cooking and juicing. In other cases the residue level may increase during processing as it often does in the case of oil from oilseeds and olives. Further, in some cases the active ingredient can be transformed during processing into degradation products that are more toxic than the parent compound.

The JMPR is aware that there is a considerable trade in manufactured foods based, for example, on fruits, vegetables, cereals and meat. However, the variety of forms under which the products are offered makes it impossible to recommend MRLs for all possible processed foods. For this reason the JMPR has specified that, in the case of processed foods for which no MRLs have been recommended, the maximum residue permitted in the processed food should not be greater than the maximum residue permitted in the equivalent weight of the raw agricultural commodity.

The JMPR frequently estimates maximum residue levels for important processed foods and feeds in international trade when residues concentrate in these products at levels higher than in the raw agricultural commodities from which they are derived (e.g. oil, bran, peel, etc.). Even when the estimates are not recommended for use as maximum residue limits or when residues do not concentrate in the processed product, the JMPR will continue to record in its monographs the effect of processing on the level and fate of residues in food. This has been found to be critical for better estimates of dietary intake of pesticides.

Processing studies are among the critical supporting studies required for the evaluation of a new or periodic review compound. See Chapter 3 section, "Fate of residues in storage and processing", for the objectives and data requirements.

All the residues (parent and relevant metabolites) determined in the RAC also have to be determined in the processed products. In addition, any degradation products found in studies of the nature of the residue which require a separate dietary risk assessment also have to be considered. The residue must be calculated according to the definition relevant for compliance with MRLs and for the estimations of dietary intake.

As a result of the processing studies, it will be possible to recognize reductions and concentrations and to calculate processing factors for important products.

Processing factor = residue level [mg/kg] in processed product ÷ residue level [mg/kg] in RAC

If more than one processing study has been conducted for a particular pesticide in the same RAC, the average processing factor for each type of process should be used for each processed commodity. If the processing factors from two trials are irreconcilable, e.g. 10-fold different, the mean is inappropriate because it would not represent either process. In this case it is preferable to choose one of the values as being representative. The highest processing factor should be chosen as the default (conservative) value if there is no other reason to choose one or the other.

When residues in the processed commodity are undetectable or <LOQ the calculated processing factor (LOQ ÷ residue level in RAC) should be reported with a "less than" (<) symbol. If residues in the processed commodity are undetectable or <LOQ in several processing studies it may mean that residues in the processed commodity are very low or essentially zero and the calculated processing factors are merely a reflection of the starting residue levels in the RAC. In this case the best estimate of the processing factor is the lowest "less than" value rather than the mean of "less than" values. Reported processing factors should be rounded to 2 significant figures.

When residues in the processed commodity and in the RAC are both undetectable the study is of no value for deriving a processing factor.

If several studies are available and a step that is routinely used in the processing of that RAC (e.g. cleaning, washing) is omitted in a study, it may be inappropriate to include that study in the calculation of the average processing factor.

To estimate a maximum residue level for a processed product the MRL or maximum residue level of the RAC is multiplied by the processing factor. For the purpose of IEDI estimation, the STMR of the RAC is multiplied by the processing factor to give the STMR-P of the processed product.

If data are available for the residues in the edible portion of the commodity (e.g. in banana pulp), an STMR should be estimated directly from the residues in the edible portion found in supervised trials at the maximum registered rate of use.

CHAPTER 6
ESTIMATION OF RESIDUE LEVELS FOR CALCULATION OF DIETARY INTAKE OF PESTICIDE RESIDUES

PROCESSING, COOKING FACTORS AND EDIBLE PORTION RESIDUE DATA

In using data on the effects on residue levels of processing or cooking practices, the mean processing factor should be applied to the STMR value estimated for the raw agricultural commodity as already described. The STMR value estimated in this way for the processed commodity should be referred to as the STMR-P.

If data are available for the residues in the edible portion of the commodity (e.g. banana pulp), an STMR value should be estimated directly using the edible portion residue values from maximum registered use trials (as opposed to using pesticide values for the whole commodity).

If the processing factors from two trials are irreconcilable, e.g. 10-fold different, the mean is inappropriate because it would not represent either process. In this case it is preferable to choose one of the values as being representative. The highest processing factor should be chosen as the default (conservative) value if there is no other reason to choose one or the other.

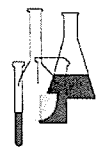
資料 2

United States Environmental Protection Agency | Prevention, Pesticides and Toxic Substances (7101) | EPA 712–C–96–154 August 1996

EPA

Residue Chemistry Test Guidelines

OPPTS 860.1520 Processed Food/Feed



INTRODUCTION

This guideline is one of a series of test guidelines that have been developed by the Office of Prevention, Pesticides and Toxic Substances, United States Environmental Protection Agency for use in the testing of pesticides and toxic substances, and the development of test data that must be submitted to the Agency for review under Federal regulations.

The Office of Prevention, Pesticides and Toxic Substances (OPPTS) has developed this guideline through a process of harmonization that blended the testing guidance and requirements that existed in the Office of Pollution Prevention and Toxics (OPPT) and appeared in Title 40, Chapter I, Subchapter R of the Code of Federal Regulations (CFR), the Office of Pesticide Programs (OPP) which appeared in publications of the National Technical Information Service (NTIS) and the guidelines published by the Organization for Economic Cooperation and Development (OECD).

The purpose of harmonizing these guidelines into a single set of OPPTS guidelines is to minimize variations among the testing procedures that must be performed to meet the data requirements of the U. S. Environmental Protection Agency under the Toxic Substances Control Act (15 U.S.C. 2601) and the Federal Insecticide, Fungicide and Rodenticide Act (7 U.S.C. 136, *et seq.*).

Final Guideline Release: This guideline is available from the U.S. Government Printing Office, Washington, DC 20402 on *The Federal Bulletin Board.* By modem dial 202–512–1387, telnet and ftp: fedbbs.access.gpo.gov (IP 162.140.64.19), internet: http://fedbbs.access.gpo.gov, or call 202–512–0132 for disks or paper copies. This guideline is also available electronically in ASCII and PDF (portable document format) from the EPA Public Access Gopher (gopher.epa.gov) under the heading "Environmental Test Methods and Guidelines."

OPPTS 860.1520 Processed food/feed.

(a) **Scope.** (1) **Applicability**. This guideline is intended to meet testing requirements of both the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) (7 U.S.C. 136, *et seq.*) and the Federal Food, Drug, and Cosmetic Act (FFDCA) (21 U.S.C. 301, *et seq.*).

(2) **Background.** The source material used in developing this harmonized OPPTS test guideline is OPP 171–4, Results of Tests on the Amount of Residue Remaining, Including a Description of the Analytical Methods Used (Pesticide Assessment Guidelines, Subdivision O: Residue Chemistry., EPA Report 540/9–82–023, October 1982). This guideline should be used in conjunction with OPPTS 860.1000, Background.

(b) **Purpose.** Processing studies are required to determine whether residues in raw commodities may be expected to degrade or concentrate during food processing. If residues do concentrate in a processed commodity, a food or feed

additive tolerance must be established under section 409 of the FFDCA (or a section 701 Maximum Residue Limit (MRL) in some cases). However, if residues do not concentrate in processed commodities, the tolerance for the raw agricultural commodity (RAC) itself applies to all processed food or feed derived from it.

