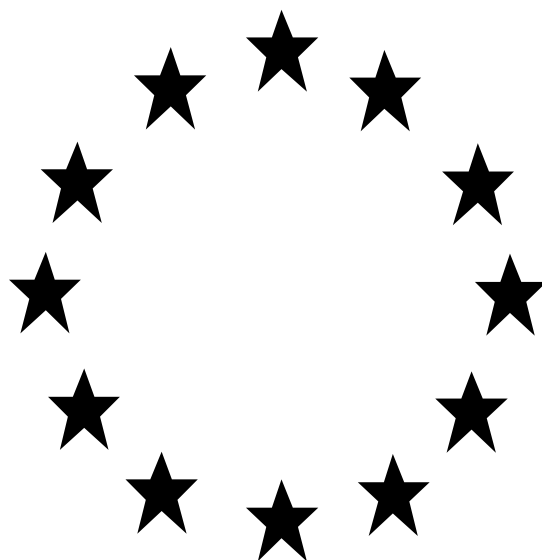




# **Draft Assessment Report (DAR)**

**- public version -**

**Initial risk assessment provided by the rapporteur Member State  
The Netherlands for the existing active substance**

**PYRIDABEN**

**of the third stage (part B) of the review programme  
referred to in Article 8(2) of Council Directive 91/414/EEC**

**Volume 3, Annex B, part 3, B.7**

**August 2007**

**B.7 Residue data****B.7.1 Metabolism, distribution and expression of residues in plants (Annex IIA 6.1 and Annex IIIA 8.1)****B.7.1.1 Primary crops****STUDY 1****Characteristics**

|                   |                                                                                                                                                                                                                                                                              |                      |                                                                                           |
|-------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------|-------------------------------------------------------------------------------------------|
| Reference         | : Mayer, F., 1992 (IIA, 6.1/01)<br>Hofmann, M., 1989a, b, c                                                                                                                                                                                                                  | Application rate     | : 3 x 300 g as/ha for spray treatment (3 x 1N)<br>1 mg/apple for apples painted           |
| Type of study     | : Distribution and metabolism                                                                                                                                                                                                                                                |                      |                                                                                           |
| Year of execution | : 1989-1992                                                                                                                                                                                                                                                                  |                      |                                                                                           |
| Test substance    | : Pyridaben-01, <sup>14</sup> C-[Bz]-NC-129 (radiochem. purity 96.16%, lot no: CP-827-2).<br>Pyridaben-01, <sup>14</sup> C-[Bz]-NC-129 (radiochem. purity 96.31%, lot no: CP-827-2).<br>Pyridaben-02 <sup>14</sup> C-[Pz]-NC-129 (radiochem. purity 97.36%, lot no. CP-928). | Concentration        | : 0.3-0.6 g/L (spray treatment)<br>10 g/L (paint application)                             |
|                   |                                                                                                                                                                                                                                                                              | Vehicle              | : BAS 9078 6 I (EC) in water                                                              |
|                   |                                                                                                                                                                                                                                                                              | Number of treatments | : 3, 1 <sup>st</sup> after end of blooming for spray treatment.<br>1, for painted apples. |
| Plant             | : apple (Cox Orange) for spray treatment<br>apple (Roter Berlepsch) for paint treatment                                                                                                                                                                                      | Area                 | Total area 1.5 m <sup>2</sup> (plastic pots)                                              |
|                   |                                                                                                                                                                                                                                                                              | Total rate           | : 900 g as/ha (3x 300 g as/ha)                                                            |
| GLP statement     | : Yes                                                                                                                                                                                                                                                                        | Harvest (DAT)        | : 25 spray application<br>40 paint application                                            |
| Guideline         | : EPA O:171-4                                                                                                                                                                                                                                                                | Acceptability        | : acceptable                                                                              |

**Study design**

Two varieties of apples were either spray treated (Cox Orange) or painted (Roter Berlepsch), with respectively, benzyl-<sup>14</sup>C-Pyridaben (PB-1) and both PB-1 and pyridazinone-<sup>14</sup>C-Pyridaben (PB-2) formulated as BAS 9078 6 I.

In May 1989, four 5-year-old apple trees (Cox Orange) were grown in plastic pots (total area 1.5m<sup>2</sup>) filled with a 3:1 mixture of loam:sand:soil. The study was performed outdoor under natural conditions. The trees were sprayed three times at a nominal rate of 300 g as/ha per application (PB-1, 3x 1N SEU, according to the GAP of citrus) at 78 (immediately after end of blooming), 50 and 25 days before harvest (spray interval 25 and 28 days) totalling 900 g as/ha. Apples were harvested 25 days after the last treatment.

Leaf samples were taken 3 to 4 hours after treatment and then stored at -20°C. Soil (0-2 and 2-5 cm) was sampled at harvest. Apples were collected 25 days after treatment, peeled, cored and quartered. Branches were coarsely cut and the soil sieved before freezing. Total residues in homogenised apple, leaf, branch and soil samples were determined by combustion/LSC. For the other two studies, paint application (1 mg/apple) of PB-1 or PB-2 took place on 26-07-1989 on 4 apple trees each. Sampling and analysis conditions were similar to those mentioned before, with the exception that samples were only taken at harvest (40 DAT). Peel, pulp (recombined cores and fruit flesh) and whole apple were extracted with acetone followed by acetone/water (8/2 v/v). Radioactivity in the extracts was determined by LSC and in post-extraction solids

(PES) by combustion/LSC. Metabolite patterns in extracts were determined by TLC. Prior to HPLC analysis, extracts were partitioned against dichloromethane and ethyl acetate. The aqueous phase was subjected to enzyme treatment to cleave polysaccharides (amylase) and to fermentation. Additional purification methods were centrifugation, filtration, solid phase extraction ( $C_{18}$ , COOH) and solid/liquid extraction with acetonitrile. Selected PES were further subjected to extractions with MeOH, MeOH- and water-Soxhlet extractions, HCl reflux and enzyme (hesperidinase) treatment. The residue after Soxhlet extraction was fractionated into starch, cellulose, lignin and proteins. Identifications were performed by comparison of retention times and of MS-spectra of isolated fractions with reference materials.

## Results

The levels of radioactivity after three applications at a rate of 300 g as PB-1/ha per application on “Cox Orange” and one paint treatment, 1 mg/apple, of PB-1 and PB-2 on “Roter Berlepsch” apples are summarised in Table B.7.1.1-01.

Total residues in apple fruits at 25 DAT were 0.138 mg eq/kg. Total extractable residues in peel were 47.5% TRR and 13.9% TRR for pulp. Unextractable residues were 32.9% TRR and 5.7% TRR for peel and pulp, respectively. Pyridaben amounted to 20% TRR (Table B.7.1.1-02). Five metabolites were identified: PB-22, PB-14, PB-17, B-1 and B-3, each  $\leq 5.1\%$  TRR ( $\leq 0.007$  mg eq/kg). Other extractables did not exceed 2.9% TRR or 0.01 mg eq/kg, with the exception of H19 (10% TRR, 0.013 mg eq/kg). H19 was characterised as a highly polar, water soluble fraction. Approximately 30% of the TRR consisted of unextractables, of which 16.5% TRR was found incorporated in plant material (cellulose, lignin and starch fractions).

The total residues after paint treatment at 40 DAT were 5.310 mg eq/kg (PB-1) and 5.411 mg eq/kg (PB-2) (Table B.7.1.1-03 and -04). Total extractable residues in apples were 74.7/70.2% TRR for peel (PB-1/PB-2) and 4.1/5.0% TRR for pulp (PB-1/PB-2). Unextractable residues were 23.9/25.0% TRR (PB-1/PB-2) and 0.3/0.6% TRR (PB-1/PB-2) for peel and pulp, respectively. A part of the unextractables (12% TRR) was incorporated into natural plant components (starch, cellulose, lignin).

**Table B.7.1.1-01** Distribution of radioactivity following three applications of [benzyl-<sup>14</sup>C] pyridaben at 300 g as/ha (spray treatment) per application in apple fruit harvested at 25 DAT and distribution of [benzyl-<sup>14</sup>C] pyridaben and [pyridazinone-<sup>14</sup>C] pyridaben at 1 mg/apple (paint treatment) at 40 DAT.

|                                        | TRR<br>(mg eq/kg) | Residue<br>(mg eq/kg of whole fruit) | Residue<br>(% of whole fruit) |
|----------------------------------------|-------------------|--------------------------------------|-------------------------------|
| <b>Foliar treatment (25 DAT)</b>       |                   |                                      |                               |
| Pulp                                   | 0.031             | 0.027                                | 19.6                          |
| Peel                                   | 0.810             | 0.111                                | 80.4                          |
| Whole fruit                            | -                 | 0.138                                | 100                           |
| <b>Paint application PB-1 (40 DAT)</b> |                   |                                      |                               |
| Pulp                                   | 0.272             | 0.231                                | 4.4                           |
| Peel                                   | 34.088            | 5.079                                | 95.6                          |
| Whole fruit                            | -                 | 5.310                                | 100                           |
| <b>Paint application PB-2 (40 DAT)</b> |                   |                                      |                               |
| Pulp                                   | 0.373             | 0.314                                | 5.8                           |
| Peel                                   | 32.055            | 5.097                                | 94.2                          |
| Whole fruit                            | -                 | 5.411                                | 100                           |

The major component of the residue was pyridaben (48.8-51.3% TRR, 2.59-2.78 mg eq/kg). Seven metabolites were identified in samples treated with PB-1 (B1, B3, B-5, D1, PB-14, PB-17 and PB-22) and four metabolites in samples treated with PB-2 (P2, PB-14, PB-17 and PB-22). All metabolites were  $\leq 2.6\%$  TRR ( $\leq 0.115$  mg eq/kg). Unidentifieds were  $\leq 2.3\%$  TRR ( $\leq 0.125$  mg eq/kg). The characterised metabolites are categorised as highly polar peaks (H), medium polar peaks (M) and non-polar peaks (U), based on their respective HPLC-retention time.

**Table B.7.1.1-02 Distribution/identification of radioactivity following three applications of [benzyl-<sup>14</sup>C] pyridaben at 300 g as/ha per application in apple fruit harvested at 25 DAT.**

| Fraction                  |  | % TRR | mg eq/kg fruit |        |
|---------------------------|--|-------|----------------|--------|
| whole fruit               |  | 100   | 0,138          |        |
| Peel                      |  | 80,4  | 0,111          |        |
| Extractables              |  | 47.5  | 0.066          |        |
| Pyridaben=U1              |  |       | 20             | 0,027  |
| H7                        |  |       | 0,9            | 0,001  |
| H14                       |  |       | 2,1            | 0,003  |
| H15                       |  |       | 2,6            | 0,004  |
| H19                       |  |       | 10             | 0,013  |
| M1=PB-22                  |  |       | 2              | 0,003  |
| M2=PB-14 + B3             |  |       | 2,9            | 0,004  |
| M4                        |  |       | 0,6            | 0,001  |
| M6=B1                     |  |       | 5,1            | 0,007  |
| M13                       |  |       | 2,9            | 0,004  |
| M21=PB-17                 |  |       | 1,4            | 0,002  |
| others                    |  |       | 4,9            | 0,008  |
| Unextractables            |  | 32.9  | 0.045          |        |
| Soxhlet MeOH <sup>3</sup> |  |       | 6.8            | 0.009  |
| Soxhlet water             |  |       | 1.1            | 0.002  |
| cellulose                 |  |       | 3.9            | 0.005  |
| MeOH/HCL-lignin           |  |       | 4.3            | 0.006  |
| starch                    |  |       | 7.2            | 0.010  |
| Pulp                      |  | 19,6  | 0,027          |        |
| Extractables              |  | 13.9  | 0.019          |        |
| organic <sup>2</sup>      |  |       | 3.8            | 0.005  |
| aqueous                   |  |       | 7.1            | 0.009  |
| Unextractables            |  | 5.7   | 0.008          |        |
| Soxhlet MeOH              |  |       | <1             | <0.001 |
| Soxhlet water             |  |       | <1             | <0.001 |
| starch                    |  |       | 1.1            | 0.002  |
| total identified          |  | 31,4  | 0.043          |        |

<sup>1</sup> at least 5 fractions, each <1% TRR (<0.001 mg eq/kg)

<sup>2</sup> at least 8 fractions, each <1% TRR (<0.001 mg eq/kg)

<sup>3</sup> identifications in Soxhlet MeOH extract are included with extractables above

**Table B.7.1.1-03 Distribution and identification of radioactivity following one paint application of [benzyl-<sup>14</sup>C] pyridaben at 1 mg as/apple in apple fruit harvested at 40 DAT.**

| Fraction                  | % TRR | mg eq/kg fruit |
|---------------------------|-------|----------------|
| whole fruit               | 100   | 5.31           |
| Peel                      | 95.6  | 5.079          |
| Extractables              | 74.7  | 3.965          |
| Pyridaben=U1              | 47.2  | 2.508          |
| H3                        | 1.2   | 0.061          |
| H5                        | 1     | 0.050          |
| H6                        | 1.1   | 0.059          |
| H8                        | 0.3   | 0.014          |
| H10                       | 0.8   | 0.041          |
| H17                       | 1.2   | 0.063          |
| H18                       | 0.6   | 0.029          |
| H19                       | 2.2   | 0.118          |
| H21                       | 0.3   | 0.013          |
| M1=PB-22                  | 0.9   | 0.047          |
| M2=PB-14 + B-3            | 1.9   | 0.102          |
| M3                        | 0.3   | 0.015          |
| M4                        | 0.4   | 0.019          |
| M6=B1                     | 0.8   | 0.039          |
| M7=B-5                    | 2.2   | 0.112          |
| M9                        | 0.5   | 0.027          |
| M11                       | 1.1   | 0.053          |
| M12                       | 1.1   | 0.052          |
| M13                       | 1.6   | 0.084          |
| M17                       | 2.3   | 0.120          |
| M21=PB-17                 | 0.9   | 0.045          |
| M22                       | 1.0   | 0.052          |
| U3                        | 1.0   | 0.052          |
| U29=D-1                   | 0.8   | 0.039          |
| U33                       | 0.5   | 0.023          |
| U37                       | 0.7   | 0.036          |
| U39                       | 0.3   | 0.013          |
| U41                       | 0.8   | 0.039          |
| Unextractables            | 23.9  | 1.269          |
| Soxhlet MeOH <sup>2</sup> | 2.0   | 0.105          |
| Soxhlet water             | 1.1   | 0.055          |
| HCL extract <sup>1</sup>  | 2.2   | 0.117          |
| hesperidinase extract     | 0.2   | 0.009          |
| Pulp                      | 4.4   | 0.231          |
| Extractables              | 4.1   | 0.217          |
| Pyridaben=U1              | 1.6   | 0.085          |
| H6                        | 0.1   | 0.003          |
| H7                        | 0.1   | 0.004          |
| H16                       | 0.1   | 0.004          |
| M2=PB-14 + B-3            | 0.1   | 0.003          |
| M6=B-1                    | 0.1   | 0.005          |
| M7=B5                     | 0.1   | 0.003          |
| U3                        | 0.3   | 0.015          |
| Unextractables            | 0.3   | 0.015          |
| total identified          | 56.6  | 3.01           |

<sup>1</sup> at least 14 fractions, each  $\leq 0.3\%$  TRR ( $\leq 0.016$  mg eq/kg)

<sup>2</sup> identifications in Soxhlet MeOH extract are included with extractables above

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**Table B.7.1.1-04**      **Distribution and identification of radioactivity following one paint application of [pyridazinone-14C] pyridaben at 1 mg as/apple in apple fruit harvested at 40 DAT.**

| Fraction                   | % TRR |      | mg eq/kg fruit |       |
|----------------------------|-------|------|----------------|-------|
| whole fruit                | 100   |      | 5.411          |       |
| Peel                       | 94.2  |      | 5.097          |       |
| Extractables               | 70.2  |      | 3.798          |       |
| Pyridaben=U1               |       | 48.6 |                | 2.63  |
| H3                         |       | 1.3  |                | 0.074 |
| H4                         |       | 0.9  |                | 0.051 |
| H5                         |       | 0.7  |                | 0.037 |
| H6                         |       | 0.8  |                | 0.041 |
| H8                         |       | 0.3  |                | 0.017 |
| H16                        |       | 0.3  |                | 0.013 |
| H18                        |       | 0.3  |                | 0.015 |
| H19                        |       | 0.2  |                | 0.009 |
| H20                        |       | 0.6  |                | 0.031 |
| H21                        |       | 0.3  |                | 0.016 |
| M1=PB-22                   |       | 1.2  |                | 0.057 |
| M2=PB-14                   |       | 2.1  |                | 0.112 |
| M7                         |       | 0.2  |                | 0.009 |
| M8=P-2                     |       | 1.5  |                | 0.079 |
| M10                        |       | 0.8  |                | 0.047 |
| M13                        |       | 2.3  |                | 0.125 |
| M17                        |       | 1.7  |                | 0.091 |
| M19                        |       | 1.3  |                | 0.071 |
| M21=PB-17                  |       | 0.8  |                | 0.044 |
| M22                        |       | 0.6  |                | 0.030 |
| U3                         |       | 1.2  |                | 0.067 |
| U5                         |       | 0.9  |                | 0.051 |
| U36                        |       | 0.5  |                | 0.024 |
| Unextractables             | 25.0  |      | 1.349          |       |
| Soxhlet MeOH <sup>1</sup>  |       | 2.0  |                | 0.101 |
| Soxhlet water <sup>1</sup> |       | 1.8  |                | 0.098 |
| cellulose                  |       | 1.0  |                | 0.058 |
| protein                    |       | <0.1 |                | 0.007 |
| starch                     |       | 1.5  |                | 0.080 |
| lignin                     |       | 9.5  |                | 0.516 |
| Pulp                       | 5.8   |      | 0.314          |       |
| Extractables               | 5.0   |      | 0.272          |       |
| Pyridaben=U1               | 2.7   |      | 0.145          |       |
| H3                         | 0.1   |      | 0.003          |       |
| H5                         | 0.2   |      | 0.011          |       |
| H6                         | 0.1   |      | 0.004          |       |
| H17                        | 0.1   |      | 0.003          |       |
| M3                         | 0.2   |      | 0.01           |       |
| M4                         | 0.1   |      | 0.006          |       |
| M8=P-2                     | 0.1   |      | 0.005          |       |
| Unextractables             | 0.6   |      | 0.033          |       |
| total identified           | 57.0  |      | 3.084          |       |

<sup>1</sup> identifications in Soxhlet extracts are included with extractables above

Because of the long duration of the study (3 years) storage stability was determined (RP TLC), in peel of painted apples and a 20% decrease of pyridaben was found, after 2.5 years of storage at -20°C, as well as an increase of metabolite spots. No new metabolites were formed during this storage period.

### Conclusions

Following three spray applications of 0.3 kg a.i./ha, total residues in apple fruits at 25 DAT were 0.138 mg eq/kg. Total extractable residues in peel/pulp were 47.5/13.9% TRR and unextractable residues were 32.9 and 5.7% TRR for peel and pulp, respectively. Pyridaben amounted to 20% TRR. Five metabolites were identified: PB-22, PB-14, PB-17, B-1 and B-3, each  $\leq 5.1\%$  TRR ( $\leq 0.007$  mg eq/kg). Other extractables did not exceed 2.9% TRR or 0.01 mg eq/kg, with the exception of H19 (10% TRR, 0.013 mg eq/kg). H19 was characterised as a highly polar, water soluble fraction. Approximately 30% of the TRR consisted of unextractables, of which 16.5% TRR was found incorporated in plant material (cellulose, lignin and starch fractions). The study is acceptable.

Total residues after paint treatment in apples harvested 40 DAT were 5.310 mg eq/kg (PB-1) and 5.411 mg eq/kg (PB-2). Total extractable residues were 74.7/70.2% TRR for peel (PB-1/PB-2) and 4.1/5.0% TRR for pulp (PB-1/PB-2). Unextractable residues were 23.9/25.0% TRR (PB-1/PB-2) and 0.3/0.6% TRR (PB-1/PB-2) for peel and pulp, respectively. A part of the unextractables (12% TRR) was incorporated into natural plant components (starch, cellulose, lignin). The major component of the residue was pyridaben (48.8-51.3% TRR, 2.59-2.78 mg eq/kg). Eight metabolites were identified: P2, B-1, B-3, B-5, D1, PB-14, PB-17 and PB-22. All metabolites were  $\leq 2.6\%$  TRR ( $\leq 0.115$  mg eq/kg). Unidentifieds were  $\leq 2.3\%$  TRR ( $\leq 0.125$  mg eq/kg). The study is acceptable.

### Guidelines and limitations

1. Because the intended use is on tomatoes and citrus, the following limitations for tomatoes and citrus were considered: According to the GAP, spray application should be no later than BBCH 83 (citrus) or BBCH 89 (tomato), i.e. fruit ripe for picking. First application in this study was immediately after end of blooming (meaning BBCH 60-71 for citrus and BBCH 61-69 for tomatoes). Apples were harvested 25-40 days after the last treatment, whereas the PHI according to GAP is 3 or 14 days (tomato and citrus, respectively). The total number of applications (of comparable rate) was higher than the GAP of tomato and citrus (3 in stead of 1).
2. Evaluation against the requirements outlined in Lundehehn (Commission of the European Communities, 1607/VI/97 rev 1 22/7/1997): Total residues in apples at a PHI of 25-40 days exceeded the trigger value for feed (0.05 mg eq/kg) and for human food (0.01 mg eq/kg) for further work. For the spray application, metabolites  $>10\%$  of TRR and/or 0.010 mg eq/kg were identified (with one exception) and metabolites  $<10\%$  of TRR were characterized. Unextractables represented 39% TRR and 0.05 mg/kg and were further characterised. Total identifieds were 31-57% TRR.

## STUDY 2

### Characteristics

|                   |                                                                                                                                                         |                      |                                                                                                                         |
|-------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------|-------------------------------------------------------------------------------------------------------------------------|
| Reference         | : Singh, M., 1994 (IIA 6.1/02)                                                                                                                          | Application rate     | : 0.57 kg a.i./ha(1.9N)<br>4.76 kg a.i./ ha(16N)                                                                        |
| Type of study     | : distribution and metabolism                                                                                                                           | Concentration        | : 0.06-0.7 g/L                                                                                                          |
| Year of execution | : 1990-1994                                                                                                                                             | Vehicle              | : formulated as 25 WP in water                                                                                          |
| Test substance    | : Pyridaben, <sup>14</sup> C-[Bz] (radiochem. purity 99%, lot no: CP-1007).<br>Pyridaben, <sup>14</sup> C-[Pz] (radiochem. purity 99%, lot no. CP-1008. | Number of treatments | : 2                                                                                                                     |
| Plant             | : Citrus, varieties: "Hamlin" and "Valencia"                                                                                                            | Area                 | : na                                                                                                                    |
| GLP statement     | : yes                                                                                                                                                   | Total rate           | : 1.14 kg/ha and 9.52 kg/ha                                                                                             |
| Guideline         | : EPA O:171-4(a)                                                                                                                                        | Harvest (DAT)        | : Hamlin<br>0, 1, 3, 7, 34, 60 and 76 DAT1; 7, 14 DAT2<br>Valencia<br>0, 1, 3, 7, 34, 60 and 234 DAT1;<br>3, 7, 14 DAT2 |
|                   |                                                                                                                                                         | Acceptability        | : acceptable                                                                                                            |

### Study design

Two varieties ("Hamlin" and "Valencia") of citrus fruit were treated with benzyl and pyridazinone-labelled pyridaben. The treatment consisted of two applications (interval 76 (Hamlin) or 234 d (Valencia)), spraying individual citrus fruits, with a mixture of <sup>14</sup>C-pyridaben and 20% WP, in an outdoor environment. The first application was post-bloom on immature fruits and the second on mature fruits. Two different rates, a low dose of 0.57 kg a.i./ha and a high dose of 4.76 kg a.i./ ha, were used. Standard applications of pesticides and fertilizer were made to keep the crop healthy. Low dosed fruit was harvested 0, 1, 3, 7, 34, 60, 76 (Hamlin) and 234 (Valencia) days after first treatment and 0, 7 and 14 days after second treatment. For the high dose treated fruit, harvest was 0 and 7 days after first treatment and 7 and 14 days after second treatment. Storage stability of samples was confirmed.

The fruit samples were fractionated into a surface wash, peel extract, peel unextractables and pulp (juice plus pulp). Fruit was washed with acetone and acetone/water (8:2 v/v). Radioactivity was determined by LSC before and after filtration. Surface wash solid residues were determined by combustion/LSC. The radioactive residues in the surface wash filtrate were subjected to HPLC and 2D-TLC. HPLC preparation of the sample consisted of solvent transfer to acetone, concentration and transfer to water/acetonitrile (8:2 v/v) and filtration (0.45 micron). For TLC analysis the samples were concentrated to dryness and redissolved in acetone. Two TLC systems were used, one to quantify pyridaben and it's metabolites of intermediate polarity and the other to quantify polar metabolites.

The washed fruit was fractionated into juice, peel, pulp and seed. Peel was homogenized with methanol/water (5:1 v/v). Radioactivity in the filtered supernatant was determined by LSC and radioactivity in post extraction solids (PES) by combustion/LSC. Pulp was blended in methanol/water (5:1 v/v), centrifuged after which the juice was added and the procedure repeated. Radioactivity in the filtered combined supernatants was determined by LSC and in PES and seeds (no results reported) by combustion/LSC. Metabolite identification was obtained by comparison of chromatographic behaviour with reference standards and by LC-MS/MS analysis.

## Results

The results for the fractionation of radioactive residues in surface wash, peel extractables, unextractable peel and pulp are presented in Tables B.7.1.1-05 and -06. The GAP for citrus involves 1 application (300 g a.i./ha) with a PHI of 14 days. The results of the sampling point 14 days after the last treatment of the low dose are most relevant to the GAP and are therefore discussed below.

Following two applications of [benzyl-<sup>14</sup>C] pyridaben and [pyridazinone-<sup>14</sup>C] pyridaben at 570 g as/ha on citrus fruits, total residues in citrus fruits at 14 DAT2 were 0.046-0.067 (benzyl-label) and 0.040-0.141 (pyridazinone-label) mg eq/kg. The majority of the residue was found in/on the peel (≥96.4% TRR, 0.039-0.139 mg eq/kg). Radioactivity in pulp was 1.2-3.6% TRR (<0.01 mg eq/kg) and not further investigated. Peel associated radioactivity was fractionated into a surface wash (61-79% TRR), extractables (9.9-19.7% TRR) and unextractables (9.6-18.7% TRR).

Identification work was performed in the 7 DAT2 samples of the low and high doses. The results are presented in Tables B.7.1.1-07 to -10. In the surface wash of the low dose samples, pyridaben was the most important identified fraction: 11.8-22.14% TRR (0.006-0.02 mg eq/kg). Up to 15 metabolite fractions were observed (each ≤4.78% TRR and ≤0.006 mg eq/kg) of which 6 were identified as PB-11, PB-14, PB-22, B-1, B-3 and P-14. In the high dose surface wash, pyridaben was 24.04-36.07% TRR. Individual metabolite fractions were ≤3.33% TRR of which 6 were identified as PB-11, PB-14, PB-22, B-1, B-3 and P-14. Small amounts of pyridaben and B-11 were observed in the peel extract (all ≤2.73% TRR and ≤0.002 mg eq/kg in the low dose samples).

**Table B.7.1.1-05 Distribution of radioactivity following two applications of [benzyl-14C] and [pyridazinone-14C] pyridaben at 570 g as/ha in "Hamlin" citrus fruit harvested at various DAT.**

|              | Hamlin (+0 DAT1) |  |                |              |  |                |
|--------------|------------------|--|----------------|--------------|--|----------------|
|              | benzyl           |  |                | pyridazinone |  |                |
|              | % TRR fruit      |  | mg eq/kg fruit | % TRR fruit  |  | mg eq/kg fruit |
| TRR          | 100              |  | 0.175          | 100          |  | 0.105          |
| surface wash | 96.54            |  | 0.169          | 89.12        |  | 0.094          |
| peel extract | 1.85             |  | 0.003          | 7.57         |  | 0.008          |
| peel marc    | 0.62             |  | 0.001          | 2.19         |  | 0.002          |
| Pulp         | 0.99             |  | 0.002          | 1.13         |  | 0.001          |
|              | Hamlin (7 DAT1)  |  |                |              |  |                |
|              | benzyl           |  |                | pyridazinone |  |                |
|              | % TRR fruit      |  | mg eq/kg fruit | % TRR fruit  |  | mg eq/kg fruit |
| TRR          | 100              |  | 0.036          | 100          |  | 0.014          |
| surface wash | 57.89            |  | 0.021          | 64.15        |  | 0.008          |
| peel extract | 13.58            |  | 0.005          | 12.38        |  | 0.002          |
| peel marc    | 24.15            |  | 0.009          | 21.74        |  | 0.003          |
| Pulp         | 4.38             |  | 0.002          | 1.73         |  | <0.001         |
|              | Hamlin (34 DAT1) |  |                |              |  |                |
|              | benzyl           |  |                | pyridazinone |  |                |
|              | % TRR fruit      |  | mg eq/kg fruit | % TRR fruit  |  | mg eq/kg fruit |
| TRR          | 100              |  | 0.023          | 100          |  | 0.010          |
| surface wash | 35.96            |  | 0.008          | 43.46        |  | 0.005          |
| peel extract | 22.78            |  | 0.005          | 15.15        |  | 0.002          |
| peel marc    | 35.87            |  | 0.008          | 36.16        |  | 0.004          |
| Pulp         | 5.40             |  | 0.001          | 5.23         |  | 0.001          |
|              | Hamlin (76 DAT1) |  |                |              |  |                |
|              | benzyl           |  |                | pyridazinone |  |                |
|              | % TRR fruit      |  | mg eq/kg fruit | % TRR fruit  |  | mg eq/kg fruit |
| TRR          | 100              |  | 0.009          | 100          |  | 0.009          |
| surface wash | 48.00            |  | 0.003          | 31.43        |  | 0.002          |
| peel extract | 25.72            |  | 0.003          | 31.31        |  | 0.003          |
| peel marc    | 17.11            |  | 0.002          | 33.47        |  | 0.003          |
| Pulp         | 9.17             |  | 0.001          | 3.79         |  | <0.001         |
|              | Hamlin (+0 DAT2) |  |                |              |  |                |
|              | benzyl           |  |                | pyridazinone |  |                |
|              | % TRR fruit      |  | mg eq/kg fruit | % TRR fruit  |  | mg eq/kg fruit |
| TRR          | 100              |  | 0.132          | 100          |  | 0.133          |
| surface wash | 85.19            |  | 0.112          | 95.13        |  | 0.127          |
| peel extract | 9.21             |  | 0.012          | 3.62         |  | 0.005          |
| peel marc    | 4.00             |  | 0.006          | 0.70         |  | 0.001          |
| Pulp         | 1.60             |  | 0.002          | 0.55         |  | 0.001          |
|              | Hamlin (7 DAT2)  |  |                |              |  |                |
|              | benzyl           |  |                | pyridazinone |  |                |
|              | % TRR fruit      |  | mg eq/kg fruit | % TRR fruit  |  | mg eq/kg fruit |
| TRR          | 100              |  | 0.084          | 100          |  | 0.122          |
| surface wash | 76.93            |  | 0.064          | 74.92        |  | 0.092          |
| peel extract | 13.08            |  | 0.011          | 13.52        |  | 0.017          |
| peel marc    | 8.92             |  | 0.008          | 10.14        |  | 0.012          |
| Pulp         | 1.07             |  | 0.001          | 1.42         |  | 0.002          |
|              | Hamlin (14 DAT2) |  |                |              |  |                |
|              | benzyl           |  |                | pyridazinone |  |                |
|              | % TRR fruit      |  | mg eq/kg fruit | % TRR fruit  |  | mg eq/kg fruit |
| TRR          | 100              |  | 0.067          | 100          |  | 0.141          |
| surface wash | 61.09            |  | 0.041          | 79.34        |  | 0.113          |
| peel extract | 19.70            |  | 0.013          | 9.90         |  | 0.013          |
| peel marc    | 15.64            |  | 0.011          | 9.57         |  | 0.013          |
| Pulp         | 3.58             |  | 0.002          | 1.20         |  | 0.002          |

**Table B.7.1.1-06** Distribution of radioactivity following a two applications of [benzyl-14C] and [pyridazinone-14C] pyridaben at 570 g as/ha in “Valencia” citrus fruit harvested at various DAT.

|              | Valencia (+0 DAT1)  |  |                |              |  |                |
|--------------|---------------------|--|----------------|--------------|--|----------------|
|              | benzyl              |  |                | pyridazinone |  |                |
|              | % TRR fruit         |  | mg eq/kg fruit | % TRR fruit  |  | mg eq/kg fruit |
| TRR          | 100                 |  | 0.042          | 100          |  | 0.029          |
| surface wash | 85.24               |  | 0.035          | 84.7         |  | 0.024          |
| peel extract | 11.70               |  | 0.005          | 7.69         |  | 0.002          |
| peel marc    | 2.15                |  | 0.001          | 6.50         |  | 0.002          |
| Pulp         | 0.92                |  | <0.001         | 1.11         |  | <0.001         |
|              | Valencia (7 DAT1)   |  |                |              |  |                |
|              | benzyl              |  |                | pyridazinone |  |                |
|              | % TRR fruit         |  | mg eq/kg fruit | % TRR fruit  |  | mg eq/kg fruit |
| TRR          | 100                 |  | 0.015          | 100          |  | 0.012          |
| surface wash | 56.78               |  | 0.008          | 55.17        |  | 0.006          |
| peel extract | 14.40               |  | 0.002          | 10.28        |  | 0.001          |
| peel marc    | 26.07               |  | 0.004          | 32.70        |  | 0.004          |
| Pulp         | 2.75                |  | <0.001         | 1.85         |  | <0.001         |
|              | Valencia (34 DAT1)  |  |                |              |  |                |
|              | benzyl              |  |                | pyridazinone |  |                |
|              | % TRR fruit         |  | mg eq/kg fruit | % TRR fruit  |  | mg eq/kg fruit |
| TRR          | 100                 |  | 0.014          | 100          |  | 0.012          |
| surface wash | 53.14               |  | 0.007          | 50.71        |  | 0.006          |
| peel extract | 11.99               |  | 0.002          | 10.53        |  | 0.001          |
| peel marc    | 28.15               |  | 0.004          | 32.63        |  | 0.004          |
| Pulp         | 6.72                |  | 0.001          | 6.13         |  | 0.001          |
|              | Valencia (234 DAT1) |  |                |              |  |                |
|              | benzyl              |  |                | pyridazinone |  |                |
|              | % TRR fruit         |  | mg eq/kg fruit | % TRR fruit  |  | mg eq/kg fruit |
| TRR          | 100                 |  | 0.004          | 100          |  | 0.006          |
| surface wash | 82.46               |  | 0.001          | 39.70        |  | 0.002          |
| peel extract | 6.39                |  | <0.001         | 25.20        |  | 0.001          |
| peel marc    | 0.96                |  | <0.001         | 31.34        |  | 0.002          |
| Pulp         | 10.19               |  | <0.001         | 3.76         |  | <0.001         |
|              | Valencia (+0 DAT2)  |  |                |              |  |                |
|              | benzyl              |  |                | pyridazinone |  |                |
|              | % TRR fruit         |  | mg eq/kg fruit | % TRR fruit  |  | mg eq/kg fruit |
| TRR          | 100                 |  | 0.133          | 100          |  | 0.097          |
| surface wash | 92.03               |  | 0.122          | 61.52        |  | 0.060          |
| peel extract | 3.95                |  | 0.005          | 22.91        |  | 0.022          |
| peel marc    | 3.68                |  | 0.005          | 13.77        |  | 0.013          |
| Pulp         | 0.34                |  | <0.001         | 1.80         |  | 0.002          |
|              | Valencia (7 DAT2)   |  |                |              |  |                |
|              | benzyl              |  |                | pyridazinone |  |                |
|              | % TRR fruit         |  | mg eq/kg fruit | % TRR fruit  |  | mg eq/kg fruit |
| TRR          | 100                 |  | 0.048          | 100          |  | 0.049          |
| surface wash | 71.96               |  | 0.034          | 77.29        |  | 0.038          |
| peel extract | 7.34                |  | 0.003          | 6.29         |  | 0.003          |
| peel marc    | 20.35               |  | 0.010          | 15.20        |  | 0.007          |
| Pulp         | 0.35                |  | <0.001         | 1.21         |  | 0.001          |
|              | Valencia (14 DAT2)  |  |                |              |  |                |
|              | benzyl              |  |                | pyridazinone |  |                |
|              | % TRR fruit         |  | mg eq/kg fruit | % TRR fruit  |  | mg eq/kg fruit |
| TRR          | 100                 |  | 0.046          | 100          |  | 0.04           |
| surface wash | 68.31               |  | 0.031          | 65.63        |  | 0.026          |
| peel extract | 14.70               |  | 0.007          | 14.32        |  | 0.006          |
| peel marc    | 15.81               |  | 0.007          | 18.66        |  | 0.007          |
| Pulp         | 1.18                |  | 0.001          | 1.39         |  | 0.001          |

