formyl-N-[2-(2,4,6-trichlorophenoxy) ethyl]urea), expressed as Prochloraz[m]	No data	No data	Not applicable

Table 2.1. (cont.) Residue definitions in USA and Canada compared to EU residue definitions for 14 pesticide active substances

	EU		USA[a]	Canada[b]	Residue definitions same for USA/ Canada and EU?
	Residue definition for risk assessment (RA)	Residue definition for enforcement (E)			
Thiabendazole	Sum of thiabendazole (2-(4-thiazolyl)-1H-benzimidazole) and its metabolite benzimidazole (free and conjugated) or Thiabendazole: 2-(4-thiazolyl)-1H-benzimidazole (post harvest treatments only)[n]	Thiabendazole: 2-(4-thiazolyl)-1H-benzimidazole[n]	Residues of thiabendazole, including its metabolites and degradates. Compliance by measuring only the sum of thiabendazole (2-(4-thiazolyl)-1H-benzimidazole) and its metabolite benzimidazole (free and conjugated), calculated as thiabendazole	Thiabendazole: 2-(4-thiazolyl)-1H-benzimidazole	USA: No (E and RA) CAN: Yes (E); No (RA pre-harvest); Yes (RA post-harvest)
Hexythiazox	Hexythiazox: (4R,5R)-rel-5-(4-chlorophenyl)-N-cyclohexyl-4-methyl-2-oxo-3-thiazolidinecarboxamide[o]	Hexythiazox: (4R,5R)-rel-5-(4-chlorophenyl)-N-cyclohexyl-4-methyl-2-oxo-3-thiazolidinecarboxamide[o]	Residues of hexythiazox, including its metabolites and degradates. Compliance by measuring only hexythiazox and its metabolites containing the (4-chlorophenyl)-4-methyl-2-oxo-3-thiazolidine moiety, calculated as hexythiazox	Hexythiazox: (4R,5R)-rel-5-(4-chlorophenyl)-N-cyclohexyl-4-methyl-2-oxo-3-thiazolidinecarboxamide	USA: No (E and RA) CAN: Yes (E and RA)

Table 2.1. (cont.) Residue definitions in USA and Canada compared to EU residue definitions for 14 pesticide active substances

	EU		USA[a]	Canada[b]	Residue definitions same for USA/ Canada and EU?
	Residue definition for risk assessment (RA)	Residue definition for enforcement (E)			
Metalaxyl / Metalaxyl-M[g]	Metalaxyl and metalaxyl-M (metalaxyl including other mixtures of constituent isomers including metalaxyl-M (sum of isomers))[p]	Metalaxyl (methyl N-(methoxyacetyl)-N-(2,6-xylyl)-DL-alaninate) and metalaxyl-M ((R)-2[2,6-di-methyl-phenyl)-(2-methoxy-acetyl)-amino]-propionic acid methyl ester) (metalaxyl including other mixtures of constituent isomers including metalaxyl-M (sum of isomers)	Metalaxyl: Combined residues of the fungicide metalaxyl [N-(2,6-dimethylphenyl)-N-(methoxyacetyl) alanine methylester] and its metabolites containing the 2,6-dimethylaniline moiety, and N-(2-hydroxy methyl-6-methylphenyl)-N-(methoxyacetyl)-alanine methyl ester, expressed as metalaxyl	Metalaxyl: Methyl N-(2,6-dimethylphenyl)-N-(methoxyacetyl)-DL-alaninate, including metabolites that can be converted to the 2,6-dimethylaniline moiety, each expressed as metalaxyl equivalents	USA: No (E and RA) CAN: No (E and RA)

