Appendix to:

EFSA (European Food Safety Authority), 2022. Conclusion on the peer review of the pesticide risk assessment of the active substance propyzamide. EFSA Journal 2022;20(2):7034, 14 pp. doi:10.2903/j.efsa.2022.7034

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Appendix A — List of end points for the active substance and the representative formulation

Section 1 Impact on Human and Animal Health
Studies performed on metabolites or impurities

| Study Details |
|---------------|
| RH-24644: the bacterial reverse mutation assay (Ames), *in vitro* micronucleus test and a 28-day study including the *in vivo* gene mutation Pig-a assay as an integrated part of the study. |
| RH-26702: the bacterial reverse mutation assay (Ames), *in vitro* micronucleus test and a 28-day study including the *in vivo* gene mutation Pig-a assay as an integrated part of the study. |
| RH-25337: the bacterial reverse mutation assay (Ames) and an *in vitro* micronucleus test. |

In addition, QSAR analyses using DEREK, OASIS TIMES, and TOPKAT were made with the parent molecule Propyzamide and the plant metabolites (RH-24644, RH-25891, RH-26702, RH-26521, RH-26059, RH-24848, and RH-25337) as well as an independent analysis of read-across using OECD QSAR Toolbox.

Based on the results from these studies, a concern for potential genotoxicity could not be excluded for plant metabolites RH-24644 (and by read across RH-25891) and RH-26702 (data gap) since the results of the *in vivo* Pig-A gene mutation analysis in the 28-day studies on metabolites RH-24644 and RH-26702 are considered inconclusive. It was agreed during TC 55 that if the TTC approach would be considered appropriate by risk managers, the TTC value for potentially genotoxic substances (0.0025 µg/kg bw/d) would in principle apply.

Furthermore, a bacterial reverse mutation assay, an *in vitro* mammalian chromosomal aberration test and an *in vitro* mammalian cell mutation assay with RH-24580 were submitted.
## Section 2 Residues in or on treated products food and feed

### Metabolism in plants (Regulation (EU) N° 283/2013, Annex Part A, points 6.2.1, 6.5.1, 6.6.1 and 6.7.1)

| Primary crops (Plant groups covered) OECD Guideline 501 | Crop groups | Crop(s) | Application(s) | DAT (days) |
|--------------------------------------------------------|-------------|---------|----------------|------------|
| Fruit crops                                            | Root crops  | Sugar beet | Foliar, 1x1.5 kg/ha BBCH 16 | 20, 148    |
|                                                       | Leafy crops | Lettuce | Pre/Post emergence, (1x2.24 kg/ha/1x2.24 kg/ha) | 0, 15, 30, 55 |
| Cereals/grass crops                                    |             |          |                |            |
| Pulses/Oilseeds                                        |             |          |                |            |
| Miscellaneous                                          |             |          |                |            |

#### Rotational crops (metabolic pattern) OECD Guideline 502

| Crop groups | Crop(s) | PBI (days) | Comments |
|-------------|---------|------------|----------|
| Root/tuber crops | Carrot | 180, 365 | Bare soil, 4.48 kg a.s./ha, ploughing at 10 cm depth. |
| Leafy crops | Lettuce | 30, 180, 365 | |
| Cereal (small grain) | Wheat | 365 | |
| Other | | | |

Rotational crop and primary crop metabolism similar? Mannoside conjugate of RH-25337 and glucoside of RH-26702 recovered predominantly in lettuce, carrot top and wheat forage and straw.

#### Processed commodities (standard hydrolysis study) OECD Guideline 507

| Conditions | Propyzamide | RH-24644 |
|------------|-------------|----------|
| 20 min, 90°C, pH 4 | 98.8% | 0 |
| 60 min, 100°C, pH 5 | 96.1% | 0 |
| 20 min, 120°C, pH 6 | 95.9% | 0.6% |

Residue pattern in processed commodities similar to residue pattern in raw commodities? Yes
Plant residue definition for monitoring (RD-Mo)
OECD Guidance, series on pesticides No 31

Propyzamide
(1) Propyzamide and (2) all metabolites (and their conjugates) bearing the 3,5-dichlorobenzoic acid (DCBA) moiety, expressed as propyzamide – Provisional – To be reconsidered pending the genotoxicity potential of RH-24644 (by read across RH-25891) and RH-26702, the outcome of the requested residue field trials respectively on lettuce and rapeseeds and analysing the magnitude of residues of all metabolites included in the plant residue definition for risk assessment and rotational crops field trials on leafy crops, root crops and cereals, small grain crops for the determination of propyzamide, mannoside conjugate of RH-25337 and glucoside of RH-26702 residues. If required, the general toxicity of these metabolites should also be addressed.

Conversion factor (monitoring to risk assessment)
Open – Pending upon the requested residue field trials respectively on lettuce and rapeseeds and analysing the magnitude of residues of all metabolites included in the plant residue definition for risk assessment and rotational crops field trials on leafy crops, root crops and cereals, small grain crops for the determination of propyzamide, mannoside conjugate of RH-25337 and glucoside of RH-26702 residues at 30 days plant back intervals (PBI) (data gaps).

Metabolism in livestock (Regulation (EU) N° 283/2013, Annex Part A, points 6.2.2, 6.2.3, 6.2.4, 6.2.5 6.7.1)

| OECD Guideline 503 and SANCO/11187/2013 rev. 3 (fish) | Animal | Dose (mg/kg bw/d) | Duration (days) | N rate/comment |
|------------------------------------------------------|--------|--------------------|-----------------|----------------|
| Animals covered                                      |        |                    |                 |                |
| Laying hen                                           | 3.67   | 10                 | 1800            |                |
| Goat/Cow                                             | 1.9–2.49 | 4   | 500 (Dairy), 625 (Lamb) |
| Pig                                                  | --     |                    |                 |                |
| Fish                                                 | --     |                    |                 |                |

(up to 250 characters)

Time needed to reach a plateau concentration in milk and eggs (days)
Milk: 3-4 days
Eggs: Not reached after 10 dosing days

Animal residue definition for monitoring (RD-Mo)
OECD Guidance, series on pesticides No 31
Propyzamide
Animal residue definition for risk assessment (RD-RA)

| (1) propyzamide and (2) all metabolites (and their conjugates) bearing the 3,5-dichlorobenzoic acid (DCBA) moiety, expressed as propyzamide – Provisional - To be reconsidered pending the outcome of the requested residue field trials on primary and rotational crops and finalisation of the plant risk assessment residue definition. |

Conversion factor (monitoring to risk assessment)

| Open – Pending finalisation of the dietary burden calculation and the potential need for ruminant and poultry feeding studies. |

Metabolism in rat and ruminant similar (Yes/No)

| Yes |

Fat soluble residues (Yes/No) (FAO, 2009)

| Yes, log $P_{OW} = 3.27$ Higher levels of total residues in fat compared to fat free muscle. |
Residues in succeeding crops (Regulation (EU) N° 283/2013, Annex Part A, point 6.6.2)

Confined rotational crop study
(Quantitative aspect)
OECD Guideline 502

Parent propyzamide was identified in significant proportions in lettuce (15% to 42% TRR) and in carrot top (17% TRR). The mannoside conjugate of RH-25337 was found to be a major compound of the total residues in lettuce (12-36% TRR), in carrot top (18-28% TRR) and in wheat forage and straw (26.6% TRR and 14.7% TRR, respectively) although the absolute concentrations of this compound in carrot and wheat plant parts were much lower compared to those recovered in lettuce. The glucoside of RH-26702 was the most abundant metabolite observed in lettuce (18%-37% TRR). Metabolites’ identification was not carried out in carrot root and wheat grain.

Field rotational crop study
OECD Guideline 504

Rotational crops field trials on leafy crops, root crops and cereals, small grain crops for the determination of propyzamide, mannoside conjugate of RH-25337 and glucoside of RH-26702 residues at 30-d PBI are required (data gap).

Stability of residues (Regulation (EU) N° 283/2013, Annex Part A, point 6.1)
OECD Guideline 506

| Plant products (Category) | Commodity | T (°C) | Stability (Months) |
|--------------------------|-----------|--------|--------------------|
|                          |           |        | Propyzamide        |
| High water content       | Apple     | -20°C  | 36                 |
|                          | Lettuce   |        |                    |
|                          | Peaches   |        |                    |
|                          | Peaches   | -20°C  | 36                 |
| High oil content         | Rapeseeds | -20°C  | 18                 |
|                          | Soya bean seeds | -20°C | 24                 |
| High protein content     | Dry bean seed | -18°C | 13                 |
| High acid content        | Grapes    | -20°C  | 36                 |