(c) **Concentration of residues on processing.** (1) Whenever there is a possibility of residue levels in processed foods/feeds exceeding the level in a RAC, processing data are required. Examples of processed foods/feeds in which residues may concentrate are apple juice and apple pomace, the hulls, meal, and refined oil from cottonseed, or the sugar, dried pulp and molasses from sugar beet roots. A list of processed byproducts is contained in Table 1 of OPPTS 860.1000, Background.

(2) Processing studies should simulate commercial practices as closely as possible. RAC samples used in processing studies should contain field treated quantifiable residues, preferably at or near the proposed tolerance level, so that concentration factors for the various byproducts can be determined. As discussed in paragraph (f)(3) of this guideline, this may require field treatment at exaggerated application rates to obtain sufficient residue levels for processing studies. Processing studies utilizing spiked samples are not acceptable, unless it can be demonstrated that the RAC residue consists entirely of a surface residue.

(3) Only one processing study is required for each crop in Table 1 of OPPTS 860.1000 having a processed commodity. However, it is advisable to have multiple samples of the RAC and processed commodities in the study. As stated in paragraph (f)(2) of this guideline, if multiple processing studies are available for a given crop, the Agency will use the average concentration factor obtained across these studies. In some cases the requirement for a processing study may be waived based on field trial data for the RAC reflecting exaggerated application rates. This is discussed in more detail in paragraph (f)(3) of this guideline.

(4) The total toxic residue should be measured in the raw agricultural commodity at the time processing is initiated and in all processed commodities of the crop listed in Table 1 of OPPTS guideline 860.1000. With the exception of the small grains, the Agency will not normally translate data between crops. In the case of small grains, a processing study on wheat satisfies the requirement for studies on barley, buckwheat, millet, oats and rye if the pesticide is applied to all these crops in a similar manner and comparable residue levels occur in the grains.

(5) Unless the processed commodities are analyzed within thirty days of their production, data demonstrating the stability of residues in representative processed commodities during storage are required as described in OPPTS

Table 1.—Maximum Theoretical Concentration Factors by Crop

Crop	Maximum Concentration Factor
Apples	>14x*
Barley	8x
Beets, sugar	>20x*
Canola	3x
Citrus	1000x
Coconut	3x
Coffee	4.5x
Corn	25x
Cottonseed	6x
Figs	3.5x
Grapes	5x*
Mint (peppermint, spearmint)	330x
Oats	8x**
Olive	10x
Peanuts	3x
Pineapple	4x
Potatoes	5x
Plums (prunes)	3.5x
Rapeseed	2x
Rice	8x
Rye	10x
Safflower	9x
Soybeans	12x
Sugarcane	>20x*
Sunflower	4.5x
Tomatoes	5.5x*
Wheat	8x

*Experimental factor
**Based on factor for wheat

(2) The list is not all inclusive as factors are not available for all processed commodities listed in Table 1 of OPPTS 860.1000. In addition, some processed commodities may have greater potential for concentration than those processed commodities for which factors were calculated. For those commodities for which higher concentrations are expected, the Agency has tabulated some experimental concentration factors, by comparing proposed and established food/feed

additive tolerances to the proposed and established tolerances for the RAC. Additional factors may be added or updated in the future as further information becomes available.

(3) There are two types of processes for which maximum theoretical concentration factors can easily be calculated. The first type is where the concentration is based on the loss of water during processing. In this case, the theoretical concentration factor is the ratio of the percent of dry matter in the processed commodity to the percent of dry matter in the RAC. For example, grapes contain 18 percent dry matter while raisins contain 85 percent dry matter. The theoretical concentration factor for the processing of grapes into raisins is 85/18 or 4.7□. The second type of process is that in which a RAC is separated into components, such as the processing of corn grain into corn oil. In this case, the theoretical concentration factor is 100 percent divided by the percentage of the processed commodity in the RAC. Corn grain may contain as little as 4 percent corn oil. The theoretical concentration factor for processing of corn into oil then is 100/4, or 25□.

(4) In cases where a crop had multiple processed fractions, only the fraction having the highest maximum theoretical concentration factor is listed in Table 1 (see paragraph (e)(1) of this guideline). In some cases, only typical yields were available for a particular RAC, particularly for grains. A factor was still calculated, but may not actually be the maximum theoretical concentration factor. The following Table 2 shows calculations for those commodities where concentration is based on loss of water, Table 3 shows calculations for those commodities where concentration is based on separation into components, and Table 4 is a tabulation of experimentally determined factors obtained by comparing proposed and established food/feed additive tolerances to the proposed and established tolerances for the RAC. A bibliography for the tables is given in paragraph (e)(5) of this guideline.

Table 2.—Theoretical Concentration Factors Based on Loss of Water

Crop	percent dry matter	Factor	Reference
Figs	22		PAM I, sec. 202.12
dry figs	76	3.5	PAM I sec., 202.12
Grapes	18		Harris Guide
raisins	85	4.7	Harris Guide
Potatoes	20		USDA
dried (flakes, granules)	93	4.7	USDA
Plums	21		PAM I, sec. 202.12
prunes	72	3.4	PAM I, sec. 202.12
Tomatoes	6		p. 311, Commercial Vegetable Processing, 2nd Ed.
puree	8.5	1.4	p. 272, Commercial Vegetable Processing, 2nd Ed.
paste	33	5.5	p. 277, Commercial Vegetable Processing, 2nd Ed.

Table 3.—Theoretical Concentration Factors Based on Separation into Components

Crop	Minimum percent of whole	Factor	Reference
Barley grain			
bran	13	7.7	based on wheat bran
pearled	82	1.2	p. 426, Principles of Field Crop Production
Beets, sugar			
sugar	8	12.5	Advances in Sugar Beet Production
molasses			
dried pulp			
Canola			
meal	52	1.9	p. 259, by difference, CRC Handbook of Processing and Utilization in Agriculture
oil	33	3.0	p. 259, CRC Handbook of Processing and Utilization in Agriculture

Table 3.—Theoretical Concentration Factors Based on Separation into Components—Continued

