J Consum Prot Food Saf (2017) 12:3–14
DOI 10.1007/s00003-016-1043-3
Journal of Consumer Protection and Food Safety
Journal für Verbraucherschutz und Lebensmittelsicherheit

RESEARCH ARTICLE

Compilation of processing factors and evaluation of quality controlled data of food processing studies

Rebekka Scholz[1] · Michael Herrmann[1] · Britta Michalski[1]

Received: 19 May 2016 / Accepted: 29 July 2016 / Published online: 6 September 2016

Abstract Often, agricultural commodities are not eaten raw but undergo processing operations prior to human consumption. These may significantly affect the residue levels of pesticides contained therein and/or thereon. Due to the physico-chemical properties of the residue, its concentration may decrease or increase in processed fractions compared to the initial concentration in the raw agricultural commodity (RAC). The resulting ratio between processed fraction and RAC is denoted as processing factor (P*f*). Information obtained from processing studies may serve for 2 different purposes: to decide on compliance of residues in processed products with legal standards for the RAC, and to refine dietary exposure estimation of humans and livestock with respect to residues in processed products. The German Federal Institute for Risk Assessment (BfR) extracted and compiled the results of several processing studies, the full reports of which had been made available to BfR in the framework of applications either for pesticide authorisation, for the setting of maximum residue levels (MRL), or within the EU active substances approval programme. Each P*f* derived from processing studies was reviewed against transparent quality criteria and statements have been made regarding the robustness and reliability of the study results. Compared to the former version, the revised BfR database includes a more extended, more detailed and more trustworthy compilation of more than 6500 processing factors accompanied by relevant information on key parameters of the underlying processing studies.

Keywords Pesticide residue · Food processing · Processing study · Quality criteria · Processing factor

1 Introduction

Some agricultural commodities are unpalatable in their raw state or may benefit from processing prior to human consumption. Several publications discuss the impact of such processing operations on the level of pesticide residues in foodstuff (Holland et al. 1994; Chavarri et al. 2005; Kaushik et al. 2009; Poulsen et al. 2007). Most of the procedures conducted to elucidate the impact of processing operations focus on industrial processing of fruits and vegetables. Much broader information is available from data packages submitted by pesticide manufacturers for authorisation of their products. The effect of food processing on residue levels depends on the commodity as well as the pesticide, and is correlated with individual physico-chemical properties of the pesticide (Burchat et al. 1998). To date, MRLs are set out in Annexes II or III to Regulation (EC) No 396/2005 only for RACs (European Commission 2005), but apply also for processed and/or composite food or feed by considering changes in the levels of pesticide residues caused by processing and/or mixing (article 20(1)). Similarly, MRLs are established for only a very small

Electronic supplementary material The online version of this article (doi:10.1007/s00003-016-1043-3) contains supplementary material, which is available to authorized users.

✉ Rebekka Scholz
rebekka.scholz@bfr.bund.de

[1] Federal Institute for Risk Assessment, Max-Dohrn-Str. 8-10, 10589 Berlin, Germany

number of simply processed commodities by Codex Alimentarius (Codex Alimentarius 2016).

Processing factors are an indispensable tool, mainly for 2 purposes:

1. Providing information to food safety inspection services on the scope of changes in residue levels during food processing operations, thus, they are crucial for assessing whether the starting material has been in compliance with legal standards.
2. Providing information to risk assessors for refined dietary exposure estimates, such as figures, to allow a more realistic assessment in cases when commodities are mainly consumed after processing. This aspect will become even more important in upcoming cumulative consumer intake assessments.

The aim of the BfR project presented here was to generate a comprehensive database on quality-controlled processing factors. The data compilation is intended to support not only risk assessors in their evaluation of consumer risks caused by pesticide residues, but all interested parties in order to improve the transparency of evaluation results.

2 Existing guidance on how to perform processing studies

Processing procedures may have a significant impact on pesticide residues, not only related to the magnitude of residue concentration (OECD 2008b), but also to the chemical transformation in (parts of) the parent residue during processing (impact on the nature of residue) (OECD 2007). Several processing operations have been identified in the OECD Guidance "Document on Overview of Residue Chemistry Studies" as being representative of the most widely used industrial and domestic food processing technologies (OECD 2009). In addition, a larger assortment of processed commodities is published in the OECD Guidance Document on Magnitude of Pesticide Residues in Processed Commodities (OECD 2008a), illustrated by examples of processing types and recommended extrapolations for typical RACs. To each core procedure and processed matrix, the corresponding OECD procedure code has been assigned (Table 1).

In addition to the fractions produced for human consumption, by-products are obtained from some processing operations that are not discarded but may be used for livestock feeding. Residues in those fractions need to be taken into account when predicting the dietary burden of livestock animals and evaluation of the residue transfer into animal commodities. The Guidance Document on Residues in Livestock (OECD 2013) provides a list of feedstuffs including by-products from food processing for human consumption. Processing studies therefore investigate processed fractions destined for human consumption as well as by-products possibly fed to livestock.