[a] https://www.globalmrl.com/db#query; [b] https://www.canada.ca/en/health-canada/services/consumer-product-safety/pesticides-pest-management/public/protecting-your-health-environment/pesticides-food/residue-definitions-chemicals-maximum-residue-limits-regulated-under-pest-control-products-act.html; [c] Conclusion on the peer review of the pesticide human health risk assessment of the active substance chlorpyrifos. EFSA Journal 2014;12(4):3640, 34 pp. doi:10.2903/j.efsa.2014.3640; [d] Review of the existing maximum residue levels for chlorpyrifos-methyl according to Article 12 of Regulation (EC) No 396/2005. EFSA Journal 2017;15(3):4737, 70 pp. doi: 10.2903/j.efsa.2017.4734; [e] http://ec.europa.eu/food/plant/pesticides/eu-pesticides-database/public/?event=activesubstance.detail&language=EN&selectedID=1222; [f] Conclusion on pesticide peer review regarding the risk assessment of the active substance 2-phenylphenol. EFSA Scientific Report (2008) 217, 1-67; [g] Conclusion on pesticide peer review regarding the risk assessment of the active substance pyriproxyfen. EFSA Scientific Report (2009) 336 1-99. 2-phenylphenol. EFSA Scientific Report (2008) 217, 1-67; [h] Conclusion regarding the peer review of the pesticide risk assessment of the active substance pyrimethanil, EFSA Scientific Report (2006) 61, 1-70; [i] RAR propiconazole, List of Endpoints. Finland, June 2016; [j] Conclusion on pesticide peer review on the risk assessment of the active substance propyzamide. EFSA Journal (2016); 14(8):4554. doi: 10.2903/j.efsa.2016.4554; [k] Conclusion regarding the peer review of the pesticide risk assessment of the active substance tebufenpyrad. EFSA Scientific Report (2008) 192,1-100; [l] Conclusion on the peer review of the pesticide risk assessment of the active substance imazalil. EFSA Journal 2010, 8(3):1526. [69 pp.]. doi:10.2903/j.efsa.2010.1526; [m] Conclusion on the peer review of the pesticide risk assessment of the active substance prochloraz. EFSA Journal 2011, 9(7):2323. [120 pp.]. doi:10.2903/j.efsa.2011.2323; [n] Reasoned opinion on the revision of the review of the existing maximum residue levels for thiabendazole. EFSA Journal 2016;14(6):4516, 45 pp. doi:10.2903/j.efsa.2016.4516; [0] Conclusion on the peer review of the pesticide risk assessment of the active substance hexythiazox. EFSA Journal 2010;8(10):1722. [78 pp.]. doi:10.2903/j.efsa.2010.1722; [p] Metalaxyl-M: RAR metalaxyl-M, List of Endpoints. Belgium, June 2016; Metalaxyl: http://ec.europa.eu/food/plant/pesticides/eu-pesticides-database/public/?event=activesubstance.selection&language=EN.

2.1.2. Conclusion

For many active substances there is no agreement between RD set in the EU, USA and Canada. This means that residues and MRLs for an active substance may not be comparable between countries / regions since they include different components as part of the RD. These differences may in reality often be quite small, since it can be assumed that all RD will comprise the major part of the residue, however, an easy extrapolation is by no means possible. Direct use of MRLs that have been set in the USA or Canada for EU purposes is therefore feasibly for those substances for which RD correspond, however, it is not feasible where RD differ.

3. Approaches to Setting Maximum Residue Limits (MRLs)

3.1. US approach and tolerances (MRLs) in processed foods

In the US, tolerances (equivalent to MRLs) for pesticides are set by the EPA under FFDCA (Federal Food Drug and Cosmetic Act) section 408. Generally, tolerances need to be set for processed foods if a pesticide residue concentrates during processing to a level that exceeds the tolerance for the raw agricultural commodity (RAC).

A distinction is thereby made between processed commodities that are «ready to eat» (RTE) and those that are «not ready to eat» (nRTE). Citrus oil belongs to the latter category as it is not consumed directly.

In order to determine whether residues in the RTE (mixed/diluted) forms of nRTE processed foods exceed the tolerances for the RAC, the Agency will develop dilution factors. These will be based on the least amount of dilution that may occur for the nRTE commodity. Currently, there is not yet a list of dilution factors available[1].

No tolerance needs to be set for the processed commodity if the pesticide residue in the nRTE food (obtained by multiplying the highest mean residue from field trials – HAFT - with the processing factor) does not exceed the tolerance for the RAC.

However, if the residue in the nRTE exceeds the RAC tolerance, that residue should be divided by the dilution factor to determine the residue

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[1] Residue Chemistry Test Guidelines OPPTS 860.1520 Processed Food/Feed. EPA 712–C–96–184, August 1996. https://www.regulations.gov/document?D=EPA-HQ-OPPT-2009-0155-0014.

level in the RTE food (e.g. soft drink). If the residue in the (diluted) RTE food is still higher than the RAC tolerance, specific tolerances for the nRTE processed commodity need to be set (formerly under FFDCA section 701 or 409, now all under FFDCA section 408[2]).

Current US tolerances for citrus fruit/lemon RAC and for citrus oil for 14 pesticide active substances are compiled in Table 31.With the exception of 2-phenylphenol, tolerances for citrus oil exist for all active substances for which RAC tolerances are available. No tolerances have been set in the US for chlorpyrifos-methyl, prochloraz, propyzamide and tebufenpyrad.