Crop	Minimum percent of whole	Factor	Reference
Citrus			
peel	30	3.3	p. 1391, Considine Foods and Food Production Encyclopedia
oil	0.1	1000	PAM I, sec. 202.12
pulp, dehydrated			
juice	50	2	p. 1387, Considine Foods and Food Production Encyclopedia
Coconut			
oil	35	2.9	PAM I, sec. 202.15
copra (dried meal)		2.1	DRES (from USDA Handbook No. 102)
Coffee			
roasted bean	1.2	18 percent loss in weight in roasting	p. 459 Considine
instant		4.4	PP no. 0E3875-based on weights in processing study
Corn grain			
oil	4	25.0	p. 243, Corn, Culture, Processing, Products
Cottonseed			
hulls	26	3.8	p. 187, CRC Handbook of Processing and Utilization in Agriculture
meal	45	2.2	p. 187, CRC Handbook of Processing and Utilization in Agriculture
oil	16	6.3	p. 187, CRC Handbook of Processing and Utilization in Agriculture
Grapes			
juice	82	1.2	Harris Guide
Mint			
oil	0.3	333	15 mL oil from 10 lb hay
Oats			
flour			
rolled oats	70	1.4	p. 577-8, Cereal Crops
Olive oil			
oil	10	108	p. 1372, Considine Foods and Food Production Encyclopedia
Peanuts			
meal	46	2.2	p. 139, by difference, see p 293, Peanuts:...
oil	36	2.8	PAM I, sec. 202.25
Pineapple			PP no. 6F0482
process residue	26	3.8	
juice			
Potatoes			
processed waste	25	4.0	NorthWest Food Processors Association
Rapeseed			
meal	52	1.9	p. 259, by difference, CRC Handbook of Processing and Utilization in Agriculture
Rice grain (rough rice)			
hulls	20	5.0	pp. 649, 652, Cereal Crops
bran	13	7.7	p. 649, 652, Cereal Crops
Rye grain			
bran	10	10.0	p. 244-5, CRC Handbook of Processing and Utilization in Agriculture
flour			
Safflower			
meal	11	9.1	p. 114, CRC Handbook of Processing and Utilization in Agriculture

Table 3.—Theoretical Concentration Factors Based on Separation into Components—Continued

Crop	Minimum percent of whole	Factor	Reference
oil (safflower)	30	3.3	p. 114, CRC Handbook of Processing and Utilization in Agriculture
Soybeans			
hulls	9	11.3	MRID No. 424482-03, Appendix B, p67
meal	46	2.2	CBRS No. 10541, D. Miller, 1/29/93
oil	8	12.0	CBRS No. 10541, D. Miller, 1/29/93
Sugarcane			
molasses			
sugar	8.5	11.8	p. 426, Principles of Field Crop Production
Sunflower			
meal	22	4.5	p. 146, by difference, CRC Hand book of Processing and Utilization in Agriculture
oil	40	2.5	p. 146, CRC Hand book of Processing and Utilization in Agriculture
Tomatoes			
juice	70	1.4	p. 303, Commercial Vegetable Processing, 2nd. Ed.
Wheat grain			
bran	13	7.7	p. 2125, Considine
flour	72	1.4	pp. 295-6, Cereal Crops
shorts	12	8.3	pp. 295-6, Cereal Crops

Table 4.—Maximum Observed (Experimental) Concentration Factors

Crop	Maximum Concentration Factor [1]
apple pomace	14×
sugar beet pulp, dry	20×
sugarcane molasses	20×

[1] These factors are based on a comparison of proposed and established food additive tolerances to the proposed and established tolerances on raw agricultural commodities.

(5) The following is a bibliography for Tables 1 through 4.

Pesticide Analytical Manual, Volume I (PAM I), 1994, Food and Drug Administration.
Agriculture Handbook No. 8, Composition of Foods: Raw, Processed, prepared, U. S. Department of Agriculture, Agricultural Research Service, B. K. Watt, and A. L. Merrill, December, 1963.
CRC Handbook of Processing and Utilization in Agriculture, Volume II, Part 2 Plant Products, I. A. Wolff, ed., CRC Press, Boca Raton, FL 1983.
Foods and Food Production Encyclopedia, D. M. Considine, and G. D. Considine, eds., Van Nostrand Reinhold, New York, 1982.
Commercial Vegetable Processing, 2nd Edition, ed. B. S. Luk, and J. G. Woodroof, Avi/Van Nostrand Reinhold, New York, 1988.
Peanuts: Production, Processing, Products, 2nd Edition, J. G. Woodroof, Avi Publishing, Westport, CT, 1973.
Corn: Culture, Processing, Products, Ed. G. E. Inglett, Avi Publishing, Westport, CT, 1970.
Oats: Chemistry and Technology, ed. F. H. Webster, American Association of Cereal Chemists, Inc., St. Paul, MN 1986.
Advances in Sugar Beet Production: Principles and Practices, eds., R. T. Johnson, et. al., Iowa State University Press, Ames, IA 1971.
Harris Guide.
Feeds & Nutrition--Complete, First Edition, Ensminger, M. E., and C. G. Olentine, Jr., Ensminger Publishing Co., Clovis, CA 1978.
Cereal Crops, Leonard, W. H., and J. H. Martin, Macmillan Co., New York, 1963.
Principles of Field Crop Production. 3rd. Edition, Martin, J. H., W. H. Leonard, and D. L. Stamp, Macmillan, New York, 1976.

(f) **Determining the need for food/feed additive tolerances**—(1) **RAC residue value.** (i) The Agency will consider using some average residue value from field trials if it can be determined that there is sufficient mixing during processing such that variation among individual samples from a field will be substantially evened out. It has been stated that "** * * the most relevant 'average' residue value from crop field trials is the highest average residue value from the series of individual field trials * * * *." This value is sometimes referred to as the HAFT (highest average field trial). Other average values (e.g. average of all field trials) may be considered if the circumstances involved in processing of the crop warrant. Such an example would be where processing is likely to involve blending of crop from across a regional or national market.

(ii) As a result of this policy, it is necessary to determine the HAFT for each RAC for which a processing study has shown concentration of residues. For each field trial reflecting the maximum residue use (i.e. maximum number and rate of application, minimum preharvest interval) and considered acceptable for determining the section 408 of FFDCA tolerance (i.e. values discarded for reasons such as contamination should not be included), residue values for all samples at that site reflecting that use should be averaged. (NOTE: If residues were corrected for low method recoveries or for losses during storage in order to determine the tolerance, the corrected values should also be used in this exercise.) The highest such average value is the HAFT and is to be used to calculate the maximum expected residue in processed commodities. For field trials in which only one sample per site reflects the maximum residue use no averaging can be done and the highest individual residue value becomes the HAFT.

(2) **Multiple processing studies.** (i) Whenever more than one processing study has been conducted for a particular pesticide on a given RAC, the average concentration factor should be used for each processed commodity when determining the need for section 409 tolerances (or section 701 MRLs under paragraph (c)(6) of this guideline). Similarly, if multiple samples or subsamples are analyzed within a processing study, the average residue value should be used for each commodity as opposed to using the lowest value from the RAC samples and the highest value for the processed fraction samples, which would result in the highest concentration factors. When averaging concentration factors across studies, factors which exceed the theoretical maximum should be lowered to the latter for averaging purposes. In no instance should a section 409 tolerance (or section 701 MRL) be based on a concentration factor greater than the theoretical maximum. If only one processing study has been conducted and the theoretical concentration factor has been exceeded, the section 409 or section 701 residue level should be based on the factor (if available) listed in Tables 1 through 4 of this guideline.

(ii) As stated in paragraph (c)(2) of this guideline, processing studies should reflect actual commercial practices. If several studies are available and a step (e.g. washing) that is routinely used in the processing of that RAC is omitted, it

may be inappropriate to include that study in the calculation of the average concentration factor.