Table 1 OECD procedure codes

OECD code	Explanation
I	Distribution in the edible/non edible portion
II	Preparation of fruit juice
III	Preparation of canned fruit
IV	Preparation of other fruit products
V	Preparation of alcoholic beverages (fermentation, distillation)
VI	Cooking vegetables, pulses and grains in water (including steaming)
VII	Preparation of vegetable juice
VIII	Preparation of canned vegetable
IX	Miscellaneous preparation of other vegetable products
X	Preparation of oil (extraction, pressing, milling in case of maize) Xa belongs to extraction, Xb belongs to pressing, Xc belongs to maize milling
XI	Distribution on milling
XII	Preparation of sugar
XIII	Infusions and extractions
XIV	Silage production
XV	Processing of products of animal origin including preparation of meat and fish (poaching, frying, baking, boiling)
XVI	Dehydration
XVII	Fermentation of soybeans, rice and others (except alcoholic beverages)
XVIII	Microwaving vegetable
XIX	Pickling

3 Data sources used to set up the database of processing factors

Previous collation work has been done and P*f* values have been published by BfR; the most recent version 3.0 was published in 2011. At that time, mainly publically available data were included, e.g. from

1. The annual Reports of the Joint Meeting on Pesticide Residues (JMPR) on the evaluations of

pesticide residues in food, published by FAO/WHO,

2. Scientific reports issued by the European Food Safety Authority (EFSA), encompassing conclusions on the peer review of pesticide risk assessments and reasoned opinions on the review or modification of existing MRLs.

In addition, data on pulp/peel distribution in citrus fruit were included, which were provided by a food business operator (Ahlers and Reichert 2007) or collected within the framework of the German food monitoring programme (BVL 2011). Since the former versions of the database merely reflected the results published by other scientific bodies, the user was left with invalidated figures on processing factors without further information. The original study reports had not been reviewed and no statement whatsoever was made, e.g. on the appropriateness of the employed analytical method or the number of individual trials.

Hence, the decision was made to completely restructure the BfR database and factors were derived only after carefully scrutinizing the underlying studies submitted to BfR in the framework of various legal procedures. It is noted that there is some overlap of the data volumes of studies submitted to BfR and the studies submitted to and evaluated by other scientific bodies, e.g. EFSA or JMPR.

According to the provisions of the OECD Guideline 508 (OECD 2008b), processing studies utilising spiked samples are explicitly referred to as "not acceptable", unless there is experimental evidence that there is no difference in distribution pattern compared to incurred residues. Based on this, studies involving spiked samples were generally considered not acceptable and were not considered in the project.

4 Eligibility criteria that need to be addressed by processing studies

Each processing factor used either in risk assessment or enforcement of legal standards should have been derived in a study which complies with a minimum of quality criteria, as regulatory decisions may largely depend on that piece of information. A set of principle requirements should be fulfilled prior to using such factors in either regulatory action of food control inspectors or refined estimation of dietary exposure. In the following, the eligibility criteria employed are outlined in more detail.

4.1 Representativeness of the employed processing procedures

Ideally, the applied experimental setup should mimic representative industrial or domestic standards as closely as possible (OECD 2008b). However, it is known that processing conditions are very versatile and a subject to continuous technological progress. Preferably, product properties as defined by food norms should be reflected in the processed product. These properties could be related to e.g. minimum fruit content in jam or marmalade, or the standard types of flour (e.g. whole meal flour or flour type 550).

In view of the importance of industrial products in trade, industrial procedures may be preferred over domestic scale operations in order to obtain more representative results. Especially fractions destined for feeding purposes are only anticipated to be available from industrial scale operations.

4.2 Residue definitions

Residue definitions of pesticidal active substances may either consist of a single compound (mostly parent) or of several compounds including relevant metabolites and degradation products. It is not uncommon that, due to different demands, the residue definition for enforcement purposes [simple marker(s), accessible to routine analysis] deviates from that for risk assessment, which focuses on the total toxicological burden.

Residue definitions for monitoring are established together with MRLs in Reg. (EC) No 396/2005 (European Commission 2005) and can be retrieved from relevant legislation or the EU Pesticide database (EU Pesticide database 2016) maintained by the European Commission services. No such statutory rules exist for the definitions for risk assessment purposes.

Furthermore, processing studies should ideally address not only the legally established residue definition but also components of the residue definition that are defined for risk assessment. However, definitions applicable for risk assessment are often subject to revision. As additional components might not have been part of the residue definition when the study was designed, the set of analytes might not comply with the actual residue definition(s) in quite a number of studies. For these reasons, the BfR data compilation focuses on the residue definitions for monitoring. In case that a residue definition for risk assessment differs from monitoring, a conversion factor needs to be considered.

