



## Summary of Studies Supporting USDA Product Licensure

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|---|---|
| Establishment Name  | Boehringer Ingelheim Animal Health USA Inc.   |
| USDA Vet Biologics Establishment Number                                   | 124   |
| Product Code  | 4X49.21   |
| True Name   | Bovine Rhinotracheitis-Virus Diarrhea-Parainfluenza 3-Respiratory Syncytial Virus Vaccine, Modified Live Virus, Mannheimia Haemolytica Toxoid |
| Tradename(s) / Distributor or Subsidiary (if different from manufacturer) | Pyramid 5 +PRESPONSE SQ - No distributor specified<br>Pyramid FP 5 + Presponse SQ - Boehringer Ingelheim (Canada) Ltd.                        |
| Date of Compilation Summary   | April 08, 2019  |

**Disclaimer: Do not use the following studies to compare one product to another. Slight differences in study design and execution can render the comparisons meaningless.**

|  |   |
|--|---|
| <b>Study Type</b>                        | Efficacy  |
| <b>Pertaining to</b>                     | Bovine Virus Diarrhea (BVD)   |
| <b>Study Purpose</b>                     | Demonstration of efficacy against BVD Type 1 clinical disease, leukopenia, and viremia  |
| <b>Product Administration</b>            |   |
| <b>Study Animals</b>                     | Bovine  |
| <b>Challenge Description</b>             | BVD1b NY-1 strain   |
| <b>Interval observed after challenge</b> |   |
| <b>Results</b>                           | Study data were evaluated by USDA-APHIS prior to product licensure and met regulatory standards for acceptance at the time of submission. No data are published because this study was submitted to USDA-APHIS prior to January 1, 2007, and APHIS only requires publication of data submitted after that date. |
| <b>USDA Approval Date</b>                | June 14, 1994   |

|  |   |
|--|---|
| <b>Study Type</b>                        | Efficacy  |
| <b>Pertaining to</b>                     | Bovine Virus Diarrhea (BVD)   |
| <b>Study Purpose</b>                     | Demonstration of efficacy against persistent infection of calves with BVD Type 1  |
| <b>Product Administration</b>            | Pregnant heifers or cows prior to breeding  |
| <b>Study Animals</b>                     | Bovine  |
| <b>Challenge Description</b>             | BVD1b 97B1415 strain  |
| <b>Interval observed after challenge</b> |   |
| <b>Results</b>                           | Study data were evaluated by USDA-APHIS prior to product licensure and met regulatory standards for acceptance at the time of submission. No data are published because this study was submitted to USDA-APHIS prior to January 1, 2007, and APHIS only requires publication of data submitted after that date. |
| <b>USDA Approval Date</b>                | December 10, 2003   |