(3) **Use of exaggerated rate studies.** (i) The Agency encourages use of field trials with exaggerated application rates in cases where residues near or below the analytical method's LOQ are expected in the RAC from the maximum registered rate (1□). For purposes of this discussion, pesticide uses can be divided into those which result in quantifiable residues in the RAC and those which do not. The former would have section 408 tolerances set above the LOQ, while the latter would usually have tolerances set at the LOQ. In either case, if possible, processing studies should use RAC samples which contain quantifiable residues.

(ii) For uses which result in quantifiable residues in the RAC from the registered application rate, exaggerated rate applications are not needed to generate RAC samples for processing if all field trials lead to residues well above the LOQ. However, if residues below or near the LOQ are observed in some field trials, it is advisable for an exaggerated application rate to be used to generate RAC samples for the processing study. Regardless of whether exaggerated application rates are used, if a section 408 tolerance is based on the presence of quantifiable residues and concentration of residues is observed in a processed commodity, that concentration factor will be used in conjunction with the HAFT or other applicable average value and other relevant factors (e.g. variability of the analytical method) to determine the need for a section 409 tolerance (or section 701 MRL). In other words, the concentration factor will *not* be adjusted for the use of exaggerated rates in cases where quantifiable residues are observed in the RAC from the registered use.

(iii) In those cases where *all* RAC samples from the field trials show residues below the LOQ and the residue data cover *all* significant growing regions for the crop as delineated in OPPTS 860.1500, it may be possible to waive the processing study and conclude that section 409 tolerances (or section 701 MRLs) are not needed based on the results of field trials conducted at exaggerated application rates. With the exception of mint and citrus, if exaggerated rate data are available and these field trials result in no quantifiable residues in the RAC, no processing study and section 409 tolerances are required provided that the rate was exaggerated by at least the highest theoretical concentration factor among all the processed commodities derived from that crop *or* 5×, whichever is less. Processing studies will be needed for citrus and mint in virtually all cases due to the extremely high potential concentration factors for citrus oil (1,000×) and mint oil (330×).

(iv) If no quantifiable residues are found in the RAC from the maximum registered rate, but the exaggerated rate does produce quantifiable residues, the latter samples should be processed and residues measured in the appropriate commodities. Any residues still above the LOQ in the processed commodities should be adjusted for the degree of exaggeration. These adjusted residues should then be compared to the LOQ for the RAC. If the adjusted residues are greater than or equal to twice the LOQ, a section 409 tolerance (or section 701 MRL) is needed. Due to the variability associated with an analytical method near its LOQ, a food additive tolerance (or section 701 MRL) will not normally be established for residues less than twice the LOQ. For example, consider a field corn RAC tolerance set at 0.05 ppm (LOQ) and residues of 0.08 ppm being found in the RAC and 0.30 ppm in the oil following a 5×application rate. Adjusting for the 5×rate, oil residues would be 0.06 ppm, which is less than twice the LOQ. Therefore, a section 409 tolerance is not necessary. However, if the oil residues were 1.0 ppm, a section 409 tolerance (or perhaps section 701 MRL) at 0.20 ppm (1.0 ppm/5) would be necessary.

(v) One additional scenario needs to be discussed regarding use of exaggerated rates. In some cases no quantifiable residues may be found in the RAC, but the exaggerated rate is less than the maximum theoretical concentration factor (or 5×, whichever is less) due to phytotoxicity limitations. In these instances a decision will be made case-by-case as to the need for a processing study. If a processing study is deemed necessary, any quantifiable residues in processed fractions would be adjusted for the degree of exaggeration as explained in the previous paragraph. Some of the factors to consider when determining if the processing study is needed include how close the degree of exaggeration comes to the theoretical factor (or 5×, whichever is less) and whether *detectable* residues (i.e. greater than limit of detection but less than LOQ) are found in any RAC samples. Another consideration would be whether the pesticide is likely to be present on a specific portion of the RAC based on when it is applied and/or its ability to translocate. For example, a pesticide applied late in the growing season would be more likely to be on the surface of a fruit and have greater potential to concentrate in pomace than one applied only
at the bloom stage or earlier.

(4) **Impact of Ready-to-Eat (RTE).** (i) The classification of a processed food as RTE or *not* RTE will determine whether or not the possibility of setting a section 701 MRL needs to be explored as discussed under paragraph (f)(5) of this guideline. Until recently, the Agency has considered any food available for sale as being

ready-to-eat. The Agency now holds that RTE food has a common sense meaning of food which is consumed without further preparation and will apply this interpretation in future actions. Therefore, food should now be considered "ready-to-eat" if it consumed "as-is" or is added to other RTE foods (e.g. condiments).

(ii) The Agency also realizes that application of this definition of RTE may be difficult in many instances. The following processed foods are examples of not-ready-to-eat: mint oil, citrus oil, guar gum, and dried tea. Examples of clearly RTE foods are raisins, olives, and potato chips. Vegetable oils are an example of foods not so easily characterized under this RTE standard. The Agency is presently analyzing information on food consumption and mixing of livestock feeds in order to classify processed commodities with respect to RTE. As such decisions are made, they will be made available to the public.

(5) **Determining the need for section 409 tolerances or section 701 MRL's.** (i) The Agency will establish food/feed additive tolerances (FATs) under section 409 of the FFDCA for processed foods or feeds that *are* classified as RTE if residues in those processed commodities are likely to exceed the corresponding section 408 tolerances. Therefore, for an RTE food such as raisins, the concentration factor (taking into account multiple processing studies and exaggerated rates, if applicable) should be multiplied by the HAFT (or other applicable average value) and that value compared to the RAC tolerance. If that number is appreciably higher than the section 408 tolerance, a food/feed additive (section 409) tolerance will be needed. The judgment as to "appreciably higher" will need to take into account how close the residue level is to the LOQ of the analytical method. If residues in the processed food are less than twice the LOQ, a section 409 tolerance is normally not needed. On the other hand, when residues in the processed food (i.e. concentration factor times HAFT) are significantly above the LOQ, a section 409 tolerance will normally be needed if those residues are approximately 1.5□the section 408 tolerance (or higher). For situations in which the processed food/feed residues are close to that level (e.g. 1.3 to 1.7□those in the RAC), all relevant information including variability in recovery data will be considered by the Agency when assessing the need for food/feed additive tolerances.

(ii) The procedure is more complex for processed foods or feeds that are *not* RTE (nRTE). If residues in an nRTE processed food exceed the section 408 tolerance, residues in the RTE forms of those foods/feeds will need to be determined and then compared to the section 408 tolerance. If the residues in the RTE (i.e. mixed/diluted) form do not exceed the RAC tolerance, the Agency will establish an MRL on the nRTE processed commodity under section 701 of the FFDCA. On the other hand, if residues in the RTE (mixed/diluted) form still appreciably exceed those in the RAC, a food/feed additive tolerance will be established for the NRTE processed commodity under section 409 of the FFDCA.

(iii) In order to determine whether residues in the RTE (mixed/diluted) forms of nRTE processed foods/feeds exceed those in the RAC, the Agency will develop dilution factors. These will be based on the least amount of dilution that may occur for the nRTE food. For example, flour, assuming it is classified as nRTE, is likely to have a relatively low dilution factor based on its use in preparation of commodities such as crackers, bagels, and tortillas. Dried tea, on the other hand, is likely to have a large dilution factor based on the relative weight of water used to brew tea. At this time there is no list of dilution factors. As these factors are derived, the Agency will announce them to the public periodically.