(1): Whole material

| Animal    | Animal commodity | T (°C) | Stability (Months) |
|-----------|------------------|--------|--------------------|
| Ruminants | Muscle           | -18°C  | 6                  |
|           | Liver            | -18°C  | 6                  |
|           | Kidney           | -18°C  | 6                  |
|           | Fat              | -18°C  | 6                  |
|           | Milk             | -20°C  | 36                 |
| Poultry   | Egg              | -18°C  | 6                  |
### Summary of residues data from the supervised residue trials (Regulation (EU) N° 283/2013, Annex Part A, point 6.3) OECD Guideline 509, OECD Guidance, series on pesticides No 66 and OECD MRL calculator

| Crop                  | Region/Indoor | Residue levels (mg/kg) observed in the supervised residue trials relevant to the supported GAPs (b) | Recommendations/comments (OECD calculations) | MRL proposals (mg/kg) | HR (mg/kg) (c) | STMR (mg/kg) (d) |
|-----------------------|---------------|---------------------------------------------------------------------------------------------------|---------------------------------------------|----------------------|----------------|----------------|
| **Representative uses** |               |                                                                                                  |                                             |                      |                |                |
| **RD-Mo:** Propyzamide |               |                                                                                                  |                                             |                      |                |                |
| **RD-RA:** (1) propyzamide and (2) all metabolites (and their conjugates) bearing the 3,5-dichlorobenzoic acid (DCBA) moiety, expressed as propyzamide (provisional) |               |                                                                                                  |                                             |                      |                |                |
| Lettuce               | NEU           | **RD-Mo:** 2x <0.01, 0.02, 2x 0.03, 0.011, 0.014, 0.015, 0.063, 0.13<br>**RD-RA:** - |                                            | 0.2                             | 0.13              | 0.018          |
| Lettuce               | SEU           | **RD-Mo:** 0.02, 0.03, 0.05, 0.07, 0.105, 0.130, 0.290, 0.330, 0.420<br>Based on the proportionality approach the corresponding residue values compliant with the SEU critical GAP are: 0.015, 0.029, 0.038, 0.053, 0.073, 0.098, 0.215, 0.244, 0.320<br>**RD-RA:** - |                                            | 0.6                             | 0.32              | 0.073          |
| Rapeseeds             | NEU           | **RD-Mo:** Seed: 8x <0.01, 0.024, 0.027, 0.034, 0.039, 0.088; 0.090<br>**RD-RA:** -<br>**RD-Mo:** Forage (whole plant): 0.016; 0.049; 0.051; 0.071<br>**RD-RA:** - |                                            | 0.15                            | 0.090             | 0.010          |
| Rapeseeds             | SEU           | **RD-Mo:** Seed: 2x <0.01, 0.011, 0.013, 0.015, 0.027, 0.053, 0.054, 0.067, 0.169<br>**RD-RA:** -<br>**RD-Mo:** Forage (whole plant): 0.008, 0.024, 0.028, 0.059<br>**RD-RA:** - | According to the Dixon´s Q-test, the value 0.169 mg/kg is an outlier. However, deviations in the experimental conditions in the field phase of this trial were not identified. Thus, this value is included in the MRL calculation. | 0.3                             | 0.169             | 0.021          |

**MRL application** (row to be deleted if not relevant)
### Summary of the data on formulation equivalence OECD Guideline 509

| Crop       | Region/Indoor (a) | Residue levels (mg/kg) observed in the supervised residue trials relevant to the supported GAPs (b) | Recommendations/comments (OECD calculations) | MRL proposals (mg/kg) | HR (mg/kg) (c) | STMR (mg/kg) (d) |
|------------|-------------------|-------------------------------------------------------------------------------------------------|---------------------------------------------|----------------------|----------------|-----------------|
|            |                   | Two types of formulations have been used: WP and EC. No differences in residues at harvest in head lettuce due to formulations were observed. |                                             |                      |                |                 |

(a): NEU or SEU for northern or southern outdoor trials in EU member states (N+SEU if both zones), Indoor for glasshouse/protected crops, Country if non-EU location.

(b): Residue levels in trials conducted according to GAP reported in ascending order (e.g. 3x <0.01, 0.01, 6x 0.02, 0.04, 0.08, 3x 0.10, 2x 0.15, 0.17). When residue definition for monitoring and risk assessment differs, use Mo/RA to differentiate data expressed according to the residue definition for Monitoring and Risk Assessment.

(c): HR: Highest residue. When residue definition for monitoring and risk assessment differs, HR according to residue definition for monitoring reported in brackets (HRMo).