| <b>Study Type</b>                        | Efficacy   |                   |                |                   |                   |           |            |                 |             |             |
|--|--|-------------------|----------------|-------------------|-------------------|-----------|------------|-----------------|-------------|-------------|
| <b>Pertaining to</b>                     | Bovine Virus Diarrhea (BVD)  |                   |                |                   |                   |           |            |                 |             |             |
| <b>Study Purpose</b>                     | Demonstration of efficacy against BVD Type 1 (respiratory disease) 217 days after vaccination  |                   |                |                   |                   |           |            |                 |             |             |
| <b>Product Administration</b>            | One dose, subcutaneously   |                   |                |                   |                   |           |            |                 |             |             |
| <b>Study Animals</b>                     | 46 bovine calves (23 vaccinates and 23 controls), 25 to 37 days of age   |                   |                |                   |                   |           |            |                 |             |             |
| <b>Challenge Description</b>             | Challenged with BVD Type 1b, Isolate CA0401186A, 217 days (7 months) after vaccination   |                   |                |                   |                   |           |            |                 |             |             |
| <b>Interval observed after challenge</b> | Calves were observed and blood was collected for 14 days after challenge to evaluate viremia and leukopenia.   |                   |                |                   |                   |           |            |                 |             |             |
| <b>Results</b>                           | <p>Results of the study are summarized as follows:</p> <p>Blood was evaluated for viremia (the presence of virus) and leukopenia (at least one white blood cell count below 60% of pre-challenge baseline).</p> <p><b>Positive for Viremia and Leukopenia:</b></p> <table border="1"> <thead> <tr> <th></th> <th><b>Viremia</b></th> <th><b>Leukopenia</b></th> </tr> </thead> <tbody> <tr> <td><b>Vaccinates</b></td> <td>0/23 (0%)</td> <td>6/23 (26%)</td> </tr> <tr> <td><b>Controls</b></td> <td>22/23 (96%)</td> <td>21/23 (91%)</td> </tr> </tbody> </table> <p>See tables on the following pages for data.</p> |                   | <b>Viremia</b> | <b>Leukopenia</b> | <b>Vaccinates</b> | 0/23 (0%) | 6/23 (26%) | <b>Controls</b> | 22/23 (96%) | 21/23 (91%) |
|  | <b>Viremia</b>   | <b>Leukopenia</b> |                |                   |                   |           |            |                 |             |             |
| <b>Vaccinates</b>                        | 0/23 (0%)  | 6/23 (26%)        |                |                   |                   |           |            |                 |             |             |
| <b>Controls</b>                          | 22/23 (96%)  | 21/23 (91%)       |                |                   |                   |           |            |                 |             |             |
| <b>USDA Approval Date</b>                | July 14, 2014  |                   |                |                   |                   |           |            |                 |             |             |

**Viremia in Vaccinates (23 bovine)**

| Animal ID | Days Post-Challenge |   |   |   |   |   |   |   |   |    |    |    |    |    | Overall Result |
|-----------|---------------------|---|---|---|---|---|---|---|---|----|----|----|----|----|----------------|
|           | 1                   | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 |                |
| 21        | -                   | - | - | - | - | - | - | - | - | -  | -  | -  | -  | -  | -              |
| 32        | -                   | - | - | - | - | - | - | - | - | -  | -  | -  | -  | -  | -              |
| 34        | -                   | - | - | - | - | - | - | - | - | -  | -  | -  | -  | -  | -              |
| 37        | -                   | - | - | - | - | - | - | - | - | -  | -  | -  | -  | -  | -              |
| 41        | -                   | - | - | - | - | - | - | - | - | -  | -  | -  | -  | -  | -              |
| 43        | -                   | - | - | - | - | - | - | - | - | -  | -  | -  | -  | -  | -              |
| 48        | -                   | - | - | - | - | - | - | - | - | -  | -  | -  | -  | -  | -              |
| 49        | -                   | - | - | - | - | - | - | - | - | -  | -  | -  | -  | -  | -              |
| 51        | -                   | - | - | - | - | - | - | - | - | -  | -  | -  | -  | -  | -              |
| 57        | -                   | - | - | - | - | - | - | - | - | -  | -  | -  | -  | -  | -              |
| 61        | -                   | - | - | - | - | - | - | - | - | -  | -  | -  | -  | -  | -              |
| 64        | -                   | - | - | - | - | - | - | - | - | -  | -  | -  | -  | -  | -              |
| 67        | -                   | - | - | - | - | - | - | - | - | -  | -  | -  | -  | -  | -              |
| 68        | -                   | - | - | - | - | - | - | - | - | -  | -  | -  | -  | -  | -              |
| 73        | -                   | - | - | - | - | - | - | - | - | -  | -  | -  | -  | -  | -              |
| 82        | -                   | - | - | - | - | - | - | - | - | -  | -  | -  | -  | -  | -              |
| 86        | -                   | - | - | - | - | - | - | - | - | -  | -  | -  | -  | -  | -              |
| 87        | -                   | - | - | - | - | - | - | - | - | -  | -  | -  | -  | -  | -              |
| 94        | -                   | - | - | - | - | - | - | - | - | -  | -  | -  | -  | -  | -              |
| 97        | -                   | - | - | - | - | - | - | - | - | -  | -  | -  | -  | -  | -              |
| 102       | -                   | - | - | - | - | - | - | - | - | -  | -  | -  | -  | -  | -              |
| 104       | -                   | - | - | - | - | - | - | - | - | -  | -  | -  | -  | -  | -              |
| 108       | -                   | - | - | - | - | - | - | - | - | -  | -  | -  | -  | -  | -              |