(iv) The procedure for assessing nRTE processed commodities is as follows. The concentration factor (accounting for multiple processing studies and exaggerated rates, if necessary) is multiplied by the HAFT (or other applicable average value) to determine residues in the nRTE processed food. If the residue in the nRTE food does not appreciably exceed the section 408 tolerance, neither a section 409 tolerance nor section 701 MRL is needed. If the residue in the nRTE processed food does appreciably exceed the RAC tolerance, that residue should be divided by the dilution factor to determine the residue level in the RTE form. If the residue in the RTE (mixed/diluted) food is basically equal to or less than the section 408 tolerance, a section 701 MRL is needed for the nRTE processed commodity. If the residue in the RTE (mixed/diluted) food still appreciably exceeds the section 408 tolerance, a section 409 (i.e. food or feed additive) tolerance is needed for the nRTE processed commodity.

(v) This procedure can be illustrated by some examples using mint and the nRTE food mint oil. The assumption is made that for three different pesticides that the HAFT value is 8.0 ppm and that the RAC tolerance is 10 ppm. The assumption is also made that the dilution factor for mint oil is 160 for its use in preparation of RTE foods. Pesticide A is observed to concentrate 1.3□in mint oil. The concentration factor times the HAFT is equal to 10.4 ppm, which is not appreciably higher than the RAC tolerance of 10 ppm. Neither a section 409 tolerance nor section 701 MRL is needed for the mint oil. Pesticide B is found to concentrate 40□in mint oil. The concentration factor (40) times the HAFT (8.0 ppm) is qual to 320 ppm, well above the RAC tolerance of 10 ppm. The residues in the RTE

(mixed/diluted) food are then calculated to be 2 ppm by dividing the mint oil residue of 320 ppm by the dilution factor of 160. The 2 ppm residue in the RTE food is below the 10 ppm RAC tolerance. Therefore, a section 701 MRL of 320 ppm should be established for the nRTE mint oil. Pesticide C is found to concentrate 320□in mint oil. The concentration factor (320) times the HAFT (8.0 ppm) is 2,560 ppm, which is well above the RAC tolerance of 10 ppm. The residues in the RTE food are then calculated to be 16 ppm by dividing the mint oil residue of 2,560 ppm by the dilution factor of 160. The 16 ppm in the RTE (mixed/diluted) food appreciably exceeds the 10 ppm RAC tolerance. Therefore, a section 409 or food additive tolerance is needed for mint oil at 2,560 ppm (or more likely at 2,500 ppm considering significant figures).

(g) **Data report format.** The following describes a suggested format for a study report, item by item. However, other formats are also acceptable, provided that the information described this paragraph is included.

(1) *Title/cover page.* Title page and additional documentation requirements (i.e. requirements for data submission and procedures for claims of confidentiality of data if relevant to the study report) should precede the content of the study. These requirements are described in PR Notice 86–5 (see paragraph (h)(5) of this guideline).

(2) *Table of contents.*

(3) *Summary/introduction.*

(4) *Materials*—(i) *Test substance.* (A) Identification of the pesticide formulated product used in the field trial from which the RAC used in the processing study was derived, including the active ingredient therein, or if fortified RAC samples were used in the processing study, identity of the fortifying substances.

(B) Identification and amount of residues in experimentally treated RAC samples at the time the processing study is initiated.

(C) Any and all additional information petitioners consider appropriate and relevant to provide a complete and thorough description and identification of the test substances used in the processing study.

(ii) *Test commodity.* (A) Identification of the RACs (crop/type/variety) and the specific crop parts used in the processing study.

(B) Sample identification (source of samples, field trial identification number; control or weathered residue sample, coding and labeling information (should be the same as or cross-referenced to the sample coding/labeling assigned at harvest)).

(C) Treatment histories (pesticides used, rates, number of applications, preharvest intervals (PHIs), etc.) of the RAC samples used in the processing study.

(D) The developmental stages, general condition (immature/mature, green/ripe, fresh/dry, etc.) and sizes of the RAC samples used in the processing
study.

(E) Any and all additional information the petitioner considers appropriate and relevant to provide a complete and thorough description of the RACs used in the processing study.

(5) *Methods*—(i) *Experimental design.* For example:

(A) Number of test/control samples.

(B) Number of replicates.

(C) Residue levels in the RACs to be used.

(D) Representativeness of test commodities to the matrices of concern, etc.

(ii) *Test procedures*—(A) Fortification (spiking) procedure, if used (detail the manner in which the test compounds were introduced to the RACs).

(B) A description of the processing procedure used and how closely it simulates commercial practice. Quantities of starting RAC and of resulting processed commodities.

(C) A description of the methods of residue analysis (see OPPTS 860.1340, Residue analytical method).

(D) A description of the means of validating the methods of residue analysis (see OPPTS 860.1340).

(E) A description of any storage stability validation studies that may have been performed (see OPPTS 860.1380, Storage stability data).

(6) *Results/discussion*—(i) *Residue results.* (A) Raw data and correction factors applied, if any.

(B) Recovery levels.

(C) Storage stability levels, if applicable.

(D) Direct comparison of residues in the RAC with those in each processed product or processing fraction derived from that sample, etc.

(ii) *Statistical treatments.* Describe tests applied to the raw data.

(iii) *Quality control.* Include if not covered elsewhere. Describe control measures/precautions followed to ensure the fidelity of the processing study.

(iv) *Other.* Constituting any and all additional information the petitioner considers appropriate and relevant to provide a complete and thorough description of the processing study or studies.

(7) *Conclusions.* Discuss conclusions that may be drawn concerning the concentration/reduction of the test compounds in the test matrices as a function of the standard commercial processing procedure, and the need for food/feed additive tolerances or section 701 MRLs.

(8) *Certification.* Certification of authenticity by the Study Director (including signature, typed name, title, affiliation, address, telephone number, date).

(9) *Tables/figures.* (i) Tables of raw data from the processing study, method recovery data, storage stability recovery data (if applicable); etc.

(ii) Graphs, figures, flowcharts, etc. (as relevant—include the processing procedure with weights of RAC and processed fractions).

(10) *Appendixes.* (i) Representative chromatograms, spectra, etc. (as applicable).

(ii) Reprints of methods and other studies (unless physically located elsewhere in the overall data submission, in which case cross-referencing will suffice) which will support the registrant's conclusions.

(iii) Other, comprising any relevant material not fitting in any of the other portions of this report.

(h) **References.** The following references should be consulted for additional background material on this test guideline.

(1) Environmental Protection Agency, Pesticide Reregistration Rejection Rate Analysis—Residue Chemistry; Follow-up Guidance for: Generating Storage Stability Data; Submission of Raw Data; Maximum Theoretical Concentration Factors; Flowchart Diagrams. EPA Report No. 737–R–93–001, February, 1993.