3.2. Canadian approach and MRLs in processed foods

MRLs in Canada are set by Health Canada and are regulated under the Pesticide Control Products Act (PCPA). Typically, an MRL applies to the identified raw agricultural food commodity as well as to any processed food product that contains it. However, where a processed product may require a higher MRL than that specified for its raw agricultural commodity, separate MRLs are specified[3].

No further information was found as to how specific MRLs for processed foods are set.

Current Canadian MRLs for citrus/lemon fruit RAC and for citrus oil for 14 pesticide active substances are shown in Table 31. MRLs for citrus fruit and oil are generally very similar to US tolerances, but fewer MRLs for citrus oil have been set than in the US. As in the USA, no tolerances are available for chlorpyrifos-methyl, prochloraz, propyzamide and tebufenpyrad.

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2 https://www.epa.gov/pesticide-registration/pesticide-registration-manual-chapter-11-tolerance-petitions.

3 https://www.canada.ca/en/health-canada/services/consumer-product-safety/pesticides-pest-management/public/protecting-your-health-environment/pesticides-food/maximum-residue-limits-pesticides.html.

Table 3.1. MRLs for lemons / citrus fruit and citrus oil in the USA and Canada for 14 pesticide active substances

	USA*		Canada**	
	Tolerance lemon RAC (ppm)	Tolerance citrus oil (ppm)	MRL citrus fruits RAC (mg/kg)	MRL citrus oil (mg/kg)
Chlorpyrifos	1	20	1	–
Chlorpyrifos-methyl	–	–	–	–
Dicofol[a]	6	200	5	–
2-Phenylphenol	10	--	10[c]	–
Pyriproxyfen	0.5	20	0.5	20
Pyrimethanil	10	150	10	150
Propiconazole	8	1000	8	1000
Propyzamide	–	–	–	–
Tebufenpyrad	–	–	–	–
Imazalil	10	200	5	–
Prochloraz	–	–	–	–
Thiabendazole	10	15	10	–
Hexythiazox	0.6	25	0.5	24
Metalaxyl / Metalaxyl-M[b]	1	7	5	–

* *https://www.globalmrl.com/db#query/20240D6242A8FD6E0755278D24FCD77E1AAED1E73832C3113F55000FD3A009353711/1/125 https://www.ecfr.gov/cgi-bin/historyECFR?gp=1&SID=5b0578d881c1162a040d4484cd061278&h=L&mc=true&ret=true.*
** *http://pr-rp.hc-sc.gc.ca/mrl-lrm/results-eng.php.*

[a] Dicofol is not approved in the EU. MRL is set at limit of quantification.
[b] Only metalaxyl in Canada.
[c] Sodium orthophenyl phenate.

3.3. Discussion of US and Canadian approaches with regard to EU

Specific MRLs for processed food commodities are set in both USA and Canada, and MRLs for citrus oil exist for a number of active substances in both countries.

The Canadian approach to how MRLs for processed commodities are set, however, is not specified in detail, therefore no further conclusion can be drawn as do its applicability to EU procedures.

The US approach to setting MRLs in processed commodities differs from the EU approach in that it distinguishes between processed foods that are eaten directly (RTE) and those that are not (nRTE), and it introduces the use of a dilution factor for nRTE foods to assess the possible residue in the edible commodity. Generally, the concept of assessing the residue concentration in the diluted food commodity of nRTE processing commodities seems interesting, since it provides an easy way of deciding whether MRLs for a processed nRTE commodity would be required.

For MRL setting of nRTE commodities in the US, data from field trials (highest average field trials – HAFT - for RAC residue) and from processing studies (for processing factors) are required. Both, field residue data and processing data are also generated for pesticide registration in the EU.

In contrast to the US, median field residue data are used (STMR) in the EU and not average (mean) data, and STMRs are only relevant for refined risk assessment calculation and not for MRL setting. In order adapt the US approach to the EU, it may be advisable not to use the HAFT (or similar field trials) value, but instead the STMR for the assessment of potential residues in the final (diluted) food commodity. In the case of citrus oil, an MRL would then have to be set if

$$RAC\ STMR\left(\frac{mg}{kg}\right) \times Processing\ factor\ \div\ Dilution\ factor > RAC\ MRL\ (mg/kg)$$

An example calculation for citrus oil is detailed in the following section.

3.4. Example calculation based on US approach

To assess the need for specific MRLs (tolerances) for processed foods in the US, normally data are taken from field residue trials and from processing studies. Since field data and generic processing factors for citrus oil are not available, in this example measured residues in citrus oil from an AILIMPO study[4] were instead used, in which residues for 14 pesticides were measured in RAC lemon fruit and in cold-pressed citrus oil.

[4] Proposal for a generic processing factor to be considered to derive MRL's from Fresh Lemons to Cold Pressed Lemon Oil (CPLO). A Practical Approach to Solve Uncertainty. AILIMPO, 17.02.2016.

In agreement with the equation above, the residue in citrus oil was multiplied with the dilution factor (0.03 % citrus oil in soft drink = 3333 x dilution) and then compared to the RAC MRL.

Residues of 14 active substances measured in cold-pressed lemon oil were directly compared to MRLs for lemon, and after taking into account the dilution in soft drink. Results are shown in Table 3.2.

Table 3.2. Assessment of residues of cold-pressed lemon oil in soft drink with regard to MRLs in lemon

	Highest residue in lemon oil* (mg/kg)	EU MRL lemon (mg/kg)**	Residue in lemon oil *vs.* lemon MRL: Exceedance of MRL?	Calculated residue in RTE soft drink[a] (mg/kg)	Residue in soft drink vs lemon MRL: Exceedance of MRL?
Chlorpyrifos	4.03	0.20	Y	0.001	N
Chlorpyrifos-methyl	0.29	0.30	N	0.000	N
Dicofol	0.09	0.02	Y	0.000	N
2-Phenylphenol	80.74	5.00	Y	0.024	N
Pyriproxyfen	5.54	0.60	Y	0.002	N
Pyrimethanil	19.94	10.00	Y	0.006	N
Propiconazole	0.56	6.00	N	0.000	N
Propyzamide	0.19	0.01	Y	0.000	N
Tebufenpyrad	0.40	0.50	N	0.000	N
Imazalil	5.54	5.00	Y	0.002	N
Prochloraz	90.74	10.00	Y	0.027	N
Thiabendazole	3.90	5.00	N	0.001	N
Hexythiazox	0.32	1.00	N	0.000	N
Metalaxyl / Metalaxyl-M	0.09	0.50	N	0.000	N

** Proposal for a generic processing factor to be considered to derive MRLs from Fresh Lemons to Cold Pressed Lemon Oil (CPLO). A Practical Approach to Solve Uncertainty. AILIMPO, 17.02.2016.*
*** http://ec.europa.eu/food/plant/pesticides/eu-pesticides-database/public/?event=pesticide.residue.selection&language=EN.*

a Residue in RTE (Ready To Eat) soft drink containing 0.03 % lemon oil=Residue in lemon oil/dilution factor 3333.

While MRLs for lemon were exceeded for a number of active substances when comparing residues in lemon oil directly with MRLs for lemon, no lemon MRL was exceeded in the diluted soft drink containing

0.03 % citrus oil. This would mean, extrapolating from the US approach, that no MRLs would need to be set for citrus oil.

Generally, since the dilution of citrus oil in soft drinks is very high (x 3333), it would seem unlikely that specific MRLs for citrus oil will be required: the dilution factor is always greater than any concentration during citrus oil processing. For the 14 active substances investigated, the highest concentration in citrus oil in the AILIMPO study was measured for chlorpyrifos, with a PF of 201.5.

3.5. Conclusion

Whereas the Canadian approach to setting MRLs in processed commodities is not specified and therefore not discussed any further, the US approach was considered further with regard to its relevance for the EU.

Due to the absence of field residue data for lemon and processing factors for lemon oil, measured residues in citrus oil were used for an example calculation of residues in the edible food soft drink. Whereas residues in citrus oil often exceeded the MRL for lemon RAC, the calculated residue concentration in the consumable soft drink was always well below the MRLs for lemon RAC. From this calculation it can be concluded that, due to the great dilution of citrus oil in soft drink, no MRLs for citrus oil would have to be set in the EU if US criteria would apply.

In addition to the above considerations, the use of dilution factors may be an easy way to decide whether residues that were measured in citrus oil are compliant with current lemon/citrus MRLs.

4. Overall Conclusions

- Direct transfer of MRLs that have been set in USA or Canada for citrus oil is not considered feasible since in many cases residue definitions differ between USA/Canada and the EU. MRLs for lemon/citrus fruit RAC also differ between USA/Canada and EU for many active substances.
- The US approach to MRL setting in processed commodities (using dilution factors for processed commodities that are not eaten directly) may be useful for establishing whether specific MRLs for

citrus oil are needed. However, field residue data and processing factors are nevertheless required.

- In the absence of reliable processing factors for citrus oil, the use of dilution factors may be a practical way of assessing whether residues measured in citrus oil comply with existing MRLs for lemon/citrus RAC. However, it is uncertain whether this would be an approach that can be translated into EU policy.