+ = positive for virus (highlighted yellow)  
 - = negative for virus

### Viremia in Controls (23 bovine)

| Animal ID | Days Post-Challenge |   |   |   |   |   |   |   |   |    |    |    |    |    | Overall Result |
|-----------|---------------------|---|---|---|---|---|---|---|---|----|----|----|----|----|----------------|
|           | 1                   | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 |                |
| 31        | -                   | - | - | - | - | + | + | - | + | -  | -  | -  | -  | -  | +              |
| 33        | -                   | - | - | - | - | + | - | - | - | -  | -  | -  | -  | -  | +              |
| 36        | -                   | + | + | + | - | + | - | - | - | -  | -  | -  | -  | -  | +              |
| 38        | -                   | - | - | + | + | + | + | - | + | -  | -  | -  | -  | -  | +              |
| 44        | -                   | - | - | + | + | + | - | - | - | -  | -  | -  | -  | -  | +              |
| 47        | -                   | - | - | + | + | - | - | - | - | -  | -  | -  | -  | -  | +              |
| 50        | -                   | - | - | - | - | + | + | - | - | -  | -  | -  | -  | -  | +              |
| 53        | -                   | - | - | - | + | + | + | + | + | -  | -  | -  | -  | -  | +              |
| 56        | -                   | - | - | + | + | + | + | - | - | -  | -  | -  | -  | -  | +              |
| 58        | -                   | - | - | + | + | + | + | - | - | -  | -  | -  | -  | -  | +              |
| 59        | -                   | - | - | + | + | + | + | + | + | -  | -  | -  | -  | -  | +              |
| 62        | -                   | - | - | - | + | - | + | - | - | -  | -  | -  | -  | -  | +              |
| 66        | -                   | - | - | - | + | + | - | + | - | -  | -  | -  | -  | -  | +              |
| 69        | -                   | - | - | - | + | - | - | - | - | -  | -  | -  | -  | -  | +              |
| 70        | -                   | - | - | - | + | + | + | - | - | -  | -  | -  | -  | -  | +              |
| 74        | -                   | - | - | - | - | - | - | - | - | -  | -  | -  | -  | -  | -              |
| 85        | -                   | - | - | - | + | + | - | - | - | -  | -  | -  | -  | -  | +              |
| 89        | -                   | - | - | - | + | + | + | - | - | -  | -  | -  | -  | -  | +              |
| 92        | -                   | - | - | - | - | + | + | - | - | -  | -  | -  | -  | -  | +              |
| 98        | -                   | - | - | - | + | + | + | - | - | -  | -  | -  | -  | -  | +              |
| 101       | -                   | - | - | - | - | + | + | + | - | -  | -  | -  | -  | -  | +              |
| 106       | -                   | - | - | - | + | - | - | - | - | -  | -  | -  | -  | -  | +              |
| 107       | -                   | - | - | - | + | + | + | - | - | -  | -  | -  | -  | -  | +              |

+ = positive for virus (highlighted yellow)