(2) Environmental Protection Agency, Pesticide Reregistration Rejection Rate Analysis – Residue Chemistry; Follow-up Guidance for: Updated Livestock Feeds Tables; Aspirated Grain Fractions (Grain Dust); A Tolerance Perspective; Calculating Livestock Dietary Exposure; Number and Location of Domestic Crop Field Trials. EPA Report No. 737–K–94–001, June, 1994.

(3) Environmental Protection Agency, Pesticide Reregistration Rejection Rate Analysis—Residue Chemistry; EPA Report No. 738–R–92–001, June, 1992.

(4) Environmental Protection Agency, FIFRA Accelerated Reregistration—Phase 3 Technical Guidance. EPA Report No. 540/09–90–078. (Available from National Technical Information Service, Springfield, VA).

(5) Environmental Protection Agency, Pesticide Registration Notice PR 86–5, Standard Format for Data Submitted under the FIFRA and Certain Provisions of the Federal Food, Drug, and Cosmetic Act (FFDCA), May 3, 1986.

資料 3

COMMISSION OF THE
EUROPEAN COMMUNITIES
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Directorate General for Agriculture

VI B II-1

APPENDIX E
PROCESSING STUDIES

1 Introduction

To evaluate the residue behaviour of plant protection products, not only the results of residue tests carried out on plants and plant products are necessary but also the results of residue tests carried out on processed plant products (processing studies) are important.

Even when plant protection products are used correctly, in accordance with Good Agricultural Practice, residues in or on plants and plant products are in many cases unavoidable. Since many of these plants and plant products then are processed before they reach the consumer or before being eaten, processing studies allow a better estimate to be made of consumers' exposure to residues. The results of these studies allow a more realistic calculation of consumers' intake of the active substances in plant protection products and/or their relevant metabolites, and thus a better risk assessment than is possible by calculating the Theoretical Maximum Daily Intake (TMDI). In addition, these studies can produce results relating to residues in commodities that may be used as animal feeding stuffs.

It is not normally necessary to analyse routinely for degradation and reaction products which are not included in the MRL-residue definition in processing studies. Such studies however have to include degradation or reaction products included in the residue definition for the estimation of dietary intake and have to be carried out where there is a reasonable expectation that processing may convert the residues into a species of greater toxicological concern. It should also be noted that a knowledge of the residues in processed plant products is a pre-requisite to estimating transfer factors as referred to in the proposal for an amendment of the Council residue Directive 97/41/EC (OJ No. L184, 12.7.1997, p.33).
The results of processing studies will not only help to give a more realistic estimate of the dietary intake and better comparability of data, but will also help to gain acceptance for maximum residue limits (MRLs) at international level. In this guideline only general advice is given on how to plan, get up and carry out studies. It may be necessary to produce separate guidelines, if required, for individual crops to work out comparable and repeatable results. The requirements of international trade are taken into account insofar as the guidelines and draft guidelines of international and national organisations and associations are taken into consideration.

2. **Objectives of processing studies**

Processing studies have four objectives:
- To obtain information about breakdown products or reaction products which may require a separate risk assessment.
- To determine the quantitative distribution of residues in the various intermediate and end products, thus enabling a recognition of reductions and concentrations and to estimate transfer factors (i.e. residue levels in processed commodity/residue levels in raw commodity).
- To enable a more realistic estimate to be made of dietary intake of plant protection products.
- In special cases, to use the test results as a basis for the fixing of Maximum Residue Limits for the various processed foodstuffs of plant origin.

3. **Effect on the nature of the residue**

3.1 Objectives

The objective of these studies is to establish whether or not breakdown or reaction products arise from residues in the raw commodities during processing which may require a separate risk assessment.

3.2 Study type

The nature of most of the processing procedures is such that it would be impossible to conduct a study using radiolabelled chemicals in a manner representative of the conditions experienced in normal practice. However, the parameter which is most likely to affect the nature of the residue during most processing operations is hydrolysis, because processes like heating would generally inactivate enzymes present in the substrate, leaving simple hydrolysis as the most important degradation mechanism. The effects of processes other than hydrolysis may also have to be investigated, where the properties of the active substance or metabolites indicate that toxicologically significant degradation products may occur as a result of these processes.
However, in the case of hydrolysis, three different hydrolysis conditions have been chosen to simulate normal processing practice. Since the substrate itself is not likely to have a major effect (apart from governing the pH level in some situations), the presence of the commodity is not necessary during the investigations.

3.3 Extent of data required

The studies are normally conducted with a radiolabelled form of the active substance.
Depending upon the potential uses of the plant protection product one or more studies will be necessary. Under normal conditions a maximum of three hydrolysis studies for the chosen representative conditions will suffice but under certain circumstances (e.g. raffination of oil, where no representative conditions are given) more studies have to be conducted.

3.4 Test guidelines

Specific guidelines to conduct such studies are included in Annex 1.

4. **Effect on the residue levels**

4.1 Objectives

The objectives of these studies are to determine the quantitative distribution of residues in the various intermediate and end products, thus enabling a recognition of reductions and concentrations and to estimate transfer factors.
Furthermore they should enable a more realistic estimate to be made of dietary intake of plant protection products. In special cases, the test results could be used as a basis for the fixing of Maximum Residue Limits for the various

processed foodstuffs of plant origin.

4.2 Study types

In order to achieve these objectives, two different types of processing studies are suggested: balance studies and follow-up studies.

The basis for the follow-up studies is always dependant on the corresponding balance studies.

These two types of studies differ from one another not only in their objectives but also in their scope.

4.2.1 Balance studies

The term 'processing study' is in principle understood to mean, first and foremost, balance studies (sometimes also known as basic studies). The aim of such studies is where possible to determine the distribution of (or to draw up a 'balance sheet' for) the residues in all intermediate and end products and, where appropriate, the waste products arising from the processing. In this way any concentrations or reductions in residues in individual products can be recognized. It must be borne in mind, however, that with volatile or heat-sensitive residues, or with residues metabolizing during processing, a 'balance sheet' can be determined only to a limited extent. However, it is intended that all the residues (active substances and relevant metabolites) determined in the original plant product will also be determined in the processed products.

Breakdown or reaction products from hydrolysis studies which require a separate risk assessment must also be determined in the processed products.

4.2.2 Follow-up studies

If as a result of the balance studies the distribution of the residues is known for all intermediate and end products, then more extensive studies can be limited to important end products or intermediate products, i. e. to products which either reach the consumer direct, as an end product, or which are used as the starting product for further processing.

In individual cases, feedingstuffs must also be investigated in this respect (e. g. molasses). Such investigations are specific residue tests, for example to determine concentration factors for specific important products. Since these more extensive studies are based on the balance studies, they are known as follow-up studies.

4.3 Planning of processing studies

The guidelines given here set out the general principles. Recommendations for individual crops and processing studies which deviate from these general guidelines should be obtained from the appropriate individual guidelines that have to be worked out in the future.

The decision as to whether it is necessary to carry out processing studies will depend on:

- the importance of a processed product in the human and animal diet
- the level of residue in the plant or plant product to be processed,
- the physico-chemical properties of the active substance or relevant metabolites, and
- the possibility that degradation products of toxicological significance may be found after processing of the plant or plant product.

The results of the studies for investigation of the nature of the residues have to be taken unto account. If no studies are carried out, the detailed reasons must be given.