4.3 Minimum number of trials

The number of replicate trials within a study is a key parameter for robustness of the derived processing factor, particularly when each individual processing factor is significantly different. Even within the same study, processing factors derived from two replicate trials may show a considerable degree of variability. When individual processing factors from the 2 trials differ by more than 50 % (with a main focus on the relevant processed fraction), OECD Guideline 508 (OECD 2008b) recommends to carry out a 3rd trial to enhance consistency of the data and strengthen confidence in the finally derived factor. In the framework of their mandate to review existing MRLs according to article 12 of Reg. (EC) No 396/2005, EFSA required minimum of 3 trials to ensure sufficient robustness prior to recommending a processing factor (EFSA 2012, 2014).

4.4 Validity of the analytical method

The analytical method used in the processing study should be described in sufficient detail. Parameters like recovery rates, repeatability, reproducibility and sensitivity should be in line with generally agreed requirements for analytical methods for pre-registration purposes (SANCO/3029/99) (European Commission 2000).

The procedural recovery should be within the range of 70–120 %. In addition, the coefficient of variation should be below 20 %. If these parameters were not fulfilled, the study was not considered acceptable.

4.5 Compliance with standards of good laboratory practice

In the area of experimental research, good laboratory practice (GLP) specifically refers to a quality system of management controls for research laboratories and organizations aiming to ensure the uniformity, consistency, reliability, reproducibility, quality, and integrity of chemical safety tests (OECD 1998). Hence, only processing studies prepared in accordance with GLP standards were considered.

4.6 Sample storage conditions

Information on the sample storage conditions and the time elapsed between sampling and extraction/analysis was considered to be essential to the validity of processing studies. The database includes information about the duration of freezer storage of the samples. This information can be related to data from storage stability studies of the analyte(s) in the respective matrix type. If the storage conditions were chosen in a way that the duration of proven storage stability was not exceeded, the study was considered valid with respect to this criterion.

5 Calculation of P*f*

The processing factor is defined as follows:

$$Pf = \frac{\text{Residue of processed fraction } \left(\frac{\text{mg}}{\text{kg}}\right)}{\text{Residue of RAC } \left(\frac{\text{mg}}{\text{kg}}\right)}$$

Processing factors have been reported after rounding to 2-digit accuracy. If rounding resulted in a value of 0.00, accuracy has been rounded to 3 digits. The range from the lowest to the highest value has been reported. If the concentration of the analyte in the processed product was below the analytical limit of quantification (<LOQ), the numerical value of the LOQ was used, and the calculated processing factor was prefixed by the symbol "<". If the concentration in the RAC was below the LOQ, a remark has been made under "comments" and the study was not considered acceptable.

If more than one processing factor is derived for a processed fraction in a study, the median value is used and set out as median P*f*. If only 2 processing factors were reported, no 3rd replicate was required when they did not deviate by more than 50 %. This is in line with the present requirements (OECD Guideline 508), but statistical power (e.g. robustness against outliers) is certainly strongly limited in that cases. If residues in the processed product were below the LOQ in all trials, both the individual and the median P*f* figures were prefixed by the symbol "<". A numerical value for the median P*f* was only provided if at least one of the individual P*f* values did not bear the prefix "<". When the residue concentrations in the RAC and in the processed product were both below the analytical LOQ in all trials, a processing factor was not applicable.

6 Procedure of creating the database

Following data acquisition, which has been described above, assignments and grouping were conducted.

At present, BfR is archiving more than 2600 processing studies, the characteristics of which have been listed by active compounds in a Microsoft Office Excel worksheet. Table 2 shows a typical screenshot of the database. In general, "not applicable" is indicated if no information on the respective criterion was reported in the study.

6.1 Crops and crop groups

The assignment of the raw agricultural commodities used in the processing studies is in accordance with the crop groupings in Reg. (EU) No 752/2014 (European Commission 2014) detailing Annex I to Reg. (EC) No. 396/2005 (European Commission 2005). The commodity list employed in Table 3 is an open list and contains all RACs for which processing studies were available to date.

The uniform classification of crops allows the user to specifically filter the database for the appropriate studies. For the sake of completeness and convenience, the assignment of terms was harmonized in those cases of unequivocally identical produce with different names. For example, the term rapeseed was uniformly used instead of canola. And we have chosen the British denomination maize (instead of the American term corn). On the other hand, grapes were divided into red and white varieties in order to cope with the specific technological differences in the production of red and white wine.

6.2 Matrices and matrix groups

Processed fractions, hereafter called matrices, may be named differently in different studies. As for RACs it was important for benefits of consistency to combine the same products/fractions by a common matrix term. The entire table of all commodities and related matrices can be retrieved from Annex 1 (supplementary data). For example, Table 4 shows the grouping of the matrices for hops: e.g. the matrix "spent grain" coincides with the term "brewer's grain". Table 4 also provides information on the number of trials in which a respective matrix term was addressed. Matrices deviating only insignificantly in their processing were considered synonymous and combined if no significant difference was anticipated for the processing factors. For example, the matrices "young beer", "cooled beer" and "beer" were combined in the common matrix group "beer".

By this means, the ca. 800 differently named processed matrices in the complete database (processed matrix as reported) were consolidated into 175. This aggregation improves not only the searchability of a processed product but also the comparison of different studies. Thus, it enhances the chance for the user of the database to actually retrieve the complete set of studies matching his or her query.