- = negative for virus

## Leukopenia in Vaccinates (23 bovine)

| ID  | White Blood Cell Count per each Day Post-Challenge |      |      |      |      |      |      |      |      |      |      |     |      |      |      | Overall Result |
|-----|--|------|------|------|------|------|------|------|------|------|------|-----|------|------|------|----------------|
|     | Base-line  | 1    | 2    | 3    | 4    | 5    | 6    | 7    | 8    | 9    | 10   | 11  | 12   | 13   | 14   |                |
| 21  | 13.5   | 10.4 | 11.3 | 11.6 | 11.9 | 11.3 | 12.4 | 12.2 | 11.6 | 12.4 | 9.6  | 9.6 | 9.3  | 9.7  | 10.4 | -              |
| 32  | 8.4  | 8.1  | 7.8  | 7.9  | NA   | 9.9  | 8.9  | 9.7  | 8.9  | 7.1  | 6.6  | 8   | 8.4  | 10.7 | 12   | -              |
| 34  | 8.9  | 8.7  | 9    | 9.3  | 9.5  | 8.5  | 8.9  | 9    | 8.6  | 8    | 8.2  | 4.7 | 5.1  | 6.9  | 8.6  | +              |
| 37  | 13.9   | 12.4 | 12.7 | 12.6 | 11.9 | 11.6 | 11   | 11.4 | 9.4  | 9.3  | 9    | 9.9 | 10.1 | 10.1 | 9.9  | -              |
| 41  | 8.1  | 8.3  | 7.8  | 9.1  | 8.3  | 7.5  | 7.3  | 7.4  | 7.5  | 5.4  | 5.3  | 5.1 | 6.2  | 7.8  | 8.1  | -              |
| 43  | 8.0  | 7.7  | 8    | 8.8  | 8.1  | 8.6  | 8    | 8.9  | 7.8  | 8.2  | 6    | 6.9 | 8.1  | 7.4  | 6.8  | -              |
| 48  | 6.2  | 6.6  | 6.8  | 7    | 6.7  | 6.5  | 6.5  | 6.8  | 7.2  | 3.1  | 3.8  | 5   | 5.6  | 5.8  | 6.1  | +              |
| 49  | 11.1   | 10.6 | 10.9 | 11.1 | 11.8 | 10.5 | 9.4  | 10.1 | 10.4 | 10.5 | 8    | 8.8 | 8.6  | 10.9 | 11.9 | -              |
| 51  | 8.0  | 8.5  | 9.4  | 10.8 | 10.4 | 11.3 | 9.7  | 10.1 | 10.3 | 8.7  | 5.5  | 6.7 | 7.4  | 7.5  | 8.2  | -              |
| 57  | 8.5  | 9.4  | 9.6  | 9.1  | 9.7  | 8.8  | 9.4  | 9.1  | 9    | 8.8  | 8.4  | 7   | 8    | 7.5  | 7.3  | -              |
| 61  | 7  | 7    | 6.8  | 7.9  | 4.6  | 3.9  | 4.5  | 6.6  | 7    | 6.8  | 6.3  | 8.2 | 8.8  | 8    | 7.9  | +              |
| 64  | 8.1  | 6.6  | 6.1  | 6.6  | 7.2  | 6.2  | 6.9  | 7.2  | 7.1  | 7.4  | 7.1  | 6.8 | 7.8  | 9.5  | 9    | -              |
| 67  | 6.2  | 5.8  | 5.9  | 6.6  | 6.7  | 6.3  | 3.5  | 4.7  | 5    | 5.1  | 5.4  | 6.4 | 6.4  | 8.2  | 6.1  | +              |
| 68  | 7.6  | 8.2  | 8.5  | 8.7  | 8.7  | 7    | 5.1  | 5.6  | 6.3  | 6.6  | 7.2  | 7.9 | 8.1  | 9.3  | 9.4  | -              |
| 73  | 8.0  | 8    | 7.9  | 8    | 8.1  | 7.8  | 7.7  | 6.1  | 5.7  | 5.8  | 5.9  | 6.1 | 7.3  | 7.4  | 9.2  | -              |
| 82  | 11.6   | 11.1 | 11.2 | 17.2 | 12.1 | 11.6 | 11.6 | 11   | 11.5 | 11.4 | 5.7  | 8.1 | 9.6  | 11.5 | 10.8 | +              |
| 86  | 6.6  | 7.2  | 7.1  | 6.8  | 6.8  | 5.9  | 6.3  | 6.1  | 5.8  | 6.7  | 4.2  | 4.6 | 5.9  | 5.9  | 7.2  | -              |
| 87  | 9.2  | 9.4  | 9.9  | 10   | 7.4  | 8.3  | 7.5  | 10.4 | 8.8  | 8.6  | 9.7  | 9.1 | 8.9  | 9.1  | 9.6  | -              |
| 94  | 11.6   | 11.2 | 11.4 | 10.6 | 10.1 | 9.3  | 9.3  | 9.4  | 9.9  | 10.2 | 8.3  | 8.6 | 9.4  | 11.4 | 11.8 | -              |
| 97  | 6.4  | 6.8  | 7    | 8.1  | 8.3  | 7.7  | 7.4  | 7.9  | 8.3  | 7.5  | 4.8  | 5.3 | 5.7  | 6.6  | 5.8  | -              |
| 102 | 8.7  | 8.3  | 8.8  | 8.7  | 8.9  | 8.2  | 8.2  | 8.5  | 8    | 6    | 3.8  | 5.5 | 6.3  | 7.1  | 8.1  | +              |
| 104 | 8.3  | 8.4  | 8.6  | 9.2  | 8.9  | 7.9  | 8.1  | 8.9  | 8.5  | 6.9  | 5.3  | 6.7 | 6.7  | 9.9  | 7.9  | -              |
| 108 | 8.1  | 8.1  | 9    | 7.7  | 8.4  | 11.4 | 7.8  | 9.3  | 11.9 | 10.3 | 10.3 | 8   | 12.7 | 10.6 | 10.2 | -              |

### White Blood Cell Count:

- Baseline is the average white blood cell (WBC) counts from 3 consecutive days, prior to challenge
- Numerical values = white blood cell count in K/ $\mu$ L
- Highlighted yellow = positive for leukopenia, meaning a 40% or more reduction in the total WBC count compared to baseline on that day
- NA = not applicable / no measurement on that day

### Overall Result:

- + = positive for leukopenia at least one day (highlighted yellow)
- = negative for leukopenia on every day

### Leukopenia in Controls (23 bovine)

| ID  | White Blood Cell Count per each Day Post-Challenge |      |      |     |     |     |     |     |      |      |     |     |     |     |      | Overall Result |
|-----|--|------|------|-----|-----|-----|-----|-----|------|------|-----|-----|-----|-----|------|----------------|
|     | Base-line  | 1    | 2    | 3   | 4   | 5   | 6   | 7   | 8    | 9    | 10  | 11  | 12  | 13  | 14   |                |
| 31  | 7.8  | 7.7  | 7.3  | 3.8 | NA  | 4.5 | 3.7 | 3.9 | 6.1  | 10.6 | 7   | 5.9 | 5.5 | 5.9 | 3.2  | +              |
| 33  | 11.3   | 10.5 | 11.9 | 6.5 | 7   | 7.3 | 5.7 | 6   | 10.3 | 7.9  | 6.8 | 7   | 7.4 | 8.1 | 7.7  | +              |
| 36  | 8.9  | 9.2  | 8.8  | 5.1 | 6.4 | 5.7 | 5.3 | 5.2 | 6.6  | 7.5  | 6.3 | 5.7 | 5.9 | 5.9 | 6    | +              |
| 38  | 6.5  | 5.9  | 7    | 4.6 | 4.6 | 3.9 | 3.6 | 3.4 | 7    | 7.3  | 6.1 | 5.4 | 5.3 | 5.6 | 5    | +              |
| 44  | 10.3   | 10.2 | 10   | 4.1 | 6.2 | 5.8 | 4.3 | 7.3 | 12.7 | 8    | 5.4 | 5.7 | 6.3 | 5.5 | 5.5  | +              |
| 47  | 7.9  | 8.1  | 7.6  | 4.8 | 5.9 | 5.8 | 4.5 | 5.3 | 7.9  | 6.5  | 6.2 | 5.8 | 5.6 | 5.6 | 6    | +              |
| 50  | 8.2  | 8.9  | 8.9  | 5.9 | 4.6 | 6   | 5.1 | 6.3 | 10.4 | 8.9  | 6.3 | 5.1 | 5.1 | 5.7 | 5.6  | +              |
| 53  | 7.5  | 8.3  | 8.5  | 3.9 | 4.5 | 4.3 | 3.1 | 3.4 | 3.6  | 7.5  | 6.1 | 4.4 | 5.6 | 5.8 | 5.5  | +              |