**Table B.7.1.1-07 Identification of radioactivity following two applications of [benzyl-<sup>14</sup>C] and [pyridazinone-<sup>14</sup>C] pyridaben at 570g as/ha in “Hamlin” citrus fruit harvested at 7 DAT2.**

|                                         | [benzyl- <sup>14</sup> C] |          | [pyridazinone- <sup>14</sup> C] |          |
|-----------------------------------------|---------------------------|----------|---------------------------------|----------|
|                                         | % TRR                     | mg eq/kg | % TRR                           | mg eq/kg |
| <b>TRR</b>                              | 100                       | 0.084    | 100                             | 0.122    |
| <b>surface wash filtrate</b>            | 60.59                     | 0.056    | 57.44                           | 0.067    |
| pyridaben                               | 21.34                     | 0.020    | 11.80                           | 0.014    |
| PB-11                                   | -                         | -        | 0.38                            | <0.001   |
| PB-14                                   | 4.55                      | 0.004    | 4.21                            | 0.005    |
| PB-22                                   | 1.38                      | 0.001    | 2.31                            | 0.003    |
| B-1+PB-11                               | 1.88                      | 0.002    | -                               | -        |
| B-3+unk-3                               | 0.62                      | 0.001    | -                               | -        |
| P-14                                    | -                         | -        | 3.61                            | 0.004    |
| unk-1                                   | 1.37                      | 0.001    | 0.66                            | 0.001    |
| unk-2                                   | 1.01                      | 0.001    | 0.85                            | 0.001    |
| unk-3                                   | -                         | -        | 0.64                            | 0.001    |
| unk-4                                   | 0.37                      | <0.001   | 0.87                            | 0.001    |
| unk-5                                   | 1.20                      | 0.001    | -                               | -        |
| unk-6                                   | 0.19                      | <0.001   | 0.17                            | <0.001   |
| unk-7                                   | 4.20                      | 0.004    | 4.78                            | 0.006    |
| unk-8                                   | 1.32                      | 0.001    | 2.10                            | 0.002    |
| unresolved                              | 21.74                     | 0.018    | 25.06                           | 0.031    |
| <b>bound (surface wash particulate)</b> | 6.82                      | 0.006    | 10.66                           | 0.012    |
| <b>Peel extract (EtOAc fraction)</b>    | 12.52                     | 0.011    | 5.74                            | 0.007    |
| non-polar                               | -                         | -        | -                               | -        |
| non-polar (pyridaben)                   | 1.90                      | 0.002    | 0.76                            | 0.001    |
| intermediate polar (B-11)               | 2.73                      | 0.002    | -                               | -        |
| intermediate polar                      | 1.36                      | 0.001    | 0.46                            | 0.001    |
| polar                                   | 4.70                      | 0.004    | 1.13                            | 0.001    |
| <b>Peel extract (aqueous fraction)</b>  | 3.45                      | 0.003    | 6.78                            | 0.008    |
| <b>Peel bound</b>                       | 10.76                     | 0.010    | 10.32                           | 0.012    |
| <b>Juice and Pulp Marc</b>              | 0.98                      | 0.001    | 1.59                            | 0.002    |
| <b>Total identified</b>                 | 34.40                     |          | 23.07                           |          |

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**Table B.7.1.1-08 Identification of radioactivity following two applications of [benzyl-<sup>14</sup>C] and [pyridazinone-<sup>14</sup>C] pyridaben at 570g as/ha in “Valencia” citrus fruit harvested at 7 DAT2.**

|                                         | [benzyl- <sup>14</sup> C] |          | [pyridazinone- <sup>14</sup> C] |          |
|-----------------------------------------|---------------------------|----------|---------------------------------|----------|
|                                         | % TRR                     | mg eq/kg | % TRR                           | mg eq/kg |
| <b>TRR</b>                              | 100                       | 0.048    | 100                             | 0.049    |
| <b>surface wash filtrate</b>            | 47.74                     | 0.023    | 57.53                           | 0.026    |
| pyridaben                               | 12.33                     | 0.006    | 22.14                           | 0.009    |
| PB-11                                   | -                         | -        | 4.09                            | 0.002    |
| PB-14                                   | 1.79                      | 0.001    | 1.53                            | 0.001    |
| PB-22                                   | 0.51                      | <0.001   | 0.37                            | <0.001   |
| B-1+PB-11                               | 4.08                      | 0.002    | -                               | -        |
| B-3+unk-3                               | -                         | -        | -                               | -        |
| P-14                                    | -                         | -        | 0.32                            | <0.001   |
| unk-1                                   | 0.80                      | <0.001   | 1.10                            | <0.001   |
| unk-2                                   | 0.93                      | <0.001   | 0.81                            | <0.001   |
| unk-3                                   | -                         | -        | 0.40                            | <0.001   |
| unk-4                                   | 1.30                      | 0.001    | 0.39                            | <0.001   |
| unk-5                                   | -                         | -        | -                               | -        |
| unk-6                                   | -                         | -        | -                               | -        |
| unk-7                                   | 2.23                      | 0.001    | 1.99                            | 0.001    |
| unk-8                                   | 2.63                      | 0.001    | 3.16                            | 0.001    |
| unresolved                              | 21.14                     | 0.010    | 21.23                           | 0.010    |
| <b>bound (surface wash particulate)</b> | 18.85                     | 0.009    | 28.76                           | 0.013    |
| <b>Peel extract (EtOAc fraction)</b>    | 4.77                      | 0.002    | 4.01                            | 0.002    |
| non-polar                               | -                         | -        | -                               | -        |
| non-polar (pyridaben)                   | 1.19                      | 0.001    | 1.08                            | 0.001    |
| intermediate polar (B-11)               | 0.66                      | <0.001   | -                               | -        |
| intermediate polar                      | 0.22                      | <0.001   | 0.69                            | <0.001   |
| polar                                   | 0.76                      | <0.001   | 0.56                            | <0.001   |
| <b>Peel extract (aqueous fraction)</b>  | 2.06                      | 0.001    | 2.38                            | 0.001    |
| <b>Peel bound</b>                       | 20.35                     | 0.009    | 15.21                           | 0.007    |
| <b>Juice and Pulp Marc</b>              | 0.35                      | <0.001   | 1.21                            | 0.001    |
| <b>Total identified</b>                 | 20.56                     |          | 29.53                           |          |

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**Table B.7.1.1-09 Identification of radioactivity following two applications of [benzyl-<sup>14</sup>C] and [pyridazinone-<sup>14</sup>C] pyridaben at 4760g as/ha in "Hamlin" citrus fruit harvested at 7DAT2.**

|                                         | [benzyl- <sup>14</sup> C] |          | [pyridazinone- <sup>14</sup> C] |          |
|-----------------------------------------|---------------------------|----------|---------------------------------|----------|
|                                         | % TRR                     | mg eq/kg | % TRR                           | mg eq/kg |
| <b>TRR</b>                              | 100                       | 0.724    | 100                             | 0.967    |
| <b>surface wash filtrate</b>            | 53.31                     | 0.386    | 49.22                           | 0.476    |
| pyridaben                               | 36.07                     | 0.261    | 26.28                           | 0.254    |
| PB-11                                   | -                         | -        | 1.08                            | 0.010    |
| PB-14                                   | 0.96                      | 0.007    | 1.90                            | 0.018    |
| PB-22                                   | 0.37                      | 0.003    | 0.68                            | 0.007    |
| B-1+PB-11                               | 1.0                       | 0.007    | -                               | -        |
| B-3+unk-3                               | 0.19                      | 0.001    | -                               | -        |
| P-14                                    | -                         | -        | 2.39                            | 0.023    |
| unk-1                                   | -                         | -        | -                               | -        |
| unk-2                                   | -                         | -        | -                               | -        |
| unk-3                                   | -                         | -        | 0.26                            | 0.003    |
| unk-4                                   | -                         | -        | 0.58                            | 0.006    |
| unk-5                                   | -                         | -        | 0.22                            | 0.002    |
| unk-6                                   | 0.30                      | 0.002    | 0.19                            | 0.002    |
| unk-7                                   | 2.92                      | 0.021    | 1.72                            | 0.017    |
| unk-8                                   | 1.12                      | 0.008    | 1.40                            | 0.014    |
| unresolved                              | 10.38                     | 0.075    | 12.52                           | 0.121    |
| <b>bound (surface wash particulate)</b> | 5.76                      | 0.042    | 7.63                            | 0.074    |
| <b>Peel extract (EtOAc fraction)</b>    | 5.73                      | 0.042    | 5.43                            | 0.058    |
| non-polar                               | -                         | -        | 0.26                            | 0.03     |
| non-polar (pyridaben)                   | 0.24                      | 0.002    | 0.91                            | 0.010    |
| intermediate polar (B-11)               | 1.14                      | 0.008    | -                               | -        |
| intermediate polar                      | 0.22                      | 0.002    | 1.13                            | 0.012    |
| polar                                   | 3.64                      | 0.027    | 2.32                            | 0.025    |
| <b>Peel extract (aqueous fraction)</b>  | 3.80                      | 0.028    | 2.98                            | 0.032    |
| <b>Peel extract (soxhlet)</b>           | 3.17                      | 0.023    | 3.05                            | 0.032    |
| <b>Peel extract (MeOH/HCL)</b>          | 1.77                      | 0.013    | 1.81                            | 0.019    |
| <b>Juice and Pulp Marc</b>              | 2.19                      | 0.016    | 6.42                            | 0.068    |
| <b>Total identified</b>                 | 39.97                     |          | 33.24                           |          |

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**Table B.7.1.1-10 Identification of radioactivity following two applications of [benzyl-<sup>14</sup>C] and [pyridazinone-<sup>14</sup>C] pyridaben at 4760g as/ha in “Valencia” citrus fruit harvested at 7DAT2**

|                                                 | [benzyl- <sup>14</sup> C] |          | [pyridazinone- <sup>14</sup> C] |          |
|-------------------------------------------------|---------------------------|----------|---------------------------------|----------|
|                                                 | % TRR                     | mg eq/kg | % TRR                           | mg eq/kg |
| <b>TRR</b>                                      | 100                       | 0.477    | 100                             | 0.359    |
| <b>surface wash filtrate</b>                    | 53.06                     | 0.253    | 49.58                           | 0.178    |
| pyridaben                                       | 27.48                     | 0.136    | 24.04                           | 0.090    |
| PB-11                                           | -                         | -        | 0.93                            | 0.003    |
| PB-14                                           | 1.02                      | 0.005    | 0.81                            | 0.003    |
| PB-22                                           | 0.24                      | 0.001    | 0.34                            | 0.001    |
| B-1+PB-11                                       | 1.33                      | 0.007    | -                               | -        |
| B-3+unk-3                                       | 0.40                      | 0.002    | -                               | -        |
| P-14                                            | -                         | -        | 0.28                            | 0.001    |
| unk-1                                           | -                         | -        | -                               | -        |
| unk-2                                           | 1.43                      | 0.007    | 1.21                            | 0.005    |
| unk-3                                           | -                         | -        | 0.36                            | 0.001    |
| unk-4                                           | 0.35                      | 0.002    | 0.36                            | 0.001    |
| unk-5                                           | -                         | -        | 0.52                            | 0.002    |
| unk-6                                           | 0.20                      | 0.001    | 0.14                            | 0.001    |
| unk-7                                           | 1.94                      | 0.010    | 3.33                            | 0.012    |
| unk-8                                           | 1.62                      | 0.008    | 2.52                            | 0.009    |
| unresolved                                      | 17.05                     | 0.081    | 14.74                           | 0.053    |
| <b>bound (surface wash particulate)</b>         | 13.37                     | 0.064    | 13.47                           | 0.050    |
| <b>Peel extract (EtOAc fraction) (Table 16)</b> | 4.55                      | 0.021    | 4.14                            | 0.015    |
| non-polar                                       | -                         | -        | 0.09                            | <0.001   |
| non-polar (pyridaben)                           | 0.56                      | 0.003    | 0.60                            | 0.002    |
| intermediate polar (B-11)                       | 0.85                      | 0.004    | -                               | -        |
| intermediate polar                              | 0.19                      | 0.001    | 0.79                            | 0.003    |
| polar                                           | 1.90                      | 0.009    | 1.81                            | 0.007    |
| <b>Peel extract (aqueous fraction)</b>          | 3.79                      | 0.018    | 2.70                            | 0.010    |
| <b>Peel extract (soxhlet)</b>                   | 2.80                      | 0.013    | 4.25                            | 0.015    |
| <b>Peel extract (MeOH/HCL)</b>                  | 1.94                      | 0.009    | 4.33                            | 0.016    |
| <b>Juice and Pulp Marc</b>                      | 0.43                      | 0.002    | 0.44                            | 0.002    |
| <b>Total identified</b>                         | 31.88                     |          | 27.00                           |          |

## Conclusions

Following two applications of [benzyl-<sup>14</sup>C] pyridaben and [pyridazinone-<sup>14</sup>C] pyridaben at 570 g as/ha on citrus fruits, total residues in citrus fruits at 14 DAT2 were 0.046-0.067 (benzyl-label) and 0.040-0.141 (pyridazinone-label) mg eq/kg. The majority of the residue was found in/on the peel (≥96.4% TRR, 0.039-0.139 mg eq/kg). Radioactivity in pulp was 1.2-3.6% TRR (<0.01 mg eq/kg) and not further investigated. Peel associated radioactivity was fractionated into a surface wash (61-79% TRR), extractables (9.9-19.7% TRR) and unextractables (9.6-18.7% TRR). In the surface wash of the low dose samples, pyridaben was the most important identified fraction: 11.8-22.14% TRR (0.006-0.02 mg eq/kg). Up to 15 metabolite fractions were observed (each ≤4.78% TRR and ≤0.006 mg eq/kg) of which 6 were identified as PB-11, PB-14, PB-22, B-1, B-3 and P-14. In the high dose surface wash, pyridaben was 24.04-36.07% TRR. Individual metabolite fractions were ≤3.33% TRR of which 6 were identified as PB-11, PB-14, PB-22, B-1, B-3 and P-14. Small amounts of pyridaben and B-11 were observed in the peel extract (all ≤2.73% TRR and ≤0.002 mg eq/kg in the low dose samples). The study is acceptable.

## Guidelines and limitations

1. The following deviations from the GAP for citrus were considered: Two applications were performed instead of one. However, as the spray interval was large, and prior to the second treatment TRR was very low, the results after the second treatment (PHI 7 and 14 days) are considered relevant for the

intended use. The total dose was 1.9N the maximum dose according to the GAP, hence absolute amounts may be overestimated.

- Evaluation against the requirements outlined in Lundehn (Commission of the European Communities, 1607/VI/97 rev 1 22/7/1997): Total residues in citrus at a PHI of 14 days exceeded the trigger value for feed (0.05 mg eq/kg) and for human food (0.01 mg eq/mg) for further work. Unidentifieds were all <0.01 mg eq/kg and all the radioactive residue was sufficiently characterised. The identified fraction was 21-40 %TRR.

### STUDY 3

#### Characteristics

|                   |                                                                                     |                      |                                                                           |
|-------------------|-------------------------------------------------------------------------------------|----------------------|---------------------------------------------------------------------------|
| Reference         | : Ogawa, K. 2003 (IIA 6.1/03)                                                       | Application rate     | : 5 mL distributed over whole plant (leaves/fruits) by brush (1 mg/plant) |
| Type of study     | : metabolism in plants                                                              | Concentration        | : 0.2 g/L                                                                 |
| Year of execution | : 2003                                                                              | Vehicle              | : EC formulation                                                          |
| Test substance    | : Pyridaben, <sup>14</sup> C-[Pz]-NC-129 (radiochem. purity 99.5% lot no. CP-1505). | Number of treatments | : 1                                                                       |
|                   |                                                                                     | Interval             | : na                                                                      |
| Plant             | : tomato (Fukujyu No.2)                                                             | Area                 | : Pot area 346.4 cm <sup>2</sup>                                          |
| GLP statement     | : yes                                                                               | Total rate           | : 1 mg/plant                                                              |
| Guideline         | : J.MAFF 12 Nohsan No. 8147, 2000                                                   | Harvest (DAT)        | : 1 (fruits), 7 (fruits), 14 (fruits and foliage)                         |
|                   |                                                                                     | Acceptability        | : acceptable                                                              |

#### Study design

From May to July 2003, tomato plants were acclimatized, after which treatment took place in a greenhouse on July 3<sup>rd</sup> of 2003. Application of pyridazinone-labelled pyridaben (formulated as EC) was by brush to leaves and fruits at a rate of 1 mg/plant. Harvest of the fruit (one tomato per pot per sampling time) took place 1, 7 and 14 days after treatment (DAT). Fruit was rinsed with acetone. Radioactivity in the rinsate was determined by LSC. After concentration, the rinsate was subjected to HPLC/TLC. The rinsed fruit was homogenised and twice extracted with MeOH. Radioactivity in the combined extract was determined by LSC and in post extraction solids by combustion/LSC. The extract was partitioned against ethyl acetate at pH 2. Radioactivity in organic and aqueous phases was determined by LSC. The organic phase was concentrated before analysis with HPLC/TLC. The foliage was harvested 14 days after treatment and analysed the same way as the tomato fruit. Metabolite identification was obtained by comparison of chromatographic behaviour with reference standards.

#### Results

The levels of radioactivity and identification work after one application of [pyridazinone-<sup>14</sup>C] pyridaben at a rate of 1 mg/plant (paint application on leaves and fruits) are summarised in Tables B.7.1.1-11 to B.7.1.1-14.

Mean total residues in tomato fruits 1, 7 and 14 DAT were 0.086, 0.082 and 0.112 mg eq/kg, respectively.

Total residues in the surface rinse of fruits were 71.4 (DAT14) to 84.7% TRR (DAT1). Extractable residues in fruit were 15.0 (DAT1) to 25.6% TRR (DAT14). Unextractable residues in fruit were 0.2-3% TRR.

Pyridaben was the major component of the residue: 91.7 (DAT14) to 98.2% TRR (DAT1). Extractable activity in tomato fruits after surface rinse consisted of  $\geq 95\%$  pyridaben. Four metabolites were identified (D1, PB-4, PB-9 and PB-14). All metabolites were  $\leq 0.7\%$  TRR in individual fruits ( $< 0.001$  mg eq/kg).

In foliage sampled at 14 DAT the mean TRR was 6.299 mg eq/kg, with pyridaben comprising 81.3% of the TRR. Unextracted residue contained 12.5% TRR (0.785 mg eq/kg). The metabolites PB-4, PB-9, PB-14, PB-22 and D-1 were  $\leq 1.1\%$  of TRR in the foliage.

**Table B.7.1.1-11 Distribution and identification of radioactivity following one paint application of [pyridazinone-14C] pyridaben at 1 mg/plant in tomato fruit harvested 1 DAT.**

|                                     | Tomato fruit DAT 1 |          |             |          |
|-------------------------------------|--------------------|----------|-------------|----------|
|                                     | replicate A        |          | replicate B |          |
|                                     | % TRR              | mg eq/kg | % TRR       | mg eq/kg |
| <b>TRR<sup>1</sup></b>              | 100                | 0.076    | 100         | 0.097    |
| <b>Surface rinse</b>                | 80.6               | 0.064    | 88.9        | 0.086    |
| pyridaben                           | 79.9               | 0.060    | 88.0        | 0.085    |
| PB-4                                | 0.2                | <0.001   | 0.2         | <0.001   |
| Diffuse                             | 0.4                | <0.001   | 0.6         | <0.001   |
| <b>Extractables (organic phase)</b> | 18.5               | 0.014    | 10.4        | 0.010    |
| pyridaben                           | 18.5               | 0.014    | 10.0        | 0.010    |
| PB-4                                | -                  | -        | 0.2         | <0.001   |
| diffuse                             | -                  | -        | 0.1         | <0.001   |
| <b>Extractables (aqueous phase)</b> | 0.6                | <0.001   | 0.6         | 0.001    |
| <b>Unextractables</b>               | 0.3                | <0.001   | 0.2         | <0.001   |
| <b>Total identified</b>             | 98.6               | -        | 98.6        | -        |

<sup>1</sup> % of TRR was determined as the sum of rinsate, extractables and unextractables.

**Table B.7.1.1-12 Distribution and identification of radioactivity following one paint application of [pyridazinone-14C] pyridaben at 1 mg/plant in tomato fruit harvested 7 DAT.**

|                                     | Tomato fruit DAT 7 |          |             |          |
|-------------------------------------|--------------------|----------|-------------|----------|
|                                     | replicate A        |          | replicate B |          |
|                                     | % TRR              | mg eq/kg | % TRR       | mg eq/kg |
| <b>TRR<sup>1</sup></b>              | 100.0              | 0.080    | 100.0       | 0.083    |
| <b>surface rinse</b>                | 76.5               | 0.061    | 74.1        | 0.062    |
| pyridaben                           | 74.9               | 0.060    | 73.1        | 0.061    |
| PB-4                                | 0.5                | <0.001   | 0.3         | <0.001   |
| PB-14                               | 0.1                | <0.001   | -           | -        |
| D-1                                 | 0.2                | <0.001   | -           | -        |
| Diffuse                             | 0.9                | 0.001    | 0.7         | 0.001    |
| <b>Extractables (organic phase)</b> | 19.2               | 0.015    | 21.9        | 0.018    |
| pyridaben                           | 17.4               | 0.014    | 21.3        | 0.018    |
| PB-4                                | -                  | -        | -           | -        |
| PB-14                               | 0.5                | <0.001   | -           | -        |
| D-1                                 | 0.5                | <0.001   | -           | -        |
| Diffuse                             | 0.9                | 0.001    | 0.5         | <0.001   |
| <b>Extractables (aqueous phase)</b> | 1.1                | 0.001    | 1.1         | 0.001    |
| <b>Unextractables</b>               | 3.1                | 0.003    | 2.9         | 0.002    |
| <b>Total identified</b>             | 94.1               | -        | 94.7        | -        |

<sup>1</sup> % of TRR was determined as the sum of rinsate, extractables and unextractables.

**Table B.7.1.1-13 Distribution and identification of radioactivity following one paint application of [pyridazinone-14C] pyridaben at 1 mg/plant in tomato fruit harvested 14 DAT.**

|                                     | Tomato fruit DAT 14 |          |       |          |
|-------------------------------------|---------------------|----------|-------|----------|
|                                     | rep A               |          | rep B |          |
|                                     | % TRR               | mg eq/kg | % TRR | mg eq/kg |
| <b>TRR<sup>1</sup></b>              | 100                 | 0.122    | 100   | 0.101    |
| <b>Surface rinse</b>                | 72.7                | 0.089    | 70.2  | 0.071    |
| pyridaben                           | 70.1                | 0.086    | 69.5  | 0.070    |
| PB-4                                | 0.5                 | 0.001    | 0.1   | <0.001   |
| PB-9                                | 0.1                 | <0.001   | -     | -        |
| PB-14                               | 0.3                 | <0.001   | -     | -        |
| D-1                                 | 0.4                 | 0.001    | 0.1   | <0.001   |
| Diffuse                             | 1.2                 | 0.001    | 0.4   | <0.001   |
| <b>Extractables (organic phase)</b> | 21.1                | 0.026    | 23.3  | 0.024    |
| pyridaben                           | 20.6                | 0.025    | 23.3  | 0.024    |
| diffuse                             | 0.5                 | 0.001    | -     | -        |
| <b>Extractables (aqueous phase)</b> | 2.9                 | 0.004    | 3.9   | 0.004    |
| <b>Unextractables</b>               | 3.3                 | 0.004    | 2.7   | 0.003    |
| <b>Total identified</b>             | 92.0                | -        | 93.0  | -        |

<sup>1</sup> % of TRR was determined as the sum of rinsate, extractables and unextractables.

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**Table B.7.1.1-14 Distribution and identification of radioactivity following one paint application of [pyridazinone-<sup>14</sup>C] pyridaben at 1 mg/plant in tomato foliage harvested 14 DAT.**

|                                     | Tomato foliage DAT 14 |              |             |              |
|-------------------------------------|-----------------------|--------------|-------------|--------------|
|                                     | rep A                 |              | rep B       |              |
|                                     | % TRR                 | mg eq/kg     | % TRR       | mg eq/kg     |
| TRR <sup>1</sup>                    | 100                   | 5.879        | 100         | 6.719        |
| Surface rinse                       | 62.7                  | 3.685        | 58.2        | 3.908        |
| pyridaben                           | 61.5                  | 3.615        | 56.6        | 3.804        |
| PB-4                                | 0.4                   | 0.026        | 0.5         | 0.034        |
| PB-9                                | 0.0                   | 0.001        | -           | -            |
| PB-14                               | 0.1                   | 0.008        | 0.1         | 0.004        |
| PB-22                               | 0.1                   | 0.003        | 0.1         | 0.004        |
| D-1                                 | 0.2                   | 0.012        | 0.4         | 0.030        |
| Diffuse                             | 0.3                   | 0.020        | 0.5         | 0.032        |
| <b>Extractables (organic phase)</b> | <b>24.1</b>           | <b>1.418</b> | <b>25.5</b> | <b>1.711</b> |
| pyridaben                           | 22.0                  | 1.295        | 22.4        | 1.508        |
| PB-4                                | 0.5                   | 0.030        | 0.7         | 0.044        |
| PB-9                                | 0.1                   | 0.004        | 0.1         | 0.006        |
| PB-14                               | 0.2                   | 0.013        | 0.4         | 0.024        |
| PB-22                               | -                     | -            | 0.0         | 0.003        |
| D-1                                 | 0.0                   | 0.003        | 0.0         | 0.003        |
| Diffuse                             | 1.3                   | 0.074        | 1.8         | 0.123        |
| <b>Extractables (aqueous phase)</b> | <b>2.0</b>            | <b>0.119</b> | <b>2.6</b>  | <b>0.176</b> |
| <b>Unextractables</b>               | <b>11.2</b>           | <b>0.658</b> | <b>13.7</b> | <b>0.924</b> |
| <b>Total identified</b>             | <b>85.1</b>           |              | <b>81.3</b> |              |

<sup>1</sup> % of TRR was determined as the sum of rinsate, extractables and unextractables.

## Conclusions

Following one paint application (to fruits and leaves) of [pyridazinone-<sup>14</sup>C] pyridaben at a rate of 1 mg/plant, mean total residues in tomato fruits 1, 7 and 14 DAT were 0.086, 0.082 and 0.112 mg eq/kg, respectively. Pyridaben was the major component of the residue: 91.7 (DAT14) to 98.2% TRR (DAT1). Four metabolites were identified in tomato fruits (D1, PB-4, PB-9 and PB-14). Metabolites were ≤0.7%TRR in individual fruits (<0.001 mg eq/kg). In conclusion, the residue in tomato fruits is sufficiently identified and characterised. The study is acceptable.

## Guidelines and limitations

None

## B.7.1.2 Succeeding and rotational crops

Laboratory DT<sub>90</sub> values for pyridaben in soil indicate that pyridaben residues in soil 100 days after treatment will be >10% of applied. Crop rotation is not relevant in citrus cultivation, but may be relevant in tomato cultivation. Hence, data on rotational or succeeding crops are required. One study was submitted and is summarised below.

## STUDY 1

### Characteristics

|                   |                                                                                                                                                                                                                                                                                                                     |                      |                                                                                                                                                     |
|-------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------|
| Reference         | : Ellenson, J.L., 1999, 2003 (IIA 6.6/01)                                                                                                                                                                                                                                                                           | Application rate     | : 0.75 kg/ha (2.5N)                                                                                                                                 |
| Type of study     | : rotational crops                                                                                                                                                                                                                                                                                                  | Concentration        | : 0.86 g/L                                                                                                                                          |
| Year of execution | : 1998-1999                                                                                                                                                                                                                                                                                                         | Vehicle              | : MeOH:water 85:15 v/v                                                                                                                              |
| Test substance    | : [Pz- <sup>14</sup> C] pyridaben (batch 98042-61-03; radiochemical purity 94.8%)                                                                                                                                                                                                                                   | Number of treatments | : 2 (interval 35 d)                                                                                                                                 |
| Plant             | : target crop: no target crop. Application was to bare soil.<br>rotational crops plant back interval 30 d: radish (var. Early Scarlet Globe), mustard greens (var. Florida Broad Leaf) and wheat (var. Featherstone 520).<br>rotational crops plant back interval 240 d: radish, swiss chard, sorghum (var. KS 585) | Sampling             | : radish (leaves/roots), mustard greens, wheat forage, hay, straw and grain at maturity, swiss chard (at early maturity) and sorghum (early forage) |
| GLP statement     | : yes                                                                                                                                                                                                                                                                                                               | Area                 | : 2.88 m <sup>2</sup>                                                                                                                               |
| Guideline         | : US EPA OPPTS 860.1850 7524/VI/95 Rev.2                                                                                                                                                                                                                                                                            | Total rate           | : 1.5 kg/ha                                                                                                                                         |
|                   |                                                                                                                                                                                                                                                                                                                     | Acceptability        | : Acceptable                                                                                                                                        |

### Study design

Bare sandy loam soil (1.9% organic matter; in a bottomless aluminium casket, 1m deep) was treated with two doses (35 days interval) of [pyridazinone-<sup>14</sup>C] pyridaben at a nominal rate of 0.75 kg as/ha by spraying. Radish, mustard greens and wheat were sown 30 days after the last soil treatment (DALT) and radish, swiss chard and sorghum also at 240 DALT. The plants were grown outside in ambient weather conditions. Harvest was 31 or 40 (radish root and leaves), 31 (sorghum forage), 40 (swiss chard, above ground part), 61 (mustard greens, above ground part), 201 (wheat forage), 201-210 (wheat hay) and 243 (wheat straw and grain) days after planting. All samples were homogenised and total radioactive residues were determined by combustion/LSC. The raw agricultural commodities (RAC) obtained from crops planted 30 DALT with a TRR >0.01 mg eq/kg, were, generally, extracted twice with water, followed by acetone/water (80:20 v:v) and acetone extraction. The two latter extracts were combined. For the crops planted 240 DALT, only the water extraction was performed. For selected RACs, post extraction solids (PES) were subjected to acid (HCl) and/or basic (NaOH) hydrolysis. Radioactivity in PES was determined by combustion/LSC. Selected extracts were subjected to TLC and/or HPLC analysis. Soil samples were taken at 30, 70, 91 and 240 DALT. Soils were extracted with 80% acetone:water followed by 20% 1N H<sub>3</sub>PO<sub>4</sub>/MeOH. The combined extract was partitioned into an organic (DCM) and aqueous phase and subjected to TLC and/or HPLC.

### Results

The radioactivity levels in soil at 30, 70, 91 and 240 DALT showed a decline from 0.534 mg/kg (30 DALT) to 0.324 mg/kg (240 DALT). In the soil extracts, parent compound and the metabolites PB-4 and PB-7 were present, with pyridaben as the major single compound at 30 DALT and 70 DALT. The same compounds were found in the soil at 240 DALT but here PB-4 was the major residue.

The levels of radioactivity in radish (roots and leaves), mustard greens, wheat forage, hay, straw and grain, sorghum forage, and swiss chard planted 30 or 240 days after two applications of [pyridazinone-<sup>14</sup>C] at a rate of 0.75 kg as/ha to bare soil are summarised in Table B.7.1.2-01. The total radioactive residues, for rotational crops planted after 30 days, were 0.013 mg eq/kg (radish root), 0.050 mg eq/kg (radish leaves), 0.019 mg eq/kg (mustard greens), 0.011 mg eq/kg (wheat forage), 0.044 mg eq/kg (wheat hay), 0.045 mg

eq/kg (wheat straw) and 0.009 mg eq/kg (wheat grain). For the crops planted 240 days after treatment, the total radioactive residues were 0.022 mg eq/kg (radish root), 0.049 mg eq/kg (radish leaves), 0.044 mg eq/kg (swiss chard) and 0.024 mg eq/kg (sorghum forage).

The extractable residues for radish root and radish leaves were 92.1 (0.012 mg eq/kg) and 97.5% (0.049 mg eq/kg), respectively. In mustard greens 93.9% 90.018 mg eq/kg) was extractable, while in wheat, 72.8% (0.008 mg eq/kg), 87.1% (0.039 mg eq/kg) and 54.7% (0.025 mg eq/kg) could be extracted from forage, hay and straw, respectively. From the crops planted at 240 DALT, extractable residues were 55.5% or 0.012 mg eq/kg for radish root, 66.2% (0.032 mg eq/kg) for radish leaves, 59.7% (0.026 mg eq/kg) for swiss chard and 47.0% or 0.011 mg eq/kg for sorghum forage.

The results for identification and further chromatographic fractionation of radioactivity for each RAC are discussed below.