4.3.1 Importance of the processed product

In considering whether processing studies should be carried out, one has to take into account the importance of the plant or plant product to be processed and the importance of the processed product (see Annex 3). The results of the studies for investigation of the nature of residues have to be taken into account.

4.3.2 Consideration of physico-chemical properties

Important conclusions concerning the behaviour of the active substance and/or its metabolites during processing can be drawn simply by looking at the distribution coefficients for n-octanol/water, hydrolysis stability, heat stability and solubility behaviour. A detailed description of the requirements are given in Annex 1. For example, when the log Pow is greater than three, one can assume that the residue will be concentrated in oil, whereas good water-solubility indicates that residues can be expected in juices.

4.3.3 Level of residues in the initial product

Processing studies are not normally necessary if no significant or no analytically determinable residues occur in the plant or plant product which would be processed, or if the total theoretical maximum daily intake (TMDI) is less than 10% of the ADI. In addition processing studies are not normally required for plants or plant products mostly eaten raw except for those with inedible portions such as citrus, banana or kiwi fruit where data on the distribution of the residue in peel/pulp may be required.

'Significant residues' generally refer to residues above 0.1 mg/kg. If the pesticide concerned has a high acute toxicity and/or a low ADI consideration must be given to conducting processing studies for determinable residues below 0.1

mg/kg.
One must also take into account the fact that in many processes the residues in the original product are diluted during processing. Therefore, processing studies on hops, for example, are only to be carried out if the Maximum Residue Level for dried hops is at or above 5 mg/kg. (.....)
In all other cases, processing studies must, in principle, be contemplated.
If no studies are carried out, then detailed reasons must be given.
Preferably only products containing incurred residues should be used for processing. Fortification of the residues, for example, to the maximum permissable levels, either by increasing the application rates, shortening the Pre-harvest Intervals and/or by spiking with the active substance and/or its metabolites in vitro, is not as a rule desirable, though in some cases it may be permissible or even necessary.

4.3.4 Test conditions

In order to estimate transfer factors and to enable a realistic estimate of dietary intake of residues of plant protection products, processing studies representative of the potential uses of the product and of household and industrial preparation of food are usually needed.
When required processing studies (both balance and follow-up) usually only have to be carried out for a core-set of representative processing procedures for representative commodities (see Annex 2).
If it is not possible to derive from the core-set of processing procedures consistent transfer factors applicable to other processed commodities or other crops, then additionnal processing studies on other crops must be carried out.
Additional studies may also be necessary if the estimate of dietary intake exceeds the ADI to allow further refinement of the dietary intake calculation. Additional studies should ideally be carried out on crops which contribute most to the ADI exceedance.

4.3.5 Number of studies

If the processed plant products play an important part in dietary intake or if, in exceptional cases, Maximum Residue Levels are to be set for processed products on the basis of processing studies, at least one reliable balance study (e.g. depending on the recovery of the active substance) and three further follow-up studies are necessary.
It should also be noted that it may be quite sufficient and appropriate to carry out the balance studies on one crop by way of an example for the whole crop group, e. g. to use processing studies on apples for all pome fruit.
Advice on the products to be analysed for the various crops and crop groups is given in Annex 3. Advice on sampling is given in document 7029/VI/95; for products or processed product types not mentioned in Annex 1 of document 7029/VI/95, the applicant, or the person carrying out the trials, must make a justified proposal.

4.4 Processing technology

The technology to be used in processing studies should always correspond as closely as possible to the actual conditions that are normally used in practice. A distinction must therefore be made between preparation in household and industrial processing. Thus, processed products that are prepared in household (e. g. cooked vegetables) should be produced using the equipment and preparation techniques that are normally used in household. On the other hand, industrially produced processed products (e. g. cereal products, preserves, fruit juices, sugar) should be produced using commercially representative technology, i. e. taking into account normal food-technology processes. Important processing practices such as peeling, washing, cooking, baking, frying, canning, freezing and drying have to be studied where appropriate.
If several major commercial processes could be routinely used, then two different processes should be used in the balance studies; i. e. preferably those representative processes that most likely lead to high residues in important processed products. It is possible, for example, that processed products could be obtained from oilseeds by extraction or by pressing, or that apple sauce could be produced using household techniques or industrial processing. In follow-up studies, the process used should be the one that is expected to leave the higher residue levels in the processed product concerned.

5 **Evaluation of results**

As a result of the studies, it will be possible:
a) to recognize reductions and concentrations, and
b) to estimate transfer factors.
If in exceptional cases Maximum Residue Levels for processed products are to be estimated on the basis of the processing studies, then the following procedure is suggested:
From the residue results obtained from the balance studies and from the follow-up studies for the processed product for which a MRL is to be set, an average transfer factor is determined. All available residue results for the plant or

plant product which has/have been processed are multiplied by this factor. The figures obtained in this way are evaluated in accordance with the calculation procedure recommended elsewhere. On the basis of the result obtained a MRL is proposed.

6 **Reporting**

A report on processing studies should include all relevant data in a suitable format. This can, for example, be achieved by using the two-stage method outlined below.

- Tabular report

The trials included in a residue study are reported individually in tabular form. The results of residue analysis of the processed products may also be recorded on these forms.

- Report of the processing study

The presentation of a processing study is, for example, sub-divided into the following sections:

- Objective
- Sample background
- Sample processing
- Preparation, measuring, assessment
- Evaluation, discussion of results.

- Objective

The Objective section of the report again describes the aims of the study in detail and formulates the questions to be dealt with in the study.

- Sample background

This section of the report describes the origin of the raw products used in the processing studies (e. g. from a residue trial, addition trial).

- Sample processing

This section describes the methods used to process the samples. Some commercial processes are quite complex. It may be useful to provide a flow diagram to explain the process.

- Preparation, measuring, assessment

This essentially describes the method used to prepare and analyse the samples.
This section of the report contains the measured results and the methods used to asses the results.

- Evaluation, discussion of results

This section of the report discusses and evaluates the reported analysis results in the light of the questions outlined in the objective section.

7 **References**

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M.Buys, G.Timme, J.C.Tournayre, B.Walz-Tylla and R.Whiteoak , 1993:
Guideline for the conduct of studies to investigate the nature of the potential residue in the products of industrial processing or household preparation - Guidelines for processing studies, European Crop Protection Association, March 1993.

ANNEX 1

Guideline for the conduct of hydrolysis studies to investigate the nature of the potential residue in the products of industrial processing or household preparation

1 **Introduction**

When residues are present in raw agricultural commodities which are generally consumed only after processing (in either industrial or household situations), it may be necessary to investigate the magnitude of residues in the processed commodities.

Depending upon the type of process involved and upon the chemical nature of the residue in the raw commodity, it may first be necessary to determine whether the nature of the residue in the processed commodities is likely to be different from that in the raw agricultural commodity. This guideline provides a way in which such preliminary investigations may be conducted.