| 56  | 9.8  | 7.6  | 9.1  | 3.9 | 6   | 4.5 | 4.4 | 5.3 | 12.2 | 9.8  | 5.4 | 5.2 | 6   | 5.5 | 6.3  | +              |
| 58  | 8.3  | 8.7  | 9.8  | 5.7 | 6.3 | 7.1 | 5.1 | 5.2 | 8.2  | 8.4  | 6.1 | 6.4 | 7.4 | 6.2 | 6.5  | -              |
| 59  | 10.1   | 11.1 | 12.2 | 8.5 | 7.3 | 8.7 | 7.6 | 7.8 | 9.4  | 12.7 | 13  | 9.9 | 9.5 | 9.9 | 21.6 | -              |
| 62  | 9.5  | 10.2 | 9.8  | 4.9 | 5.5 | 5.1 | 4.2 | 3.9 | 7.5  | 10.7 | 8.6 | 7   | 6.1 | 6.2 | 5.5  | +              |
| 66  | 6.7  | 8.5  | 8    | 4.5 | 6   | 5.2 | 4.5 | 5.8 | 7    | 5.8  | 4.8 | 4.6 | 5.1 | 5.4 | 3.9  | +              |
| 69  | 11.1   | 12.1 | 11.4 | 5.1 | 8.1 | 8.8 | 7.2 | 9.4 | 11.3 | 10.5 | 7.8 | 7.4 | 7.1 | 7.4 | 7.7  | +              |
| 70  | 10.7   | 10.1 | 9    | 4.4 | 6   | 5.8 | 4.4 | 4.5 | 7.5  | 10.8 | 8.5 | 7.4 | 5.6 | 6.4 | 5.8  | +              |
| 74  | 5.8  | 6.2  | 6.4  | 4.2 | 4.7 | 4.2 | 3.3 | 3   | 4    | 7    | 5.2 | 4.4 | 4.6 | 4.1 | 4.5  | +              |
| 85  | 8.6  | 8    | 7.8  | 5.7 | 6.8 | 5.4 | 4.5 | 4.3 | 5    | 6.1  | 6.3 | 7.4 | 7.2 | 7.6 | 7.4  | +              |
| 89  | 8.9  | 8.4  | 8.5  | 3.9 | 5.8 | 6.1 | 4.6 | 4.1 | 9.1  | 8.6  | 5.7 | 4.7 | 5.2 | 5.1 | 5.7  | +              |
| 92  | 7.8  | 7.4  | 5.9  | 4.4 | 4.6 | 3.8 | 3.2 | 3.6 | 4.1  | 4.6  | 3.6 | 3.8 | 3.8 | 4.5 | 4.4  | +              |
| 98  | 7.9  | 7.4  | 8    | 4.5 | 5.9 | 4.2 | 4.1 | 4.1 | 6.5  | 7.3  | 6.5 | 5.8 | 6.1 | 5.9 | 5.8  | +              |
| 101 | 9.9  | 9.3  | 10.5 | 8.5 | 7.6 | 7.2 | 5.6 | 5.5 | 5.3  | 13.4 | 9.6 | 7.2 | 6.5 | 7   | 5.4  | +              |
| 106 | 7.1  | 7.2  | 7.3  | 4.4 | 5.3 | 4.6 | 3.7 | 5.2 | 7.6  | 5.3  | 5.1 | 6.4 | 5.6 | 6.3 | 6.9  | +              |
| 107 | 10.7   | 10.5 | 10.1 | 6.7 | 7.9 | 7   | 5.5 | 5.7 | 7.8  | 8.9  | 8.7 | 7.5 | 7.1 | 7.6 | 8.8  | +              |

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- NA = not applicable / no measurement on that day

#### Overall Result:

- + = positive for leukopenia at least one day (highlighted yellow)
- = negative for leukopenia on every day



|  |   |
|--|---|
| <b>Study Type</b>                        | Efficacy  |
| <b>Pertaining to</b>                     | Bovine Virus Diarrhea (BVD)   |
| <b>Study Purpose</b>                     | Demonstration of efficacy against persistent infection of calves with BVD Type 2  |
| <b>Product Administration</b>            | Pregnant heifers or cows prior to breeding  |
| <b>Study Animals</b>                     | Bovine  |
| <b>Challenge Description</b>             | BVD2a 96B2222 strain  |
| <b>Interval observed after challenge</b> |   |
| <b>Results</b>                           | Study data were evaluated by USDA-APHIS prior to product licensure and met regulatory standards for acceptance at the time of submission. No data are published because this study was submitted to USDA-APHIS prior to January 1, 2007, and APHIS only requires publication of data submitted after that date. |
| <b>USDA Approval Date</b>                | December 10, 2003   |

|  |   |
|--|---|
| <b>Study Type</b>                        | Efficacy  |
| <b>Pertaining to</b>                     | Bovine Virus Diarrhea (BVD)   |
| <b>Study Purpose</b>                     | Demonstration of efficacy against BVD Type 2 clinical disease, leukopenia, and viremia  |
| <b>Product Administration</b>            |   |
| <b>Study Animals</b>                     | Bovine  |
| <b>Challenge Description</b>             | BVD2a IAF 103, BT-4A-2 strain   |
| <b>Interval observed after challenge</b> |   |
| <b>Results</b>                           | Study data were evaluated by USDA-APHIS prior to product licensure and met regulatory standards for acceptance at the time of submission. No data are published because this study was submitted to USDA-APHIS prior to January 1, 2007, and APHIS only requires publication of data submitted after that date. |
| <b>USDA Approval Date</b>                | August 4, 2003  |

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| <b>Study Type</b>                        | Efficacy  |
| <b>Pertaining to</b>                     | Infectious Bovine Rhinotracheitis (IBR)   |
| <b>Study Purpose</b>                     | Demonstration of efficacy against IBR (respiratory disease)   |
| <b>Product Administration</b>            |   |
| <b>Study Animals</b>                     | Bovine  |
| <b>Challenge Description</b>             |   |
| <b>Interval observed after challenge</b> |   |
| <b>Results</b>                           | Study data were evaluated by USDA-APHIS prior to product licensure and met regulatory standards for acceptance at the time of submission. No data are published because this study was submitted to USDA-APHIS prior to January 1, 2007, and APHIS only requires publication of data submitted after that date. |
| <b>USDA Approval Date</b>                | September 9, 1994   |

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|--|---|
| <b>Study Type</b>                        | Efficacy  |
| <b>Pertaining to</b>                     | <i>Mannheimia haemolytica</i>   |
| <b>Study Purpose</b>                     | Demonstration of efficacy against <i>Mannheimia haemolytica</i>   |
| <b>Product Administration</b>            |   |
| <b>Study Animals</b>                     | Bovine  |
| <b>Challenge Description</b>             |   |
| <b>Interval observed after challenge</b> |   |
| <b>Results</b>                           | Study data were evaluated by USDA-APHIS prior to product licensure and met regulatory standards for acceptance at the time of submission. No data are published because this study was submitted to USDA-APHIS prior to January 1, 2007, and APHIS only requires publication of data submitted after that date. |
| <b>USDA Approval Date</b>                | July 17, 1996   |

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| <b>Study Type</b>                        | Efficacy  |
| <b>Pertaining to</b>                     | Bovine Parainfluenza Type 3 (PI <sub>3</sub> )  |
| <b>Study Purpose</b>                     | Demonstration of efficacy against PI <sub>3</sub>   |
| <b>Product Administration</b>            |   |
| <b>Study Animals</b>                     | Bovine  |
| <b>Challenge Description</b>             |   |
| <b>Interval observed after challenge</b> |   |
| <b>Results</b>                           | Study data were evaluated by USDA-APHIS prior to product licensure and met regulatory standards for acceptance at the time of submission. No data are published because this study was submitted to USDA-APHIS prior to January 1, 2007, and APHIS only requires publication of data submitted after that date. |
| <b>USDA Approval Date</b>                | June 10, 2002   |