**Table B.7.1.2-01** Total radioactive residues and distribution of radioactivity in radish (roots/leaves), mustard greens, wheat forage and wheat hay/straw/grain planted 30 days or radish (roots/leaves), swiss chard and sorghum forage planted 240 days after two treatments of soil with [pyridazinone-<sup>14</sup>C] pyridaben at a nominal rate of 0.75 kg as/ha per application.

| Commodity/fraction | plant back interval 30 days |                   |  | plant back interval 240 days |                   |  |
|--------------------|-----------------------------|-------------------|--|------------------------------|-------------------|--|
|                    | TRR (%)                     | mg eq/kg          |  | TRR (%)                      | mg eq/kg          |  |
| radish root        | 100                         | 0.013             |  | 100                          | 0.022             |  |
| ERR <sup>1</sup>   | 92.1                        | 0.012             |  | 55.5                         | 0.012             |  |
| water ext.         | 61.7                        | 0.008             |  | 55.5                         | 0.012             |  |
| acetone:water ext. | 16.9                        | 0.002             |  | np                           | np                |  |
| hydrolysis         | 13.5                        | 0.002             |  | np                           | np                |  |
| PES <sup>2</sup>   | 13.9                        | 0.002             |  | 44.5                         | 0.010             |  |
| radish leaves      | 100                         | 0.050             |  | 100                          | 0.049             |  |
| ERR                | 97.5                        | 0.049             |  | 66.2                         | 0.032             |  |
| water ext.         | 51.6                        | 0.026             |  | 66.2                         | 0.032             |  |
| acetone:water ext. | 21.7                        | 0.011             |  | np                           | np                |  |
| hydrolysis         | 24.2                        | 0.012             |  | np                           | np                |  |
| PES                | 5.4                         | 0.003             |  | 33.8                         | 0.017             |  |
| mustard greens     | 100                         | 0.019             |  | -( <sup>3</sup> )            | -( <sup>3</sup> ) |  |
| ERR                | 93.9                        | 0.018             |  | -                            | -                 |  |
| water ext.         | 76.0                        | 0.014             |  | -                            | -                 |  |
| acetone:water ext. | 8.9                         | 0.002             |  | -                            | -                 |  |
| hydrolysis         | 9.0                         | 0.002             |  | -                            | -                 |  |
| PES                | 7.05                        | 0.001             |  | -                            | -                 |  |
| wheat forage       | 100                         | 0.011             |  | -( <sup>3</sup> )            | -( <sup>3</sup> ) |  |
| ERR                | 72.8                        | 0.008             |  | -                            | -                 |  |
| water ext.         | np                          | np                |  | -                            | -                 |  |
| acetone:water ext. | np                          | np                |  | -                            | -                 |  |
| hydrolysis         | 72.8                        | 0.008             |  | -                            | -                 |  |
| PES                | 31.8                        | 0.003             |  | -                            | -                 |  |
| wheat hay          | 100                         | 0.044             |  | -( <sup>3</sup> )            | -( <sup>3</sup> ) |  |
| ERR                | 87.1                        | 0.039             |  | -                            | -                 |  |
| water ext.         | 64.8                        | 0.029             |  | -                            | -                 |  |
| acetone:water ext. | 22.3                        | 0.010             |  | -                            | -                 |  |
| hydrolysis         | np                          | np                |  | -                            | -                 |  |
| PES                | 27.0                        | 0.012             |  | -                            | -                 |  |
| wheat straw        | 100                         | 0.045             |  | -( <sup>3</sup> )            | -( <sup>3</sup> ) |  |
| ERR                | 54.7                        | 0.025             |  | -                            | -                 |  |
| water ext.         | 54.7                        | 0.025             |  | -                            | -                 |  |
| acetone:water ext. | np                          | np                |  | -                            | -                 |  |
| hydrolysis         | np                          | np                |  | -                            | -                 |  |
| PES                | 45.3                        | 0.020             |  | -                            | -                 |  |
| wheat grain        | 100                         | 0.009             |  | -( <sup>3</sup> )            | -( <sup>3</sup> ) |  |
| swiss chard        | -( <sup>3</sup> )           | -( <sup>3</sup> ) |  | 100                          | 0.044             |  |
| ERR (only water)   | -                           | -                 |  | 59.7                         | 0.026             |  |
| PES                | -                           | -                 |  | 40.3                         | 0.018             |  |
| sorghum forage     | -( <sup>3</sup> )           | -( <sup>3</sup> ) |  | 100                          | 0.024             |  |
| ERR (only water)   | -                           | -                 |  | 47.0                         | 0.011             |  |
| PES                | -                           | -                 |  | 53.0                         | 0.013             |  |

<sup>1</sup> ERR: extractable radioactive residues

<sup>2</sup> PES: post extraction solids

<sup>3</sup> not relevant (crop not grown)

np: not performed

### Radish roots

The extractable aqueous residue of 30 DALT sown radish roots eluted (HPLC) as a polar peak (20.5% TRR, 0.003 mg eq/kg) and 7 regions, all <10% TRR (<0.001 mg eq/kg). Further fractionation of the polar peak resulted in two resolvable peaks with 11.9% TRR and 8.0% TRR, respectively. The largest of these peaks was fractionated further into three peaks, of which the largest represented 8% TRR (0.0011 mg eq/kg). In the organic extract a total of 1.5% TRR (<0.001 mg eq/kg) could be identified as parent compound. In the organic fraction, after hydrolysis, 4% TRR (<0.001 mg eq/kg) could be attributed to polar components.

In radish roots planted 240 DALT, the aqueous extraction consisted of 55.5% and could be fractionated into one polar peak of 30% TRR (0.007 mg eq/kg), two regions <10% TRR ( $\leq 0.001$  mg eq/kg) and unresolved radioactivity (12.1% TRR, 0.003 mg eq/kg).

#### **Radish leaves**

The extractable residues in radish leaves (sown 30 DALT) consisted mostly of polar residues. The major residue in the aqueous fraction represents 7% TRR (0.0036 mg eq/kg), all other 10 peaks were <10% TRR and <0.004 mg eq/kg. Parent compound was measured in the organic extract and determined to be less than 1% TRR. Acid and base hydrolysis released 13.8% (0.007 mg eq/kg) and 10.4% TRR (0.005 mg eq/kg), respectively (both characterised as very polar in nature).

In radish leaves planted 240 DALT, two peaks accounted for 11% TRR and 9% TRR, or 0.005 mg eq/kg and 0.004 mg eq/kg, of the characterised residue in the aqueous extract. Six other peaks were <10% TRR (<0.005 mg eq/kg) in the aqueous extract.

#### **Mustard greens**

In mustard greens planted 30 DALT, the aqueous extractable residues were characterised as polar residues with one peak of 17% TRR (0.003 mg eq/kg) and 10 additional regions <10% TRR ( $\leq 0.002$  mg eq/kg). In the organic extract minor amounts of parent compound (<1% TRR, <0.001 mg eq/kg) could be detected. At least 11 further regions, all <10% TRR (<0.001 mg eq/kg) were observed. About 6% TRR (9 peaks, of which one 2% TRR and 0.0004 mg eq/kg but others <1% TRR), could be attributed to very polar residues in the water-soluble hydrolysate.

#### **Wheat forage**

Concentrations were so low in wheat forage that only the aqueous extraction was fractionated in one polar region representing 13% TRR (0.001 mg eq/kg), one less polar region representing 14.3% TRR (0.002 mg eq/kg), and ten additional regions, each less than 4% TRR (<0.001 mg eq/kg).

#### **Wheat hay**

The residues in the aqueous fraction of wheat hay sown 30 DALT, was fractionated into two major regions. The most polar region accounted for 9.9% TRR (0.004 mg eq/kg) and was further separated into six different regions (largest region 4.7% TRR, 0.002 mg eq/kg). The second region was 11.5% TRR (0.005 mg eq/kg) and was further fractionated into six different regions with 5% TRR (0.002 mg eq/kg) as the largest fraction. In the organic extract, two regions could be distinguished (both <0.001 mg eq/kg, 1.4% and 1.6% TRR respectively).

#### **Wheat straw**

Wheat straw planted 30 DALT contained residues in the aqueous extract of 41.2% TRR, which were fractionated into one polar peak of 10% TRR (0.005 mg eq/kg) and 8 regions <10% TRR.

### Wheat grain

Total TRR was 0.009 mg eq/kg, so less than 0.01, therefore no further extractions were performed.

### Swiss chard

The aqueous extraction (53% TRR, 0.023 mg eq/kg) of Swiss chard (planted 240 DALT) was fractionated into one polar peak (15% TRR, 0.007 mg eq/kg) and 12 other regions all <10% TRR and <0.004 mg eq/kg.

### Sorghum forage

In sorghum forage (sown 240 DALT) the residues of the aqueous extraction (36% TRR) were fractionated into 15 regions, with two polar peaks of 6% TRR (0.001 mg eq/kg) and 7% TRR (0.002 mg eq/kg). The other 13 regions were all <6% TRR or 0.002 mg eq/kg.

### Conclusions

The levels of radioactivity in radish (leaves and roots), mustard greens, wheat forage, hay, straw and grain sown 30 days after two applications of [Pyridazinone-<sup>14</sup>C] pyridaben at a rate of 0.75 kg as/ha to bare soil were 0.013 mg eq/kg (radish root), 0.050 mg eq/kg (radish leaves), 0.019 mg eq/kg (mustard greens), 0.011 mg eq/kg (wheat forage), 0.044 mg eq/kg (wheat hay), 0.045 mg eq/kg (wheat straw) and 0.009 mg eq/kg (wheat grain). Individual residues consisted mainly of polar unidentified residues in the aqueous extractables of RACs, all were <0.01 mg eq/kg and <10% TRR, except one polar peak in 30 DALT mustard greens (17% TRR). Parent compound was determined in the organic fraction of radish roots, leaves and in mustard greens but was <0.001 mg eq/kg (and ≤1.5% TRR).

### Guidelines & Limitations

None

#### B.7.1.3 Summary of studies in plants

Three studies were submitted on the metabolism of Pyridaben: one in apple, one in orange and one in tomato. The study in apple is not included in the summary below since the intended use of pyridaben is on citrus and tomato only (note: metabolism in apple, citrus and tomato was similar). In the study with oranges, the number of applications (two instead of one) deviated from the cGAP. However the results are considered relevant for the intended use since the spray interval was large and TRR prior to second treatment low. Absolute amounts may have been overestimated since total dose was 1.9N the maximum dose according to the GAP.

In study 2, following two spray applications of [Benzyl-<sup>14</sup>C] and [Pyridazinone-<sup>14</sup>C] pyridaben at 570 g as/ha on citrus fruits, total residues in citrus fruits at 14 DAT2 were 0.040-0.141 mg eq/kg. The majority of the residue was found in/on the peel (≥96.4% TRR, 0.039-0.139 mg eq/kg). Radioactivity in pulp was 1.2-3.6% TRR (<0.01 mg eq/kg). Peel associated radioactivity was fractionated into a surface wash (61-79% TRR),

extractables (9.9-19.7% TRR) and unextractables (9.6-18.7% TRR). In the surface wash pyridaben was the most important identified fraction: 11.8-22.14% TRR (0.006-0.02 mg eq/kg). Up to 15 metabolite fractions were observed (each  $\leq 4.78\%$  TRR and  $\leq 0.006$  mg eq/kg) of which 6 were identified as PB-11, PB-14, PB-22, B-1, B-3 and P-14. Small amounts of pyridaben and B-11 were observed in the peel extract (all  $\leq 2.73\%$  TRR and  $\leq 0.002$  mg eq/kg in the low dose samples). The study is acceptable.

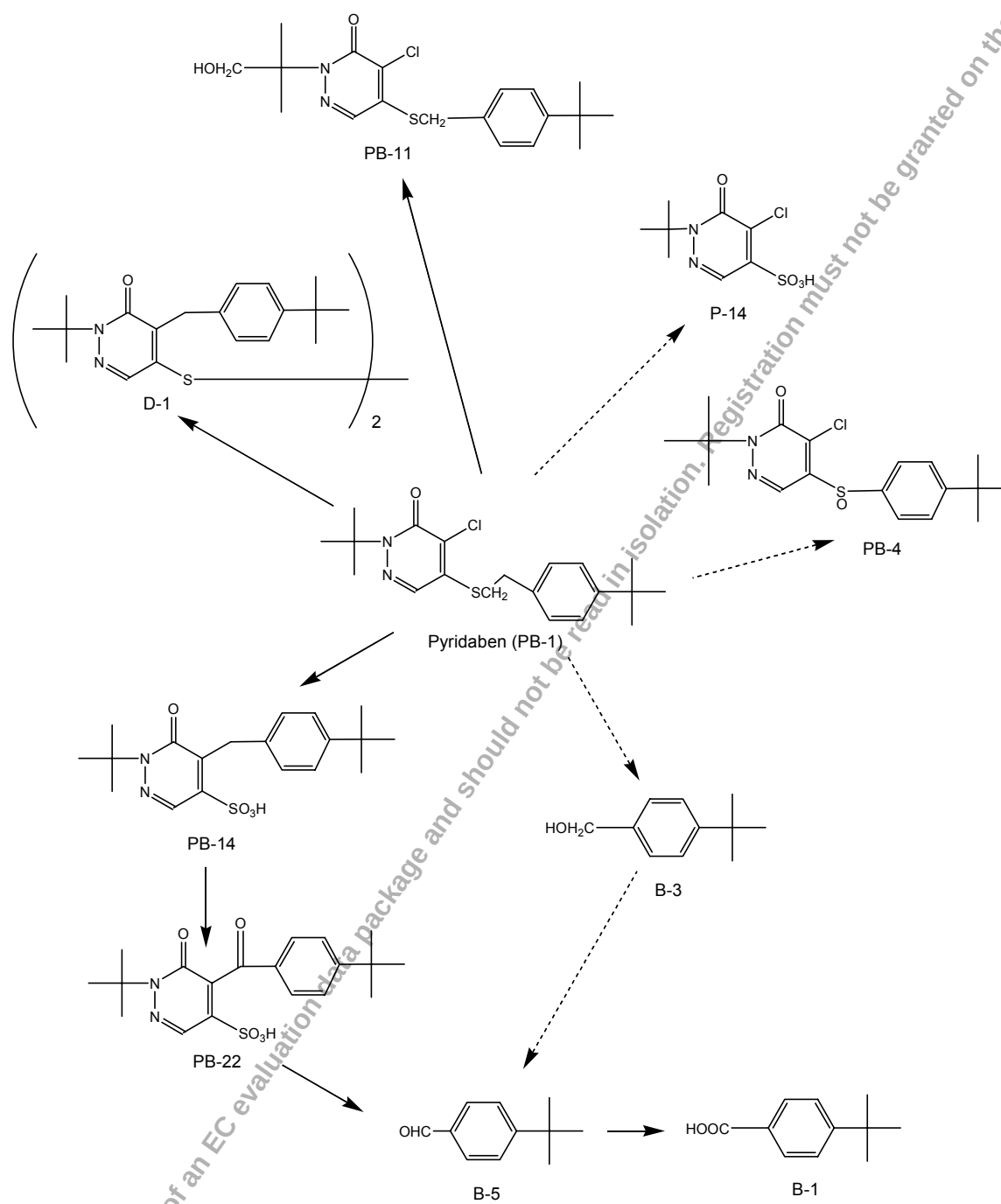
In study 3, following one paint application (to fruits and leaves) of [pyridazinone- $^{14}\text{C}$ ] pyridaben at a rate of 1 mg/plant, mean total residues in tomato fruits 1, 7 and 14 DAT were 0.082-0.112 mg eq/kg. Pyridaben was the major component of the residue: 91.7%-98.2% TRR. Four metabolites (D1, PB-4, PB-9 and PB-14) were identified in individual fruits, all  $\leq 0.7\%$  TRR ( $< 0.001$  mg eq/kg).

One confined crop rotational study was submitted including the relevant crop categories (cereals, leaf and root crop). The levels of radioactivity in radish (leaves and roots), mustard greens, wheat forage, hay, straw and grain sown 30 days after two applications of [Pyridazinone- $^{14}\text{C}$ ] pyridaben at a rate of 0.75 kg as/ha to bare soil were 0.013 mg eq/kg (radish root), 0.050 mg eq/kg (radish leaves), 0.019 mg eq/kg (mustard greens), 0.011 mg eq/kg (wheat forage), 0.044 mg eq/kg (wheat hay), 0.045 mg eq/kg (wheat straw) and 0.009 mg eq/kg (wheat grain). The residues consisted mainly of polar unidentifieds (all  $< 0.01$  mg eq/kg and  $< 10\%$  TRR, except one polar peak in 30 DALT mustard greens (17% TRR)). Parent compound was determined in radish roots, leaves and in mustard greens ( $< 0.001$  mg eq/kg and  $\leq 1.5\%$  TRR).

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**B.7.1.4 List of identified compounds**

| Code             | Compounds                                                                                                  | Description | Crop/Commodity                                    | Animal/Tissue                                    |
|------------------|------------------------------------------------------------------------------------------------------------|-------------|---------------------------------------------------|--------------------------------------------------|
| Pyridaben (PB-1) | 2-tert-butyl-5-(4-tert-butylbenzylthio)-4-chloropyridazin-3(2H)-one                                        | Parent      | Apple (fruit)                                     | Goat (faeces, liver)                             |
| P-1              | tert-butyl-4-chloro-5-mercapto-pyridazin-3(2H)-one                                                         | Metabolite  | -                                                 | Goat (liver)                                     |
| P-2              | 2-tert-butyl-4-chloro-5-methylthiopyridazin-3(2H)-one                                                      | Metabolite  | Apple (fruit)                                     | -                                                |
| P-3              | 2-tert-butyl-4-chloro-5-hydroxypyridazin-3(2H)-one                                                         | Metabolite  | -                                                 | Goat (bile, kidney)                              |
| P-14             | 2-tert-butyl-4-chloropyridazin-3(2H)-one-5-sulfonic acid                                                   | Metabolite  | Citrus (fruit)                                    | -                                                |
| B-1              | 4-tert-butyl-benzoic acid                                                                                  | Metabolite  | Apple (fruit)<br>Citrus (fruit)                   | Goat (faeces, fat)                               |
| B-3              | 4-tert-butyl-benzylalcohol                                                                                 | Metabolite  | Apple (fruit)<br>Citrus (fruit)                   | Goat (faeces)                                    |
| B-5              | 4-tert-butyl-benzaldehyde                                                                                  | Metabolite  | Apple (fruit)                                     | -                                                |
| B-7              | 2-(4-carboxyphenyl)-2-methylpropionic acid                                                                 | Metabolite  | -                                                 | Goat (faeces, kidney)<br>Hen (excreta)           |
| B-8              | 2-(4-hydroxymethylphenyl)-2-methyl-1-propanol                                                              | Metabolite  | -                                                 | Goat (faeces, bile)                              |
| B-11             | 2-(4-carboxyphenyl)-2-methyl-1-propanol                                                                    | Metabolite  | -                                                 | Hen (fat)                                        |
| D-1              | di-[2-tert-butyl-4-(4-tert-butylbenzyl)pyridazin-3(2H)-one-5-yl]disulfide                                  | Metabolite  | Apple (fruit)<br>Tomato (fruit)                   | Hen (eggs)                                       |
| PB-3             | 2-tert-butyl-5-(4-tert-butylbenzylsulfonyl)-4-chloropyridazin-3(2H)-one                                    | Metabolite  | -                                                 | Goat (urine, faeces)                             |
| PB-4             | 2-tert-butyl-5-(4-tert-butylbenzylsulfinyl)-4-chloropyridazin-3(2H)-one                                    | Metabolite  | Tomato (fruit)                                    | Goat (faeces)<br>Hen (excreta)                   |
| PB-7             | 2-tert-butyl-5-[4-(1-carboxy-1-methylethyl)benzylthio]-4-chloropyridazin-3(2H)-one                         | Metabolite  | -                                                 | Goat (urine, faeces, liver)<br>Hen (liver, skin) |
| PB-9             | 2-tert-butyl-4-chloro-5-[4-(1,1-dimethyl-2-hydroxyethyl)benzylthio]pyridazin-3(2H)-one                     | Metabolite  | Tomato (fruit)                                    | Goat (faeces, bile, liver)<br>Hen (liver, skin)  |
| PB-11            | 5-(4-tert-butylbenzylthio)-4-chloro-2-(1,1-dimethyl-2-hydroxyethyl)-pyridazin-3(2H)-one                    | Metabolite  | Citrus (fruit)                                    | Goat (urine, liver, kidney)<br>Hen (fat)         |
| PB-12            | 5-(4-tert-butylbenzylthio)-2-(1-carboxy-1-methylethyl)-4-chloropyridazin-3(2H)-one                         | Metabolite  | -                                                 | Goat (faeces, fat)<br>Hen (excreta, liver)       |
| PB-13            | 4-chloro-2-(1,1-dimethyl-2-hydroxyethyl)-5-[4-(1,1-dimethyl-2-hydroxyethyl)benzylthio]-pyridazin-3(2H)-one | Metabolite  | -                                                 | Goat (faeces)<br>Hen (excreta, liver, eggs)      |
| PB-14            | 2-tert-butyl-4-(4-tert-butylbenzyl)pyridazin-3(2H)-one                                                     | Metabolite  | Apple (fruit)<br>Citrus (fruit)<br>Tomato (fruit) | -                                                |
| PB-17            | 2-tert-butyl-4-(4-tert-butylbenzyl)-pyridazin-3(2H)-one                                                    | Metabolite  | Apple (fruit)                                     | -                                                |
| PB-22            | 2-tert-butyl-4-(4-tert-butylbenzyl)pyridazin-3(2H)-one-5-sulfonic acid                                     | Metabolite  | Apple (fruit)<br>Citrus (fruit)                   | -                                                |

**B.7.1.5 Metabolic pathway****Figure B.7.1.5-01 Metabolic pathway of pyridaben in citrus**

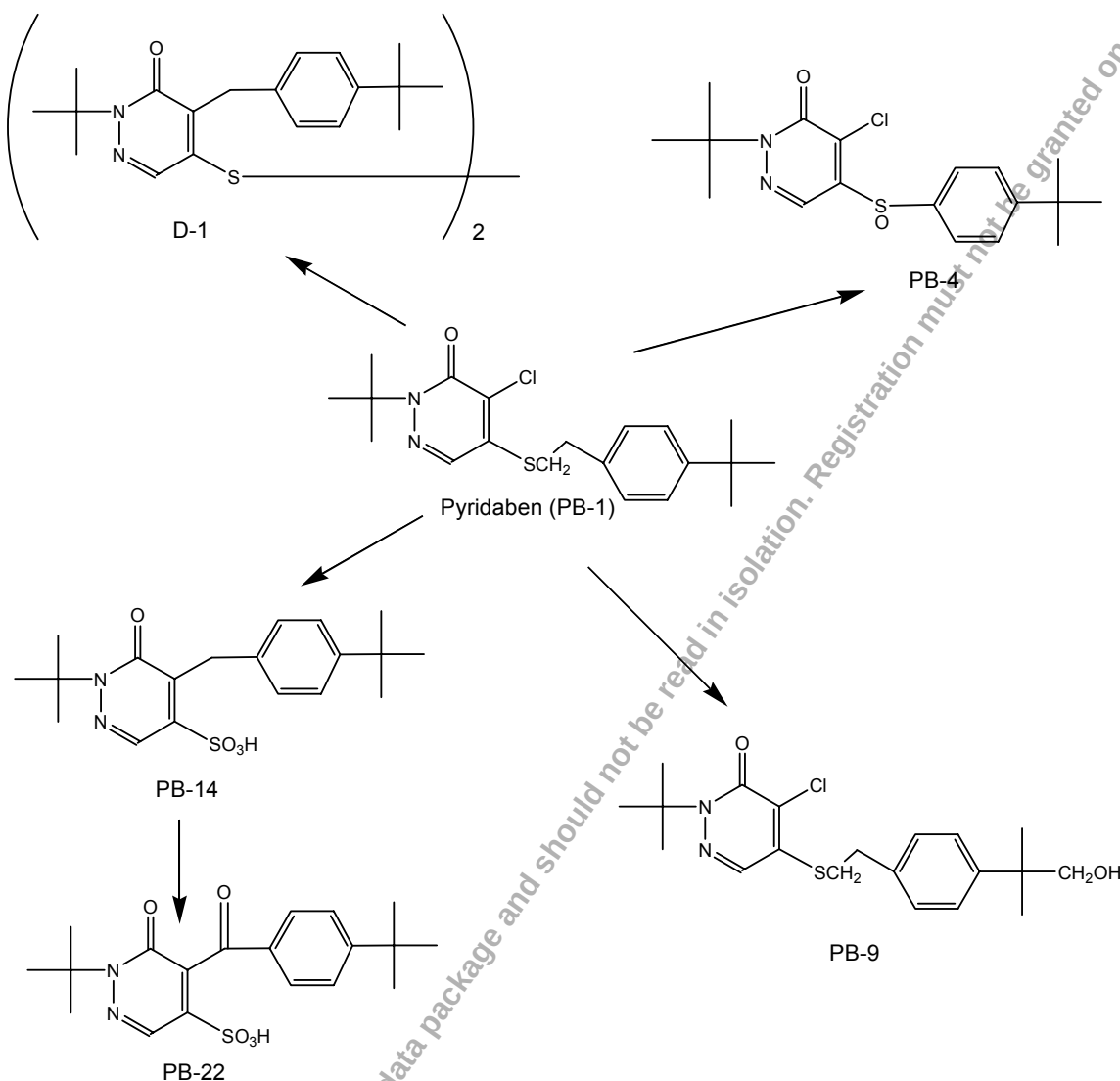


**Figure B.7.1.5-02 Metabolic pathway of pyridaben in tomato**

## **B.7.2 Metabolism, distribution and expression of residues in livestock (Annex IIA 6.2 and Annex IIIA 8.1)**

Metabolism studies in livestock are required because pyridaben residues in animal feed (cattle) exceed 0.1 mg/kg dry feed. Studies in poultry are not required as wet pomace is not a constituent of poultry feed. (Note: the intake calculation for cattle was based on a HR (whole fruit, oranges) of 0.12 mg/kg and a wet pomace processing factor of 1.1. The HR value is provisional as the field residue trials were not conducted under least favourable conditions).

### B.7.2.1 Ruminants

#### STUDY 1

##### Characteristics

|                   |                                                                                                                                                                                                                                                 |               |                                                                                                                 |
|-------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------|-----------------------------------------------------------------------------------------------------------------|
| Reference         | : Hallifax, D., 1994 (IIA, 6.2/01)<br>O'Connor, J., 1996 (addendum to report)                                                                                                                                                                   | GLP statement | : yes                                                                                                           |
| Type of study     | : distribution and metabolism                                                                                                                                                                                                                   | Guideline     | : EPA O: 171-4 (b)                                                                                              |
| Year of execution | : 1991-1994                                                                                                                                                                                                                                     | Dose          | : 0.5 mg/day or 20 mg/day, for 5 consecutive days                                                               |
| Test substance    | : [pyridazinone- <sup>14</sup> C] pyridaben (radiochem. purity ≥97.4%, lot no. CP-1008).<br>[benzyl- <sup>14</sup> C] pyridaben (radiochem. purity ≥96.6%, lot no. CP-1007).<br>non-labelled pyridaben (chemical purity 99.6% lot no. 129T8604) | Vehicle       | : gelatin capsules                                                                                              |
|                   |                                                                                                                                                                                                                                                 | Concentration | : 0.2 and 6.9-7.8 mg/kg feed as received                                                                        |
|                   |                                                                                                                                                                                                                                                 | Total dose    | : 5.5-6.5 MBq/ 2.5 mg (low dose)<br>22.5-27 MBq / 100 mg (high dose)                                            |
| Animal            | : lactating goats                                                                                                                                                                                                                               | Sampling      | : Urine, faeces, cage wash, blood, milk, liver, fat, kidneys, muscle, bile and gastrointestinal tract+ contents |

##### Study design

Four lactating goats received daily oral doses of pyridazinone-<sup>14</sup>C-labelled (Pz) or benzyl-<sup>14</sup>C- labelled (Bz) pyridaben contained in gelatin capsules for 5 consecutive days at a rate of 0.5 or 20 mg/day (2 goats each) (equivalent to 0.2 and 6.9-7.8 mg/kg diet as received). The goats had been acclimated for 4-5 weeks before dosing. One control goat was included in the study.

The goats were milked twice a day, once prior to dosing (morning) and once in the evening. Urine and faeces were collected separately as 24-hour samples. The cage was cleaned at the end of the study and radioactivity in the washing was determined by LSC. Blood samples (5-10 mL) were taken daily, immediately before dosing. The goats were sacrificed 24h (low dose) and 5 h (high dose) after the final (5<sup>th</sup>) dose. The following tissues were sampled: liver, perirenal fat, mesenteric fat, subcutaneous fat, kidneys, and muscle from triceps, gracilis and longissimus dorsi. Additionally, bile and the contents of the gastrointestinal tract were collected.

Total radioactivity in homogenised samples was determined by LSC, combustion/LSC or after solubilising by LSC.

Urine, bile and milk samples were extracted with ethyl acetate (2x) after acidification of the sample to pH 2 with 6M HCl. The faeces, tissue and organ samples were extracted with methanol (2x), after which the extract was concentrated to the aqueous phase and extracted with ethyl acetate. Radioactivity in aqueous and organic phases was determined by LSC. Ethyl acetate phases were concentrated prior to 1-D or 2-D TLC analysis. Subsamples of the aqueous phase were subjected to hydrolysis with acid (1M HCl) or base (1M NaOH) and partitioned against ethyl acetate. Radioactivity in organic and aqueous phases was determined by LSC and the ethyl acetate phases were concentrated prior to 1-D or 2-D TLC analysis. Portions of urine, faeces and liver were also subjected to enzymatic hydrolysis (β-glucuronidase/sulphatase)

in a 0.2M acetate buffer (37°C, 6 hours, pH 5). After this incubation more  $\beta$ -glucuronidase/sulphatase was added and further incubated for 18 hours. The extract was partitioned against ethyl acetate. Radioactivity in organic and aqueous phases was determined by LSC and the ethyl acetate phases were concentrated prior to 1-D or 2-D TLC analysis. The solid residue of the MeOH-extracted liver samples was treated with a non-specific protease (Pronase E) in triethylamine acetate buffer (37°C, 18 hours, pH 7.4), after which more enzyme was added and the incubation continued, this time for 3 hours, to release bound material. The extract was partitioned against ethyl acetate. Radioactivity in organic and aqueous phase was determined by LSC. Ethyl acetate phases of liver extracts were also analysed by reversed phase HPLC-RAM.

All samples that could not be analysed immediately were stored frozen (-20°C) as soon as possible after collection. Storage stability was determined, after storage up to 27 months at -20°C, with HPLC-analysis and found acceptable.

Metabolite identification was obtained in high-dose samples by co-chromatography with reference compounds.

## Results

Total radioactivity in urine, faeces, cage wash, blood, milk, liver, fat (perirenal, mesenteric and subcutaneous), kidneys, muscle (triceps, gracilis and longissimus dorsi), bile and gastrointestinal tract contents is given in Table B.7.2.1-01. The recovery of radioactivity in the low dose group was 71.4% (Pz) and 67.4% (Bz), while in the high dose group 60.1% (Pz) and 45.7% (Bz) was recovered.

Further fractionation of radioactivity is given in Tables B.7.2-02 and -03. Metabolite identifications are given in the text below.

No radioactivity was detected in blood from goats in the low dose group, except in plasma from the Pz-treated goat (0.4-0.6  $\mu\text{g eq/L}$ ). In the high dose group (after doses 1-4), concentrations in blood ranged between 1.3 and 2.1  $\mu\text{g eq/L}$  for the Pz-treated goat and 1.6 and 4.1  $\mu\text{g eq/L}$  for the Bz-treated goat. After the final dose the concentrations were 6.1 and 4.7  $\mu\text{g eq/L}$  respectively.

In milk 0.4% (Pz) and 0.2% (Bz), corresponding to 1  $\mu\text{g eq/L}$  for each label, was recovered in the low dose group, while in the high dose group the concentrations ranged between 3.5-9.3  $\mu\text{g eq/mL}$  for Pz-milk and 1.4-2.9  $\mu\text{g eq/L}$  for Bz-milk. A plateau was reached between 2 and 3 days for the residue levels in milk from both doses and both labels.

In tissues and organs, of low dosed goats, the residue levels for Pz-labelled pyridaben were all smaller than 0.01 mg eq/kg except fat (0.012 mg eq/kg). For Bz-labelled pyridaben residues in all tissues and organs were below 0.01 mg eq/kg. In the high dosed Pz-group, residue levels were 0.14 mg eq/kg for liver, 0.03 mg eq/kg in kidney, 0.009 mg eq/kg in muscle and 0.06 mg eq/kg for fat. In the high dosed Bz-group, residues

were found in liver (0.11 mg eq/kg), 0.02 mg eq/kg in kidney, 0.005 mg eq/kg in muscle and 0.03 mg eq/kg in fat.

In ethyl acetate extracts of urine from Pz- and Bz-treated goats, PB-3 (0.09% of mean daily dose (MDD)) and PB-7 (<0.01% MDD) were the only two identified fractions. Other fractions (10,  $\leq 0.86\%$  MDD) could not be attributed to single reference compounds. Acid/alkali treatment or enzyme treatments released PB-11 (0.20% MDD). Other released fractions (at least 6,  $\leq 1.49\%$  MDD) could not be attributed to a single reference compound. Identifications and quantifications in urine are tentative as TLC regions were poorly resolved and no confirmation with a second technique was obtained.

In the ethyl acetate extracts of Pz- and Bz-faeces, two metabolites were identified: PB-7 (0.66% MDD) and PB-9 (1.61% MDD). Other fractions (at least 4,  $\leq 14.8\%$  mean daily dose) could not be attributed to single reference compounds. Acid/alkali treatment or enzyme treatments released several fractions which corresponded to PB-1 (=parent) (2.29% MDD), PB-3 (19.13% MDD), PB-4 (1.22% MDD), PB-12 (0.39% MDD), PB-13 (0.89% MDD), B-1 (0.08% MDD), B-3 (0.09% MDD), B-7 (0.22% MDD) and B-8 (0.07% MDD). Identifications and quantifications in faeces are tentative as TLC regions were often poorly resolved and no confirmation with a second technique was obtained.

In Pz- and Bz-bile, at least 9 fractions were observed, of which three were identified as P-3 (<0.01% MDD), B-8 (<0.01% MDD) and PB-9 (<0.01% MDD). Other fractions ( $\leq 0.13\%$  MDD) could not be attributed to single reference compounds.

In the ethyl acetate extracts of Pz- and Bz-liver, 3 to 5 fractions were observed, of which three were identified as P-1 (0.05% MDD), PB-9 (0.01% MDD) and PB-11 (<0.01% MDD). Other fractions ( $\leq 0.09\%$  MDD) could not be attributed to single reference compounds. In extracts following acid/alkali treatment or enzyme treatment, several fractions ( $\leq 0.18\%$  MDD) were observed which did not match with single reference compounds. Based on HPLC analysis, PB-1 (=parent) (17.6% TRR, 0.025 mg eq/kg), PB-7 (3.75% TRR, 0.005 mg eq/kg) and PB-9 (5.11% TRR, 0.007 mg eq/kg) were identified in the liver (and confirmed by TLC).

In the ethyl acetate extracts of Pz- and Bz-kidney, 5 fractions were observed, of which three were identified as P-3 (<0.01% MDD), PB-11 (0.01% MDD) and B-7 (<0.01% MDD). Other fractions ( $\leq 0.01\%$  MDD) could not be attributed to a single reference compound. Identifications are tentative as no confirmation with a second technique was obtained.

In muscle, at least 3 fractions were observed (<0.01% MDD) which did not match with single reference compounds.

In fat, 3-5 fractions (all <0.01% MDD) were observed of which two were identified as PB-12 (<0.01% MDD) and B-1 (<0.01% MDD). Other fractions could not be attributed to single reference compounds. Identifications are tentative as no confirmation with a second technique was obtained.

**Table B.7.2.1-01** Distribution of radioactivity in goat tissues, milk and excreta after 5 doses [pyridazinone-<sup>14</sup>C] or [benzyl-<sup>14</sup>C] pyridaben at 0.5 or 20 mg/day (% of total dose)

|           | % of total dose                 |           |                           |           |
|-----------|---------------------------------|-----------|---------------------------|-----------|
|           | [pyridazinone- <sup>14</sup> C] |           | [benzyl- <sup>14</sup> C] |           |
|           | 0.5 mg/day                      | 20 mg/day | 0.5 mg/day                | 20 mg/day |
| Urine     | 3.1                             | 2.2       | 5.9                       | 2.6       |
| Faeces    | 60.1                            | 45.9      | 56.7                      | 31.4      |
| Cage wash | 0.0                             | 0.0       | 0.0                       | 0.0       |
| Milk      | 0.4                             | 0.0       | 0.2                       | 0.0       |
| Bile      | 0.0                             | 0.1       | 0.1                       | 0.1       |
| Tissues   | 0.4                             | 0.2       | 0.1                       | 0.1       |
| GIT       | 7.4                             | 11.7      | 4.4                       | 11.5      |
| Total     | 71.4                            | 60.1      | 67.4                      | 45.7      |

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**Table B.7.2.1-02** Total radioactivity in goat tissues, milk and excreta after 5 doses [pyridazinone-<sup>14</sup>C] or [benzyl-<sup>14</sup>C] pyridaben at 0.5 mg/day (expressed as % of mean daily dose).

|                     | [pyridazinone- <sup>14</sup> C] |                     | [benzyl- <sup>14</sup> C] |                     |
|---------------------|---------------------------------|---------------------|---------------------------|---------------------|
|                     | % mean daily dose               | mg eq/kg or mg eq/L | % mean daily dose         | mg eq/kg or mg eq/L |
| Urine               |                                 |                     |                           |                     |
| Urine day 1         | 2.8 <sup>(B)</sup>              | nr <sup>(A)</sup>   | 5.5 <sup>(B)</sup>        | nr                  |
| Urine day 2         | 1.9 <sup>(B)</sup>              | nr                  | 6.0 <sup>(B)</sup>        | nr                  |
| Urine day 3         | 2.6 <sup>(B)</sup>              | nr                  | 7.8 <sup>(B)</sup>        | nr                  |
| Urine day 4         | 2.8 <sup>(B)</sup>              | nr                  | 7.6 <sup>(B)</sup>        | nr                  |
| Urine day 5         | 5.4 <sup>(B)</sup>              | nr                  | 2.8 <sup>(B)</sup>        | nr                  |
| Faeces              |                                 |                     |                           |                     |
| Faeces day 1        | 29.0 <sup>(B)</sup>             | nr                  | 34.3 <sup>(B)</sup>       | nr                  |
| Faeces day 2        | 55.4 <sup>(B)</sup>             | nr                  | 55.7 <sup>(B)</sup>       | nr                  |
| Faeces day 3        | 67.6 <sup>(B)</sup>             | nr                  | 64.5 <sup>(B)</sup>       | nr                  |
| Faeces day 4        | 76.7 <sup>(B)</sup>             | nr                  | 64.9 <sup>(B)</sup>       | nr                  |
| Faeces day 5        | 71.5 <sup>(B)</sup>             | nr                  | 64.9 <sup>(B)</sup>       | nr                  |
| Cage wash           | 0.0                             |                     | 0.2                       |                     |
| Blood               |                                 |                     |                           |                     |
| Blood day 1         | nd <sup>(C)</sup>               | nd <sup>(C)</sup>   | nd <sup>(C)</sup>         | nd <sup>(C)</sup>   |
| Blood day 2         | nd <sup>(C)</sup>               | nd <sup>(C)</sup>   | nd <sup>(C)</sup>         | nd <sup>(C)</sup>   |
| Blood day 3         | nd <sup>(C)</sup>               | nd <sup>(C)</sup>   | nd <sup>(C)</sup>         | nd <sup>(C)</sup>   |
| Blood day 4         | nd <sup>(C)</sup>               | nd <sup>(C)</sup>   | nd <sup>(C)</sup>         | nd <sup>(C)</sup>   |
| Blood day 5         | nd <sup>(C)</sup>               | nd <sup>(C)</sup>   | nd <sup>(C)</sup>         | nd <sup>(C)</sup>   |
| Plasma              |                                 |                     |                           |                     |
| Plasma day 1        | nr                              | 0.0004              | nr                        | nd <sup>(C)</sup>   |
| Plasma day 2        | nr                              | nd <sup>(C)</sup>   | nr                        | nd <sup>(C)</sup>   |
| Plasma day 3        | nr                              | 0.0006              | nr                        | nd <sup>(C)</sup>   |
| Plasma day 4        | nr                              | 0.0005              | nr                        | nd <sup>(C)</sup>   |
| Plasma day 5        | nr                              | 0.0004              | nr                        | nd <sup>(C)</sup>   |
| Milk                |                                 |                     |                           |                     |
| Milk day 1 pm       | 0.1                             | 0.0008              | 0.1                       | 0.0007              |
| am                  | 0.2                             | 0.0008              | 0.1                       | 0.0005              |
| Milk day 2 pm       | 0.2                             | 0.0011              | 0.1                       | 0.0007              |
| am                  | 0.3                             | 0.0010              | 0.2                       | 0.0007              |
| Milk day 3 pm       | 0.2                             | 0.0012              | 0.1                       | 0.0006              |
| am                  | 0.3                             | 0.0010              | 0.1                       | 0.0006              |
| Milk day 4 pm       | 0.2                             | 0.0013              | 0.1                       | 0.0006              |
| am                  | 0.3                             | 0.0008              | 0.1                       | 0.0005              |
| Milk day 5 pm       | 0.1                             | 0.0011              | 0.1                       | 0.0007              |
| am                  | 0.3                             | 0.0010              | 0.1                       | 0.0005              |
| Liver               | 0.8                             | 0.0043              | 0.5                       | 0.0018              |
| Fat                 |                                 |                     |                           |                     |
| perirenal           | 0.5                             | 0.0116              | nd <sup>(C)</sup>         | nd <sup>(C)</sup>   |
| mesenteric          | 0.3                             | 0.0116              | nd <sup>(C)</sup>         | nd <sup>(C)</sup>   |
| subcutaneous        | 0.0                             | 0.0065              | nd <sup>(C)</sup>         | nd <sup>(C)</sup>   |
| Kidneys             | 0.0                             | 0.0011              | 0.0                       | 0.0007              |
| Muscle              |                                 |                     |                           |                     |
| triceps             | 0.0                             | 0.0009              | nd <sup>(C)</sup>         | nd <sup>(C)</sup>   |
| gracilis            | 0.0                             | 0.0024              | nd <sup>(C)</sup>         | nd <sup>(C)</sup>   |
| longissimus dorsi   | nd <sup>(C)</sup>               | nd <sup>(C)</sup>   | nd <sup>(C)</sup>         | nd <sup>(C)</sup>   |
| Bile                | 0.1                             | 0.0506              | 0.5                       | 0.0575              |
| GI tract + contents | 37.1                            |                     | 21.9                      |                     |
| intestinal contents | 26.7                            | 0.0407              | 17.9                      | 0.0382              |
| rumen contents      | 10.4                            | 0.0063              | 4.0                       | 0.0034              |

(A) nr: not reported

(B) Recovery of radioactivity in urine or faeces, 24 hours after each of the 5 daily doses

(C) Results within background range

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**Table B.7.2.1-03** Total radioactivity in goat excreta, cage wash, blood, milk, tissues, bile and gastrointestinal tract + contents after 5 doses [pyridazinone-<sup>14</sup>C] or [benzyl-<sup>14</sup>C] pyridaben at 20 mg/day (expressed as % of mean daily dose).

|                              | [pyridazinone- <sup>14</sup> C] |                     | [benzyl- <sup>14</sup> C] |                     |
|------------------------------|---------------------------------|---------------------|---------------------------|---------------------|
|                              | % mean daily dose               | mg eq/kg or mg eq/L | % mean daily dose         | mg eq/kg or mg eq/L |
| <b>Urine<sup>(C)</sup></b>   |                                 |                     |                           |                     |
| Urine day 1                  | 1.2 <sup>(B)</sup>              | nr <sup>(A)</sup>   | 2.7 <sup>(B)</sup>        | nr <sup>(A)</sup>   |
| Urine day 2                  | 1.6 <sup>(B)</sup>              | nr                  | 3.2 <sup>(B)</sup>        | nr                  |
| Urine day 3                  | 0.8 <sup>(B)</sup>              | nr                  | 3.0 <sup>(B)</sup>        | nr                  |
| Urine day 4                  | 1.5 <sup>(B)</sup>              | nr                  | 3.2 <sup>(B)</sup>        | nr                  |
| Urine day 5                  | 0.4 <sup>(B)</sup>              | nr                  | 1.1 <sup>(B)</sup>        | nr                  |
| <b>Faeces<sup>(D)</sup></b>  |                                 |                     |                           |                     |
| Faeces day 1                 | 37.4 <sup>(B)</sup>             | nr <sup>(A)</sup>   | 29.6 <sup>(B)</sup>       | nr <sup>(A)</sup>   |
| Faeces day 2                 | 48.5 <sup>(B)</sup>             | nr                  | 40.8 <sup>(B)</sup>       | nr                  |
| Faeces day 3                 | 71.6 <sup>(B)</sup>             | nr                  | 40.2 <sup>(B)</sup>       | nr                  |
| Faeces day 4                 | 65.9 <sup>(B)</sup>             | nr                  | 34.5 <sup>(B)</sup>       | nr                  |
| Faeces day 5                 | 6.0 <sup>(B)</sup>              | nr                  | 12.1 <sup>(B)</sup>       | nr                  |
| <b>Cage wash</b>             | 0.1                             |                     | 0.2                       |                     |
| <b>Blood</b>                 |                                 |                     |                           |                     |
| Blood day 1                  | nr <sup>(A)</sup>               | 0.0016              | nr <sup>(A)</sup>         | 0.0021              |
| Blood day 2                  | nr                              | 0.0021              | nr                        | 0.0026              |
| Blood day 3                  | nr                              | 0.0013              | nr                        | 0.0016              |
| Blood day 4                  | nr                              | 0.0021              | nr                        | 0.0041              |
| Blood day 5                  | nr                              | 0.0061              | nr                        | 0.0047              |
| <b>Plasma</b>                |                                 |                     |                           |                     |
| Plasma day 1                 | nr <sup>(A)</sup>               | 0.0033              | nr <sup>(A)</sup>         | 0.0032              |
| Plasma day 2                 | nr                              | 0.0031              | nr                        | 0.0045              |
| Plasma day 3                 | nr                              | 0.0045              | nr                        | 0.0035              |
| Plasma day 4                 | nr                              | 0.0027              | nr                        | 0.0049              |
| Plasma day 5                 | nr                              | 0.0084              | nr                        | 0.0069              |
| <b>Milk<sup>(E)</sup></b>    |                                 |                     |                           |                     |
| Milk day 1                   | 0.0                             | 0.0045              | 0.0                       | 0.0014              |
|                              | 0.0                             | 0.0035              | 0.0                       | 0.0018              |
| Milk day 2                   | 0.0                             | 0.0093              | 0.0                       | 0.0029              |
|                              | 0.0                             | 0.0043              | 0.0                       | 0.0019              |
| Milk day 3                   | 0.0                             | 0.0067              | 0.0                       | 0.0023              |
|                              | 0.0                             | 0.0038              | 0.0                       | 0.0020              |
| Milk day 4                   | 0.0                             | 0.0068              | 0.0                       | 0.0028              |
|                              | 0.0                             | 0.0039              | 0.0                       | 0.0019              |
| Milk day 5                   | 0.0                             | 0.0049              | 0.0                       | 0.0023              |
| <b>Liver<sup>(F)</sup></b>   | 0.7                             | 0.139               | 0.7                       | 0.106               |
| <b>Fat<sup>(G)</sup></b>     | 0.0                             | 0.0588              | 0.0                       | 0.0261              |
| <b>Kidneys<sup>(H)</sup></b> | 0.0                             | 0.0335              | 0.0                       | 0.0190              |
| <b>Muscle<sup>(I)</sup></b>  | 0.0                             | 0.0093              | 0.0                       | 0.0049              |
| <b>Bile<sup>(J)</sup></b>    | 0.3                             | 2.890               | 0.3                       | 1.730               |
| <b>GI tract + contents</b>   | 58.9                            | 1.470               | 57.5                      | 1.640               |

(A) nr: not reported.

(B) Recovery of radioactivity in urine or faeces, 24 hours after each of the 5 daily doses.

(C) ethyl acetate extracted 34% radioactive material from the Pz-urine and 71% from Bz-urine, acid/alkali treatment resulted in 65%/46% (Pz) and 63%/58% (Bz), and  $\beta$ -glucuronidase/sulphatase in 52% (Pz) and 71% (Bz) extraction.

(D) ethyl acetate extracted 30% radioactive material from the Pz-faeces and 47% from Bz-faeces, acid/alkali treatment resulted in 80%/73% (Pz) and 90%/66% (Bz), and  $\beta$ -glucuronidase/sulphatase (with/without) in 81%/76% (Pz) and 79%/68% (Bz) extraction.

(E) ethyl acetate extracted 66% radioactive material from the Pz-milk and 81% from Bz-milk.

(F) ethyl acetate extracted 30% radioactive material from both Pz-liver and Bz-liver, acid/alkali treatment resulted in 53%/76% (Pz) and 75%/52% (Bz), and  $\beta$ -glucuronidase/sulphatase (with/without) in 78%/67% (Pz) and 75%/74% (Bz) extraction.

(G) ethyl acetate extracted 40% radioactive material from the Pz-fat and 60% from Bz-fat.

(H) ethyl acetate extracted 80% radioactive material from both Pz-kidney and Bz-kidney.

(I) ethyl acetate extracted 80% radioactive material from both Pz-muscle and Bz-muscle.

(J) ethyl acetate extracted 66% radioactive material from the Pz-bile and 60% from Bz-bile.

## Conclusions

After five daily dose administrations of [Pyridazinone-<sup>14</sup>C] or [Benzyl-<sup>14</sup>C] pyridaben at 0.5 or 20 mg/day, 34-63.2% of the total administered dose was recovered in excreta (urine, faeces and cage wash). In total, 4.6-12.0% of the administered dose was recovered in the tissues, of which 94.9-98.3% in the gastrointestinal tract and its contents. Total recovery of radioactivity was 45.7-71.4% of the total administered dose. Total residue levels in the low dose tissues were highest in fat (Pz-only, 0.012 mg eq/kg), followed by liver (max 0.0043 mg eq/kg), muscle (max 0.0024 mg eq/kg) and kidney (max 0.0011 mg eq/kg). The maximum residue level in milk was 0.0013 mg eq/kg (day 4). A plateau was reached after 2-3 days. The total residue levels in the high dose tissues were highest in liver (0.139 mg eq/kg), followed by fat (0.0588 mg eq/kg), kidneys (0.0335 mg eq/kg) and muscle (0.0093 mg eq/kg). The maximum residue in milk was 0.0093 mg eq/L (day 2).

In urine PB-3 (0.09% of mean daily dose (MDD)) and PB-7 (<0.01% MDD) were the only two tentatively identified fractions. Other fractions were ≤0.86% MDD. Acid/alkali treatment or enzyme treatments released PB-11 (0.20% MDD). Other released fractions were ≤1.49% MDD. Identifications and quantifications in urine are tentative as TLC regions were poorly resolved and no confirmation with a second technique was obtained.

In faeces, two metabolites were tentatively identified: PB-7 (0.66% MDD) and PB-9 (1.61% MDD). Other fractions were ≤14.8% MDD. Acid/alkali treatment or enzyme treatments released several fractions which corresponded to PB-1 (2.29% MDD), PB-3 (19.13% MDD), PB-4 (1.22% MDD), PB-12 (0.39% MDD), PB-13 (0.89% MDD), B-1 (0.08% MDD), B-3 (0.09% MDD), B-7 (0.22% MDD) and B-8 (0.07% MDD). Identifications and quantifications in faeces are tentative as TLC regions were often poorly resolved and no confirmation with a second technique was obtained.

In bile three fractions were tentatively identified as P-3 (<0.01% MDD), B-8 (<0.01% MDD) and PB-9 (<0.01% MDD). Other fractions were ≤0.13% MDD. Identifications are tentative as no confirmation with a second technique was obtained.

In the liver three fractions were tentatively identified as P-1 (0.05% MDD), PB-9 (0.01%) and PB-11 (<0.01% MDD). Other fractions were ≤0.09% MDD. In extracts following acid/alkali treatment or enzyme treatment, several fractions (≤0.18% MDD) were observed which did not match with single reference compounds. Based on HPLC analysis, PB-1 (17.6% TRR, 0.025 mg eq/kg), PB-7 (3.75% TRR, 0.005 mg eq/kg) and PB-9 (5.11% TRR, 0.007 mg eq/kg) were identified in the liver (and confirmed by TLC).

In kidney three fractions were tentatively identified as P-3 (<0.01% MDD), PB-11 (0.01% MDD) and B-7 (<0.01% MDD). Other fractions were ≤0.01% MDD. In muscle, at least 3 fractions were observed (<0.01% of

MDD) which did not match with single reference compounds. In fat, 3-5 fractions (all <0.01% MDD) were observed of which two were identified as PB-12 (<0.01% MDD) and B-1 (<0.01% MDD).

### Guidelines and limitations

1. Metabolite identifications were not confirmed by a second analytical technique, with the exception of liver metabolites.
2. The low dose was 0.2 mg/kg feed as received (and >0.2 mg/kg dry feed). Provisional intake calculations for cattle resulted in a maximum feed concentration of 0.17 mg/kg dry weight, which is lower than the lowest dose in this study. (Note: the intake calculation for cattle was based on a HR (whole fruit, oranges) of 0.12 mg/kg and a wet pomace processing factor of 1.1. The HR value is provisional as the field residue trials were not conducted under least favourable conditions)

### B.7.2.2 Poultry

#### STUDY 1

##### Characteristics

|                   |                                                                                                                                                                                                                                                 |               |                                                                                                      |
|-------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------|------------------------------------------------------------------------------------------------------|
| Reference         | : Hallifax, D., 1994 (IIA, 6.2/02)<br>O'Connor, J., 1996 (addendum to report)                                                                                                                                                                   | GLP statement | : yes                                                                                                |
| Type of study     | : distribution and metabolism                                                                                                                                                                                                                   | Guideline     | : EPA O: 171-4 (b)                                                                                   |
| Year of execution | : 1991-1993                                                                                                                                                                                                                                     | Dose          | : 12.5 µg/day or 1 mg/day for 8 consecutive days                                                     |
| Test substance    | : [pyridazinone- <sup>14</sup> C] pyridaben (radiochem. purity ≥97.4%, lot no. CP-1008).<br>[benzyl- <sup>14</sup> C] pyridaben (radiochem. purity ≥96.6%, lot no. CP-1007).<br>non-labelled pyridaben (chemical purity 99.6% lot no. 129T8604) | Vehicle       | : gelatin capsules filled with cellulose                                                             |
|                   |                                                                                                                                                                                                                                                 | Concentration | : ca. 0.1 mg/kg (low dose) or ca 7 mg/kg (high dose) feed as received                                |
|                   |                                                                                                                                                                                                                                                 | Total dose    | : low dose: 224-264 kBq/100 µg<br>high dose: 17.6-21.6 MBq/8 mg                                      |
| Animal            | : laying hens (Stirling Ranger strain)                                                                                                                                                                                                          | Sampling      | : eggs, excreta, cage wash, muscle, liver, fat, skin with fat, and gastrointestinal tract + contents |

##### Study design

Groups of 10 laying hens (Stirling Ranger strain) received daily oral doses of [Pyridazinone-<sup>14</sup>C] or [Benzyl-<sup>14</sup>C] pyridaben, contained in gelatin capsules for 8 consecutive days at a rate of 0.1 mg/kg diet as received or 7 mg/kg diet as received. The hens had been acclimated between 2 and 3 weeks before dosing. Ten control hens were included in the study.

Eggs were collected daily and the shell separated from the white and yolk which were combined. Excreta were collected once daily. At the end of dosing, the cages were rinsed with methanol and radioactivity in the rinsates was determined by LSC. Hens were sacrificed 24 h (low dose) or 5 h (high dose) after administration of the last (8<sup>th</sup>) dose and breast and thigh muscle, liver, abdominal fat and skin with fat and the gastrointestinal tract and contents were collected.

Total radioactivity in homogenised samples was determined by LSC, combustion/LSC or by solubilising/LSC. The excreta, liver, muscle, fat and skin homogenates were extracted with methanol (2x). The extract was

concentrated to the aqueous phase, adjusted to pH 2 with 6M HCL and extracted twice with ethyl acetate. Radioactivity in organic and aqueous phases was determined by LSC. The organic phase was concentrated prior to TLC and HPLC (liver only) analysis. The aqueous phase was subjected to acid (1M HCl) and base (1M NaOH) hydrolysis (reflux, 2 h). After hydrolysis, the extract was adjusted to pH 2 with 6M HCL and extracted with ethyl acetate. Radioactivity in organic and aqueous phases was determined by LSC. The organic phase was concentrated prior to TLC analysis. Further portions of excreta and liver homogenates were hydrolysed with  $\beta$ -glucuronidase/sulphatase. First, the homogenates were adjusted with HCl to pH 5 and then incubated with  $\beta$ -glucuronidase/sulphatase in 0.2M acetate buffer (6 hours, 37°C), after this, more enzyme was added and the sample incubated for another 18 hours. After enzyme treatment, the extract was adjusted to pH 2 with 6M HCL and extracted with ethyl acetate. Radioactivity in organic and aqueous phases was determined by LSC. The organic phase was concentrated prior to TLC analysis.

Storage stability was determined in liver samples which were stored at -20°C and reextracted after 15 and 26 months and found acceptable.

Metabolite identification was obtained in high dose samples by co-chromatography with reference compounds.

## Results

The distribution of radioactivity in tissues, eggs, excreta and cage wash is given in Table B.7.2.2-01 and B.7.2.2-02. Of the total administered dose, 61.9-78.2% (Pz-label) and 70.1-88.2% (Bz-label) was recovered in excreta (including cage wash). Total recovery of radioactivity was 74.3-79.3% (Pz) and 64.3-89.1% (Bz). Daily cumulative excretion of radioactivity is given in Table B.7.2.2-03.

The maximum residue level in eggs (yolk/white combined), after the high dose treatment, was 0.0142 mg eq/kg (Pz-label) and 0.019 mg eq/kg (Bz-label) (Table B.7.2.2-04). For the low dose, egg residues were <0.001 mg eq/kg. In total maximum 0.05% of the total administered dose was recovered in eggs. No plateau was reached for both the Pz- and Bz-label.

In the tissues (including GI-tract), 1.1-4.2% (Pz) and 0.9-2.4% (Bz) of the total administered dose was recovered. The Pz-label residue levels were 0.0249/5.89 mg eq/kg (GI-tract, low/high dose), 0.0002/0.119 mg eq/kg (liver, low/high dose), 0.0001/0.010 mg eq/kg (muscle, low/high dose) and 0.0001/0.056 mg eq/kg (skin, low/high dose). The Bz-label residue levels were 0.0253/3.32 mg eq/kg (GI-tract, low/high dose), nd/0.089 mg eq/kg (liver, low/high dose), nd/0.015 mg eq/kg (muscle, low/high dose) and nd/0.042 mg eq/kg (skin, low/high dose). (nd = not detected).

Results of extraction and chromatography of samples are given in Tables B.7.2.2-05. In ethyl acetate of excreta from Pz- and Bz-treated hens, PB-12 (2.35% of mean daily dose (MDD)) and PB-13 (0.9% MDD) were the only two identified fractions. Other fractions (4-7,  $\leq$ 12.16% MDD) could not be attributed to single

reference compounds. Acid/alkali treatment or enzyme treatments released B-7 (1.54% MDD) and PB-4 (2.26% MDD). Other released fractions (4-7,  $\leq 31.24\%$  MDD) could not be attributed to single reference compounds. Identifications and quantifications in hen excreta are tentative as TLC regions were poorly resolved and no confirmation with a second technique was obtained.

In the ethyl acetate extracts of Pz- and Bz-liver, at least 4 fractions were observed, of which three were identified as PB-12 (0.01% MDD), PB-9 (0.01% MDD) and PB-7 (0.14% MDD). Other fractions ( $\leq 0.11\%$  MDD) could not be attributed to single reference compounds. In extracts following acid/alkali treatment or enzyme treatment, several fractions ( $\leq 0.12\%$  MDD) were observed of which one was identified as PB-13 (0.03% MDD). Identifications of PB-12 and PB-13 are tentative (not confirmed by a second method). PB-7 and PB-9 were confirmed by HPLC and TLC.

In the ethyl acetate extracts of Pz- and Bz-eggs, 4-5 fractions were observed, of which one was identified as D-1 ( $<0.05\%$  MDD). Other fractions ( $<0.05\%$  MDD) could not be attributed to single reference compounds. Identifications are tentative as no confirmation with a second technique was obtained.

In muscle, at least 3 fractions were observed ( $<0.05\%$  MDD) of which one was identified as PB-13 ( $<0.05\%$  MDD). Identifications are tentative as no confirmation with a second technique was obtained.

In fat, 3-4 fractions (all  $<0.05\%$  MDD) were observed of which two were identified as PB-11 ( $<0.05\%$  MDD) and B-11 ( $<0.05\%$  MDD). Other fractions could not be attributed to single reference compounds. Identifications are tentative as no confirmation with a second technique was obtained.

In skin, 2.6 fractions (all  $<0.05\%$  MDD) were observed of which two were identified as PB-7 ( $<0.05\%$  MDD) and PB-9 ( $<0.05\%$  MDD). Other fractions could not be attributed to single reference compounds. Identifications are tentative as no confirmation with a second technique was obtained.

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**Table B.7.2.2-01** Total radioactivity in hen excreta, eggs, tissues and organs after 8 doses [pyridazinone-<sup>14</sup>C] or [benzyl-<sup>14</sup>C] pyridaben at 12.5 µg/day

|                  | [pyridazinone- <sup>14</sup> C] |          | [benzyl- <sup>14</sup> C] |          |
|------------------|---------------------------------|----------|---------------------------|----------|
|                  | % of total dose                 | mg eq/kg | % of total dose           | mg eq/kg |
| Excreta          | 77.7                            | -        | 87.4                      | -        |
| Egg (yolk+white) | 0.01                            | -        | <0.01                     | -        |
| Egg shell        | nd                              | -        | nd                        | nd       |
| Cage wash+debris | 0.49                            | -        | 0.84                      | -        |
| Liver            | <0.05                           | 0.0002   | nd                        | nd       |
| Skin             | <0.05                           | 0.0001   | nd                        | nd       |
| Fat              |                                 |          |                           |          |
| abdominal        | nd                              | nd       | nd                        | nd       |
| skin             | nd                              | nd       | nd                        | nd       |
| Muscle           |                                 |          | nd                        | nd       |
| breast           | <0.05                           | 0.0001   | nd                        | nd       |
| thigh            | nd                              | nd       | nd                        | nd       |
| GI-tract         | 1.1                             | 0.0249   | 0.88                      | 0.0253   |
| Total            | 79.3                            | -        | 89.1                      | -        |

nd: not detected

**Table B.7.2.2-02** Total radioactivity in hen excreta, eggs, tissues and organs after 8 doses [pyridazinone-<sup>14</sup>C] or [benzyl-<sup>14</sup>C] pyridaben at 1 mg/day

|                  | [pyridazinone- <sup>14</sup> C] |          | [benzyl- <sup>14</sup> C] |          |
|------------------|---------------------------------|----------|---------------------------|----------|
|                  | % of total dose                 | mg eq/kg | % of total dose           | mg eq/kg |
| Excreta          | 69.4                            | -        | 61.5                      | -        |
| Egg (yolk+white) | 0.04                            | -        | 0.05                      | -        |
| Egg shell        | <0.01                           | -        | <0.01                     | -        |
| Cage wash+debris | 0.65                            | -        | 0.40                      | -        |
| Liver            | 0.08                            | 0.119    | 0.06                      | 0.089    |
| Skin             | <0.01                           | 0.056    | <0.01                     | 0.042    |
| Fat              |                                 |          |                           |          |
| abdominal        | <0.01                           | 0.028    | <0.01                     | 0.027    |
| skin             | <0.01                           | 0.028    | <0.01                     | 0.031    |
| Muscle           |                                 |          |                           |          |
| breast           | <0.01                           | 0.009    | <0.01                     | 0.010    |
| thigh            | <0.01                           | 0.010    | <0.01                     | 0.015    |
| GI-tract         | 4.10                            | 5.89     | 2.33                      | 3.320    |
| Total            | 74.3                            | -        | 64.3                      | -        |

nd: not detected

**Table B.7.2.2-03** Total cumulative radioactivity in excreta after 8 doses [pyridazinone-<sup>14</sup>C] or [benzyl-<sup>14</sup>C] pyridaben at 12.5 µg/day or 1 mg/day

| excreta sample | [pyridazinone- <sup>14</sup> C] |                   | [benzyl- <sup>14</sup> C] |                   |
|----------------|---------------------------------|-------------------|---------------------------|-------------------|
|                | low                             | high              | low                       | high              |
|                | % mean daily dose               | % mean daily dose | % mean daily dose         | % mean daily dose |
| day 1          | 67.6                            | 59.9              | 76.3                      | 67.8              |
| day 2          | 69.1                            | 61.9              | 79.8                      | 66.0              |
| day 3          | 71.3                            | 62.5              | 84.5                      | 63.7              |
| day 4          | 73.5                            | 62.6              | 85.2                      | 67.2              |
| day 5          | 73.3                            | 65.7              | 86.8                      | 68.7              |
| day 6          | 74.6                            | 68.1              | 86.4                      | 67.3              |
| day 7          | 76.5                            | 71.8              | 86.1                      | 65.8              |
| day 8          | 77.7                            | 69.4              | 87.4                      | 61.5              |

**Table B.7.2.2-04** Total radioactivity in eggs after 8 doses [pyridazinone-<sup>14</sup>C] or [benzyl-<sup>14</sup>C] pyridaben at 12.5 µg/day or 1 mg/day

| egg<br>sample | [pyridazinone- <sup>14</sup> C] |             |                      |             | [benzyl- <sup>14</sup> C] |             |                      |             |
|---------------|---------------------------------|-------------|----------------------|-------------|---------------------------|-------------|----------------------|-------------|
|               | low                             |             | high                 |             | low                       |             | high                 |             |
|               | % mean<br>daily dose            | mg<br>eq/kg | % mean<br>daily dose | mg<br>eq/kg | % mean<br>daily dose      | mg<br>eq/kg | % mean<br>daily dose | mg<br>eq/kg |
| day 1         | nd                              | nd          | <0.05                | 0.0011      | nd                        | nd          | <0.05                | 0.0003      |
| day 2         | nd                              | nd          | <0.05                | 0.0025      | nd                        | nd          | <0.05                | 0.0031      |
| day 3         | nd                              | nd          | <0.05                | 0.0054      | nd                        | nd          | <0.05                | 0.0049      |
| day 4         | nd                              | nd          | <0.05                | 0.0054      | nd                        | nd          | <0.05                | 0.0085      |
| day 5         | nd                              | nd          | <0.05                | 0.0092      | nd                        | nd          | 0.1                  | 0.0113      |
| day 6         | nd                              | nd          | 0.1                  | 0.0104      | <0.05                     | 0.0001      | 0.1                  | 0.0149      |
| day 7         | nd                              | nd          | 0.1                  | 0.0126      | <0.05                     | 0.0002      | 0.1                  | 0.0165      |
| day 8         | 0.1                             | 0.0001      | 0.1                  | 0.0142      | <0.05                     | 0.0001      | 0.1                  | 0.0190      |

WARNING: This document forms part of an EC evaluation data package and should not be read in isolation. Registrants must not be misled on the basis of this document.

**Table B.7.2.2-05** Characterization/Identification<sup>(A)</sup> of radioactive residues in hen excreta, eggs, tissues and organs after 8 doses [pyridazinone-<sup>14</sup>C] or [benzyl-<sup>14</sup>C] pyridaben at 1 mg/day

|                        | [pyridazinone- <sup>14</sup> C] |                      | [benzyl- <sup>14</sup> C] |                      |
|------------------------|---------------------------------|----------------------|---------------------------|----------------------|
|                        | % mean daily dose               | mg eq/kg             | % mean daily dose         | mg eq/kg             |
| Excreta                | 65.83                           | -                    | 40.11                     | -                    |
| ethyl acetate          | 27.04                           | -                    | 21.17                     | -                    |
| PB-13                  | 0.90                            | -                    | nd                        | -                    |
| PB-12                  | 2.35                            | -                    | nd                        | -                    |
| Aqueous                | 19                              | -                    | 8.84                      | -                    |
| Residue                | 19.79                           | -                    | 10.10                     | -                    |
| Egg (yolk+white)       | 0.04                            | 0.0142               | 0.05                      | 0.0190               |
| Organic                | <0.05                           | nd                   | <0.05                     | <0.05                |
| Aqueous                | <0.05                           |                      | <0.05                     |                      |
| Residue                | 0.04                            |                      | 0.05                      |                      |
| Skin                   | <0.05                           | 0.056                | <0.05                     | 0.042                |
| Organic                | <0.05                           |                      | <0.05                     |                      |
| PB-9                   | <0.05                           |                      | nd                        |                      |
| PB-7                   | <0.05                           |                      | nd                        |                      |
| Aqueous                | <0.05                           |                      | <0.05                     |                      |
| Residue                | <0.05                           |                      | <0.05                     |                      |
| Fat (abdominal + skin) | <0.05                           | 0.028 <sup>(B)</sup> | <0.05                     | 0.029 <sup>(B)</sup> |
| organic                | <0.05                           |                      | <0.05                     |                      |
| B-11                   | nd                              |                      | <0.05                     |                      |
| PB-11                  | nd                              |                      | <0.05                     |                      |
| Aqueous                | <0.05                           |                      | <0.05                     |                      |
| Residue                | <0.05                           |                      | <0.05                     |                      |
| Liver                  | 0.53                            | 0.119                | 0.46                      | 0.089                |
| Organic                | 0.16                            | 0.036                | 0.26                      | 0.050                |
| PB-12                  | 0.01                            | 0.002                | nd                        |                      |
| PB-7                   | 0.10                            | 0.022                | 0.14                      | 0.028                |
| PB-9                   | 0.01                            | 0.002                | nd                        | nd                   |
| Aqueous                | 0.16                            | 0.036                | 0.09                      | 0.017                |
| Residue                | 0.21                            | 0.047                | 0.11                      | 0.021                |
| Muscle (breast)        | <0.05                           | 0.009                | <0.05                     | 0.010                |
| Organic                | <0.05                           |                      | <0.05                     |                      |
| Aqueous                | <0.05                           |                      | <0.05                     |                      |
| Residue                | <0.05                           |                      | <0.05                     |                      |
| Muscle (thigh)         | <0.05                           | 0.010                | <0.05                     | 0.015                |
| Organic                | <0.05                           |                      | <0.05                     |                      |
| PB-13                  | <0.05                           |                      | nd                        |                      |
| Aqueous                | <0.05                           |                      | <0.05                     |                      |
| Residue                | <0.05                           |                      | <0.05                     |                      |

(A) Identifications are tentative (not confirmed by second technique) with the exception of PB-7 and PB-9 in liver.

(B) Mean of abdominal and skin fat

## Conclusions

After eight daily dose administrations of [Pyridazinone-<sup>14</sup>C] or [Benzyl-<sup>14</sup>C] dosed at 12.5 µg/day or 1 mg/day, 61.9-78.2% (Pz-label) and 70.1-88.2% (Bz-label) of the total administered dose was recovered in excreta (including cage wash) and 1.1-4.2% (Pz) and 0.9-2.4% (Bz) in the tissues (including GI tract). Maximum 0.05% of the total administered dose was recovered in eggs and no plateau was reached within the study period (8 days).

The maximum residue level in eggs (yolk/white combined), after the high dose treatment, was 0.0142 mg eq/kg (Pz-label) and 0.019 mg eq/kg (Bz-label) (Table B.7.2.2-04). For the low dose, egg residues were <0.001 mg eq/kg. Maximum residue levels in tissues were 0.0002/0.119 mg eq/kg (liver), 0.0001/0.015 mg eq/kg (muscle), 0.0001/0.056 mg eq/kg (skin) and nd/0.031 mg eq/kg (fat) for low/high dose, respectively. (nd = not detected).

In excreta, PB-12 (2.35% of mean daily dose (MDD)) and PB-13 (0.9% MDD) were the only two tentatively identified fractions. Other fractions (4-7) were ≤12.16% MDD. Acid/alkali treatment or enzyme treatments released B-7 (1.54% MDD) and PB-4 (2.26% MDD).

In the liver, at least 4 fractions were observed, of which three were identified as PB-12 (tentative, 0.01% MDD), PB-9 (confirmed, 0.01% MDD) and PB-7 (confirmed, 0.14% MDD). Other fractions were ≤0.11% MDD. In extracts following acid/alkali treatment or enzyme treatment, several fractions (≤0.12% MDD) were observed of which one was tentatively identified as PB-13 (0.03% MDD).

In eggs, 4-5 fractions were observed, of which one was tentatively identified as D-1 (<0.05% MDD). In muscle, at least 3 fractions were observed (<0.05% MDD) of which one was tentatively identified as PB-13 (<0.05% MDD). In fat, 3-4 fractions (all <0.05% MDD) were observed of which two were tentatively identified as PB-11 (<0.05% MDD) and B-11 (<0.05% MDD). In skin, 2-6 fractions (all <0.05% MDD) were observed of which two were tentatively identified as PB-7 (<0.05% MDD) and PB-9 (<0.05% MDD).

#### Guidelines and limitations

1. Metabolite identifications were not confirmed by a second analytical technique, with the exception of liver metabolites PB-7 and PB-9.
2. The study is supplementary as citrus pomace and tomatoes are not a constituent of poultry feed.

#### B.7.2.3 Summary of studies in ruminants and poultry

Two studies were submitted on the metabolism of pyridaben in livestock, one study in lactating goat and one in laying hen. The study in hen is supplementary as citrus and tomatoes are not fed to chicken. Both studies were acceptable.

In the goat study, after five daily dose administrations of [Pyridazinone-<sup>14</sup>C] or [Benzyl-<sup>14</sup>C] pyridaben at 0.5 or 20 mg/day, 34-63.2% of the total administered dose was recovered in excreta and 4.6-12.0% in the tissues (of which 94.9-98.3% in the GI tract). Total recovery of radioactivity was 45.7-71.4%. Total residue levels in the low dose tissues were highest in fat (Pz-only, 0.012 mg eq/kg), followed by liver (max 0.0043 mg eq/kg), muscle (max 0.0024 mg eq/kg) and kidney (max 0.0011 mg eq/kg). The maximum residue level in milk was 0.0013 mg eq/kg (day 4). A plateau was reached after 2-3 days. The following identifications were obtained in high dose samples, In urine PB-3 (0.09% of mean daily dose (MDD)) and PB-7 (<0.01%

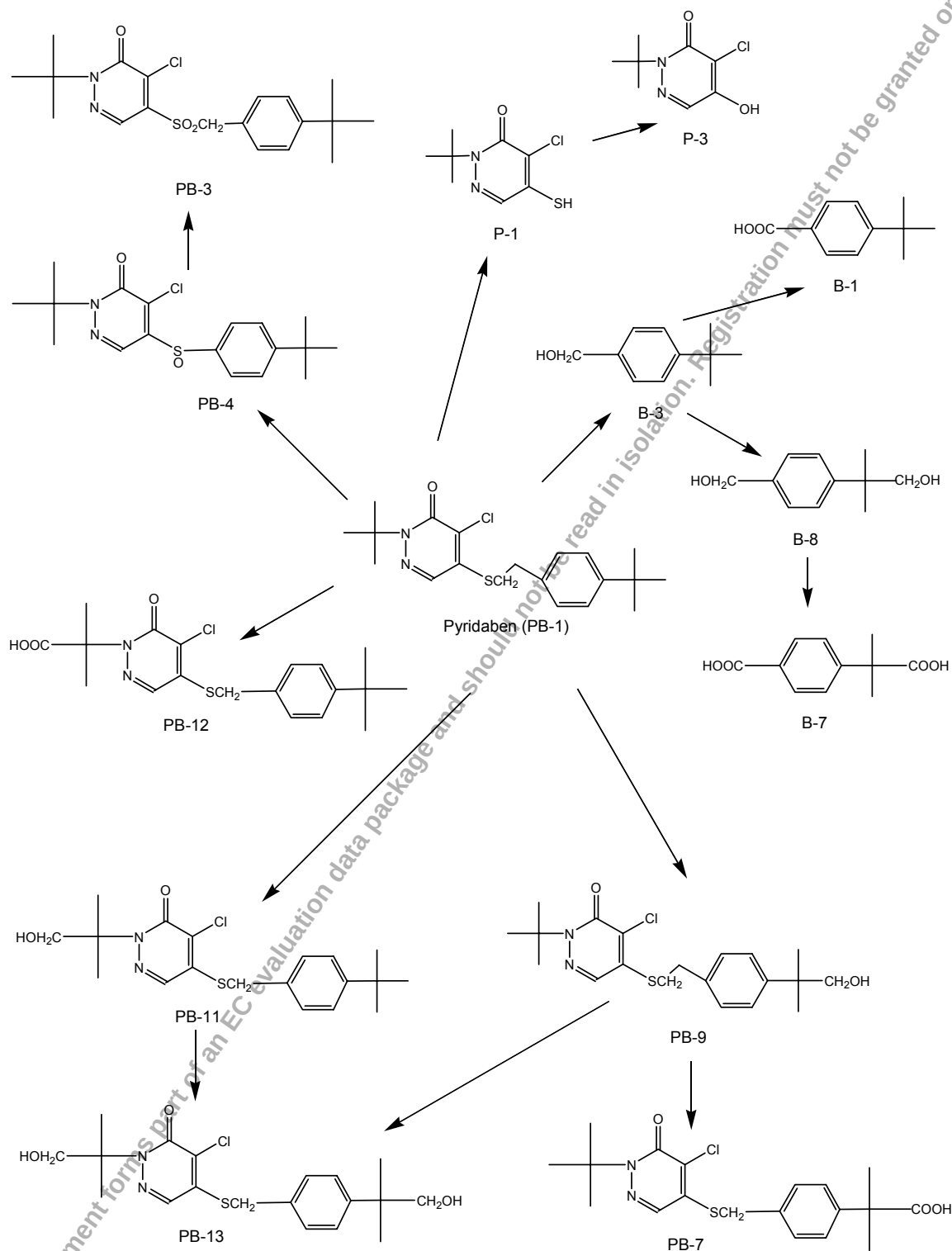
MDD) were tentatively identified. Other fractions were  $\leq 0.86\%$  MDD. In faeces, two metabolites were tentatively identified: PB-7 (0.66% MDD) and PB-9 (1.61% MDD). Other fractions were  $\leq 14.8\%$  MDD. Acid/alkali treatment or enzyme treatments released several fractions ( $\leq 19.13\%$  MDD) which corresponded (tentatively) to PB-1, PB-3, PB-4, PB-12, PB-13, B-1, B-3, B-7 and B-8. In bile, three fractions ( $< 0.01\%$  MDD) were tentatively identified as P-3, B-8 and PB-9. Other fractions were  $\leq 0.13\%$  MDD. In the liver two fractions ( $\leq 0.05\%$  MDD) were tentatively identified as P-1 and PB-11. Other fractions were  $\leq 0.09\%$  MDD. Based on HPLC analysis, PB-1 (17.6% TRR, 0.025 mg eq/kg), PB-7 (3.75% TRR, 0.005 mg eq/kg) and PB-9 (5.11% TRR, 0.007 mg eq/kg) were identified in the liver (and confirmed by TLC). In kidney three fractions ( $\leq 0.01\%$  MDD) were tentatively identified as P-3, PB-11 and B-7. Other fractions were  $\leq 0.01\%$  MDD. In muscle, at least 3 fractions were observed ( $< 0.01\%$  of MDD). In fat, 3-5 fractions (all  $< 0.01\%$  MDD) were observed of which two were identified as PB-12 and B-1.

In the study in hens, after eight daily dose administrations of [Pyridazinone- $^{14}\text{C}$ ] or [Benzyl- $^{14}\text{C}$ ] dosed at 12.5  $\mu\text{g/day}$  or 1 mg/day, 61.9-88.2% of the total administered dose was recovered in excreta and 0.9-4.2% in the tissues (including GI tract). Maximum 0.05% of the total administered dose was recovered in eggs and no plateau was reached within the study period (8 days). The maximum residue level in eggs, after the high dose treatment, was 0.019 mg eq/kg. For the low dose, egg residues were  $< 0.001$  mg eq/kg. Maximum residue levels in tissues were  $< 0.01$  mg eq/kg for the low dose and 0.119 mg eq/kg (liver), 0.015 mg eq/kg (muscle), 0.056 mg eq/kg (skin) and 0.031 mg eq/kg (fat). In excreta, PB-12 (2.35% of mean daily dose (MDD)) and PB-13 (0.9% MDD) were tentatively identified. Other fractions were  $\leq 12.16\%$  MDD. Acid/alkali treatment or enzyme treatments released B-7 (1.54% MDD) and PB-4 (2.26% MDD). In the liver PB-12 (tentative, 0.01% MDD), PB-9 (confirmed, 0.01% MDD) and PB-7 (confirmed, 0.14% MDD) were identified. Other fractions were  $\leq 0.11\%$  MDD. PB-13 (0.03% MDD) was observed after hydrolysis. In eggs D-1 was tentatively identified ( $< 0.05\%$  MDD). In muscle, at least 3 fractions were observed ( $< 0.05\%$  MDD) of which one was tentatively identified as PB-13. In fat, 3-4 fractions (all  $< 0.05\%$  MDD) were observed of which two were tentatively identified as PB-11 and B-11. In skin, 2-6 fractions (all  $< 0.05\%$  MDD) were observed of which two were tentatively identified as PB-7 and PB-9.

The low dose in the goat study was 0.2 mg/kg feed as received (and  $> 0.2$  mg/kg dry feed, actual concentration based on dry weight not determined). Provisional intake calculations for cattle resulted in a maximum feed concentration of 0.17 mg/kg dry weight, which is lower than the lowest dose in this study. (Note: the intake calculation for cattle was based on a HR (whole fruit, oranges) of 0.12 mg/kg and a wet pomace processing factor of 1.1. The HR value is provisional as the field residue trials were not conducted under least favourable conditions). It is however not anticipated that the concentration in the diet will exceed 0.2 mg/kg diet as received. Hence, residues in edible animal tissues are expected to be well below 0.01 mg eq/kg. A final assessment will be made after the residue situation under least favourable conditions is determined (see B.7.6).

**B.7.2.4 List of identified compounds**

| Code             | Compounds                                                                                                  | Description | Crop/Commodity                                    | Animal/Tissue                                    |
|------------------|------------------------------------------------------------------------------------------------------------|-------------|---------------------------------------------------|--------------------------------------------------|
| Pyridaben (PB-1) | 2-tert-butyl-5-(4-tert-butylbenzylthio)-4-chloropyridazin-3(2H)-one                                        | Parent      | Apple (fruit)                                     | Goat (faeces, liver)                             |
| P-1              | tert-butyl-4-chloro-5-mercapto-pyridazin-3(2H)-one                                                         | Metabolite  | -                                                 | Goat (liver)                                     |
| P-2              | 2-tert-butyl-4-chloro-5-methylthiopyridazin-3(2H)-one                                                      | Metabolite  | Apple (fruit)                                     | -                                                |
| P-3              | 2-tert-butyl-4-chloro-5-hydroxypyridazin-3(2H)-one                                                         | Metabolite  | -                                                 | Goat (bile, kidney)                              |
| P-14             | 2-tert-butyl-4-chloropyridazin-3(2H)-one-5-sulfonic acid                                                   | Metabolite  | Citrus (fruit)                                    | -                                                |
| B-1              | 4-tert-butyl-benzoic acid                                                                                  | Metabolite  | Apple (fruit)<br>Citrus (fruit)                   | Goat (faeces, fat)                               |
| B-3              | 4-tert-butyl-benzylalcohol                                                                                 | Metabolite  | Apple (fruit)<br>Citrus (fruit)                   | Goat (faeces)                                    |
| B-5              | 4-tert-butyl-benzaldehyde                                                                                  | Metabolite  | Apple (fruit)                                     | -                                                |
| B-7              | 2-(4-carboxyphenyl)-2-methylpropionic acid                                                                 | Metabolite  | -                                                 | Goat (faeces, kidney)<br>Hen (excreta)           |
| B-8              | 2-(4-hydroxymethylphenyl)-2-methyl-1-propanol                                                              | Metabolite  | -                                                 | Goat (faeces, bile)                              |
| B-11             | 2-(4-carboxyphenyl)-2-methyl-1-propanol                                                                    | Metabolite  | -                                                 | Hen (fat)                                        |
| D-1              | di-[2-tert-butyl-4-(4-tert-butylbenzyl)pyridazin-3(2H)-one-5-yl]disulfide                                  | Metabolite  | Apple (fruit)<br>Tomato (fruit)                   | Hen (eggs)                                       |
| PB-3             | 2-tert-butyl-5-(4-tert-butylbenzylsulfonyl)-4-chloropyridazin-3(2H)-one                                    | Metabolite  | -                                                 | Goat (urine, faeces)                             |
| PB-4             | 2-tert-butyl-5-(4-tert-butylbenzylsulfinyl)-4-chloropyridazin-3(2H)-one                                    | Metabolite  | Tomato (fruit)                                    | Goat (faeces)<br>Hen (excreta)                   |
| PB-7             | 2-tert-butyl-5-[4-(1-carboxy-1-methylethyl)benzylthio]-4-chloropyridazin-3(2H)-one                         | Metabolite  | -                                                 | Goat (urine, faeces, liver)<br>Hen (liver, skin) |
| PB-9             | 2-tert-butyl-4-chloro-5-[4-(1,1-dimethyl-2-hydroxyethyl)benzylthio]pyridazin-3(2H)-one                     | Metabolite  | Tomato (fruit)                                    | Goat (faeces, bile, liver)<br>Hen (liver, skin)  |
| PB-11            | 5-(4-tert-butylbenzylthio)-4-chloro-2-(1,1-dimethyl-2-hydroxyethyl)-pyridazin-3(2H)-one                    | Metabolite  | Citrus (fruit)                                    | Goat (urine, liver, kidney)<br>Hen (fat)         |
| PB-12            | 5-(4-tert-butylbenzylthio)-2-(1-carboxy-1-methylethyl)-4-chloropyridazin-3(2H)-one                         | Metabolite  | -                                                 | Goat (faeces, fat)<br>Hen (excreta, liver)       |
| PB-13            | 4-chloro-2-(1,1-dimethyl-2-hydroxyethyl)-5-[4-(1,1-dimethyl-2-hydroxyethyl)benzylthio]-pyridazin-3(2H)-one | Metabolite  | -                                                 | Goat (faeces)<br>Hen (excreta, liver, eggs)      |
| PB-14            | 2-tert-butyl-4-(4-tert-butylbenzyl)pyridazin-3(2H)-one                                                     | Metabolite  | Apple (fruit)<br>Citrus (fruit)<br>Tomato (fruit) | -                                                |
| PB-17            | 2-tert-butyl-4-(4-tert-butylbenzyl)-pyridazin-3(2H)-one                                                    | Metabolite  | Apple (fruit)                                     | -                                                |
| PB-22            | 2-tert-butyl-4-(4-tert-butylbenzoyl)pyridazin-3(2H)-one-5-sulfonic acid                                    | Metabolite  | Apple (fruit)<br>Citrus (fruit)                   | -                                                |

**B.7.2.5 Metabolic pathway****Figure B.7.2.3-01 Metabolic pathway of Pyridaben in goat**



**B.7.3 Definition of the residue (Annex IIA 6.7; Annex IIIA 8.6)****B.7.3.1 Definition of the residue in plant material**

The major component of the residue in whole fruit oranges was pyridaben (approximately 12-22% TRR). Other metabolites were <0.006 mg eq/kg and <10% TRR. Some of these minor metabolites (P-14, B-5, PB-14 and PB-22) were not observed in rat metabolism studies, but were structurally similar to pyridaben and other rat metabolites. In conclusion, no toxicologically relevant metabolites were observed in citrus.

The major component of the residue in tomatoes was pyridaben (approximately 92-98% TRR). Other metabolites were <0.001 mg eq/kg and ≤0.7% TRR. Some of these minor metabolites (PB-14 and PB-22) were not observed in rat metabolism studies, but were structurally similar to pyridaben and other rat metabolites. In conclusion, no toxicologically relevant metabolites were observed in tomatoes.

Metabolism in apple was similar to citrus and tomatoes.

Based on the above, the following residue definitions are proposed:

**Residue definition for monitoring:** pyridaben (fruits: citrus/tomato/apple)

**Residue definition risk assessment:** pyridaben (fruits: citrus/tomato/apple)

**Conversion factor, CF:** 1

**B.7.3.2 Definition of the residue in animal products**

Because no definitive residue data are available (see B.7.6) under the least favourable conditions, no final concentration of pyridaben in cattle diet can be calculated and no final conclusion on the need for a residue definition in animal products can be made at this moment.

However, provisional intake calculations for cattle resulted in a maximum feed concentration of 0.17 mg/kg dry weight (the intake calculation for cattle was based on a provisional HR (whole fruit, oranges) of 0.12 mg/kg and a wet pomace processing factor of 1.1. The HR value is provisional as the field residue trials were not conducted under least favourable conditions). Based on the goat metabolism study and the livestock feeding study in cows (both performed at higher concentrations), no pyridaben residues >0.01 mg/kg are expected in edible animal products. Hence, it is expected that no definition of residues in animal products will be required.

**B.7.4 Use pattern**

The formulation NEXTER PRO 75 WP, a 750 g as/kg formulation of pyridaben, is submitted for use in Northern and Southern Europe as an insecticide against mites and whitefly in the cultivation of citrus and tomatoes. The intended uses for Northern and Southern European regions are given in Table B.7.4-01 and Table B.7.4-02, respectively.

**Table B.7.4-01 Intended use pattern of Northern European regions**

| INTENDED USE PATTERN, NORTHERN EUROPE |                         |           |                                    |             |            |             |                                       |                                |                 |                    |            |
|---------------------------------------|-------------------------|-----------|------------------------------------|-------------|------------|-------------|---------------------------------------|--------------------------------|-----------------|--------------------|------------|
| Crop and/or situation                 | Member State or Country | F, G or I | Pests or group of pests controlled | Formulation |            | Application |                                       | Application rate per treatment |                 |                    | Remarks:   |
|                                       |                         |           |                                    | type        | conc of as | method kind | growth stage                          | number (range)                 | interval (days) | as (kg/ha)         | PHI (days) |
| Tomato                                | North EU                | G         | Mites, Whitefly                    | WP          | 750 g/kg   | Spray       | At infestation, no later than BBCH 89 | 1                              | na              | 0.02-0.025 (kg/ha) | 3          |
|                                       |                         |           |                                    |             |            |             |                                       |                                |                 | 1000-1250 (l/ha)   | -          |
|                                       |                         |           |                                    |             |            |             |                                       |                                |                 | 0.25 (kg/ha)       |            |

**Table B.7.4-02 Intended use pattern of Southern European regions**

| INTENDED USE PATTERN, SOUTHERN EUROPE |                         |           |                                    |             |            |             |                                       |                                |                 |                    |            |
|---------------------------------------|-------------------------|-----------|------------------------------------|-------------|------------|-------------|---------------------------------------|--------------------------------|-----------------|--------------------|------------|
| Crop and/or situation                 | Member State or Country | F, G or I | Pests or group of pests controlled | Formulation |            | Application |                                       | Application rate per treatment |                 |                    | Remarks:   |
|                                       |                         |           |                                    | type        | conc of as | method kind | growth stage                          | number (range)                 | interval (days) | as (kg/ha)         | PHI (days) |
| Citrus                                | South EU                | F         | Mites, Whitefly                    | WP          | 750 g/kg   | Spray       | At infestation, no later than BBCH 83 | 1                              | na              | 0.02 (kg/ha)       | 14         |
|                                       |                         |           |                                    |             |            |             |                                       |                                |                 | 1500 (l/ha)        | -          |
|                                       |                         |           |                                    |             |            |             |                                       |                                |                 | 0.3 (kg/ha)        |            |
| Tomato                                | South EU                | G         | Mites, Whitefly                    | WP          | 750 g/kg   | Spray       | At infestation, no later than BBCH 89 | 1                              | na              | 0.02-0.025 (kg/ha) | 3          |
|                                       |                         |           |                                    |             |            |             |                                       |                                |                 | 1000-1250 (l/ha)   | -          |
|                                       |                         |           |                                    |             |            |             |                                       |                                |                 | 0.25 (kg/ha)       |            |

**B.7.5 Identification of critical GAPs**

A summary of the cGAPs for Northern and Southern European regions is given in Table B.7.5-01 and Table B.7.5-02, respectively.

**Table B.7.5-01 Identification of the cGAP of Northern European regions**

| INTENDED USE PATTERN, NORTHERN EUROPE |                         |           |                                    |             |            |             |                                       |                |                 |                                |              |              |            |          |
|---------------------------------------|-------------------------|-----------|------------------------------------|-------------|------------|-------------|---------------------------------------|----------------|-----------------|--------------------------------|--------------|--------------|------------|----------|
| Crop and/or situation                 | Member State or Country | F, G or I | Pests or group of pests controlled | Formulation |            | Application |                                       |                |                 | Application rate per treatment |              |              | PHI (days) | Remarks: |
|                                       |                         |           |                                    | type        | conc of as | method kind | growth stage                          | number (range) | interval (days) | as (kg/.hl)                    | water (l/ha) | as (kg/ha)   |            |          |
| Tomato                                | North EU                | G         | Mites, Whitefly                    | WP          | 750 g/kg   | Spray       | At infestation, no later than BBCH 89 | 1              | na              | 0.025<br>0.02                  | 1000<br>1250 | 0.25<br>0.25 | 3          | -        |

The notifier is requested to identify the spray concentration-spray volume combination which should be considered cGAP

**Table B.7.5-02 Identification of the cGAP of Southern European regions**

| INTENDED USE PATTERN, SOUTHERN EUROPE |                         |           |                                    |             |            |             |                                       |                |                 |                                |              |              |    |            |          |
|---------------------------------------|-------------------------|-----------|------------------------------------|-------------|------------|-------------|---------------------------------------|----------------|-----------------|--------------------------------|--------------|--------------|----|------------|----------|
| Crop and/or situation                 | Member State or Country | F, G or I | Pests or group of pests controlled | Formulation |            | Application |                                       |                |                 | Application rate per treatment |              |              |    | PHI (days) | Remarks: |
|                                       |                         |           |                                    | type        | conc of as | method kind | growth stage                          | number (range) | interval (days) | as (kg/.hl)                    | water (l/ha) | as (kg/ha)   |    |            |          |
| Citrus                                | South EU                | F         | Mites, Whitefly                    | WP          | 750 g/kg   | Spray       | At infestation, no later than BBCH 83 | 1              | na              | 0.02                           | 1500         | 0.3          | 14 | -          |          |
| Tomato                                | South EU                | G         | Mites, Whitefly                    | WP          | 750 g/kg   | Spray       | At infestation, no later than BBCH 89 | 1              | na              | 0.025<br>0.02                  | 1000<br>1250 | 0.25<br>0.25 | 3  | -          |          |

The notifier is requested to identify the spray concentration-spray volume combination which should be considered cGAP

## **B.7.6 Residues resulting from supervised trials (Annex IIA 6.3; Annex IIIA 8.2)**

### **B.7.6.1 Methods of analysis applied in the supervised trials**

Pyridaben residues in citrus fruit were determined by analytical method BAS 938/1 (studies 01 to 04 and 06 to 09) and analytical method D9309 (study 05). Pyridaben residues in tomatoes were determined by analytical method D9312 (studies 10 and 11). In validation studies for BAS 938/1, the LOQ of 0.05 mg/kg was rejected because of significant (>30% LOQ) interferences in control samples. As no interferences were seen in untreated samples and residues at the relevant PHI were generally >LOQ, the results obtained by BAS 938/1 are accepted. In validation studies for D9309, the LOQ of 0.05 mg/kg was rejected because of significant (>30% LOQ) interferences in control samples and insufficient replications. As no interferences were seen in untreated samples, residues at the relevant PHI were generally >LOQ, and procedural recoveries at the LOQ were adequate, the results obtained by D9309 are accepted. Analytical method D9312 was fully validated with an LOQ of 0.05 mg/kg. Concurrent procedural recoveries were included in each supervised field trial. Additional recoveries were provided in a separate study (Weidenauer et al. 1993, study 12). For studies 01, 02, 03, 07, 08 and 09 the recoveries were acceptable for whole fruits and pulp. The number of recovery samples was too low for citrus peel (1 sample at 0.05 and 0.1 mg/kg and 2 samples at 0.2 mg/kg) and the recovery was around 60%. However, since residue levels in whole fruit and pulp were adequately determined, processing factors can be proposed. In study 10, concurrent procedural recoveries at 10xLOQ were included, but not at the LOQ, while results were at or around LOQ level. This is accepted, since the study on method validation (Tate S. 2001, IIA 4.2.1/09), provides 5 additional recoveries at 0.05 mg/kg with a procedural recovery of 85 ± 11% In the other studies, procedural recoveries were acceptable (at LOQ, 2xLOQ and/or 10xLOQ). The maximum storage period (freezer) in any supervised residue field trial was 7 months. Storage stability of pyridaben in citrus/tomato during frozen storage was demonstrated for a period of at least one year.

### **B.7.6.2 Supervised residue trials**

#### **General remark**

For citrus, trials are performed with different dose rate expressed as kg ai/ha. The notifier provided a statement. For high trees, the dose rate should be expressed as kg ai/hL. For the trials provided, it is shown that trials performed with higher dose rate (around 0.5 kg ai/ha) and high water volumes (around 2500L/ha) are in general older/taller trees compared to those with lower dose rate (around 0.3 kg ai/ha) and lower water volumes (around 1500L/ha). When the spraying concentration is the same (0.02 kg ai/hL), the results of both populations overlap. The cGAP was defined as a spraying concentration of 0.02kg ai/hL, to a maximum of 0.25 kg ai/ha (tomato) or 0.30 kg ai/ha (citrus).

### Oranges

In total 10 residue trials (studies 01, 02, 03, 04 and 05) were submitted performed in Southern Europe covering two growing seasons. The formulation used in the studies was a 200 g/kg WP, which is different from the representative formulation (750 g/kg WP). This difference will however not lead to a different residue situation (same formulation) and is therefore accepted.

Nine trials performed with 1 application of 0.02 kg ai/hL and the appropriate PHI of 14 days are selected for MRL calculation.

### Mandarines

In total 9 residue trials (studies 05, 06 and 07) were submitted performed in Southern Europe covering at least two growing seasons. In study 07, no residues for the whole fruit were determined. Four trials performed with 1 application of 0.02 kg ai/hL and the appropriate PHI of 14 days are selected for MRL calculation.

Residues in mandarines (under comparable trial conditions) are different from orange, hence, a separate MRL is required for mandarines and no MRL can be set for citrus as a group. An additional 4 trials is required for setting an MRL for mandarin or the whole group of citrus.

### Lemon

In total 2 residue trials (studies 08 and 09) were submitted performed in Southern Europe covering at least two growing seasons. The formulation used in the studies was a 200 g/kg WP, which is different from the representative formulation (750 g/kg WP). This difference will however not lead to a different residue situation (same formulation) and is therefore accepted. For high trees, the dose rate should be expressed as kg ai/hL. Only one of both trials is performed with a dose level within the 25% deviation form 0.02 kg ai/hL. One residue value can be selected for the setting of the MRL.

### Tomatoes

In total 8 residue trials (studies 10 and 11) were submitted. One study was performed in Northern Europe and one in Southern Europe, both under glass. The formulation used in the studies was a 750 g/kg WP, which is similar to the representative formulation. When the rate is expressed in terms of kg a.i/ha, the rates in both studies are within 25% of the GAP. Samples were taken at the appropriate PHI of 3 days. Trials performed under glass in Southern and Northern Europe are considered comparable. Since the two data sets showed overlapping residue levels, they are combined to one data set for tomatoes grown in greenhouses.

### Overall conclusion

For orange, 9 residue trials are acceptable for MRL setting. An MRL will be proposed (see B.7.12). For mandarins, only 4 trials are acceptable. Since 8 trials are required for MRL setting, no MRL is proposed for mandarin. For lemons, only 1 trial is acceptable. Since 8 trials with lemon are required for MRL setting (or 8 trials with orange and 8 trials with mandarin for a group tolerance), no MRL is proposed for lemons.

**Table B.7.6.2-01 Summary of supervised trials with tomatoes for the Northern European regions**

| SUPERVISED RESIDUE TRIALS, Northern Europe |                       |                                                       |                             |                                |                 |                         |                                                  |                                                    |                     |                                            |        |                                                |
|--------------------------------------------|-----------------------|-------------------------------------------------------|-----------------------------|--------------------------------|-----------------|-------------------------|--------------------------------------------------|----------------------------------------------------|---------------------|--------------------------------------------|--------|------------------------------------------------|
| Location                                   | Commodity/<br>Variety | Data of<br>1. Sowing or<br>2. Flowering<br>3. Harvest | Method<br>of treat-<br>ment | Application rate per treatment |                 |                         | Number<br>of treat-<br>ments<br>and last<br>date | Growth<br>stage at<br>last<br>treatment<br>or date | Portion<br>analysed | Residues<br>(mg/kg)<br>Parent<br>pyridaben | DAT    | Reference,<br>Interval between<br>applications |
|                                            |                       |                                                       |                             | as (kg/hL)<br>pyridaben        | Water<br>(L/ha) | as (kg/ha)<br>pyridaben |                                                  |                                                    |                     |                                            |        |                                                |
| TOMATOES GREENHOUSE                        |                       |                                                       |                             |                                |                 |                         |                                                  |                                                    |                     |                                            |        |                                                |
| Eishout, the<br>Netherlands                | Mondeo                | 1. 23-12-99<br>2. n.d.<br>3. 17-10-00                 | spray                       | 0.026                          | 1021            | 0.261                   | 1<br>17-10-00                                    | BBCH<br>60-87                                      | Fruits              | 0.06<br><u>0.07</u>                        | 0<br>3 | Blaschke, 2002<br>(IIA 6.3/10)                 |
| Oosterhout,<br>the<br>Netherlands          | Tomcat                | 1.29-08-00<br>2.n.d.<br>3.07-11-00                    | spray                       | 0.026                          | 1006            | 0.257                   | 1<br>07-11-00                                    | BBCH<br>60-89                                      | Fruits              | <0.05<br><u>&lt;0.05</u>                   | 0<br>3 | Blaschke, 2002<br>(IIA 6.3/10)                 |
| Oosterhout,<br>the<br>Netherlands          | Tomcat                | 1.30-08-00<br>2.n.d.<br>3.07-11-00                    | spray                       | 0.026                          | 1015            | 0.260                   | 1<br>07-11-00                                    | BBCH<br>60-89                                      | Fruits              | <0.05<br><u>&lt;0.05</u>                   | 0<br>3 | Blaschke, 2002<br>(IIA 6.3/10)                 |
| Eishout, the<br>Netherlands                | Durinta               | 1.19-05-00<br>2.n.d.<br>3.13-11-00                    | spray                       | 0.026                          | 996             | 0.255                   | 1<br>13-11-00                                    | BBCH<br>60-89                                      | Fruits              | 0.05<br><u>&lt;0.05</u>                    | 0<br>3 | Blaschke, 2002<br>(IIA 6.3/10)                 |

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**Table B.7.6.2-02 Summary of supervised trials with tomatoes for the Southern European regions**

| SUPERVISED RESIDUE TRIALS, Southern Europe |                       |                                                                   |                             |                                |                 |                         |                                                     |                                                    |                     |                                            |        |                                                |
|--------------------------------------------|-----------------------|-------------------------------------------------------------------|-----------------------------|--------------------------------|-----------------|-------------------------|-----------------------------------------------------|----------------------------------------------------|---------------------|--------------------------------------------|--------|------------------------------------------------|
| Location                                   | Commodity/<br>Variety | Data of<br>1. Sowing or<br>planting<br>2. Flowering<br>3. Harvest | Method<br>of treat-<br>ment | Application rate per treatment |                 |                         | Number<br>of treat-<br>ments<br>and<br>last<br>date | Growth<br>stage at<br>last<br>treatment<br>or date | Portion<br>analysed | Residues<br>(mg/kg)<br>Parent<br>pyridaben | DAT    | Reference,<br>Interval between<br>applications |
|                                            |                       |                                                                   |                             | as (kg/hL)<br>pyridaben        | Water<br>(L/ha) | as (kg/ha)<br>pyridaben |                                                     |                                                    |                     |                                            |        |                                                |
| TOMATOES GREENHOUSE                        |                       |                                                                   |                             |                                |                 |                         |                                                     |                                                    |                     |                                            |        |                                                |
| Valencia,<br>Majal<br>(Xeresa),<br>Spain   | Bond                  | 1. 11-00<br>2.<br>3. 18-05-01                                     | spray                       | 0.021                          | 1267            | 0.269                   | 1<br>18-05-01                                       | BBCH<br>69-89                                      | Fruits              | 0.05<br><u>0.07</u>                        | 0<br>3 | Blaschke, 2002<br>(IIA 6.3/11)                 |
| Betera,<br>El<br>Palustre,<br>Spain        | Rami                  | 4. 12-00<br>5. n.d.<br>6. 18-05-01                                | spray                       | 0.021                          | 1314            | 0.279                   | 1<br>18-05-01                                       | BBCH<br>69-89                                      | Fruits              | 0.06<br><u>0.05</u>                        | 0<br>3 | Blaschke, 2002<br>(IIA 6.3/11)                 |
| Mazarron,<br>Las<br>Pecheras,<br>Spain     | Brillante             | 4. 13-03-01<br>5. n.d.<br>6. 21-05-01                             | spray                       | 0.025                          | 1005            | 0.256                   | 1<br>21-05-01                                       | BBCH<br>69-89                                      | Fruits              | 0.08<br><u>0.07</u>                        | 0<br>3 | Blaschke, 2002<br>(IIA 6.3/11)                 |
| Mazarron,<br>Leiva, Spain                  | Brillante             | 4. 20-12-00<br>5. n.d.<br>6. 21-05-01                             | spray                       | 0.021                          | 1236            | 0.262                   | 1<br>21-05-01                                       | BBCH<br>69-89                                      | Fruits              | 0.06<br><u>0.05</u>                        | 0<br>3 | Blaschke, 2002<br>(IIA 6.3/11)                 |

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**Table B.7.6.2-03 Summary of supervised trials with oranges for the Southern European regions**

| SUPERVISED RESIDUE TRIALS, Southern Europe |                       |                                                                   |                             |                                |                 |                         |                                                     |                                                    |                     |                                            |     |                                                |
|--------------------------------------------|-----------------------|-------------------------------------------------------------------|-----------------------------|--------------------------------|-----------------|-------------------------|-----------------------------------------------------|----------------------------------------------------|---------------------|--------------------------------------------|-----|------------------------------------------------|
| Location                                   | Commodity/<br>Variety | Data of<br>4. Sowing or<br>planting<br>5. Flowering<br>6. Harvest | Method<br>of treat-<br>ment | Application rate per treatment |                 |                         | Number<br>of treat-<br>ments<br>and<br>last<br>date | Growth<br>stage at<br>last<br>treatment<br>or date | Portion<br>analysed | Residues<br>(mg/kg)<br>Parent<br>pyridaben | DAT | Reference,<br>Interval between<br>applications |
|                                            |                       |                                                                   |                             | as (kg/hL)<br>pyridaben        | Water<br>(L/ha) | as (kg/ha)<br>pyridaben |                                                     |                                                    |                     |                                            |     |                                                |
| Oranges                                    |                       |                                                                   |                             |                                |                 |                         |                                                     |                                                    |                     |                                            |     |                                                |
| Coria,<br>Sevilla,<br>Spain                | Cadenera              | 1.n.d.<br>2.n.d.<br>3.22-09-92                                    | spray                       | 0.02                           | 2750            | 0.55                    | 1<br>22-09-92                                       | BBCH<br>75-77                                      | Fruit               | 0.38                                       | 0   | Anonymous,<br>1994 (IIA 6.3/01)                |
|                                            |                       |                                                                   |                             |                                |                 |                         |                                                     |                                                    |                     | 0.24                                       | 7   |                                                |
|                                            |                       |                                                                   |                             |                                |                 |                         |                                                     |                                                    |                     | 0.12                                       | 14  |                                                |
|                                            |                       |                                                                   |                             |                                |                 |                         |                                                     |                                                    |                     | 0.09                                       | 21  |                                                |
|                                            |                       |                                                                   |                             |                                |                 |                         |                                                     |                                                    | <0.05               | 28                                         |     |                                                |
| Coria,<br>Sevilla,<br>Spain                | Navelina              | 1.n.d.<br>2.n.d.<br>3.22-09-92                                    | spray                       | 0.02                           | 2750            | 0.55                    | 1<br>22-09-92                                       | BBCH<br>75-77                                      | Fruit               | 0.35                                       | 0   | Anonymous,<br>1994 (IIA 6.3/01)                |
|                                            |                       |                                                                   |                             |                                |                 |                         |                                                     |                                                    |                     | 0.16                                       | 7   |                                                |
|                                            |                       |                                                                   |                             |                                |                 |                         |                                                     |                                                    |                     | 0.10                                       | 14  |                                                |
|                                            |                       |                                                                   |                             |                                |                 |                         |                                                     |                                                    |                     | 0.09                                       | 21  |                                                |
|                                            |                       |                                                                   |                             |                                |                 |                         |                                                     |                                                    | 0.07                | 28                                         |     |                                                |
| Llivia,<br>Valencia,<br>Spain              | Navelina              | 1. n.d.<br>2. n.d.<br>3. 15-09-92                                 | spray                       | 0.02                           | 2500            | 0.5                     | 1<br>15-09-92                                       | BBCH<br>77                                         | Fruit               | 0.13                                       | 0   | Anonymous,<br>1994 (IIA 6.3/02)                |
|                                            |                       |                                                                   |                             |                                |                 |                         |                                                     |                                                    |                     | <0.05                                      | 7   |                                                |
|                                            |                       |                                                                   |                             |                                |                 |                         |                                                     |                                                    |                     | <0.05                                      | 14  |                                                |
|                                            |                       |                                                                   |                             |                                |                 |                         |                                                     |                                                    |                     | <0.05                                      | 21  |                                                |
|                                            |                       |                                                                   |                             |                                |                 |                         |                                                     |                                                    | <0.05               | 28                                         |     |                                                |
| Llivia,<br>Valencia,<br>Spain              | Newhall               | 1.n.d.<br>2.n.d.<br>3.06-10-92                                    | spray                       | 0.02                           | 2500            | 0.5                     | 2<br>06-10-92                                       | BBCH<br>77                                         | Fruit               | 0.22                                       | 0   | Anonymous,<br>1994 (IIA 6.3/02)<br>21 days     |
|                                            |                       |                                                                   |                             |                                |                 |                         |                                                     |                                                    |                     | 0.07                                       | 7   |                                                |
|                                            |                       |                                                                   |                             |                                |                 |                         |                                                     |                                                    |                     | 0.06                                       | 14  |                                                |
|                                            |                       |                                                                   |                             |                                |                 |                         |                                                     |                                                    |                     |                                            |     |                                                |
| Coria,<br>Sevilla,<br>Spain                | Cadenera              | 1.n.d.<br>2.n.d.<br>3.22-09-92                                    | spray                       | 0.02                           | 2750            | 0.55                    | 1<br>22-09-92                                       | BBCH<br>75-77                                      | Fruit               | 0.12                                       | 0   | Anonymous,<br>1994 (IIA 6.3/02)                |
|                                            |                       |                                                                   |                             |                                |                 |                         |                                                     |                                                    |                     | 0.13                                       | 7   |                                                |
|                                            |                       |                                                                   |                             |                                |                 |                         |                                                     |                                                    |                     | 0.08                                       | 14  |                                                |
|                                            |                       |                                                                   |                             |                                |                 |                         |                                                     |                                                    |                     | <0.05                                      | 21  |                                                |
|                                            |                       |                                                                   |                             |                                |                 |                         |                                                     |                                                    | <0.05               | 28                                         |     |                                                |
| Coria,<br>Sevilla,<br>Spain                | Navelina              | 1.n.d.<br>2.n.d.<br>3.22-09-92                                    | spray                       | 0.02                           | 2750            | 0.55                    | 1<br>22-09-92                                       | BBCH<br>75-77                                      | Fruit               | 0.11                                       | 0   | Anonymous,<br>1994 (IIA 6.3/02)                |
|                                            |                       |                                                                   |                             |                                |                 |                         |                                                     |                                                    |                     | 0.14                                       | 7   |                                                |
|                                            |                       |                                                                   |                             |                                |                 |                         |                                                     |                                                    |                     | 0.05                                       | 14  |                                                |
|                                            |                       |                                                                   |                             |                                |                 |                         |                                                     |                                                    |                     | 0.06                                       | 21  |                                                |
|                                            |                       |                                                                   |                             |                                |                 |                         |                                                     |                                                    | <0.05               | 28                                         |     |                                                |

| SUPERVISED RESIDUE TRIALS, Southern Europe |                       |                                                                   |                             |                                |                 |                         |                                                     |                                                    |                     |                                            |     |                                                |
|--------------------------------------------|-----------------------|-------------------------------------------------------------------|-----------------------------|--------------------------------|-----------------|-------------------------|-----------------------------------------------------|----------------------------------------------------|---------------------|--------------------------------------------|-----|------------------------------------------------|
| Location                                   | Commodity/<br>Variety | Data of<br>4. Sowing or<br>planting<br>5. Flowering<br>6. Harvest | Method<br>of treat-<br>ment | Application rate per treatment |                 |                         | Number<br>of treat-<br>ments<br>and<br>last<br>date | Growth<br>stage at<br>last<br>treatment<br>or date | Portion<br>analysed | Residues<br>(mg/kg)<br>Parent<br>pyridaben | DAT | Reference,<br>Interval between<br>applications |
|                                            |                       |                                                                   |                             | as (kg/hL)<br>pyridaben        | Water<br>(L/ha) | as (kg/ha)<br>pyridaben |                                                     |                                                    |                     |                                            |     |                                                |
| Oranges                                    |                       |                                                                   |                             |                                |                 |                         |                                                     |                                                    |                     |                                            |     |                                                |
| Argos,<br>Peloponnes<br>e, Greece          | Washington<br>Navel   | 1. n.d.<br>2. n.d.<br>3. 09-01-93                                 | spray                       | 0.02                           | 4473            | 0.895                   | 1<br>08-01-93                                       | BBCH<br>n.d.                                       | Fruit               | 0.28                                       | 1   | Anonymous,<br>1993 (IIA 6.3/03)                |
|                                            |                       |                                                                   |                             |                                |                 |                         |                                                     |                                                    | Pulp                | <0.05                                      | 7   |                                                |
|                                            |                       |                                                                   |                             |                                |                 |                         |                                                     |                                                    | Peel                | 0.41                                       | 14  |                                                |
|                                            |                       |                                                                   |                             |                                |                 |                         |                                                     |                                                    | Pulp                | <0.05                                      | 21  |                                                |
|                                            |                       |                                                                   |                             |                                |                 |                         |                                                     |                                                    | Peel                | 0.27                                       | 28  |                                                |
| Siracusa,<br>Sicily, Italy                 | Navelina              | 1. 1982<br>2. n.d.<br>3. 28-10-93                                 | spray                       | 0.02                           | 1250            | 0.287                   | 1<br>28-10-93                                       | BBCH<br>nd                                         | Fruit               | 0.16                                       | 0   | Udrisard, 1994<br>(IIA 6.3/04)                 |
|                                            |                       |                                                                   |                             |                                |                 |                         |                                                     |                                                    |                     | 0.05                                       | 14  |                                                |
|                                            |                       |                                                                   |                             |                                |                 |                         |                                                     |                                                    |                     |                                            |     |                                                |
|                                            |                       |                                                                   |                             |                                |                 |                         |                                                     |                                                    |                     |                                            |     |                                                |
|                                            |                       |                                                                   |                             |                                |                 |                         |                                                     |                                                    |                     |                                            |     |                                                |
| Catania,<br>Sicily, Italy                  | Tarocco<br>Nucellare  | 1. 1987<br>2. n.d.<br>3. 04-11-93                                 | spray                       | 0.02                           | 1200            | 0.287                   | 1<br>04-11-93                                       | BBCH<br>nd                                         | Fruit               | 0.11                                       | 0   | Udrisard, 1994<br>(IIA 6.3/04)                 |
|                                            |                       |                                                                   |                             |                                |                 |                         |                                                     |                                                    |                     | 0.06                                       | 14  |                                                |
|                                            |                       |                                                                   |                             |                                |                 |                         |                                                     |                                                    |                     |                                            |     |                                                |
|                                            |                       |                                                                   |                             |                                |                 |                         |                                                     |                                                    |                     |                                            |     |                                                |
|                                            |                       |                                                                   |                             |                                |                 |                         |                                                     |                                                    |                     |                                            |     |                                                |
| Cagnano<br>Varano<br>(FG), Italy           | Navelinas             | 1. 1983<br>2. 05-02<br>3. 30-10-02                                | spray                       | 0.02                           | 1519            | 0.3108                  | 1<br>30-10-02                                       | BBCH<br>87-88                                      | Fruit               | 0.31                                       | 0   | Blaschke, 2003<br>(IIA 6.3/05)                 |
|                                            |                       |                                                                   |                             |                                |                 |                         |                                                     |                                                    |                     | 0.26                                       | 3   |                                                |
|                                            |                       |                                                                   |                             |                                |                 |                         |                                                     |                                                    |                     | 0.18                                       | 7   |                                                |
|                                            |                       |                                                                   |                             |                                |                 |                         |                                                     |                                                    |                     | 0.12                                       | 10  |                                                |
|                                            |                       |                                                                   |                             |                                |                 |                         |                                                     |                                                    |                     | 0.10                                       | 14  |                                                |
|                                            | 0.45                  | 14                                                                |                             |                                |                 |                         |                                                     |                                                    |                     |                                            |     |                                                |
|                                            | <0.05                 | 14                                                                |                             |                                |                 |                         |                                                     |                                                    |                     |                                            |     |                                                |

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**Table B.7.6.2-04 Summary of supervised trials with mandarines for the Southern European regions**

| SUPERVISED RESIDUE TRIALS, Southern Europe |                            |                                                                   |                             |                                |                 |                         |                                                  |                                                    |                     |                                            |     |                                                |    |
|--------------------------------------------|----------------------------|-------------------------------------------------------------------|-----------------------------|--------------------------------|-----------------|-------------------------|--------------------------------------------------|----------------------------------------------------|---------------------|--------------------------------------------|-----|------------------------------------------------|----|
| Location                                   | Commodity/<br>Variety      | Data of<br>1. Sowing or<br>planting<br>2. Flowering<br>3. Harvest | Method<br>of treat-<br>ment | Application rate per treatment |                 |                         | Number<br>of treat-<br>ments<br>and last<br>date | Growth<br>stage at<br>last<br>treatment<br>or date | Portion<br>analysed | Residues<br>(mg/kg)<br>Parent<br>pyridaben | DAT | Reference,<br>Interval between<br>applications |    |
|                                            |                            |                                                                   |                             | as (kg/hL)<br>pyridaben        | Water<br>(L/ha) | as (kg/ha)<br>pyridaben |                                                  |                                                    |                     |                                            |     |                                                |    |
| Mandarins                                  |                            |                                                                   |                             |                                |                 |                         |                                                  |                                                    |                     |                                            |     |                                                |    |
| Ischitella,<br>Italy                       | Tondo liscio<br>di Paterno | 1. 1981<br>2. 05-02<br>3. 30-10-02                                | spray                       | 0.02                           | 1462            | 0.2991                  | 1<br>30-10-02                                    | BBCH<br>82                                         | Fruit               | 0.24                                       | 0   | Blaschke, 2003<br>(IIA 6.3/05)                 |    |
|                                            |                            |                                                                   |                             |                                |                 |                         |                                                  |                                                    |                     | 0.28                                       |     |                                                | 3  |
|                                            |                            |                                                                   |                             |                                |                 |                         |                                                  |                                                    |                     | 0.24                                       |     |                                                | 7  |
|                                            |                            |                                                                   |                             |                                |                 |                         |                                                  |                                                    |                     | 0.21                                       |     |                                                | 10 |
|                                            |                            |                                                                   |                             |                                |                 |                         |                                                  |                                                    |                     | 0.08                                       |     |                                                | 14 |
|                                            |                            |                                                                   |                             |                                |                 |                         |                                                  |                                                    |                     | 0.36                                       |     |                                                | 14 |
| 0.05                                       | 14                         |                                                                   |                             |                                |                 |                         |                                                  |                                                    |                     |                                            |     |                                                |    |
| Bernalda<br>(MT), Italy                    | Avana                      | 1. 1983<br>2. 4/5-02<br>3. 31-10-02                               | spray                       | 0.02                           | 1502            | 0.3074                  | 1<br>31-10-02                                    | BBCH<br>85                                         | Fruit               | 0.47                                       | 0   | Blaschke, 2003<br>(IIA 6.3/05)                 |    |
|                                            |                            |                                                                   |                             |                                |                 |                         |                                                  |                                                    |                     | 0.47                                       |     |                                                | 3  |
|                                            |                            |                                                                   |                             |                                |                 |                         |                                                  |                                                    |                     | 0.43                                       |     |                                                | 7  |
|                                            |                            |                                                                   |                             |                                |                 |                         |                                                  |                                                    |                     | 0.38                                       |     |                                                | 10 |
|                                            |                            |                                                                   |                             |                                |                 |                         |                                                  |                                                    |                     | 0.22                                       |     |                                                | 14 |
|                                            |                            |                                                                   |                             |                                |                 |                         |                                                  |                                                    |                     | 1.01                                       |     |                                                | 14 |
| 0.05                                       | 14                         |                                                                   |                             |                                |                 |                         |                                                  |                                                    |                     |                                            |     |                                                |    |
| Alcala<br>Guadaira,<br>Sevilla,<br>Spain   | Clemenules                 | 4. 1965<br>5.n.d.<br>6. 24-10-96                                  | spray                       | 0.03                           | 1880            | 0.540                   | 1<br>24-10-96                                    | BBCH<br>79-83                                      | Fruit               | 0.53                                       | 0   | Weidenauer,<br>1997 (IIA 6.3/06)               |    |
|                                            |                            |                                                                   |                             |                                |                 |                         |                                                  |                                                    |                     | 0.15                                       |     |                                                | 7  |
|                                            |                            |                                                                   |                             |                                |                 |                         |                                                  |                                                    |                     | 0.13                                       |     |                                                | 14 |
|                                            |                            |                                                                   |                             |                                |                 |                         |                                                  |                                                    |                     |                                            |     |                                                |    |
|                                            |                            |                                                                   |                             |                                |                 |                         |                                                  |                                                    |                     |                                            |     |                                                |    |
|                                            |                            |                                                                   |                             |                                |                 |                         |                                                  |                                                    |                     |                                            |     |                                                |    |
| Alcala<br>Guadaira,<br>Sevilla,<br>Spain   | Oroval                     | 1. 1965<br>2.n.d.<br>3. 17-10-96                                  | spray                       | 0.02                           | 2110            | 0.523                   | 1<br>17-10-96                                    | BBCH<br>79-83                                      | Fruit               | 0.42                                       | 0   | Weidenauer,<br>1997 (IIA 6.3/06)               |    |
|                                            |                            |                                                                   |                             |                                |                 |                         |                                                  |                                                    |                     | 0.53                                       |     |                                                | 7  |
|                                            |                            |                                                                   |                             |                                |                 |                         |                                                  |                                                    |                     | 0.31                                       |     |                                                | 14 |
|                                            |                            |                                                                   |                             |                                |                 |                         |                                                  |                                                    |                     |                                            |     |                                                |    |
|                                            |                            |                                                                   |                             |                                |                 |                         |                                                  |                                                    |                     |                                            |     |                                                |    |
|                                            |                            |                                                                   |                             |                                |                 |                         |                                                  |                                                    |                     |                                            |     |                                                |    |
| Palacios,<br>Sevilla,<br>Spain             | Clemenules                 | 1. 1982<br>2.n.d.<br>3. 30-10-96                                  | spray                       | 0.03                           | 1790            | 0.543                   | 1<br>30-10-96                                    | BBCH<br>79-83                                      | Fruit               | 0.52                                       | 0   | Weidenauer,<br>1997 (IIA 6.3/06)               |    |
|                                            |                            |                                                                   |                             |                                |                 |                         |                                                  |                                                    |                     | 0.42                                       |     |                                                | 7  |
|                                            |                            |                                                                   |                             |                                |                 |                         |                                                  |                                                    |                     | 0.25                                       |     |                                                | 14 |
|                                            |                            |                                                                   |                             |                                |                 |                         |                                                  |                                                    |                     |                                            |     |                                                |    |
|                                            |                            |                                                                   |                             |                                |                 |                         |                                                  |                                                    |                     |                                            |     |                                                |    |
|                                            |                            |                                                                   |                             |                                |                 |                         |                                                  |                                                    |                     |                                            |     |                                                |    |
| Mazagon,<br>Huelva,<br>Spain               | Clemenules                 | 1. 1981<br>2.n.d.<br>3. 07-11-96                                  | spray                       | 0.03                           | 1970            | 0.536                   | 1<br>07-11-96                                    | BBCH<br>79-82                                      | Fruit               | 0.50                                       | 0   | Weidenauer,<br>1997 (IIA 6.3/06)               |    |
|                                            |                            |                                                                   |                             |                                |                 |                         |                                                  |                                                    |                     | 0.25                                       |     |                                                | 7  |
|                                            |                            |                                                                   |                             |                                |                 |                         |                                                  |                                                    |                     | 0.21                                       |     |                                                | 14 |
|                                            |                            |                                                                   |                             |                                |                 |                         |                                                  |                                                    |                     |                                            |     |                                                |    |
|                                            |                            |                                                                   |                             |                                |                 |                         |                                                  |                                                    |                     |                                            |     |                                                |    |
|                                            |                            |                                                                   |                             |                                |                 |                         |                                                  |                                                    |                     |                                            |     |                                                |    |
| Lliria,<br>Valencia,<br>Spain              | Clemenules                 | 1. 1981<br>2.n.d.<br>3. 04-12-96                                  | spray                       | 0.02                           | 2280            | 0.539                   | 1<br>04-12-96                                    | BBCH<br>79-81                                      | Fruit               | 0.68                                       | 0   | Weidenauer,<br>1997 (IIA 6.3/06)               |    |
|                                            |                            |                                                                   |                             |                                |                 |                         |                                                  |                                                    |                     | 0.36                                       |     |                                                | 7  |
|                                            |                            |                                                                   |                             |                                |                 |                         |                                                  |                                                    |                     | 0.23                                       |     |                                                | 14 |
|                                            |                            |                                                                   |                             |                                |                 |                         |                                                  |                                                    |                     |                                            |     |                                                |    |
|                                            |                            |                                                                   |                             |                                |                 |                         |                                                  |                                                    |                     |                                            |     |                                                |    |
|                                            |                            |                                                                   |                             |                                |                 |                         |                                                  |                                                    |                     |                                            |     |                                                |    |



**B.7.6.3 Storage stability****STUDY 1****Characteristics**

|                   |                                              |               |                   |
|-------------------|----------------------------------------------|---------------|-------------------|
| Reference         | : Burkey, J. D., 1995 (IIA 6.0/01)           | GLP           | : yes             |
| Type of study     | : storage stability                          | Guideline     | : EPA 171-4       |
| Year of execution | : 1993-1994                                  | Acceptability | : acceptable      |
| Test substance    | : Pyridaben; batch: CH39/169-1; purity 99.7% | Stability     | : see conclusions |

**Study design**

Untreated frozen specimens of orange, dried orange pulp, molasses and orange oil were homogenised and fortified with pyridaben at 1 mg/kg. Fortified samples and controls were stored at <-5°C up to 12 months. Residues were analyzed according to the validated method BASF Analytical Method D9309. Orange, orange molasses and dried orange pulp were extracted with a acetone/water mixture. After extraction, solvent partitioning (dichloromethane for orange, acetonitrile for dried orange pulp and molasses) and clean-up over Florisil or silica, the extract was analysed by GC-ECD. Oil was dissolved in hexane, solvent transferred to acetonitrile and analysed after clean-up by GC-ECD. Freshly fortified samples (1 mg/kg) were included at each storage interval.

**Results**

Concentrations and (average) recoveries of stored fortified samples are shown in Tables B.7.6.3-01 to Table B.7.6.3-04. Pyridaben recoveries in 12 months stored fortified samples ranged from 82 to 97%. The range of recoveries of the stored samples was not different from the recoveries of the freshly fortified samples (at 12 months: 82-89%). The results demonstrate that pyridaben residues in orange, dried orange pulp, orange molasses and orange oil were stable during storage at <-5°C for a period of 12 months.

**Table B.7.6.3-01 Recovery of pyridaben in fortified samples (1 mg/kg) of oranges after storage at <-5°C.**

| Months of storage | Concentration in stored samples <sup>(A)</sup><br>(mg/kg) |      | Average recovery stored samples <sup>(B)</sup><br>(%) | Recovery freshly fortified specimens (%) |
|-------------------|-----------------------------------------------------------|------|-------------------------------------------------------|------------------------------------------|
| 0                 | 0.79                                                      | 0.77 | 78                                                    | 78                                       |
| 1                 | 0.80                                                      | 0.76 | 78                                                    | 78                                       |
| 3                 | 0.67                                                      | 0.69 | 68                                                    | 78                                       |
| 6                 | 0.56                                                      | 0.61 | 58                                                    | 86                                       |
| 7                 | 0.55                                                      | 0.71 | 0.63                                                  | 90                                       |
| 12                | 0.87                                                      | 0.91 | 0.89                                                  | 86                                       |

<sup>(A)</sup> Not corrected for recovery of freshly fortified samples

<sup>(B)</sup> Relative to nominal (1 mg/kg)

**Table B.7.6.3-02 Recovery of pyridaben in fortified samples (1 mg/kg) of dried orange pulp after storage at <-5°C.**

| Months of storage | Concentration in stored samples <sup>(A)</sup><br>(mg/kg) |      | Average recovery stored samples <sup>(B)</sup><br>(%) | Recovery freshly fortified specimens (%) |
|-------------------|-----------------------------------------------------------|------|-------------------------------------------------------|------------------------------------------|
| 0                 | 0.93                                                      | 0.93 | 93                                                    | 94                                       |
| 1                 | 0.93                                                      | 0.93 | 93                                                    | 94                                       |
| 3                 | 0.93                                                      | 0.91 | 92                                                    | 94                                       |
| 6                 | 0.91                                                      | 0.86 | 88                                                    | 84                                       |
| 12                | 0.88                                                      | 0.86 | 87                                                    | 82                                       |

<sup>(A)</sup> Not corrected for recovery of freshly fortified samples<sup>(B)</sup> Relative to nominal (1 mg/kg)**Table B.7.6.3-03 Recovery of pyridaben in fortified samples (1 mg/kg) of orange molasses after storage at <-5°C.**

| Months of storage | Concentration in stored samples <sup>(A)</sup><br>(mg/kg) |      | Average recovery stored samples <sup>(B)</sup><br>(%) | Recovery freshly fortified specimens (%) |
|-------------------|-----------------------------------------------------------|------|-------------------------------------------------------|------------------------------------------|
| 0                 | 0.99                                                      | 0.96 | 98                                                    | 88                                       |
| 1                 | 0.97                                                      | 0.88 | 92                                                    | 88                                       |
| 3                 | 0.85                                                      | 1.05 | 95                                                    | 88                                       |
| 6                 | 0.92                                                      | 0.95 | 94                                                    | 90                                       |
| 12                | 0.94                                                      | 1.00 | 97                                                    | 89                                       |

<sup>(A)</sup> Not corrected for recovery of freshly fortified samples<sup>(B)</sup> Relative to nominal (1 mg/kg)**Table B.7.6.3-04 Recovery of pyridaben in fortified samples (1 mg/kg) of orange oil after storage at <-5°C.**

| Months of storage | Concentration in stored samples <sup>(A)</sup><br>(mg/kg) |      | Average recovery stored samples <sup>(B)</sup><br>(%) | Recovery freshly fortified specimens (%) |
|-------------------|-----------------------------------------------------------|------|-------------------------------------------------------|------------------------------------------|
| 0                 | 0.74                                                      | *    | 74                                                    | 76                                       |
| 1                 | 0.77                                                      | 0.80 | 79                                                    | 76                                       |
| 3                 | 0.79                                                      | 0.80 | 80                                                    | 76                                       |
| 6                 | 0.80                                                      | 0.85 | 82                                                    | 76                                       |
| 12                | 0.81                                                      | 0.84 | 82                                                    | 82                                       |

<sup>(A)</sup> Not corrected for recovery of freshly fortified samples<sup>(B)</sup> Relative to nominal (1 mg/kg)

## Conclusions

Pyridaben in orange, dried orange pulp, orange molasses and orange oil is stable during storage at <-5° C for a period of 12 months.

## Guidelines & Limitations

None

## STUDY 2

### Characteristics

|                   |                                              |               |                   |
|-------------------|----------------------------------------------|---------------|-------------------|
| Reference         | : Tilting, N., 1994 (IIA 6.0/02)             | GLP           | : yes             |
| Type of study     | : storage stability                          | Guideline     | : EPA 171-4       |
| Year of execution | : 1992-1994                                  | Acceptability | : acceptable      |
| Test substance    | : Pyridaben; batch: CH39/169-1; purity 99.7% | Stability     | : see conclusions |

## Study design

Untreated frozen specimens (50 g) of apples, oranges and grapes were homogenised and fortified with pyridaben at 0.5 mg/kg. Fortified samples and controls were stored at -20°C up to 552 days. Residues were analyzed according to the validated (sufficiently for this purpose) method BASF Analytical Method 938/1. Apple and grape samples were extracted with acetone/water mixture. After extraction, solvent partitioning (dichloromethane) and clean-up over Florisil, the extract was analysed by GC-ECD. Orange samples were extracted with acetone/water mixture, after solvent transfer to n-hexane and clean-up over Florisil, the extract was analysed by GC-ECD. Freshly fortified samples (0.5 mg/kg) were included at each storage interval.

## Results

Concentrations and (average) recoveries of stored fortified samples are shown in Tables B.7.6.3-05 to Table B.7.6.3-07. The mean pyridaben recovery in 18 months stored fortified apple samples was 69.1% (in combination with a fresh procedural recovery of 83.5%). Recoveries at other time points were 71.7 to 107%. It is therefore concluded that pyridaben is stable in frozen apple for 552 days (~18 months). The mean pyridaben recovery in 18 months stored fortified orange samples was 59.7% (in combination with a fresh procedural recovery of 65%). At 360 days, the recovery in frozen orange samples was 99.7% (in combination with a fresh procedural recovery of 102.2%). Recoveries at other time points were 77.0-97.4%. The result of day 182 (35% recovery) is considered an outlier. It is therefore concluded that pyridaben is stable in frozen oranges for 360 days (12 months). The mean pyridaben recovery in 18 months stored fortified grape samples was 84.3% (in combination with a fresh procedural recovery of 63.0%). Recoveries at other time points were 75.7 to 101%. It is therefore concluded that pyridaben is stable in frozen grapes for 552 days (~18 months).

**Table B.7.6.3-05 Recovery of pyridaben in fortified samples (0.5 mg/kg) of apples after storage at -20°C.**

| Days of storage | Concentration in stored samples <sup>(A)</sup><br>(mg/kg) |       | Average recovery stored samples <sup>(B)</sup><br>(%) | Recovery freshly fortified specimens (%) |
|-----------------|-----------------------------------------------------------|-------|-------------------------------------------------------|------------------------------------------|
| 0               | 0.528                                                     | 0.502 | 103.0                                                 | 88.6                                     |
| 14              | 0.396                                                     | 0.461 | 85.7                                                  | 97.4                                     |
| 32              | 0.444                                                     | 0.375 | 81.9                                                  | 60.6                                     |
| 60              | 0.439                                                     | 0.406 | 84.5                                                  | 77.7                                     |
| 120             | 0.360                                                     | 0.357 | 71.7                                                  | 65.9                                     |
| 180             | 0.372                                                     | 0.371 | 74.3                                                  | 103.0                                    |
| 300             | 0.526                                                     | 0.544 | 107.0                                                 | 108.7                                    |
| 361             | 0.537                                                     | 0.484 | 102.1                                                 | 104.4                                    |
| 552             | 0.364                                                     | 0.327 | 69.1                                                  | 83.5                                     |

<sup>(A)</sup> Not corrected for recovery of freshly fortified samples

<sup>(B)</sup> Relative to nominal (0.5 mg/kg)

**Table B.7.6.3-06 Recovery of pyridaben in fortified samples (0.5 mg/kg) of oranges after storage at -20°C.**

| Days of storage | Concentration in stored samples <sup>(A)</sup><br>(mg/kg) |       | Average recovery stored samples <sup>(B)</sup><br>(%) | Recovery freshly fortified specimens (%) |
|-----------------|-----------------------------------------------------------|-------|-------------------------------------------------------|------------------------------------------|
| 0               | 0.441                                                     | 0.456 | 89.7                                                  | 87.2                                     |
| 14              | 0.438                                                     | 0.380 | 81.8                                                  | 90.4                                     |
| 30              | 0.398                                                     | 0.397 | 79.5                                                  | 68.7                                     |
| 60              | 0.418                                                     | 0.352 | 77.0                                                  | 82.6                                     |
| 120             | 0.459                                                     | 0.470 | 92.9                                                  | 77.5                                     |
| 182             | 0.159                                                     | 0.191 | 35.0                                                  | 61.3                                     |
| 302             | 0.493                                                     | 0.481 | 97.4                                                  | 94.1                                     |
| 360             | 0.503                                                     | 0.494 | 99.7                                                  | 102.2                                    |
| 557             | 0.312                                                     | 0.285 | 59.7                                                  | 65.0                                     |

<sup>(A)</sup> Not corrected for recovery of freshly fortified samples<sup>(B)</sup> Relative to nominal (0.5 mg/kg)**Table B.7.6.3-07 Recovery of pyridaben in fortified samples (0.5 mg/kg) of grapes after storage at -20°C.**

| Days of storage | Concentration in stored samples <sup>(A)</sup><br>(mg/kg) |       | Average recovery stored samples <sup>(B)</sup><br>(%) | Recovery freshly fortified specimens (%) |
|-----------------|-----------------------------------------------------------|-------|-------------------------------------------------------|------------------------------------------|
| 0               | 0.476                                                     | 0.492 | 96.8                                                  | 95.4                                     |
| 14              | 0.446                                                     | 0.411 | 85.7                                                  | 99.2                                     |
| 32              | 0.499                                                     | 0.477 | 97.6                                                  | 92.6                                     |
| 60              | 0.497                                                     | 0.453 | 95.0                                                  | 101.5                                    |
| 120             | 0.420                                                     | 0.464 | 88.4                                                  | 104.5                                    |
| 180             | 0.387                                                     | 0.370 | 75.7                                                  | 93.6                                     |
| 300             | 0.506                                                     | 0.481 | 98.7                                                  | 113.1                                    |
| 361             | 0.521                                                     | 0.489 | 101.0                                                 | 102.4                                    |
| 552             | 0.462                                                     | 0.381 | 84.3                                                  | 63.0                                     |

<sup>(A)</sup> Not corrected for recovery of freshly fortified samples<sup>(B)</sup> Relative to nominal (0.5 mg/kg)

## Conclusions

Pyridaben residues in apples and grapes are stable during storage at -20° C for a period of 18 months. In oranges, stored at -20°C, pyridaben residues are stable for a period of 12 months.

## Guidelines & Limitations

None.

### B.7.6.4 Summary of storage stability studies

Pyridaben residues in orange, dried orange pulp, orange molasses and orange oil were stable during storage at <-5° C for a period of 12 months. In a second study, pyridaben residues in apples and grapes were stable during storage (-20° C) for a period of 18 months and, again, in oranges for a period of 12 months.

## **B.7.7 Effects of industrial processing and/or household preparation (Annex IIA 6.5; Annex IIIA 8.4)**

### **B.7.7.1 Nature of the residue**

#### **STUDY 1**

##### **Characteristics**

|                   |                                                                                          |               |                                             |
|-------------------|------------------------------------------------------------------------------------------|---------------|---------------------------------------------|
| Reference         | : Wicks, R., 2002 (IIA 6.5.1/01)                                                         | GLP           | : yes                                       |
| Type of study     | : nature of the residue                                                                  | Guideline     | : Lundehehn (Appendix E, 7035/VI/95 rev. 5) |
| Year of execution | : 2001                                                                                   | Acceptability | : yes                                       |
| Test substance    | : [pyridazinone- <sup>14</sup> C]pyridaben (radiochemical purity 97.2%, Lot nr. CP-1505) |               |                                             |

##### **Study design**

The behaviour of [pyridazinone-<sup>14</sup>C] pyridaben was studied under conditions simulating pasteurisation, baking/brewing/boiling and sterilisation, and in compliance with GLP.

Aliquots (0.865 mL) of the dose solution, a mixture of [pyridazinone-<sup>14</sup>C] pyridaben in acetone (2.89 µg/ml), were evaporated to dryness and 500 mL of pH 4, pH 5 and pH 6 buffer solutions (all 0.01 M) were added to obtain a nominal concentration of 5 µg/L. After sonication, duplicate samples were taken to determine the initial test substance concentration (which was confirmed to be 88-96% of nominal). The treated buffer solutions were incubated in the dark as follows: 20 minutes at 90°C (pH 4), 60 minutes at 100°C (pH 5) and 20 minutes at 120°C (pH 6). After incubation, test solutions were adjusted with HCl to pH 2 and two times extracted with ethyl acetate. The extracts were separated into an aqueous and organic phase. Radioactivity in both phases was determined by LSC. The organic phase was concentrated and analysed by reversed phase HPLC with radiodetection. Temperature was monitored and weight loss determined during incubation.

##### **Results**

During incubation the temperature was within 2°C of the target and weight loss was less than 3.1%. From 88.7% to 103.6% AR was extracted from the acidified buffer solutions. In the aqueous phase, 3.1% to 5.3% AR remained. Overall recoveries of radioactivity were 92.6% to 106.8% AR (Table B.7.7.1-01). Besides pyridaben (85.2-97.8% AR), one unknown component was detected in the organic phase (3.2-4.9% AR). This unknown was also present in the starting material at 2.2%.

**Table B.7.7.1-01 Recovery and identification of radioactivity after incubation of [pyridazinone-<sup>14</sup>C] pyridaben under pasteurisation, baking/brewing/boiling and sterilisation simulating conditions.**

|                             | % of applied <sup>(A)</sup>             |                                                  |                                         |
|-----------------------------|-----------------------------------------|--------------------------------------------------|-----------------------------------------|
|                             | pH 4 (90°C, 20 min)<br>(pasteurisation) | pH 5 (100°C, 60 min)<br>(baking/brewing/boiling) | pH 6 (120°C, 20 min)<br>(sterilisation) |
| prior to incubation (total) | 100                                     | 100                                              | 100                                     |
| post incubation (total)     | 106.8                                   | 99.4                                             | 92.6                                    |
| ethyl acetate               | 103.6                                   | 94.1                                             | 88.7                                    |
| pyridaben                   | 97.8                                    | 90.0                                             | 85.2                                    |
| unknown <sup>(B)</sup>      | 4.9                                     | 4.0                                              | 3.2                                     |
| aqueous residue             | 3.1                                     | 5.3                                              | 3.9                                     |

<sup>(A)</sup> mean of duplicate samples

<sup>(B)</sup> also present in the starting material at 2.2%

## Conclusions

Pyridaben was stable under conditions simulating pasteurisation, baking/brewing/boiling and sterilisation. One unknown component was detected which accounted for 3.2-4.9% AR. The study is acceptable.

## Guidelines & Limitations

None.

## B.7.7.2 Effects on residue levels

### STUDY 1

#### Characteristics

|                   |                                                |               |                 |
|-------------------|------------------------------------------------|---------------|-----------------|
| Reference         | : Abdel-Baky, S., 1994 (IIA 6.5.2/01)          | GLP           | : yes           |
| Type of study     | : nature of the residue (processing)           | Guideline     | : EPA: 171-4(1) |
| Year of execution | : 1992-1993                                    | Acceptability | : acceptable    |
| Test substance    | : Pyridaben 75% WP (lot nr. OAJ 030; 74.9% ai) |               |                 |

#### Study design

Orange samples were collected from one site in California to determine if pyridaben concentrates into processed orange fractions. Orange trees were treated three times at an exaggerated rate of 5.6 kg ai/ha (formulated as 75% WP). Applications took place 176-178 days before harvest, 88-90 days before harvest and on the day of harvest. After harvest, oranges were processed into wet and dry pulp, molasses, oil and orange juice following commercial practices as closely as possible. Residues were analysed according to the validated method BASF D9309. In short, residues were extracted from all matrices with acetone/hexane, except for orange oil (dissolution in hexane). After partitioning into different organic phases and solid phase clean up, samples were analysed using GC-ECD with a LOQ of 0.05 mg/kg. Procedural recoveries at the LOQ and 10-300xLOQ were included and were 90±10% (n=14) on average. Storage stability was confirmed for the storage period relevant for this study (storage at <-5°C for maximum 4.5 months).

## Results

Pyridaben residues were 0.52 mg/kg in unwashed whole orange samples. After washing, pyridaben residues were 0.25 mg/kg. Pyridaben residues were 0.39 and 1.8 mg/kg for wet and dry pulp, respectively. In orange molasses, orange oil and orange juice the residues were 0.15 mg/kg, 13.1 mg/kg and <0.05 mg/kg. See Table B.7.7.2-01. Processing factors were <1 for wet pulp (0.75), washed whole oranges (0.49), molasses (0.30) and orange juice (<0.1). Residues were concentrated in dry pulp (x3.5) and orange oil (x25.3).

**Table B.7.7.2-01 Residues and processing factors in orange and processed orange products after three treatments with pyridaben (formulated as 75% WP) at 5.6 kg ai/ha.**

| Product<br>Orange     | Pyridaben         |                   |                                               |
|-----------------------|-------------------|-------------------|-----------------------------------------------|
|                       | Pyridaben (mg/kg) | Processing factor | recovery fortified samples (%) <sup>(A)</sup> |
| unwashed whole orange | 0.52              | -                 | 78 (0.05/5 mg/kg)                             |
| washed whole orange   | 0.25              | 0.49              | 85 (0.05/0.5 mg/kg)                           |
| wet pulp              | 0.39              | 0.75              | 99 (0.05/0.5 mg/kg)                           |
| dry pulp              | 1.8               | 3.5               | 91 (0.05/0.5 mg/kg)                           |
| orange molasses       | 0.15              | 0.30              | 94 (0.05/0.5 mg/kg)                           |
| orange oil            | 13.1              | 25.3              | 100 (0.05/15 mg/kg)                           |
| orange juice          | <0.05             | <0.1              | 87 (0.05/0.5 mg/kg)                           |

<sup>(A)</sup> average of two determinations

## Conclusions

Processing factors (pyridaben residues) were <1 for wet pulp (0.75), washed whole oranges (0.49), molasses (0.30) and orange juice (<0.1). Residues were concentrated in dry pulp (x3.5) and orange oil (x25.3). The study is acceptable.

## Guidelines & Limitations

None

## STUDY 2

### Characteristics

|                   |                                                 |               |                        |       |
|-------------------|-------------------------------------------------|---------------|------------------------|-------|
| Reference         | : Blaschke, U., 2003 (IIA 6.5.2/02)             | GLP           | : yes                  |       |
| Type of study     | : nature of the residue (processing)            | Guideline     | : 7029/VI/95 (Lundehn) | rev.5 |
| Year of execution | : 2002-2003                                     | Acceptability | : acceptable           |       |
| Test substance    | : Pyridaben 20WP (batch nr. OAK 207; 20.46% ai) |               |                        |       |

### Study design

"Navelina" Oranges were harvested from two plots at one site in Italy to determine the magnitude of the pyridaben residues at harvest and to determine residues in processed commodities. Orange trees were treated with a single application of Pyridaben 20WP at 0.3 kg ai/ha (normal rate, plot 2) or 1.5 kg ai/ha (exaggerated rate, plot 3). Oranges were harvested 14 days after application. Oranges were separated into peel and pulp or subjected to processing into wet and dry pomace, juice, marmalade and canned oranges. Pyridaben residues were determined by validated method NAS/366 (equivalent to BASF D9309). In short, all samples, except dry pomace, were extracted with acetone/water (80:20 v:v), followed by clean-up by liquid/liquid partitioning and solid phase extraction and analysed by GC-ECD. Dry pomace was extracted

with acetone:0.5N hydrochloric acid (50:50 v:v) followed by clean up, prior to analysis. The limit of quantitation (LOQ) was 0.05 mg/kg and limit of detection (LOD) was 0.02 mg/kg for all matrices. Procedural recoveries with fortified samples were included and ranged from 72 to 109%. RAC and processed samples were collected and frozen (<-18°C) for 60-80 days. Pyridaben residues are stable during frozen storage for 80 days as was demonstrated elsewhere (B.7.7.2, STUDY 1).

## Results

Residues in whole oranges and processed fractions are presented in Table B.7.7.2-02. Pyridaben residues in whole unwashed oranges were 0.17-0.19 and 0.56-0.78 mg/kg for the low and high dose, respectively. Residues in unwashed peel were 0.63-0.73 and 2.19-2.64 mg/kg for the low and high dose, respectively. Residues in pulp were <LOQ for the low dose and 0.12 for the high dose. In the processed samples, residues were <LOD for marmalade, canned oranges, and pasteurised juice (low dose) and 0.12, <LOD, 0.08 mg/kg, respectively for the high dose treatment. In wet pomace, pyridaben residues were 0.18 and 0.62 mg/kg for the low and high dose, respectively. In dry pomace, pyridaben residues were 0.61 and 2.88 mg/kg for the low and high dose, respectively. Processing factors and % transference are presented in Table B.7.7.2-03. Processing factors were <1 for washed whole oranges (0.37-0.66), pulp (<0.09-<0.12), juice (<0.12-0.14), marmalade (<0.12-0.21) and canned fruit (<0.04-<0.12). Residues were concentrated in dry pomace (3.57-5.16) and wet pomace (1.05-1.11).

**Table B.7.7.2-02 Residues in orange and processed orange products after one treatment with Pyridaben (formulated as 20WP) at 0.3 kg ai/ha or 1.5 kg ai/ha**

|                               | Pyridaben (mg/kg)   |                     |                  |                   |                     |                     |
|-------------------------------|---------------------|---------------------|------------------|-------------------|---------------------|---------------------|
|                               | Total fruit         |                     | Peel             |                   | Pulp                |                     |
|                               | 2 <sup>(1)</sup>    | 3 <sup>(2)</sup>    | 2 <sup>(1)</sup> | 3 <sup>(2)</sup>  | 2 <sup>(1)</sup>    | 3 <sup>(2)</sup>    |
| RAC (14 DAA)                  | 0.17 <sup>(A)</sup> | 0.56 <sup>(A)</sup> | 0.73             | 2.19              | ND <sup>(B)</sup>   | ND <sup>(B)</sup>   |
| Prior to processing, unwashed | 0.19 <sup>(A)</sup> | 0.78 <sup>(A)</sup> | 0.63             | 2.64              | <LOQ <sup>(C)</sup> | 0.12                |
|                               | total fruit         |                     | orange peel      |                   | peeled oranges      |                     |
| During orange canning, washed | 0.06 <sup>(A)</sup> | 0.37 <sup>(A)</sup> | 0.23             | 1.38              | ND <sup>(B)</sup>   | <LOQ <sup>(C)</sup> |
|                               | wet pomace          |                     | dry pomace       |                   | pasteurised juice   |                     |
| During juice production       | 0.18                | 0.62                | 0.61             | 2.88              | ND <sup>(B)</sup>   | 0.08                |
|                               | marmalade           |                     |                  |                   |                     |                     |
|                               | 2                   |                     |                  | 3                 |                     |                     |
| During marmalade production   | ND <sup>(B)</sup>   |                     |                  | 0.12              |                     |                     |
|                               | Canned oranges      |                     |                  |                   |                     |                     |
|                               | 2                   |                     |                  | 3                 |                     |                     |
| During orange canning         | ND <sup>(B)</sup>   |                     |                  | ND <sup>(B)</sup> |                     |                     |

(1) plot 2, application rate is 0.3 kg ai/ha

(2) plot 3, application rate is 1.5 kg ai/kg

(B) calculated value from peel and pulp residue

(C) ND= Less than limit of detection of 0.02 mg/kg

(D) <LOQ= Less than limit of quantitation of 0.05 mg/kg

**Table B.7.7.2-03 Transfer factors and % transference in orange and processed orange products after one treatment with Pyridaben (formulated as Pyridaben 20WP) at 0.3 kg ai/ha or 1.5 kg ai/ha**

| Product:<br>Orange                        | recovery                                 | Transfer factor  |                  | % Transference <sup>(B, C)</sup> |                  |
|-------------------------------------------|------------------------------------------|------------------|------------------|----------------------------------|------------------|
|                                           |                                          | 2 <sup>(1)</sup> | 3 <sup>(2)</sup> | 2 <sup>(1)</sup>                 | 3 <sup>(2)</sup> |
| Total fruit RAC <sup>(A)</sup> (unwashed) |                                          | 1.00             | 1.00             | 100                              | 100              |
| Total fruit (washed)                      |                                          | 0.37             | 0.66             | 38                               | 66               |
| Peel (washed)                             | 72% <sup>(D)</sup><br>80% <sup>(E)</sup> | 1.35             | 2.47             | 37                               | 62               |
| Pulp (washed)                             | 93% <sup>(D)</sup>                       | <0.12            | <0.09            | 0                                | 3                |
| wet pomace                                | 95% <sup>(D)</sup>                       | 1.05             | 1.11             | 65                               | 68               |
| dry pomace                                | 93% <sup>(D)</sup>                       | 3.57             | 5.16             | 52                               | 77               |
| pasteurised juice                         | 85% <sup>(D)</sup>                       | <0.12            | 0.14             | 0                                | 4                |
| marmalade                                 | 89% <sup>(D)</sup>                       | <0.12            | 0.21             | 0                                | 75               |
| canned oranges                            | 109% <sup>(D)</sup>                      | <0.12            | <0.04            | 0                                | 0                |

<sup>(1)</sup> plot 2, application rate is 0.3 kg ai/ha

<sup>(2)</sup> plot 3, application rate is 1.5 kg ai/kg

<sup>(A)</sup> calculated value from peel and pulp residue

<sup>(B)</sup> for ND residue values, 0 mg/kg is used for calculation

<sup>(C)</sup> for residue values <LOQ, 0.025 mg/kg, half the LOQ, is used for calculation

<sup>(D)</sup> procedural recovery determined with fortified samples at 0.5 mg/kg

<sup>(E)</sup> procedural recovery determined with fortified samples at 1.0 mg/kg

## Conclusions

Processing factors (pyridaben residues) were <1 for washed whole oranges (0.37-0.66), pulp (<0.09-<0.12), juice (<0.12-0.14), marmalade (<0.12-0.21) and canned fruit (<0.04-<0.12). Pyridaben residues were concentrated in dry pomace (3.57-5.16) and wet pomace (1.05-1.11). The study is acceptable.

## Guidelines & Limitations

1. None

### B.7.7.3 Summary of the processing studies

Three processing studies were submitted, one on the nature of the residue and two on the effects on residue levels in citrus products (oranges). All studies were acceptable. Processing studies in citrus are required as residue levels in citrus are >0.1 mg eq/kg. Processing studies in tomatoes are not required as residue levels are <0.1 mg eq/kg. The statement on tomato is subject to revision pending on the generation of new residue data under least favourable conditions (see B.7.6).

In the study on the nature of the residue, pyridaben was shown to be stable under conditions simulating pasteurisation, baking/brewing/boiling and sterilisation.

In the processing study in oranges, the processing factors (pyridaben residues) were <1 for wet pulp (0.75), washed whole oranges (0.49), molasses (0.30) and orange juice (<0.1). Residues were concentrated in dry pulp (x3.5) and orange oil (x25.3). In the second study in oranges, processing factors (pyridaben residues) were <1 for washed whole oranges (0.37-0.66), pulp (<0.09-<0.12), juice (<0.12-0.14), marmalade (<0.12-

0.21) and canned fruit (<0.04-<0.12). Pyridaben residues were concentrated in dry pomace (3.57-5.16) and wet pomace (1.05-1.11).

### B.7.8 Livestock feeding studies (Annex IIA 6.4; Annex III 8.5)

Although pyridaben residues in animal feed (cattle) exceed 0.1 mg/kg dry feed, livestock feeding studies are not required because the metabolism study in goat indicated no residues >0.01 mg eq/kg in edible animal tissues and milk. Studies in poultry are not required as wet pomace is not a constituent of poultry feed. (Note: the intake calculation for cattle was based on a HR (whole fruit, oranges) of 0.12 mg/kg and a wet pomace processing factor of 1.1. The HR value is provisional as the field residue trials were not conducted under least favourable conditions). A livestock feeding study in cow was performed and is summarized below. The above statement may have to be revised pending on the HR/STMR obtained under least favourable conditions.

#### B.7.8.1 Ruminants

##### STUDY 1

##### Characteristics

|                   |                                                                                   |                 |                                                                                                                                            |
|-------------------|-----------------------------------------------------------------------------------|-----------------|--------------------------------------------------------------------------------------------------------------------------------------------|
| Reference         | : Riley, M-E., Abdel-Baky, S. and Jordan, J., 1996 (IIA, 6.4/01)                  | Animal products | : Muscle, liver, kidney, fat, and milk                                                                                                     |
| Type of study     | : Magnitude of residues in animal tissues and animal products (livestock feeding) | GLP statement   | : yes                                                                                                                                      |
| Year of execution | : 1994                                                                            | Guideline       | : EPA O:171-4                                                                                                                              |
| Test substance    | : pyridaben, lot nr. 900304; purity 100%                                          | Dose levels     | : 2.5 (XXN), 7.5 (XXN) and 25 (XXN) mg pyridaben per kg dm feed equivalent to 0.08, 0.25, and 0.76 mg pyridaben per kg bw/day for 29 days. |
| Type of animal    | : Lactating dairy cow (Holstein)                                                  | Acceptability   | : Acceptable                                                                                                                               |

XX: no exact comparison with the expected feed concentration could be made due to the lack of residue data under least favourable conditions.

##### Study design

Three groups of 3 (low, middle and high dose) lactating dairy cows (Holstein, 3-4 years of age) were administered gelatine capsules containing pyridaben once a day for 29 consecutive days. The dose levels were 2.5 (XXN TMDI cattle), 7.5 (XXN), and 25 (XXN) mg pyridaben per kg dm feed, equivalent to 0.08, 0.25, and 0.76 mg per kg bw/day (XX: no exact comparison with the expected feed concentration could be made due to the lack of residue data under least favourable conditions, see B.7.6). A control group (3 animals) was included. Gelatine capsules were prepared weekly. Gelatine capsules were stored in at ≤15°C. The dose and stability was confirmed by HPLC-UV analysis. Dosing took place mid-morning after morning milking. Cows were milked twice daily. Proportional composite milk samples were prepared per cow and day (day -1, 1, 3, 5, 7, 10, 14, 17, 21, 24 and 28 milk samples collected) and stored frozen (≤6.5 months) for later analysis.

At the end of the dosing period (5 hours after the last dose) on day 29, the cows of each treatment group and control animals were slaughtered. Liver, kidney, muscle (composite thigh and loin) and fat (composite

mesenteric and peripheral) samples (approximately 1-2 kg per sample each) were removed, homogenised and stored frozen ( $\leq 6.5$  months) for later analysis.

Samples were analysed for pyridaben, PB-7 and PB-9 according to method D9405. The method involved extraction with acetone:water 80/20 (fat and tissues) or acetone (milk). Extracts were derivatised using diazomethane (methylation) and purified on a C-18 column prior to GC-ECD analysis. The LOQ was 0.01 mg/kg for milk and 0.05 mg/kg for tissues. Freshly fortified samples (all matrices, pyridaben, PB-7, PB-9) at the LOQ and up to 20-100 x LOQ were included yielding mean recoveries within 70 to 110% except for PB-9 (mean recoveries within 70-121%).

## Results

The cows remained in good health during the study. No treatment-related effects on body weight, milk production, or feed intake during the dosing period were observed. At *post-mortem*, no treatment-related abnormalities were observed.

Storage stability of pyridaben, PB-7 and PB-9 in beef muscle, liver, and milk was demonstrated for up to 5 months frozen storage (see B.7.8.3-01). Based upon the results after 5 months of storage, sufficient stability is also assumed after 6.5 months of frozen storage (with the possible exception of pyridaben in muscle). As no residues of pyridaben were detected in muscle of the highest dose group, the results are accepted.

Measured residues are given in Tables B.7.8.1-01 to B.7.8.1-05.

In milk, no PB-7 and PB-9 residues above the LOQ (0.01 mg/kg) were found for the low, middle and high dose treatment level. Pyridaben was not detected at the low dose, only once at the middle dose (max 0.01 mg/kg) and occasionally at the high dose (max 0.02 mg/kg).

PB-9 was not detected in any tissue at any dose level. PB-7 was only detected in liver of the middle and high dose levels, at maximum 0.05 and 0.15 mg/kg, respectively. Pyridaben was only detected in fat samples of the high dose group at maximum 0.08 mg/kg (mean 0.07 mg/kg).

**Table B.7.8.1-01** Mean residues of pyridaben, PB-7 and PB-9 in whole milk samples from lactating cows receiving diet fortified at 2.5 mg pyridaben per kg dm feed.

| Days of dosing              | Pyridaben, PB-7 and PB-9 mean <sup>(C)</sup> residues in whole milk (mg/kg) |       |       |                               |       |       |
|-----------------------------|-----------------------------------------------------------------------------|-------|-------|-------------------------------|-------|-------|
|                             | control                                                                     |       |       | 2.5 mg pyridaben / kg dm feed |       |       |
|                             | pyridaben                                                                   | PB-7  | PB-9  | pyridaben                     | PB-7  | PB-9  |
| -1                          | <0.01                                                                       | <0.01 | <0.01 | <0.01                         | <0.01 | <0.01 |
| 1                           | <0.01                                                                       | <0.01 | <0.01 | <0.01                         | <0.01 | <0.01 |
| 3                           | <0.01                                                                       | <0.01 | <0.01 | <0.01                         | <0.01 | <0.01 |
| 5                           | <0.01                                                                       | <0.01 | <0.01 | <0.01                         | <0.01 | <0.01 |
| 7                           | <0.01                                                                       | <0.01 | <0.01 | <0.01                         | <0.01 | <0.01 |
| 10                          | <0.01                                                                       | <0.01 | <0.01 | <0.01                         | <0.01 | <0.01 |
| 14                          | <0.01                                                                       | <0.01 | <0.01 | <0.01                         | <0.01 | <0.01 |
| 17                          | <0.01                                                                       | <0.01 | <0.01 | <0.01                         | <0.01 | <0.01 |
| 21                          | <0.01                                                                       | <0.01 | <0.01 | <0.01                         | <0.01 | <0.01 |
| 24                          | <0.01                                                                       | <0.01 | <0.01 | <0.01                         | <0.01 | <0.01 |
| 28                          | <0.01                                                                       | <0.01 | <0.01 | <0.01                         | <0.01 | <0.01 |
| overall mean <sup>(A)</sup> | <0.01                                                                       | <0.01 | <0.01 | <0.01                         | <0.01 | <0.01 |
| maximum <sup>(B)</sup>      | <0.01                                                                       | <0.01 | <0.01 | <0.01                         | <0.01 | <0.01 |

<sup>(A)</sup> Mean of days 1-28<sup>(B)</sup> Individual animal maximum observed during the study<sup>(C)</sup> Mean of 3 cows**Table B.7.8.1-02** Mean residues of pyridaben, PB-7 and PB-9 in whole milk samples from lactating cows receiving diet fortified at 7.5 and 25 mg pyridaben per kg dm feed.

| Days of dosing              | Pyridaben, PB-7 and PB-9 mean <sup>(C)</sup> residues in whole milk (mg/kg) |       |       |                              |       |       |
|-----------------------------|-----------------------------------------------------------------------------|-------|-------|------------------------------|-------|-------|
|                             | 7.5 mg pyridaben / kg dm feed                                               |       |       | 25 mg pyridaben / kg dm feed |       |       |
|                             | pyridaben                                                                   | PB-7  | PB-9  | pyridaben                    | PB-7  | PB-9  |
| -1                          | <0.01                                                                       | <0.01 | <0.01 | <0.01                        | <0.01 | <0.01 |
| 1                           | <0.01                                                                       | <0.01 | <0.01 | <0.01                        | <0.01 | <0.01 |
| 3                           | <0.01                                                                       | <0.01 | <0.01 | <0.02                        | <0.01 | <0.01 |
| 5                           | <0.02                                                                       | <0.01 | <0.01 | <0.02                        | <0.01 | <0.01 |
| 7                           | <0.01                                                                       | <0.01 | <0.01 | <0.01                        | <0.01 | <0.01 |
| 10                          | <0.01                                                                       | <0.01 | <0.01 | <0.01                        | <0.01 | <0.01 |
| 14                          | <0.01                                                                       | <0.01 | <0.01 | <0.01                        | <0.01 | <0.01 |
| 17                          | <0.01                                                                       | <0.01 | <0.01 | <0.02                        | <0.01 | <0.01 |
| 21                          | <0.01                                                                       | <0.01 | <0.01 | <0.01                        | <0.01 | <0.01 |
| 24                          | <0.01                                                                       | <0.01 | <0.01 | <0.01                        | <0.01 | <0.01 |
| 28                          | <0.01                                                                       | <0.01 | <0.01 | <0.02                        | <0.01 | <0.01 |
| overall mean <sup>(A)</sup> | <0.01                                                                       | <0.01 | <0.01 | <0.01                        | <0.01 | <0.01 |
| maximum <sup>(B)</sup>      | 0.01                                                                        | <0.01 | <0.01 | 0.02                         | <0.01 | <0.01 |

<sup>(A)</sup> Mean of days 1-28<sup>(B)</sup> Individual animal maximum observed during the study<sup>(C)</sup> Mean of 3 cows**Table B.7.8.1-03** Mean and maximum residues of pyridaben in tissue samples from three groups of lactating cows receiving diet fortified at 2.5, 7.5 and 25 mg per kg dm feed.

| Dose group (mg per kg dm feed) | Mean <sup>(A)</sup> and maximum pyridaben residues in tissue samples (mg/kg) |                    |       |                    |        |                    |       |                    |
|--------------------------------|------------------------------------------------------------------------------|--------------------|-------|--------------------|--------|--------------------|-------|--------------------|
|                                | kidney                                                                       |                    | liver |                    | muscle |                    | fat   |                    |
|                                | mean                                                                         | max <sup>(B)</sup> | mean  | max <sup>(B)</sup> | mean   | max <sup>(B)</sup> | mean  | max <sup>(B)</sup> |
| 2.5                            | <0.05                                                                        | <0.05              | <0.05 | <0.05              | <0.05  | <0.05              | <0.05 | <0.05              |
| 7.5                            | <0.05                                                                        | <0.05              | <0.05 | <0.05              | <0.05  | <0.05              | <0.05 | <0.05              |
| 25                             | <0.05                                                                        | <0.05              | <0.05 | <0.05              | <0.05  | <0.05              | 0.07  | 0.08               |
| 0 (control)                    | <0.05                                                                        | <0.05              | <0.05 | <0.05              | <0.05  | <0.05              | <0.05 | <0.05              |

<sup>(A)</sup> Mean of 3 cows.<sup>(B)</sup> Individual animal maximum.

**Table B.7.8.1-04 Mean and maximum residues of PB-7 in tissue samples from three groups of lactating cows receiving diet fortified at 2.5, 7.5 and 25 mg per kg dm feed.**

| Dose group<br>(mg per kg<br>dm feed) | Mean <sup>(A)</sup> and maximum PB-7 residues in tissue samples (mg/kg) |                    |       |                    |        |                    |       |                    |
|--------------------------------------|-------------------------------------------------------------------------|--------------------|-------|--------------------|--------|--------------------|-------|--------------------|
|                                      | kidney                                                                  |                    | liver |                    | muscle |                    | fat   |                    |
|                                      | mean                                                                    | max <sup>(B)</sup> | mean  | max <sup>(B)</sup> | mean   | max <sup>(B)</sup> | mean  | max <sup>(B)</sup> |
| 2.5                                  | <0.05                                                                   | <0.05              | <0.05 | <0.05              | <0.05  | <0.05              | <0.05 | <0.05              |
| 7.5                                  | <0.05                                                                   | <0.05              | ≤0.05 | 0.05               | <0.05  | <0.05              | <0.05 | <0.05              |
| 25                                   | <0.05                                                                   | <0.05              | 0.11  | 0.15               | <0.05  | <0.05              | <0.05 | <0.05              |
| 0 (control)                          | <0.05                                                                   | <0.05              | <0.05 | <0.05              | <0.05  | <0.05              | <0.05 | <0.05              |

<sup>(A)</sup> Mean of 3 cows.<sup>(B)</sup> Individual animal maximum.**Table B.7.8.1-05 Mean and maximum residues of PB-9 in tissue samples from three groups of lactating cows receiving diet fortified at 2.5, 7.5 and 25 mg per kg dm feed.**

| Dose group<br>(mg per kg<br>dm feed) | Mean <sup>(A)</sup> and maximum PB-9 residues in tissue samples (mg/kg) |                    |       |                    |        |                    |       |                    |
|--------------------------------------|-------------------------------------------------------------------------|--------------------|-------|--------------------|--------|--------------------|-------|--------------------|
|                                      | kidney                                                                  |                    | liver |                    | muscle |                    | fat   |                    |
|                                      | mean                                                                    | max <sup>(B)</sup> | mean  | max <sup>(B)</sup> | mean   | max <sup>(B)</sup> | mean  | max <sup>(B)</sup> |
| 2.5                                  | <0.05                                                                   | <0.05              | <0.05 | <0.05              | <0.05  | <0.05              | <0.05 | <0.05              |
| 7.5                                  | <0.05                                                                   | <0.05              | <0.05 | <0.05              | <0.05  | <0.05              | <0.05 | <0.05              |
| 25                                   | <0.05                                                                   | <0.05              | <0.05 | <0.05              | <0.05  | <0.05              | <0.05 | <0.05              |
| 0 (control)                          | <0.05                                                                   | <0.05              | <0.05 | <0.05              | <0.05  | <0.05              | <0.05 | <0.05              |

<sup>(A)</sup> Mean of 3 cows.<sup>(B)</sup> Individual animal maximum.

## Conclusions

Lactating cows were administered capsules fortified with pyridaben at levels of 2.5 (XXN TMDI cattle), 7.5 (XXN) and 25 (XXN) mg per kg dm feed over a period of 29 days (equivalent to 0.08, 0.25 and 0.76 mg pyridaben per kg bw/day). (XX: no exact comparison with the expected feed concentration could be made due to the lack of residue data under least favourable conditions, see B.7.6). In milk, no PB-7 and PB-9 residues above the LOQ (0.01 mg/kg) were found for the low, middle and high dose treatment level. Pyridaben was not detected at the low dose, only once at the middle dose (max 0.01 mg/kg) and occasionally at the high dose (max 0.02 mg/kg). PB-9 was not detected in any tissue at any dose level. PB-7 was only detected in liver of the middle and high dose levels, at maximum 0.05 and 0.15 mg/kg, respectively. Pyridaben was only detected in fat samples of the high dose group at maximum 0.08 mg/kg (mean 0.07 mg/kg). The study is acceptable.

## Guidelines and limitations

1. No exact comparison with the expected feed concentration could be made due to the lack of residue data under least favourable conditions, see B.7.6.

### B.7.8.2 Summary of the livestock feeding studies

Although pyridaben residues in animal feed (cattle) exceed 0.1 mg/kg dry feed, livestock feeding studies are not required because the metabolism study in goat indicated no residues >0.01 mg eq/kg in edible animal tissues and milk at normal feeding rates. Studies in poultry are not required as wet pomace/tomato is not a

constituent of poultry feed. (Note: the intake calculation for cattle was based on a HR (whole fruit, oranges) of 0.12 mg/kg and a wet pomace processing factor of 1.1. The HR value is provisional as the field residue trials were not conducted under least favourable conditions). The above statement may have to be revised pending on the HR obtained under least favourable conditions.

The lowest dose used in the study in cattle was 2.5 mg/kg dry matter feed. This dose is a factor 15 higher than the maximum estimated concentration in animal feed for cattle of approximately 0.17 mg/kg dm feed (provisional calculation, see B.7.15). The results of the livestock feeding study at the low dose indicate no residues of pyridaben above the LOQ (0.01 (milk) and 0.05 mg/kg (tissues)) in milk and all tissues.

### B.7.8.3 Stability (in animal products) of residues prior to analysis (Annex IIA 6.0)

#### STUDY 1

##### Characteristics

|                   |                                                                                                                                                                                |               |              |
|-------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------|--------------|
| Reference         | : Riley, M-E, Abdel-Baky, S. 1995 (IIA 6.0/03)                                                                                                                                 | GLP           | : yes        |
| Type of study     | : Storage stability in animal tissues                                                                                                                                          | Guideline     | : EPA 171-4  |
| Year of execution | : 1994-1995                                                                                                                                                                    | Acceptability | : acceptable |
| Test substance    | Pyridaben, batch: CH 39/169-1, purity: 99.7%,<br>pyridaben metabolite PB-7, batch: PB7-S920822, purity: 98.8%, pyridaben metabolite<br>PB-9, batch: PB9-S920910, purity: 98.7% |               |              |

##### Study design

Samples of dairy cow liver, muscle and milk were homogenised and fortified with a mixture of pyridaben and its metabolites PB-7 and PB-9 at 1 mg/kg. Fortified samples and controls were stored at <-5°C up to 5 months. Residues were analyzed according to the validated method (sufficiently for this purpose) BASF analytical method D9405. The residues were extracted with an 80% acetone in water solution for the tissues and 100% acetone for milk. After methylation (diazomethane) the samples were cleaned over a C<sub>18</sub>-column and analysed with GC-ECD. Freshly fortified samples (1 mg/kg) were included at each storage interval.

##### Results

Concentrations and (average) recoveries of stored fortified samples for pyridaben and its metabolites PB-7 and PB-9 are shown in Tables B.7.8.3-01 to Table B.7.8.3-09. Mean pyridaben recoveries in 5 months stored fortified samples were 88 (liver), 70 (muscle) and 100% (milk) (in combination with procedural recoveries of 95, 100 and 97%, respectively). Therefore it can be concluded that pyridaben is stable in frozen (<-5°C) liver, muscle and milk for 5 months. Mean PB-7 recoveries in 5 months stored fortified samples were 95 (liver), 76 (muscle) and 109% (milk) (in combination with procedural recoveries of 91, 82 and 106%, respectively). Therefore it can be concluded that PB-7 is stable in frozen (<-5°C) liver, muscle and milk for 5 months. Mean PB-9 recoveries in 5 months stored fortified samples were 107 (liver), 106 (muscle) and 86% (milk) (in combination with procedural recoveries of 106, 110 and 83%, respectively). Therefore it can be concluded that PB-9 is stable in frozen (<-5°C) liver, muscle and milk for 5 months.

**Table B.7.8.3-01 Recovery of pyridaben in fortified samples (1 mg/kg) of liver after storage at <-5°C.**

| Months of storage | Concentration in stored samples <sup>(A)</sup><br>(mg/kg) |      | Average recovery stored samples <sup>(B)</sup><br>(%) | Recovery freshly fortified specimens (%) |
|-------------------|-----------------------------------------------------------|------|-------------------------------------------------------|------------------------------------------|
| 0                 | 0.89                                                      | 0.88 | 89                                                    | 94                                       |
| 1                 | 0.73                                                      | 0.87 | 80                                                    | 94                                       |
| 3                 | 0.85                                                      | 0.88 | 87                                                    | 94                                       |
| 5                 | 0.85                                                      | 0.91 | 88                                                    | 95                                       |

<sup>(A)</sup> Not corrected for recovery of freshly fortified samples<sup>(B)</sup> Relative to nominal (1 mg/kg)**Table B.7.8.3-02 Recovery of pyridaben in fortified samples (1 mg/kg) of muscle after storage at <-5°C.**

| Months of storage | Concentration in stored samples <sup>(A)</sup><br>(mg/kg) |      | Average recovery stored samples <sup>(B)</sup><br>(%) | Recovery freshly fortified specimens (%) |
|-------------------|-----------------------------------------------------------|------|-------------------------------------------------------|------------------------------------------|
| 0                 | 0.84                                                      | 0.88 | 86                                                    | 96                                       |
| 1                 | 0.79                                                      | 0.81 | 80                                                    | 96                                       |
| 3                 | 0.64                                                      | 0.69 | 67                                                    | 96                                       |
| 5                 | 0.71                                                      | 0.69 | 70                                                    | 100                                      |

<sup>(A)</sup> Not corrected for recovery of freshly fortified samples<sup>(B)</sup> Relative to nominal (1 mg/kg)**Table B.7.8.3-03 Recovery of pyridaben in fortified samples (1 mg/kg) of milk after storage at <-5°C.**

| Months of storage | Concentration in stored samples <sup>(A)</sup><br>(mg/kg) |       | Average recovery stored samples <sup>(B)</sup><br>(%) | Recovery freshly fortified specimens (%) |
|-------------------|-----------------------------------------------------------|-------|-------------------------------------------------------|------------------------------------------|
| 0                 | 0.93                                                      | 0.94  | 94                                                    | 92                                       |
| 1                 | 0.92                                                      | 0.89  | 91                                                    | 92                                       |
| 3                 | 0.84                                                      | 0.88  | 86                                                    | 92                                       |
| 5                 | 1.014                                                     | 0.983 | 99.9                                                  | 97                                       |

<sup>(A)</sup> Not corrected for recovery of freshly fortified samples<sup>(B)</sup> Relative to nominal (1 mg/kg)**Table B.7.8.3-04 Recovery of pyridaben metabolite PB-7 in fortified samples (1 mg/kg) of liver after storage at <-5°C.**

| Months of storage | Concentration in stored samples <sup>(A)</sup><br>(mg/kg) |      | Average recovery stored samples <sup>(B)</sup><br>(%) | Recovery freshly fortified specimens (%) |
|-------------------|-----------------------------------------------------------|------|-------------------------------------------------------|------------------------------------------|
| 0                 | 0.96                                                      | 0.95 | 96                                                    | 94                                       |
| 1                 | 0.83                                                      | 0.93 | 88                                                    | 94                                       |
| 3                 | 0.89                                                      | 0.92 | 91                                                    | 94                                       |
| 5                 | 0.91                                                      | 0.99 | 95                                                    | 91                                       |

<sup>(A)</sup> Not corrected for recovery of freshly fortified samples<sup>(B)</sup> Relative to nominal (1 mg/kg)**Table B.7.8.3-05 Recovery of pyridaben metabolite PB-7 in fortified samples (1 mg/kg) of muscle after storage at <-5°C.**

| Months of storage | Concentration in stored samples <sup>(A)</sup><br>(mg/kg) |      | Average recovery stored samples <sup>(B)</sup><br>(%) | Recovery freshly fortified specimens (%) |
|-------------------|-----------------------------------------------------------|------|-------------------------------------------------------|------------------------------------------|
| 0                 | 0.81                                                      | 0.82 | 82                                                    | 80                                       |
| 1                 | 0.79                                                      | 0.80 | 80                                                    | 80                                       |
| 3                 | 0.72                                                      | 0.74 | 73                                                    | 80                                       |
| 5                 | 0.75                                                      | 0.76 | 76                                                    | 82                                       |

<sup>(A)</sup> Not corrected for recovery of freshly fortified samples<sup>(B)</sup> Relative to nominal (1 mg/kg)

**Table B.7.8.3-06 Recovery of pyridaben metabolite PB-7 in fortified samples (1 mg/kg) of milk after storage at <-5°C.**

| Months of storage | Concentration in stored samples <sup>(A)</sup><br>(mg/kg) |       | Average recovery stored samples <sup>(B)</sup><br>(%) | Recovery freshly fortified specimens (%) |
|-------------------|-----------------------------------------------------------|-------|-------------------------------------------------------|------------------------------------------|
| 0                 | 1.00                                                      | 1.00  | 100                                                   | 99                                       |
| 1                 | 0.99                                                      | 0.98  | 99                                                    | 99                                       |
| 3                 | 0.91                                                      | 0.93  | 92                                                    | 99                                       |
| 5                 | 1.135                                                     | 1.054 | 109                                                   | 106                                      |

<sup>(A)</sup> Not corrected for recovery of freshly fortified samples<sup>(B)</sup> Relative to nominal (1 mg/kg)**Table B.7.8.3-07 Recovery of pyridaben metabolite PB-9 in fortified samples (1 mg/kg) of liver after storage at <-5°C.**

| Months of storage | Concentration in stored samples <sup>(A)</sup><br>(mg/kg) |      | Average recovery stored samples <sup>(B)</sup><br>(%) | Recovery freshly fortified specimens (%) |
|-------------------|-----------------------------------------------------------|------|-------------------------------------------------------|------------------------------------------|
| 0                 | 0.98                                                      | 1.03 | 101                                                   | 105                                      |
| 1                 | 0.90                                                      | 0.94 | 92                                                    | 105                                      |
| 3                 | 0.89                                                      | 0.90 | 90                                                    | 105                                      |
| 5                 | 1.05                                                      | 1.09 | 107                                                   | 106                                      |

<sup>(A)</sup> Not corrected for recovery of freshly fortified samples<sup>(B)</sup> Relative to nominal (1 mg/kg)**Table B.7.8.3-08 Recovery of pyridaben metabolite PB-9 in fortified samples (1 mg/kg) of muscle after storage at <-5°C.**

| Months of storage | Concentration in stored samples <sup>(A)</sup><br>(mg/kg) |      | Average recovery stored samples <sup>(B)</sup><br>(%) | Recovery freshly fortified specimens (%) |
|-------------------|-----------------------------------------------------------|------|-------------------------------------------------------|------------------------------------------|
| 0                 | 1.12                                                      | 1.10 | 111                                                   | 116                                      |
| 1                 | 1.07                                                      | 1.06 | 107                                                   | 116                                      |
| 3                 | 0.98                                                      | 0.96 | 97                                                    | 116                                      |
| 5                 | 1.05                                                      | 1.07 | 106                                                   | 110                                      |

<sup>(A)</sup> Not corrected for recovery of freshly fortified samples<sup>(B)</sup> Relative to nominal (1 mg/kg)**Table B.7.8.3-09 Recovery of pyridaben metabolite PB-9 in fortified samples (1 mg/kg) of milk after storage at <-5°C.**

| Months of storage | Concentration in stored samples <sup>(A)</sup><br>(mg/kg) |       | Average recovery stored samples <sup>(B)</sup><br>(%) | Recovery freshly fortified specimens (%) |
|-------------------|-----------------------------------------------------------|-------|-------------------------------------------------------|------------------------------------------|
| 0                 | 1.18                                                      | 1.22  | 120                                                   | 118                                      |
| 1                 | 1.29                                                      | 1.29  | 129                                                   | 118                                      |
| 3                 | 1.16                                                      | 1.19  | 118                                                   | 118                                      |
| 5                 | 0.905                                                     | 0.807 | 86                                                    | 83                                       |

<sup>(A)</sup> Not corrected for recovery of freshly fortified samples<sup>(B)</sup> Relative to nominal (1 mg/kg)

## Conclusions

Pyridaben and its metabolites PB-7 and PB-9 are stable during storage at <-5° C for a period of 5 months in dairy cow liver, muscle and milk.

## Guidelines & Limitations

None.

### B.7.8.4 Summary of the storage stability studies in animal products

Pyridaben and its metabolites PB-7 and PB-9 are stable during storage at <-5° C for a period of 5 months in dairy cow liver, muscle and milk.

**B.7.9 Residues in succeeding or rotational crops (Annex IIA 6.6; Annex III 8.5)**

No field studies on residues in succeeding or rotational crops were required (a confined rotational crop study indicated no significant residues in rotational crops, see B.7.1.2).

**B.7.10 Proposed pre-harvest intervals for envisaged use, or withholding periods, in the case of post-harvest uses (Annex IIA 6.8; Annex IIIA 8.7)**

A PHI of 14 days is proposed for citrus. The proposed PHI for tomatoes is 3 days.

**B.7.11 Community MRLs and MRLs in EU Member States (Annex IIIA 12.2)**

No community MRLs have been established yet. Established MRLs in EU Member States (including Switzerland) are listed in Table B.7.11-01 (data taken from the notifier).

**Table B.7.11-01 Established MRLs in EU Member States**

| Country     | Commodity     | MRL (mg/kg) | Residue definition |
|-------------|---------------|-------------|--------------------|
| Austria     | Grape         | 0.2         | Pyridaben          |
|             | Pome fruit    | 0.2         | Pyridaben          |
|             | Stone fruit   | 0.2         | Pyridaben          |
|             | Others        | 0.05        | Pyridaben          |
| Belgium     | Plum          | 0.5         | Pyridaben          |
|             | Pome fruit    | 0.5         | Pyridaben          |
| France      | Grape (fruit) | 0.3         | Pyridaben          |
|             | Grape (wine)  | 0.05*       | Pyridaben          |
|             | Olive (oil)   | 0.05*       | Pyridaben          |
|             | Olive         | 0.1         | Pyridaben          |
|             | Walnut        | 0.05        | Pyridaben          |
|             | Pome fruit    | 0.5         | Pyridaben          |
|             | Stone fruit   | 0.5         | Pyridaben          |
| Germany     | Grape         | 0.2         | Pyridaben          |
|             | Plum          | 0.2         | Pyridaben          |
|             | Pome fruit    | 0.5         | Pyridaben          |
|             | Others        | 0.05*       | Pyridaben          |
| Italy       | Grape         | 0.2         | Pyridaben          |
|             | Peach         | 0.5         | Pyridaben          |
|             | Olive         | 0.5         | Pyridaben          |
|             | Olive (oil)   | 1           | Pyridaben          |
|             | Apple         | 0.2         | Pyridaben          |
| Luxembourg  | Pome fruit    | 0.5         | Pyridaben          |
|             | Others        | 0.05*       | Pyridaben          |
| Netherlands | Others        | 0.05*       | Pyridaben          |
|             | Plum          | 0.2         | Pyridaben          |
|             | Pome fruit    | 0.2         | Pyridaben          |
| Portugal    | Grape (fruit) | 0.5         | Pyridaben          |
|             | Grape (wine)  | 0.5         | Pyridaben          |
|             | Pear          | 0.2         | Pyridaben          |
|             | Apple         | 0.2         | Pyridaben          |
| Spain       | Olive (fruit) | 1           | Pyridaben          |
|             | Pome fruit    | 1           | Pyridaben          |
|             | Stone fruit   | 1           | Pyridaben          |
|             | Citrus        | 2           | Pyridaben          |
|             | Grape         | 1           | Pyridaben          |

### B.7.12 Proposed EU MRLs and justification for the acceptability of those MRLs (Annex IIA 6.7; Annex IIIA 8.6)

#### B.7.12.1 Proposed MRLs

The MRLs proposed by the notifier are:

| Crops              | MRL<br>Pyridaben (mg/kg) | STMR |
|--------------------|--------------------------|------|
| Oranges and lemons | 0.2                      | -    |
| Orange juice       | 0.05                     | -    |
| Canned oranges     | 0.05                     | -    |
| Marmalade          | 0.05                     | -    |
| Mandarins          | 0.5                      | -    |
| Tomatoes           | 0.1                      | -    |

#### B.7.12.2 Justification of proposed MRLs

The residue trials in citrus and tomato were not performed under least favourable conditions. Hence no residue values could be selected for the setting of the MRL. See B.7.6. for details.

**Table B.7.12.2-01 Residues used for MRL determination**

|        |                                     |       |       |       |             |             |      |      |      |      |
|--------|-------------------------------------|-------|-------|-------|-------------|-------------|------|------|------|------|
| Tomato | Northern and Southern member states | <0.05 | <0.05 | <0.05 | <u>0.05</u> | <u>0.05</u> | 0.07 | 0.07 | 0.07 |      |
| Orange | Southern member states              | <0.05 | 0.05  | 0.05  | 0.06        | <u>0.06</u> | 0.08 | 0.10 | 0.10 | 0.12 |

Calculation of MRLs, tomato (greenhouse):

Rber = 0.09 mg/kg

Rmax = 0.14 mg/kg

Calculation of MRLs, citrus:

Rber = 0.15 mg/kg

Rmax = 0.20 mg/kg

#### B.7.12.3 Summary of proposed MRLs

MRLs, STMRs and HRs could be obtained from the available residue trials for tomato and orange

**Table B.7.12.3-01 Proposed MRL, STMR and HR by the RMS**

| Crop group | Crops     | MRL (mg/kg)<br>(Pyridaben) | STMR (mg/kg)<br>(Pyridaben) | HR (mg/kg)<br>(Pyridaben) |
|------------|-----------|----------------------------|-----------------------------|---------------------------|
| Citrus     | Oranges   | 0.2                        | 0.06                        | 0.12                      |
| Citrus     | Mandarins | -                          | -                           | -                         |
| Citrus     | Lemon     | -                          | -                           | -                         |
| Tomato     | Tomato    | 0.1                        | 0.05                        | 0.07                      |

**B.7.13 Proposed EU Import tolerances and justification for the acceptability of those residues**

Not applicable, since no non-EU applications are proposed in the intended use pattern.

**B.7.14 Basis for differences, if any, in conclusions reached having regard to established or proposed CAC MRLs**

Not applicable, since no Codex MRLs have been established or proposed yet.

**B.7.15 Estimates of potential and actual dietary exposure through diet and other means (Annex IIA 6.9; Annex IIIA 8.8)****B.7.15.1 Intakes by domestic animals**

Intake of residues by domestic animals may be expected from fruit pomace only (tomatoes are not a constituent of animal feed). Calculations were based on a HR (oranges) of 0.12 mg/kg and a processing factor of 1.1 (wet pomace).

Based on the plant metabolism study, the residue considered relevant for the intake calculations consists of pyridaben only. No other toxicologically relevant metabolites are present in feeding crops.

**Cattle**

Intake of residues by dairy cattle and beef cattle may be expected from wet pomace only. Intake of residues through rotational crops used as animal feed is not relevant for use of pyridaben on citrus or tomatoes. Residue intakes were calculated using a HR-P of 0.13 mg/kg.

*Dairy cattle*

| Group/Crop | % of diet as crop | Intakes of dry matter from crop (kg/animal/day) | % dry matter | Intake fresh material (kg/animal/day) | Residues in crop (mg/kg) | Residue intake (mg/animal/day) |
|------------|-------------------|-------------------------------------------------|--------------|---------------------------------------|--------------------------|--------------------------------|
| Wet pomace | 10                | 2                                               | 23           | 8.7                                   | 0.13                     | 1.130                          |

TMDI dairy cattle (550 kg): = 0.0021 mg/kg bw/day  
 = 0.0565 mg/kg diet (dry weight)

*Beef cattle*

| Group/Crop | % of diet as crop | Intakes of dry matter from crop (kg/animal/day) | % dry matter | Intake fresh material (kg/animal/day) | Residues in crop (mg/kg) | Residue intake (mg/animal/day) |
|------------|-------------------|-------------------------------------------------|--------------|---------------------------------------|--------------------------|--------------------------------|
| Wet pomace | 30                | 5                                               | 23           | 19.6                                  | 0.13                     | 2.543                          |

TMDI beef cattle (350 kg): = 0.0073 mg/kg bw/day  
 = 0.1696 mg/kg diet (dry weight)

**Chicken**

Wet pomace or tomato is not a constituent of poultry diet.

**Pig**

Wet pomace or tomato is not a constituent of pig diet.

**B.7.15.2 Intakes by humans (long-term)**

The chronic risk assessment is performed using the WHO-EU diet and the UK diet. And the ADI of 0.01 mg/kg bw/d. Chronic intake is highest for the UK-toddlers (35.4% of the ADI).

**Table B.7.15.2-01a Calculation of the Theoretical Maximum Daily Intake using the WHO standard European diet (60 kg bw) and an ADI of 0.01 mg/kg bw/d**

| Commodity                  | consumption (g/pers/day) | MRL (mg/kg) | TMDI (µg/pers/day) | %ADI       |
|----------------------------|--------------------------|-------------|--------------------|------------|
| <b>FRUITS</b>              |                          |             |                    |            |
| Orange                     | 29.8                     | 0.2         | 6.0                | 1.0        |
| <b>FRUITING VEGETABLES</b> |                          |             |                    |            |
| Tomato                     | 66,6                     | 0,1         | 6,7                | 1.1        |
| <b>Total</b>               |                          |             |                    | <b>2.1</b> |

**Table B.7.15.2-01b Calculation of the Theoretical Maximum Daily Intake using the UK diet for adults (60 kg bw) and an ADI of 0.01 mg/kg bw/d**

| Commodity           | consumption (g/pers/day) | MRL (mg/kg) | TMDI (µg/pers/day) | %ADI       |
|---------------------|--------------------------|-------------|--------------------|------------|
| FRUITS              |                          |             |                    |            |
| Orange              | 43                       | 0.2         | 0.0462             | 7.7        |
| FRUITING VEGETABLES |                          |             |                    |            |
| Tomato              | 33                       | 0.1         | 0.0084             | 1.4        |
| <b>Total</b>        |                          |             |                    | <b>9.1</b> |

**Table B.7.15.2-01c Calculation of the Theoretical Maximum Daily Intake using the UK diet for toddlers (114.5kg bw) and an ADI of 0.01 mg/kg bw/d**

| Commodity           | consumption (g/pers/day) | MRL (mg/kg) | TMDI (µg/pers/day) | %ADI        |
|---------------------|--------------------------|-------------|--------------------|-------------|
| FRUITS              |                          |             |                    |             |
| Orange              | 29                       | 0.2         | 0.04756            | 32.8        |
| FRUITING VEGETABLES |                          |             |                    |             |
| Tomato              | 9                        | 0.1         | 0.00037            | 2.6         |
| <b>Total</b>        |                          |             |                    | <b>35.4</b> |

**B.7.15.3 National estimate for short term intake by humans (acute)**

The acute risk assessment is performed using the ARfD of 0.05 mg/kg bw/d. Risk assessment is performed using the WHO-EU diet and the UK diets for adults and toddlers.

Acute intake is highest for UK toddlers for orange (59.6% of the ARfD).

**Table B.7.15.3-01a Calculation of the National Estimated Short Term Intake using the UK diet for adults (60 kg bw) and an ARfD of 0.05 mg/kg bw/d**

| Commodity           | Consumption 97.5 percentile (g/pers/day) | HR (mg/kg) | NESTI (µg/pers/day) | %ARfD |
|---------------------|------------------------------------------|------------|---------------------|-------|
| FRUITS              |                                          |            |                     |       |
| Orange              | 0.5725                                   | 0.12       | 0.002623            | 5.2   |
| FRUITING VEGETABLES |                                          |            |                     |       |
| Tomato              | 0.2446                                   | 0.07       | 0.000754            | 1.5   |

**Table B.7.15.3-01b Calculation of the National Estimated Short Term Intake using the UK diet for toddlers (11 kg bw) and an ARfD of 0.05 mg/kg bw/d**

| Commodity           | Consumption 97.5 percentile (g/pers/day) | HR (mg/kg) | NESTI (µg/pers/day) | %ARfD |
|---------------------|------------------------------------------|------------|---------------------|-------|
| FRUITS              |                                          |            |                     |       |
| Orange              | 0.4813                                   | 0.12       | 0.011928            | 23.8  |
| FRUITING VEGETABLES |                                          |            |                     |       |
| Tomato              | 0.0905                                   | 0.07       | 0.002899            | 5.8   |

**B.7.16 Summary and evaluation of residue behaviour (Annex IIA 6.10; Annex IIIA 8.9)**

The formulation NEXTER PRO 75 WP, a 750 g as/kg formulation of pyridaben, is submitted for use in Northern and Southern Europe as an insecticide against mites and whitefly in the cultivation of citrus and tomatoes.

Three studies were submitted on the metabolism of pyridaben: one in apple, one in orange and one in tomato. The study in apple is not included in the summary below since the intended use of pyridaben is on citrus and tomato only. In the study with oranges, the number of applications (two instead of one) deviated from the cGAP. However the results are considered relevant for the intended use since the spray interval was large and TRR prior to second treatment low. Absolute amounts in oranges may have been overestimated since total dose was 1.9N the maximum dose according to the GAP.

In whole oranges, following two spray applications of [Benzyl-<sup>14</sup>C] and [Pyridazinone-<sup>14</sup>C] pyridaben at 570 g as/ha, total residues at 14 DAT were 0.040-0.141 mg eq/kg. The majority of the residue was found in/on the peel ( $\geq 96.4\%$  TRR, 0.039-0.139 mg eq/kg). Radioactivity in pulp was 1.2-3.6% TRR ( $< 0.01$  mg eq/kg). Peel associated radioactivity was fractionated into a surface wash (61-79% TRR), extractables (9.9-19.7% TRR) and unextractables (9.6-18.7% TRR). In the surface wash pyridaben was the most important identified fraction: 11.8-22.14% TRR (0.006-0.02 mg eq/kg). Up to 15 metabolite fractions were observed (each  $\leq 4.78\%$  TRR and  $\leq 0.006$  mg eq/kg) of which 6 were identified as PB-11, PB-14, PB-22, B-1, B-3 and P-14. Small amounts of pyridaben and B-11 were observed in the peel extract (all  $\leq 2.73\%$  TRR and  $\leq 0.002$  mg eq/kg in the low dose samples). The study is acceptable.

In tomatoes, following one paint application (to fruits and leaves) of [pyridazinone-<sup>14</sup>C] pyridaben at a rate of 1 mg/plant, mean total residues in tomato fruits 1, 7 and 14 DAT were 0.082-0.112 mg eq/kg. pyridaben was the major component of the residue: 91.7%-98.2% TRR. Four metabolites (D1, PB-4, PB-9 and PB-14) were identified in individual fruits, all  $\leq 0.7\%$  TRR ( $< 0.001$  mg eq/kg).

One confined crop rotational study was submitted including the relevant crop categories (cereals, leaf and root crop). The levels of radioactivity in radish (leaves and roots), mustard greens, wheat forage, hay, straw and grain sown 30 days after two applications of [Pyridazinone-<sup>14</sup>C] pyridaben at a rate of 0.75 kg as/ha to bare soil were 0.013 mg eq/kg (radish root), 0.050 mg eq/kg (radish leaves), 0.019 mg eq/kg (mustard greens), 0.011 mg eq/kg (wheat forage), 0.044 mg eq/kg (wheat hay), 0.045 mg eq/kg (wheat straw) and 0.009 mg eq/kg (wheat grain). The residues consisted mainly of polar unidentifieds (all  $< 0.01$  mg eq/kg and  $< 10\%$  TRR, except one polar peak in 30 DALT mustard greens (17% TRR)).

Two studies were submitted on the metabolism of pyridaben in livestock, one study in lactating goat and one in laying hen. The study in hen is supplementary as citrus and tomatoes are not fed to chicken and not included in the summary below.

In the goat study, after five daily dose administrations of [Pyridazinone-<sup>14</sup>C] or [Benzyl-<sup>14</sup>C] pyridaben at 0.5 or 20 mg/day, 34-63.2% of the total administered dose was recovered in excreta and 4.6-12.0% in the tissues (of which 94.9-98.3% in the GI tract). Total recovery of radioactivity was 45.7-71.4%. Total residue levels in the low dose tissues were highest in fat (Pz-only, 0.012 mg eq/kg), followed by liver (max 0.0043 mg eq/kg), muscle (max 0.0024 mg eq/kg) and kidney (max 0.0011 mg eq/kg). The maximum residue level

in milk was 0.0013 mg eq/kg (day 4). A plateau was reached after 2-3 days. The following identifications were obtained in high dose samples, In urine PB-3 (0.09% of mean daily dose (MDD)) and PB-7 (<0.01% MDD) were tentatively identified. Other fractions were  $\leq 0.86\%$  MDD. In faeces, two metabolites were tentatively identified: PB-7 (0.66% MDD) and PB-9 (1.61% MDD). Other fractions were  $\leq 14.8\%$  MDD. Acid/alkali treatment or enzyme treatments released several fractions ( $\leq 19.13\%$  MDD) which corresponded (tentatively) to PB-1, PB-3, PB-4, PB-12, PB-13, B-1, B-3, B-7 and B-8. In bile, three fractions (<0.01% MDD) were tentatively identified as P-3, B-8 and PB-9. Other fractions were  $\leq 0.13\%$  MDD. In the liver two fractions ( $\leq 0.05\%$  MDD) were tentatively identified as P-1 and PB-11. Other fractions were  $\leq 0.09\%$  MDD. Based on HPLC analysis, PB-1 (17.6% TRR, 0.025 mg eq/kg), PB-7 (3.75% TRR, 0.005 mg eq/kg) and PB-9 (5.11% TRR, 0.007 mg eq/kg) were identified in the liver (and confirmed by TLC). In kidney three fractions ( $\leq 0.01\%$  MDD) were tentatively identified as P-3, PB-11 and B-7. Other fractions were  $\leq 0.01\%$  MDD. In muscle, at least 3 fractions were observed (<0.01% of MDD). In fat, 3-5 fractions (all <0.01% MDD) were observed of which two were identified as PB-12 and B-1.

The low dose in the goat study was 0.2 mg/kg feed fresh weight (and >0.2 mg/kg dry feed, actual concentration based on dry weight not determined). Provisional intake calculations for cattle resulted in a maximum feed concentration of 0.17 mg/kg dry weight, which is lower than the lowest dose in this study. Since intake of cattle is lower than the lowest dose group from the goat metabolism study, residues in edible animal tissues are expected to be <0.01 mg eq/kg

The residue definition in citrus and tomato for post-registration monitoring and for risk assessment is proposed as pyridaben.

Wet pomace is a constituent of cattle feed at levels >0.1 mg/kg dw diet. However, based on the goat metabolism study and the livestock feeding study in cows, no pyridaben residues >0.01 mg/kg are expected in edible animal products. Hence, no definition of residues in animal products is required and MRLs need not to be set..

Residues for setting the MRL could be selected for tomato (greenhouse) and orange (field). The proposed MRL for tomato is 0.1 mg/kg (STMR of 0.05 mg/kg and HR of 0.07 mg/kg) and for orange the proposed MRL is 0.2 mg/kg (STMR 0.06 and HR 0.12 mg/kg). Data sets for derivation of an MRL for mandarin and lemon were incomplete. At least 4 additional trials for mandarin according to cGAP are required.

Pyridaben in orange, dried orange pulp, orange molasses and orange oil is stable during storage at  $<-5^{\circ}\text{C}$  for a period of 12 months.

Pyridaben was shown to be stable under conditions simulating pasteurisation, baking/brewing/boiling and sterilisation. In the processing study in oranges, the processing factors (pyridaben residues) were <1 for wet pulp (0.75), washed whole oranges (0.49), molasses (0.30) and orange juice (<0.1). Residues were

concentrated in dry pulp (x3.5) and orange oil (x25.3). In a second study in oranges, processing factors (pyridaben residues) were <1 for washed whole oranges (0.37-0.66), pulp (<0.09-<0.12), juice (<0.12-0.14), marmalade (<0.12-0.21) and canned fruit (<0.04-<0.12). Pyridaben residues were concentrated in dry pomace (3.57-5.16) and wet pomace (1.05-1.11). Processing studies in tomatoes are not required as residue levels are <0.1 mg eq/kg. The statement on tomato is subject to revision pending on the generation of new residue data under least favourable conditions.

The lowest dose used in the livestock feeding study in cattle was 2.5 mg/kg dry matter feed. This dose is a factor 15 higher than the maximum estimated concentration in animal feed for cattle of approximately 0.17 mg/kg dm feed (provisional calculation). The results of the livestock feeding study at the low dose indicate no residues of pyridaben above the LOQ (0.01 (milk) and 0.05 mg/kg (tissues)) in milk and tissues. The results supports the conclusion from the goat metabolism study that no residues above 0.01 mg/kg are expected in animal products at the anticipated feeding level. No residue definition for animal products is needed and no MRLs need to be set.

Studies in poultry are not required as wet pomace/tomato is not a constituent of poultry feed.

Pyridaben and its metabolites PB-7 and PB-9 are stable during storage at <-5° C for a period of 5 months in dairy cow liver, muscle and milk.

Consumer chronic risk assessment show that chronic intake is 2.1% for the WHO-EU diet, 9.1% of the ADI for UK adults and 35.4% for UK-toddlers. Consumer acute risk assessment show that maximal 5.2% of the ARfD is filled for UK adults and 23.8% of the ARfD is filled for UK-toddlers. Therefore, safe uses are proven for orange and tomato when NEXTER PRO 75 WP is applied according to GAP.

**B.7.17 References relied on**

| <b>Annex point/<br/>reference number</b> | <b>Author(s)</b>             | <b>Year</b> | <b>Title<br/>Source (where different from company)<br/>Company, Report No<br/>GLP or GEP status (where relevant),<br/>Published or not</b>                                                                                                            | <b>Data<br/>Protection<br/>Claimed<br/>Y/N</b> | <b>Owner<br/>**</b> |
|------------------------------------------|------------------------------|-------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------|---------------------|
| IIA, 6.0/01                              | Burkey, J. D.                | 1995        | Freezer storage stability of BAS 300 I (Pyridaben) in orange and orange processed commodities<br>BASF Corporation<br>BASF Aktiengesellschaft<br>Report no. R123<br>GLP, Unpublished                                                                   | Y                                              | BASF                |
| IIA, 6.0/02                              | Tilting, N.                  | 1994        | Two years storage stability of Pyridaben residues in apples, oranges and grapes<br>BASF Aktiengesellschaft<br>Report no. R125<br>GLP, Unpublished                                                                                                     | Y                                              | BASF                |
| IIA, 6.0/03                              | Riley, M.;<br>Abdel-Baky, S. | 1995        | Freezer storage stability of BASF 300 I (Pyridaben) and its metabolites, PB-7 and PB-9, in animal tissues (liver and muscle) and milk after 5 months of storage<br>BASF Corporation<br>BASF Aktiengesellschaft<br>Report no. R126<br>GLP, Unpublished | Y                                              | BASF                |
| IIA, 6.1/01                              | Mayer, F.                    | 1992        | The metabolism of <sup>14</sup> C-Pyridaben in apples<br>BASF Aktiengesellschaft<br>Report no. R101<br>GLP, Unpublished                                                                                                                               | Y                                              | BASF                |
| IIA, 6.1/01                              | Hofmann, M.                  | 1989<br>a   | Plant uptake study with <sup>14</sup> C-Pyridaben in apples<br>BASF Aktiengesellschaft<br>Report no. R101a<br>GLP, Unpublished                                                                                                                        | Y                                              | BASF                |
| IIA, 6.1/01                              | Hofmann, M                   | 1989<br>b   | Plant uptake study with <sup>14</sup> C-Pyridaben in apples<br>BASF Aktiengesellschaft<br>Report no. R101b<br>GLP, Unpublished                                                                                                                        | Y                                              | BASF                |
| IIA, 6.1/01                              | Hofmann, M                   | 1989<br>c   | Plant uptake study with <sup>14</sup> C-Pyridaben in apples<br>BASF Aktiengesellschaft<br>Report no. R101c<br>GLP, Unpublished                                                                                                                        | Y                                              | BASF                |
| IIA, 6.1/02                              | Singh, M.                    | 1994        | Nature of the residue of <sup>14</sup> C-BAS 300 I in citrus<br>BASF Corporation<br>BASF Aktiengesellschaft<br>Report no. R104<br>GLP, Unpublished                                                                                                    | Y                                              | BASF                |
| IIA, 6.1/03                              | Ogawa, K.                    | 2003        | Metabolism of pyridaben in tomatoes<br>Nissan Chemical Industries, Ltd.<br>Report no R8<br>GLP, Unpublished                                                                                                                                           | Y                                              | NCI                 |

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|----------------------------------|---------------------------------|------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------|--------------|
| IIA, 6.2/01                      | Hallifax, D.                    | 1994 | NC-129: Absorption, distribution, metabolism (nature of the residue) and excretion study in the lactating goat<br>[REDACTED]<br>Nissan Chemical Industries, Ltd.<br>Report no. M106<br>GLP, Unpublished                                          | Y                                        | NCI          |
| IIA, 6.2/01                      | O'Connor, J.                    | 1996 | NC-129: Absorption, distribution, metabolism (nature of the residue) and excretion study in the lactating goat<br>[REDACTED]<br>Nissan Chemical Industries, Ltd.<br>Report no. M106-2<br>GLP, Unpublished                                        | Y                                        | NCI          |
| IIA, 6.2/02                      | Hallifax, D.                    | 1994 | NC-129: Absorption, distribution, metabolism (nature of the residue) and excretion study in the laying hen<br>[REDACTED]<br>Nissan Chemical Industries, Ltd.<br>Report no. M105<br>GLP, Unpublished                                              | Y                                        | NCI          |
| IIA, 6.2/02                      | O'Connor, J.                    | 1997 | NC-129: Absorption, distribution, metabolism (nature of the residue) and excretion study in the laying hen<br>[REDACTED]<br>Nissan Chemical Industries, Ltd.<br>Report no. M105-2<br>GLP, Unpublished                                            | Y                                        | NCI          |
| IIA, 6.3/01                      | Not specified                   | 1994 | Residues of Pyridaben in oranges (30014 I 92/8A)<br>BASF Aktiengesellschaft<br>Report no. R500<br>Non-GLP, Unpublished                                                                                                                           | Y                                        | BASF         |
| IIA, 6.3/02                      | Not specified                   | 1994 | Residues of Pyridaben in oranges (30006 I 92/6A)<br>BASF Aktiengesellschaft<br>Report no. R504<br>Non-GLP, Unpublished                                                                                                                           | Y                                        | BASF         |
| IIA, 6.3/03                      | Not specified                   | 1993 | Pesticide residue analysis Pyridaben 200 g/l, orange (30006 I 93/1A)<br>BASF Aktiengesellschaft<br>Report no. R505<br>Non-GLP, Unpublished                                                                                                       | Y                                        | BASF         |
| IIA, 6.3/04                      | Udrisard, T.;<br>Weidenauer, M. | 1994 | Magnitude of residues of Pyridaben in the raw agricultural commodity of oranges after application of BAS 300 06 I under field conditions (Italy - season 1993)<br>Battelle<br>BASF Aktiengesellschaft<br>Report no. R506<br>Non-GLP, Unpublished | Y                                        | BASF         |

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|----------------------------------|----------------|------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------|--------------|
| IIA, 6.3/05                      | Blaschke, U.   | 2003 | Pyridaben: Residue decline study with Pyridaben 200 g as/kg WP applied to orange and mandarins in Italy 2002<br>Huntingdon Life Sciences Ltd.<br>Nissan Chemical Industries, Ltd.<br>Report no. R170<br>GLP, Unpublished                      | Y                                        | NCI          |
| IIA, 6.3/06                      | Weidenauer, M. | 1997 | Magnitude of residue of Pyridaben in the raw agricultural commodity of mandarins after application of BAS 300 14 I under field conditions (Spain - season 1996)<br>Battelle<br>BASF Aktiengesellschaft<br>Report no. R501<br>GLP, Unpublished | Y                                        | BASF         |
| IIA, 6.3/07                      | Not specified  | 1992 | Pesticide residue analysis Pyridaben 200 g/l, mandarin (90786 I 91/4A)<br>BASF Aktiengesellschaft<br>Report no. R503<br>Non-GLP, Unpublished                                                                                                  | Y                                        | BASF         |
| IIA, 6.3/08                      | Not specified  | 1992 | Residue reports for import tolerances (90/10965)<br>BASF Aktiengesellschaft<br>Report no. R57<br>Non-GLP, Unpublished                                                                                                                         | Y                                        | BASF         |
| IIA, 6.3/09                      | Not specified  | 1992 | Pesticide residue analysis Pyridaben 200 g/l, lemon (90786 I 91/6A)<br>BASF Aktiengesellschaft<br>Report no. R502<br>Non-GLP, Unpublished                                                                                                     | Y                                        | BASF         |
| IIA, 6.3/10                      | Blaschke, U.   | 2002 | Pyridaben: Residue decline study with Pyridaben 750 g as/kg WP applied to glasshouse tomatoes in Holland 2000 (+ 1 amendment)<br>Huntingdon Life Sciences Ltd.<br>Nissan Chemical Industries, Ltd.<br>Report no. R151<br>GLP, Unpublished     | Y                                        | NCI          |
| IIA, 6.3/11                      | Blaschke, U.   | 2002 | Pyridaben: Residue decline study with Pyridaben 750 g as/kg WP applied to glasshouse tomatoes in Spain 2001 (+ 1 amendment)<br>Huntingdon Life Sciences Ltd.<br>Nissan Chemical Industries, Ltd.<br>Report no. R152<br>GLP, Unpublished       | Y                                        | NCI          |

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| IIA, 6.3./12                     | Weidenauer, M.<br>Udrissard, T<br>Mollard, L.        | 1993 | Determination of residues of pyridaben in peaches, apples, grapes and oranges treated with BAS 300 06I, BAS 200 10I or BAS 200 14I (Spain, season 1992)<br>Nissan Chemical Industries, Ltd.<br>Report no. R507<br>GLP, unpublished | Y                                        | NCI         |
| IIA, 6.4/01                      | Riley, M.;<br>Abdel-Baky, S.; Jordan, J.             | 1995 | A meat and milk magnitude of the residue study with Pyridaben in lactating dairy cows<br>[REDACTED]<br>BASF Aktiengesellschaft<br>Report no. R400<br>GLP, Unpublished                                                              | Y                                        | BASF        |
| IIA, 6.5.1/01                    | Wicks, R.                                            | 2002 | Pyridaben: Hydrolysis under simulated processing conditions<br>Huntingdon Life Sciences Ltd.<br>Nissan Chemical Industries, Ltd.<br>Report no. R304<br>GLP, Unpublished                                                            | Y                                        | NCI         |
| IIA, 6.5.2/01                    | Abdel-Baky, S.; Burkey, J.; Jackson, S., Riley, M-E. | 1994 | The magnitude of Pyridaben residue in orange process commodities: Ground application<br>BASF Corporation<br>BASF Aktiengesellschaft<br>Report no. R300<br>GLP, Unpublished                                                         | Y                                        | BASF        |
| IIA, 6.5.2/02                    | Blaschke, U.                                         | 2003 | Pyridaben: Processing study with Pyridaben 200 g as/kg WP applied to oranges in Italy 2002<br>Huntingdon Life Sciences Ltd.<br>Nissan Chemical Industries, Ltd.<br>Report no. R305<br>GLP, Unpublished                             | Y                                        | NCI         |
| IIA, 6.6/01                      | Ellenson, J. L.                                      | 1999 | Confined rotational crop study with 14C-BAS 300 I (+ amended study report F14-2)<br>BASF Corporation<br>BASF Aktiengesellschaft<br>Report no. F14<br>GLP, Unpublished                                                              | Y                                        | BASF        |