(d): STMR: Supervised Trials Median Residue. When residue definition for monitoring and risk assessment differs, STMR according to definition for monitoring reported in brackets (STMRMo).
Inputs for animal burden calculations – Propyzamide residues\(^{(2)}\)

| Feed commodity          | Median dietary burden (mg/kg) | Comment                  | Maximum dietary burden (mg/kg) | Comment                  |
|-------------------------|-------------------------------|--------------------------|-------------------------------|--------------------------|
| Rapeseed meal           | 0.021                         | STMR value               | 0.021                         | STMR value               |
|                         |                               | Residue trials from SEU  |                               | Residue trials from SEU  |
| Rapeseeds forage        | 0.040                         | STMR value               | 0.071                         | HR value                 |
| (whole plant)           |                               |                          |                               | Residue trials from NEU  |

\(^{(2)}\) Calculated dietary burden regarded as provisional pending the outcome of the outstanding data on the magnitude of residues in primary and rotational crops of all the relevant metabolites included in the provisional plant residue definition for risk assessment (data gaps).
Residues from livestock feeding studies (Regulation (EU) N° 283/2013, Annex Part A, points 6.4.1, 6.4.2, 6.4.3 and 6.4.4) OECD Guideline 505 and OECD Guidance, series on pesticides No 73

| MRL calculations | Ruminant | Pig/Swine | Poultry | Fish |
|------------------|----------|-----------|---------|------|
| **Highest expected intake**<sup>(2)</sup> (mg/kg bw/d) | | | |
| Beef cattle | 0.001 | | | |
| Dairy cattle | 0.001 | | | |
| Ram/Ewe | 0.003 | | | |
| Lamb | 0.004 | | | |
| Finishing | <0.001 | | | |
| Breeding | 0.001 | | | |
| Broiler | | | | |
| Layer | 0.002 | | | |
| Turkey | <0.001 | | | |
| **Intake >0.004 mg/kg bw** | No | Yes | No | No |
| Feeding study submitted | Not requested | Not requested | Not requested | Not requested |
| **Representative feeding level** (mg/kg bw/d, mg/kg DM for fish) and N rates | Level | Beef: N Dairy: N | Level | Lamb: N Ewe: N | Level | N rate Breed/Finish | Level | B or T: N Layer: N | Level | N rate Carp/Trout |
| Estimated HR<sup>(a)</sup> at 1N | MRL proposals | Estimated HR<sup>(a)</sup> at 1N | MRL proposals | Estimated HR<sup>(a)</sup> at 1N | MRL proposals | Estimated HR<sup>(a)</sup> at 1N | MRL proposals | Estimated HR<sup>(a)</sup> at 1N | MRL proposals |
| Muscle | | | | | | | | | |
| Fat | | | | | | | | | |
| Meat<sup>(b)</sup> | | | | | | | | | |
| Liver | | | | | | | | | |
| Kidney | | | | | | | | | |
| Milk<sup>(a)</sup> | | | | | | | | | |
| Eggs | | | | | | | | | |
| **Method of calculation**<sup>(c)</sup> | | | | | | | | | |

(a): Estimated HR calculated at 1N level (estimated mean level for milk).

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(b): HR in meat calculated for mammalian on the basis of 20% fat + 80% muscle and 10% fat + 90% muscle for poultry

(c): The OECD guidance document on residues in livestock (series on pesticides 73) recommends three different approaches to derive MRLs for animal products; by applying a transfer factor (Tf), by extrapolation (It) or by linear regression (Ln). Fill in method(s) considered to derive the MRL proposals.
### STMR calculations

#### Median expected intake (mg/kg bw/d) (mg/kg DM for fish)

| Ruminant         | Pig/Swine | Poultry | Fish   |
|------------------|-----------|---------|--------|
| Beef cattle      | 0.0004    | Breeding| Broiler|
| Dairy cattle     | 0.0006    | Finishing| Layer  |
| Ram/Ewe          | 0.0019    | <0.001  | 0.001  |
| Lamb             | 0.0024    |         | 0.001  |
|          |           |         | 0.001  |
|          |           |         | Trout  |
|          |           |         |        |
|          |           |         | Turkey |
|          |           |         |        |

#### Representative feeding level (mg/kg bw/d, mg/kg DM for fish) and N rates

| Level | Beef: N | Level | Lamb: N | Level | N rate Breed/Finish | Level | B or T: N | Level | N rate Carp/Trount |
|-------|---------|-------|---------|-------|---------------------|-------|-----------|-------|-------------------|
| Mean level in feeding level | Estimated STMR(b) at 1N | Mean level in feeding level | Estimated STMR(b) at 1N | Mean level in feeding level | Estimated STMR(b) at 1N | Mean level in feeding level | Estimated STMR(b) at 1N | Mean level in feeding level | Estimated STMR(b) at 1N |
| Muscle |         | Fat   |         | Meat(a) | Liver | Kidney | Milk | Eggs | Method of calculation(c) |

(a): STMR in meat calculated for mammalian on the basis of 20% fat + 80% muscle and 10% fat + 90% muscle for poultry
(b): When the mean level is set at the LOQ, the STMR is set at the LOQ.
(c): The OECD guidance document on residues in livestock (series on pesticide 73) recommends three different approaches to derive MRLs for animal products; by applying a transfer factor (Tf), by intrapolation (It) or by linear regression (Ln). Fill in method(s) considered to derive the MRL proposals.
Conversion Factors (CF) for monitoring to risk assessment

Animal products
Open – Pending finalisation of the dietary burden calculation and the need for ruminant and poultry feeding studies.