Another assignment was made for the classification of flour types (Table 5). Especially for the RACs wheat grain and rye grain, various terms were reported in processing studies for flour types.

An overview of the processing procedures evaluated within the framework of this project is illustrated graphically in a total of 35 flow charts in Annex 2 (supplementary data). They describe idealized processes, encompassing all matrix groups of a commodity or of an entire sub-crop group. For instance, Fig. 1 shows the idealised flow chart for the processing of hops into beer. The processed products are coloured differently depending on their use as food or animal feed.

6.3 Comments

The "comments" box provides any further information that is deemed as relevant for the interpretation of the study, e.g.

1. Additional information on metabolites, enantiomers and/or isomers, which are not part of an actual residue definition,
2. Indication of a starting residue concentration in the RAC below the LOQ,
3. Special processing procedures which do not fall into any of the categories addressed elsewhere in the table,
4. Significant deviations from the published analytical method, and
5. Any other deviations/irregularities/remarks.

6.4 Acceptance of a study

It is the final responsibility of the assessor to decide on the acceptability of a processing study and the reliability of the reported results. One of the aims of the BfR project was to check all studies based on identical and particularly transparent criteria. With no significant discrepancies from generally agreed standards noted, a study is labelled as "acceptable". If one of the key criteria was not fulfilled, the information content of the study was flagged as "indicative". With more than one of the key parameters not addressed adequately, the study was rendered as "not acceptable" in order to provide

Table 2 Excerpt of the BfR database. Please note that the table rows are being continued on the following page providing further information on study parameters for the respective residue definition-commodity-matrix combinations. For ease of allocation the rows were numbered (1) to (13)

Line no.	Residue definition	Main crop group	Sub crop group	Commodity	Processed matrix consolidated	OECD procedure code	Individual P*f*	Median P*f*	Number of trials
(1)	Ametoctradin	Vegetables	Fruiting vegetables	Tomatoes	Puree	VII	0.44–1.15	0.88	4
(2)	Boscalid	Fruits	Berries and small fruits	Grapes, red	Pomace, wet	V	2.40–2.60	2.50	2
(3)	Boscalid	Fruits	Berries and small fruits	Grapes, red	Must, heated	V	0.09–0.18	0.14	2
(4)	Boscalid	Fruits	Berries and small fruits	Grapes, red	Wine, red	V	0.08–0.12	0.10	2
(5)	Boscalid	Fruits	Pome fruits	Apples	Fruit, washed	IV	0.4–1.00	0.65	4
(6)	Boscalid	Fruits	Pome fruits	Apples	Pomace, wet	II	5.8–8.2	6.55	4
(7)	Boscalid	Fruits	Pome fruits	Apples	Juice	II	0.05–0.10	0.08	4
(8)	Boscalid	Fruits	Pome fruits	Apples	Puree	II	0.70–1.10	0.90	4
(9)	Glyphosate (incl. trimesium aka sulfosate)	Fruits	Citrus fruits	Oranges	Pulp, dried	XVI	>1.20	>1.20	1
(10)	Glyphosate (incl. trimesium aka sulfosate)	Fruits	Citrus fruits	Oranges	Molasses	II	>1.40	>1.40	1
(11)	Glyphosate (incl. trimesium aka sulfosate)	Fruits	Citrus fruits	Oranges	Oil	X	Not applicable	Not applicable	3
(12)	Picoxystrobin	Cereals		Barley	Brewer's grain	V	>0.50	>0.50	1
(13)	Picoxystrobin	Cereals		Barley	Beer	V	<0.25–<0.50	<0.38	2

line No.	acceptability of study	GLP	storage conditions	analytical method	procedural recovery	further comments	reference	EFSA reference
(1)	Yes	Yes	Stored at −18 °C	BASF method no. L0078	91 %, SD 14, CV 15 %	Metabolite (7-amino-5-ethyl[1,2,4]triazolo[1,5-a]pyrimidine-6-y-l)acetic acid) and metabolite (7-amino-5-ethyl[1,2,4]triazolo[1,5-a]pyrimidine-6-carboxylic acid) are included; P*f* derived from sum of parent compound and metabolites	[58]	EFSA Journal 2012;10(6):2771
(2)	Yes	Yes	Stored "frozen" less than 9 month	BASF method no. 445/0	87.7 %, SD 4.0, CV 4.6 %		[1]	EFSA Journal 2014;12(7):3799
(3)	Yes	Yes	Stored "frozen" less than 9 month	BASF method no. 445/0	87.7 %, SD 4.0, CV 4.6 %	Mash heated to approx. 60 °C	[1]	EFSA Journal 2014;12(7):3799