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| <b>Study Type</b>                        | Efficacy  |
| <b>Pertaining to</b>                     | Bovine Respiratory Syncytial Virus (BRSV)   |
| <b>Study Purpose</b>                     | Demonstration of efficacy against BRSV  |
| <b>Product Administration</b>            |   |
| <b>Study Animals</b>                     | Bovine  |
| <b>Challenge Description</b>             |   |
| <b>Interval observed after challenge</b> |   |
| <b>Results</b>                           | Study data were evaluated by USDA-APHIS prior to product licensure and met regulatory standards for acceptance at the time of submission. No data are published because this study was submitted to USDA-APHIS prior to January 1, 2007, and APHIS only requires publication of data submitted after that date. |
| <b>USDA Approval Date</b>                | June 14, 1994   |

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| <b>Study Type</b>                        | Safety  |
| <b>Pertaining to</b>                     | All fractions   |
| <b>Study Purpose</b>                     | To demonstrate safety under field conditions  |
| <b>Product Administration</b>            |   |
| <b>Study Animals</b>                     | Bovine: pregnant cows and calves nursing pregnant cows provided the cows were vaccinated pre-breeding   |
| <b>Challenge Description</b>             |   |
| <b>Interval observed after challenge</b> |   |
| <b>Results</b>                           | Study data were evaluated by USDA-APHIS prior to product licensure and met regulatory standards for acceptance at the time of submission. No data are published because this study was submitted to USDA-APHIS prior to January 1, 2007, and APHIS only requires publication of data submitted after that date. |
| <b>USDA Approval Date</b>                | December 6, 2005  |

| <b>Study Type</b>                        | Safety  |               |                  |   |    |     |    |   |    |     |   |
|--|---|---------------|------------------|---|----|-----|----|---|----|-----|---|
| <b>Pertaining to</b>                     | All fractions   |               |                  |   |    |     |    |   |    |     |   |
| <b>Study Purpose</b>                     | To demonstrate safety under field conditions  |               |                  |   |    |     |    |   |    |     |   |
| <b>Product Administration</b>            | One dose, subcutaneously  |               |                  |   |    |     |    |   |    |     |   |
| <b>Study Animals</b>                     | 217 Bovine calves, 5 – 6.6 months of age  |               |                  |   |    |     |    |   |    |     |   |
| <b>Challenge Description</b>             | Not applicable  |               |                  |   |    |     |    |   |    |     |   |
| <b>Interval observed after challenge</b> | Not applicable  |               |                  |   |    |     |    |   |    |     |   |
| <b>Results</b>                           | <p>There were no local or systemic adverse reactions related to vaccination noted in any of the 217 calves during the 14 day post-vaccination observation period. The demographics of the calves is summarized as follows:</p> <table border="1"> <thead> <tr> <th>Months of Age</th> <th>Number of Calves</th> </tr> </thead> <tbody> <tr> <td>5</td> <td>27</td> </tr> <tr> <td>5.5</td> <td>90</td> </tr> <tr> <td>6</td> <td>94</td> </tr> <tr> <td>6.6</td> <td>6</td> </tr> </tbody> </table> | Months of Age | Number of Calves | 5 | 27 | 5.5 | 90 | 6 | 94 | 6.6 | 6 |
| Months of Age                            | Number of Calves  |               |                  |   |    |     |    |   |    |     |   |
| 5  | 27  |               |                  |   |    |     |    |   |    |     |   |
| 5.5                                      | 90  |               |                  |   |    |     |    |   |    |     |   |
| 6  | 94  |               |                  |   |    |     |    |   |    |     |   |
| 6.6                                      | 6   |               |                  |   |    |     |    |   |    |     |   |
| <b>USDA Approval Date</b>                | October 22, 2007  |               |                  |   |    |     |    |   |    |     |   |