Plant products
Open – data gaps for residue field trials respectively on lettuce and rapeseed and analysing the magnitude of residues of all metabolites included in the residue definition for risk assessment and rotational crops field trials on leafy crops, root crops and cereals, small grain crops for the determination of propyzamide, mannoside conjugate of RH-25337 and glucoside of RH-26702 residues at 30 days PBI.

Processing factors (Regulation (EU) N° 283/2013, Annex Part A, points 6.5.2 and 6.5.3) OECD Guideline 508 and OECD Guidance, series on testing and assessment No 96

| Crop (RAC)/Edible part or Crop (RAC)/Processed product | Number of studies(a) | Processing Factor (PF) | Conversion Factor (CF<sub>P</sub>) for RA(b) |
|--------------------------------------------------------|----------------------|------------------------|---------------------------------------------|
|                                                        |                      | Individual values | Median PF |                                    |
| Press cake                                             | 2                    | 0.95; 0.70          | 0.82      | Open                                |
| Crude oil                                              |                      | 1.3; 1.5            | 1.4       | Open                                |
| Refined oil                                            |                      | 1.5; 1.5            | 1.5       | Open                                |

(a): Studies with residues in the RAC at or close to the LOQ should be disregarded (unless concentration)
(b): When the residue definition for risk assessment differs from the residue definition for monitoring

Consumer risk assessment<sup>(3)</sup> (Regulation (EU) N° 283/2013, Annex Part A, point 6.9)
Including all uses (representative uses and uses related to an MRL application)

|                     |                             |
|---------------------|-----------------------------|
|ADI                  | 0.05 mg/kg bw per day       |
|TMDI according to EFSA PRIMO | Highest TMDI: <1 % ADI (Spanish adult) |
|NTMDI, according to (to be specified) | Not calculated |
|IEDI (% ADI), according to EFSA PRIMO | Not calculated |
|NEDI (% ADI), according to (to be specified) | Not calculated |
|Factors included in the calculations                     |                             |

|                     |                             |
|---------------------|-----------------------------|
|ARfd                 | 0.13 mg/kg bw               |
|IESTI (% ARfd), according to EFSA PRIMO | Highest IESTI: 12 % ARFD (lettuce) |
|NESTI (% ARfd), according to (to be specified) | Not calculated |
|Factors included in IESTI and NESTI                     |                             |

<sup>(3)</sup>: The consumer dietary risk assessment is conducted in regard to residues of parent propyzamide only. The consumer risk assessment cannot be finalised with regard to all the pertinent metabolites (and their conjugates) bearing the 3,5-dichlorobenzoic acid (DCBA) moiety, considering the outstanding data to address their magnitude of residues in lettuce and rapeseed and in rotational crops and the inconclusive data on the genotoxicity of RH-24644 (by read across RH-25891) and RH-26702.
Additional contribution to the consumer intakes through drinking water resulting from groundwater metabolite(s) expected to be present above 0.75 µg/L

| Metabolite(s) | RH-24580 |
|---------------|----------|
| ADI (mg/kg bw per day) | Open |
| Intake of groundwater metabolites (% ADI) | Open |

| Metabolite(s) | RH-24580 |
|---------------|----------|
| ADI (mg/kg bw per day) | Open |
| Intake of groundwater metabolites (% ADI) | Open |

| Metabolite(s) | RH-24580 |
|---------------|----------|
| ADI (mg/kg bw per day) | Open |
| Intake of groundwater metabolites (% ADI) | Open |

Proposed MRLs (Regulation (EU) No 283/2013, Annex Part A, points 6.7.2 and 6.7.3)

| Code(a) | Commodity/Group | MRL/Import tolerance(b) (mg/kg) and Comments |
|---------|-----------------|--------------------------------------------|
| **Plant commodities** | | |
| **Representative uses** (row to be deleted if not relevant) | | |
| 0251020 | Lettuce | 0.6 | Provisional(3) |
| 0401060 | Rapeseeds | 0.3 | Provisional(3) |
| **Animal commodities** | | |
| 1000000 | Open(2), (3) | | |

(a): Commodity code number, as listed in Annex I of Regulation (EC) No 396/2005
(b): MRLs proposed at the LOQ, should be annotated by an asterisk (*) after the figure.