Table 2 continued

line No.	acceptability of study	GLP	storage conditions	analytical method	procedural recovery	further comments	reference	EFSA reference
(4)	Yes	Yes	Stored "frozen" less than 9 month	BASF method no. 445/0	87.7 %, SD 4.0, CV 4.6 %		[1]	EFSA Journal 2014;12(7):3799
(5)	Yes	Yes	Stored at −18 °C for 5 months	BASF method no. 445/0	92.1 %, SD 10.9, CV 11.8 %		[16]	EFSA Journal 2014;12(7):3799
(6)	Yes	Yes	Stored at −18 °C for 5 months	BASF method no. 445/0	92.1 %, SD 10.9, CV 11.8 %		[16]	EFSA Journal 2014;12(7):3799
(7)	Yes	Yes	Stored at −18 °C for 5 months	BASF method no. 445/0	92.1 %, SD 10.9, CV 11.8 %		[16]	EFSA Journal 2014;12(7):3799
(8)	Yes	Yes	Stored at −18 °C for 5 months	BASF method no. 445/0	92.1 %, SD 10.9, CV 11.8 %		[16]	EFSA Journal 2014;12(7):3799
(9)	No	No	Stored for 22 months	GLC-FPD	74 %	Active metabolite (aminomethylphosphonic acid) reported; RAC < LOQ	[716]	not applicable
(10)	No	No	Stored for 22 months	GLC-FPD	74 %	Active metabolite (aminomethylphosphonic acid) reported; RAC < LOQ	[716]	not applicable
(11)	No	No	Stored for 22 months	GLC-FPD	74 %	Active metabolite (aminomethylphosphonic acid) reported; RAC < LOQ	[716]	not applicable
(12)	No	Yes	Stored frozen for 10 months	SOP RAM 288/01	93 %, CV 3.04 %	RAC < LOQ	[991]	EFSA Journal 2011;9(12):2488
(13)	Yes	Yes	Stored frozen for 10 months	SOP RAM 288/01	93 %, CV 3.04 %		[991]	EFSA Journal 2011;9(12):2488

Table 3 Group assignment of crops/commodities

Main crop group	Sub crop group	Commodity
Fruits	Citrus fruits	Grapefruit
		Lemons
		Limes
		Mandarins
		Oranges
	Pome fruits	Apples
		Pears
	Stone fruits	Apricots
		Cherries
		Peaches
		Plums
	Berries and small fruits	Grapes, red
		Grapes, white
		Black currants
		Strawberries
Vegetables	Root and tuber vegetables	Potatoes
		Carrots
	Bulb vegetables	Onions
	Fruiting vegetables	Tomatoes
		Chili peppers
		Sweet peppers
		Gherkins
		Melons
		Pumpkins
	Brassica vegetables	Head cabbage
		Savoy cabbage
	Leaf vegetables, herbs and edible flowers	Lettuce
		Spinach
		Mint
	Legume vegetables	Beans
		Peas
	Fungi, mosses and lichens	Mushroom
Oilseeds and Oilfruits	Oil seeds	Linseed
		Peanut
		Sunflower seed
		Rapeseed
		Soya bean
		Cotton seed
	Oil fruits	Olive
Cereals		Barley
		Maize
		Oats
		Rice
		Rye
		Sorghum
		Wheat
Teas, coffee, herbal infusions and cocoa	Teas	*Camellia sinensis*
		Coffee beans
Hops		Hops
Sugar plants		Sugar beet
		Sugar cane

reliable P*f* information. It is explicitly emphasized that this categorization scheme is that of the creator of the database. Depending on the background of his or her own experience and specific needs, the user of the data base may come to a diverging conclusion.

6.5 References and bibliographic information

For the identification of the underlying processing studies, full bibliographic information has been given, such as title of the study, authors(s) and year of publishing. If there was a Reasoned Opinion available by EFSA on the review of the existing MRLs for the active substance according to Article 12 of Reg. (EC) No 396/2005 (European Commission 2005), this is additionally referenced. However, due to lack of details from the reports, normally it cannot be reproduced which particular processing studies were underlying the processing factors recommended by the EFSA. The resulting processing factors may therefore differ between EFSA's Reasoned Opinion and the BfR database for the same pesticide/commodity/processing procedure combination.

7 Results and discussion

More than 2600 processing studies on 193 active substances have been reviewed in the project. Such studies are normally data-protected and not publicly accessible. Earlier versions of the BfR database and other projects like a compilation run by the National Institute for Health and Environment (RIVM) in the The Netherlands (RIVM, 2015) suffer from only reproducing results of evaluation studies done by other scientific bodies like EFSA or JMPR. In contrast, the new BfR processing factors database reflects the outcome of an exercise in which each individual processing study was thoroughly scrutinized under aspects of acceptability criteria for a set of key parameters governing the reliability of the study

Table 4 Matrix grouping for the processed fractions resulting from hops in beer brewing

Commodity	Processed matrix as reported	Processed matrix consolidated	Number of trials
Hops	Green cones	Cones	17
	Dried cones	Cones, dried	75
	Malt	Malt	3
	Brewer's malt	Malt	8
	Extracted hops	Hops, extracted	3
	Wort	Wort	1
	Wort after filtration	Wort, filtrated	4
	Wort cooked	Wort, cooked	4
	Young beer	Beer	5
	Beer	Beer	92
	Beer, cooled	Beer	8
	Brewer's grain	Brewer's grain	21
	Spent grain	Brewer's grain	1
	Yeast	Yeast	2
	Brewer's yeast	Brewer's yeast	16
	Spent yeast	Brewer's yeast	4
	Lees	Hops draff	2
	Hops draff	Hops draff	18
	Spent hops	Hops draff	13

Table 5 Classification of flour types

Commodity	Flour types	
Wheat	Type 140	Low grade flour (feeding)
	Type 405	Patent flour
	Type 550	White flour
	Type 812	High gluten flour
	Type 1050	Brown flour
	Type 1600	Whole meal flour
Rye	Type 815	Light rye flour
	Type 997	Rye flour
	Type 1050	Heavy rye flour

results. The outcome has been reported in the database on a single study basis. In order to build the desired degree of confidence in the derived processing factors, a number of critical parameters were verified. The information extracted from the corresponding study reports on each quality criterion can be retrieved from the database. This enables the use of the information according to specific needs. A total of 6500 processing factors were reported in the studies, out of which circa 1100 could not be reproduced because the residues in the processed matrix and in the RAC were lower than LOQ. For reasons of completeness, they were, however, not omitted. About 2800 processing factors reached the minimum quality requirements and the derived processing factors have been tagged as "acceptable". 17 % of the processing factors recorded in the database were flagged as "not acceptable", because more than one critical parameter was not met, and 40 % were flagged as "indicative" due to one parameter not having been met.

The experience gained from the comprehensive review of the large number of studies allows for some critical remarks on the general design of processing studies and the processing procedures described therein. In particular, the following striking aspects are highlighted for further improvements.

The OECD guidance does not specify or prescribe any details of the processing technique(s) that should be simulated in studies. This deliberate flexibility is to leave room for the broad range of different types of processing techniques, ranging from industrial scale food producers continually improving their practice on one end, to artisan food or domestic produce at the other end. Such limited specification of processes leaves the regulatory assessor with a difficult decision on the representativeness of a single study from which a processing factor is taken. Furthermore, information is frequently lacking on the actual range of factors for a processed produce which may be encountered in practice due to diverging processing technologies. A typical example for this is the production of beer. Meanwhile, about 30–35 % of the beers are produced from hop extracts, a procedure

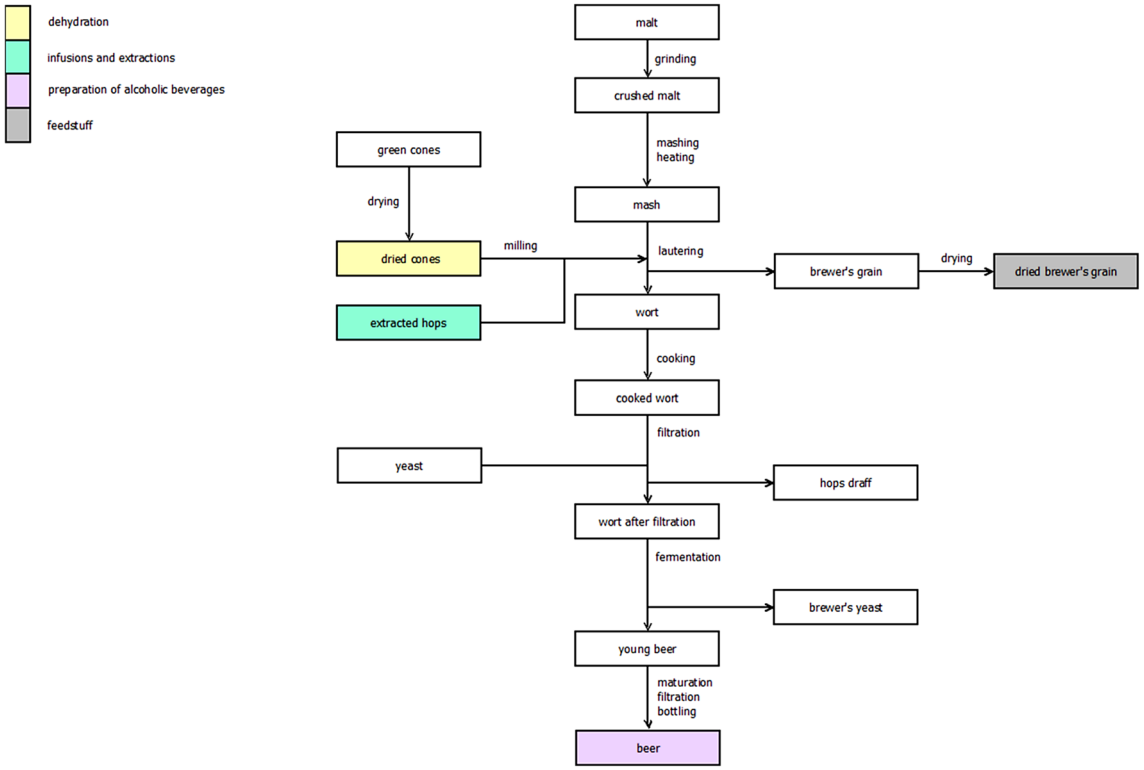

Fig. 1 Flow chart of the processing of hops into beer

not reflected by the majority of the available studies involving the use of dried hop cones (or hop pellets). Likewise, there have been numerous developments concerning the preservation of food. In many cases, a statement regarding the extent to which the simulated processing operation in the lab actually mimics recent developments in the food processing industry would be helpful, as well as a comparison of the applied technology to competing technologies.

Another source of confusion and erroneous interpretation of processing factors is a non-standardized designation of processed fractions. In the evaluated studies, more than 800 differently named processed fractions were registered. For benefits of consistency, it was deemed prudent to combine the more or less identical (but differently named) products/fractions into 175 consolidated terms for processed matrices. This significantly improves the ability to retrieve the complete information from the database, but is also for ease of comparing results of studies using deviant terminologies. One experience gained in the project is that harmonisation and amplification of the current classification/denomination of processed matrices are highly desirable—preferably associated by a coding system for processing operations and processed fractions.

Some of the study reports suffer severely from the lack of information on important parameters, e.g. duration and temperature of heating steps, which would substantially facilitate the affiliation of the study outcome. In the absence of such information, judgement on the representativeness of the procedure is difficult and intercomparison with results from other studies is impeded. Similarly, products have been characterized sparsely and/or in a very general manner in some of the study reports, for example, whether the end product was double or triple concentrated tomato paste.

Another striking obstacle preventing the derivation of processing factors in some studies is that experiments employed a starting material (RAC) with residues below the LOQ of the analytical method. Even in case of an expected accumulation in processed fractions ($Pf > 1$) such studies are not suitable to provide processing factors in a quantitative manner, hence rendering the study results obsolete.

Finally, it is considered worthwhile to further explore possibilities of extrapolation of study results to similar commodities/processes. The Guidance Document on magnitude of pesticide residues in processed commodities (OECD 2008a) indicates that

for commodities of the same commodity group undergoing the same processing procedure; the results obtained for one commodity can be extrapolated to the other similarly processed commodities within this group. These recommendations are basically confirmed by the studies recorded in the BfR database. For example, the results from processing oranges into orange juice may be extrapolated to other citrus fruits. Nevertheless, even this apparently strikingly clear rule should be cautiously applied with a closer scrutiny of the processed fraction. For example, rather divergent factors were found in juices originating from pome fruit, which on a closer look were due to different processing procedures yielding either clear or turbid juice.

With a view to the large number of processed products, an extension of the existing rules for extrapolation should be explored. However, any new extrapolation has to be based on at least a minimum number of side-by-side processing studies. In the past, processing studies were almost exclusively conducted on a very limited number of representative crops. This does not give leeway for substantiating new extrapolations to other RACs which are important in trade or make up a significant share of consumer group diets.

Likewise, it might be worthwhile to explore possibilities of processing factors being extrapolated from one substance to another, given that those are closely rated in terms of structure and/or physicochemical properties.

8 Conclusion

Processing factors are valuable tools both for concluding on whether processed food or feed was produced in compliance with legal standards and for refining dietary exposure assessments. The revised BfR database offers a detailed compilation of such processing factors. Quality information on key parameters of the processing studies allows for rating of robustness and reliability of the results. Thus, the BfR database may be considered a milestone in providing a scientific background for establishing Annex VI to Regulation (EC) No 396/2005. To further develop the collected information towards a common instrument for regulatory decision making across the EU, a close cooperation is scheduled with partners of other European institutions. Furthermore, some recommendations concerning the set-up and interpretation of processing studies might find their way into existing international guidance.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

References

Ahlers W, Reichert T (2007) Oberflächen-Konservierungsstoffe und Akute Referenzdosis—Ergebnisse einer Testreihe bei Zitrusfrüchten, Kooperation des lebensmittelchemischen Untersuchungsrings des Landesverbands Baden-Württemberg des Früchte-Import- und -Großhandels e.V. und der Atlanta AG (actually: Univeg Deutschland GmbH)

BfR (2016) http://www.bfr.bund.de. Accessed 1 July 2016

Burchat CS, Ripley BD, Leishman PD, Ritcey GM, Kakuda Y, Stephenson GR (1998) The distribution of nine pesticides between the juice and pulp of carrots and tomatoes after home processing. Food Addit Contam 15:61–71. doi:10.1080/02652039809374599

BVL (2011) Berichte zur Lebensmittelsicherheit 2011, Monitoring. http://www.bvl.bund.de/SharedDocs/Downloads/01_Lebensmittel/01_lm_mon_dokumente/01_Monitoring_Berichte/archiv/lmm_bericht_2011.pdf?__blob=publicationFile&v=4. Accessed 26 July 2016

Chavarri MJ, Herrera A, Ariño A (2005) The decrease in pesticides in fruit and vegetables during commercial processing. Int J Food Sci Technol 40:205–211. doi:10.1111/j.1365-2621.2004.00932.x

Codex Alimentarius (2016) Codex pesticides residues in food online database. http://www.fao.org/fao-who-codexalimentarius/standards/pesticide-mrls/en/. Accessed 28 February 2016

EU Pesticide database (2016). http://ec.europa.eu/food/plant/pesticides/eu-pesticides-database/public/?event=homepage&language=EN. Accessed 28 Feb 2016

EFSA (2012) Reasoned opinion on the review of the existing maximum residue levels (MRLs) for fosetyl according to Article 12 of Regulation (EC) No 396/2005. http://www.efsa.europa.eu/sites/default/files/scientific_output/files/main_documents/2961.pdf. Accessed 23 March 2016

EFSA (2014) Reasoned opinion on the review of the existing maximum residue levels (MRLs) for thiabendazole according to Article 12 of Regulation (EC) No 396/2005. http://www.efsa.europa.eu/sites/default/files/scientific_output/files/main_documents/3750.pdf. Accessed 23 March 2016

ENV/JM/MONO(2013)8 (2013). http://www.oecd.org/env/ehs/pesticides-biocides/publicationsonpesticideresidues.htm. Accessed 28 Feb 2016

European Commission (1997) Guidelines for the generation of data concerning residues as provided in Annex II part A, section 6 and Annex III, part A, section 8 of Directive 91/414/EEC concerning the placing of plant protection products on the market, Appendix E—Processing Studies, 7035/VI/95-rev.5. http://ec.europa.eu/food/plant/pesticides/guidance_documents/docs/app-e.pdf. Accessed 28 Feb 2016

European Commission (2000) Residues: Guidance for generating and reporting methods of analysis in support of pre-registration data requirements for Annex II (part A, Section 4) and Annex III (part A, Section 5) of Directive 91/414. SANCO/3029/99 rev. 4. http://ec.europa.eu/food/plant/pesticides/guidance_documents/docs/wrkdoc12_en.pdf. Accessed 23 March 2016

European Commission (2005) Commission Regulation (EC) No 396/2005 on maximum residue levels of pesticides in or on food and feed of plant and animal origin and amending Council Directive 91/414/EEC (OJ L 70/1, 16.3.2005)

European Commission (2009) Commission Regulation (EU) No 1107/2009 concerning the placing of plant protection products on the market and repealing Council Directives (OJ L 903/24, 3.11.2009)

European Commission (2013) Commission Regulation (EC) No 283/2013 setting out the data requirements for active substances, in accordance with Regulation (EC) No. 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market (OJ L 93/1, 3.4.2013)

European Commission (2014) Commission Regulation (EU) No 752/2014 replacing Annex I to Regulation (EC) No. 396/2005 of the European Parliament and of the Council (OJ L 208/1, 15.07.2014)

Holland PT, Hamilton D, Ohlin B, Skidmore MW (1994) Effects of storage and processing on pesticide residues in plant products. Pure Appl Chem 66:335–356

Kaushik G, Satya S, Naik SN (2009) Food processing a tool to pesticide residue dissipation—A review. Food Res Int 42:26–40. doi:10.1016/j.foodres.2008.09.009

OECD (1998) OECD Series on Principles of Good Laboratory Practice and Compliance Monitoring, Number 1; ENV/MC/CHEM(98)17. http://www.oecd.org/env/ehs/testing/oecdseriesonprinciplesofgoodlaboratorypracticeglpandcompliancemonitoring.htm. Accessed 28 Feb 2016

OECD (2007) Test Guideline No. 507: Nature of the Pesticide Residues in Processed Commodities—High Temperature Hydrolysis, OECD Guidelines for the Testing of Chemicals, Section 5, OECD Publishing. doi:10.1787/9789264067431-en

OECD (2008a) OECD Guidance Document on the Magnitude of Pesticide Residues in Processed Commodities ENV/JMMONO(2008)23. http://www.oecd.org/env/ehs/pesticides-biocides/publicationsonpesticideresidues.htm. Accessed 28 February 2016

OECD (2008b) Test Guideline No. 508: Magnitude of the Pesticide Residues in Processed Commodities, OECD Guidelines for the Testing of Chemicals, Section 5, OECD Publishing. doi:10.1787/9789264067622-en

OECD (2009) OECD Guidance Document on Overview of Residue Chemistry Studies; Series on Pesticides, No. 32; Series on Testing and Assessment, No. 64; ENV/JM/MONO(2009)31. http://www.oecd.org/env/ehs/pesticides-biocides/publicationsonpesticideresidues.htm. Accessed 28 Feb 2016

OECD (2013) OECD Guidance Document on Residues in Livestock; Series on Pesticides, No. 73

Poulsen ME, Hansen HK, Sloth JJ, Christensen HB, Andersen JH (2007) Survey of pesticide residues in table grapes: determination of processing factors, intake and risk assessment. Food Addit Contam 24:886–895. doi:10.1080/02652030701245320

RIVM (2015) List of processing factors to evaluate pesticide residues measured in The Netherlands. https://acceptatie.chemkap.rivm.nl/en/Topics/C/ChemKAP/Fruit_and_Vegetables/Processing_factors. Accessed 23 June 2016