2 **Processing types**

Six procedures have been identified which are representative of the most widely used processes in industry and the home. These are:

- cooking vegetables in water
- preparation of fruit preserves
- preparation of fruit juices
- preparation of oil
- preparation of beer and wine
- preparation of bread

The nature of most of these procedures is such that it would be impossible to conduct a study using radio labelled chemicals in a manner representative of the conditions experienced in normal practice. However, the parameter which is most likely to affect the nature of the residue during most processing operations is hydrolysis, because processes like heating would generally inactivate enzymes present in the substrate, leaving primarily simple hydrolysis as a degradation mechanism. This guideline therefore describes a range of hydrolytic conditions which may be employed to simulate normal processing practice. Since the substrate itself is not likely to have a major effect (apart from governing the pH level in some situations), the guideline does not require the presence of the commodity during these investigations.

3 **Representative hydrolytic conditions**

Hydrolysis data are normally generated for a plant protection product at 25°C for one month and at pH 5, 7 and 9. The objective of these studies is primarily related to environmental conditions. By contrast, processing operations typically involve higher temperatures but for much shorter periods and, in some cases, more extreme pH values.

Table 1 summarises the typical conditions which prevail for each type of process, for the significant parameters of temperature, time and pH.

Table 1

Significant parameters during processing operations

Type of process	Critical operation	Temperature (°C)	Time (min)	pH
Cooking vegetables	Boiling	100 [1]	15 - 50 [2]	4.5 - 7
Preserves				
- fruits	Pasteurisation	90 - 95 [3]	1 - 20 [4]	3 - 4.5
- vegetables	Sterilisation	118 - 125 [5]	5 - 20 [6]	4.5 - 7
Fruit Juice	Pasteurisation	82 - 90 [7]	1 - 2 [8]	3 - 4.5
Oil	Raffination	190 - 270 [9]	20 - 360 [10]	6 -7
Beer	Brewing	100	60 - 120	4.1 - 4.7
Red wine [11]	Heating of grape mash	60	2 [12]	2.8 - 3.8
Bread	Baking	100 - 120 [13]	20 - 40 [14]	4 - 6

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(1) Temperature of the vegetables during cooking
(2) Time, the vegetables have 100°C
(3) Temperature within the fruit preserves during pasteurisation
(4) Time, the content of the fruit preserves have 90 - 95°C
(5) Temperature within the vegetable preserves during sterilisation
(6) Time, the content of the preserves have 118 - 125°C
(7) Temperature of the fruit juice during pasteurisation
(8) Time, the fruit juice has 82 - 90°C
(9) Temperature of the desodorisation during raffination
(10) Time of the desodorisation
(11) White wine is not heated
(12) Subsequently either chilled quickly or allowed to cool slowly (overnight)
(13) Temperature within the loaf and on the surface during 20 - 40 minutes
(14) Time, the loaf and the surface have 100 - 120 °C

From the above details, three representative sets of conditions are defined in Table 2. These should be used to investigate the effects of hydrolysis as appropriate for the relevant processing operations.

Table 2
Representative hydrolytic conditions

Error! Bookmark not defined. Temperature (°C)	Time (min)	pH	Processes represented
90	20	4	Pasteurisation
100	60	5	Baking, Brewing, Boiling
120	20	6	Sterilisation

The extreme conditions which would be required to mimic the raffination of oil, have been omitted from this set of representative conditions. The major consideration for the processing of oil seeds is the possible concentration or reduction in residues during the pressing or extraction of oil. In most cases, residues will be very low at this stage and only in exceptional circumstances will it be necessary to conduct further studies on the nature of the residue. Because of the extreme conditions, these further studies should be discussed with the regulatory authorities. By contrast, hydrolytic conditions during the preparation of wine are very mild compared with those in other processes and are therefore not included in Table 2.

4 **Conduct of studies**

Depending upon the potential range of uses of the plant protection product, one or more of the above representative hydrolysis situations should be investigated (an autoclave will be needed for the temperatures above 100°C). The studies should be generally conducted with a radio labelled form of the active substance, in order to maximise the identification of components at the end of the study. The studies must be conducted in compliance with Good Laboratory Practice with reference to Standard Operating Procedures.

In cases where the residue in the raw commodity consists primarily of a metabolite, the need to conduct hydrolysis studies with that metabolite should be considered on a case by case basis. For example, comparison of its structure with those of the parent compound and the hydrolysis products of the parent compound may suggest that additional studies are unnecessary.

5 **Interpretation of results**

An individual hydrolysis product need not be identified if it is clear by calculation that its concentration in the final processed commodities will be less than 0.05 mg/kg. Such calculations should take account of its magnitude in the hydrolysis study (as a proportion of the starting material), dilution (or concentration) factors during processing and the initial residue levels in the raw commodity.

If the hydrolysis products are the same as the transformation products already identified as the residue of toxicological significance in the raw commodity, the same residue methodology principle is appropriate for use in subsequent studies on the magnitude of residues in processed commodities.

ANNEX 2

Core Processing Procedures

Error! Bookmark not defined.processing type	crop [1]
distibution in the edible / non edible portion	citrus bananas
preparation of fruit juice	citrus apples [2]
preparation of other fruit products	apples [2] or other fruit
preparation of canned fruit	stone fruit or berries [2]
preparation of wine	grapes
preparation of beer	hops barley
cooking vegetables in water	one representative vegetable crop [2] or potatoes
preparation of vegetable juice and other products	one representative vegetable crop [2] potatoes
preparation of oil	rape seed [2]
distibution on milling and preparation of bread	wheat
preparation of sugar	sugar beets

1) Studies with the listed crops only necessary if there is a GAP or expected GAP
2) The selection of crop depends on the use pattern of the pesticide

ANNEX 3

Processed commodities per crop group and procedure

When it comes to the products that are to be tested for residues in a processing study, a distinction should be made according to the objective being pursued. In a balance study, all intermediate products, end products and waste products should if possible be included, in order to guarantee that a "balance sheet" will be obtained (see also 4.2.1). In the follow-up studies, only those intermediate and end products that are still relevant need to be tested. These products, which it is suggested should be tested in a follow-up study, appear in single underlined type in the following list. The residues in the initial material should in all cases be determined and reported as well.

1 Fruits

Beside the already mentioned core processing procedure other procedures may be necessary to conduct like drying. For individual crop groups, the following crops are suggested:

Crop	Processing type	Products
Citrus fruit	Distribution in the edible/non edible portion	Peel, pulp
Bananas		Peel, pulp
Kiwifruits		Peel, pulp
Pineapples		Peel, pulp
Oranges	Preparation of fruit juice	Industrially produced juice, pomace (wet, dried)
Apples		Industrially produced juice, pomace (wet, dried)
Currants (black)		Juice
Cherries	Preparation of canned fruit	Washed cherries, canned
Strawberry		Canned
Apples	Preparation of other fruit products	Washed apples, apple sauce
Plums		Washed plums, plum puree
Currants		Washed currants, jam/jelly
Strawberry		Washed strawberries, jam
Plums		Prunes
Grapes		Raisins
Oranges		Marmelade
Olives	Preparation of oil	Oil
Wine grapes	Preparation of wine	Juice, wine

2

Vegetables

Beside the already mentioned core processing procedure other procedures may be necessary to conduct like drying, fermentation and concentration.

For individual crop groups, the following crops are suggested: