# Summary of Studies Supporting USDA Product Licensure

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|---|---|
| Establishment Name | Epitopix, LLC |
| USDA Vet Biologics Establishment Number | 365 |
| Product Code | 2879.00 |
| True Name | Klebsiella Pneumoniae Bacterial Extract |
| Tradename(s) / Distributor or Subsidiary (if different from manufacturer) | Klebvax - Agri Laboratories, Ltd. |
| Date of Compilation Summary | April 19, 2018 |

**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.**

<table>
<tr><td>Study Type</td><td>Efficacy</td></tr>
<tr><td>Pertaining to</td><td>Klebsiella pneumoniae</td></tr>
<tr><td>Study Purpose</td><td>To demonstrate effectiveness against Klebsiella mastitis in cattle.</td></tr>
<tr><td>Product Administration</td><td>Two doses administered at 3-week intervals by subcutaneous route.</td></tr>
<tr><td>Study Animals</td><td>Study animals were housed at a commercial dairy and included 569 head of Holstein or Jersey dairy cows and heifers. Animals were randomized to treatment group with 281 head in the placebo group, and 288 head in the Klebsiella vaccinated group.</td></tr>
<tr><td>Challenge Description</td><td>The challenge was through natural exposure of Klebsiella pneumoniae present in the environment at the dairy.</td></tr>
<tr><td>Interval observed after challenge</td><td>The cows were milked three times daily and monitored for mastitis for 90 days post-calving.</td></tr>
<tr><td>Results</td><td>
<table>
<tr><td></td><td>Klebsiella Negative</td><td>Klebsiella pneumoniae positive</td></tr>
<tr><td>Placebo</td><td>211</td><td>14</td></tr>
<tr><td>Vaccinates</td><td>221</td><td>4</td></tr>
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</td></tr>
<tr><td>USDA Approval Date</td><td>September 23, 2016</td></tr>
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|---|---|
| **Study Type** | Safety |
| **Pertaining to** | ALL |
| **Study Purpose** | To demonstrate safety of the product under field conditions. |
| **Product Administration** | Two doses administered at 3-4 week intervals by subcutaneous route. |
| **Study Animals** | 833 head of commercial dairy cattle were housed at four separate commercial dairies in four geographically distinct regions of the United States. At each site, 1/3 of the animals were non-lactating and less than 22 months of age while the other 2/3 of the animals were lactating and at various ages >22 months of age. Region 1 included 209 cattle. Region 2 included 214 cattle. Region 3 included 200 cattle. Region 4 included 210 cattle. |
| **Challenge Description** | Not applicable |
| **Interval observed after challenge** | On day of vaccination cattle were observed for local and systemic reactions. Local swelling of the injection site was evaluated by palpation the day after vaccination, and three weeks later. |
| **Results** | Raw data on tables below. Injection site swellings resolved within 3 weeks after vaccination. |
| **USDA Approval Date** | February 1, 2018 |

**Tables show the number of cattle with injection site reactions after the 1st vaccination**

Region 1*

| | Prior to 1st vacc | 1 day following 1st vacc | 3 weeks post 1st vacc |
|---|---|---|---|
| No swelling | 208 (99.5%) | 163 (79.1%) | 200 (98.5%) |
| < 1.5 cm | 1 (0.5%) | 14 (6.8%) | 0 |
| 1.5 - 5.0 cm | 0 | 16 (7.8%) | 3 (1.5%) |
| > 5 cm | 0 | 13 (6.3%) | 0 |
| Total Animals | 209 | 206 | 203 |

* One 20-month gestating heifer died at the Region 1 dairy approximately 48 hours after 1st vaccination due to a systemic reaction.

Region 2

| | Prior to 1st vacc | 1 day following 1st vacc | 3 weeks post 1st vacc |
|---|---|---|---|
| No swelling | 205 (95.8%) | 90 (42.1%) | 212 (100%) |
| < 1.5 cm | 2 (0.9%) | 3 (1.4%) | 0 |
| 1.5 - 5.0 cm | 4 (1.9%) | 37 (17.3%) | 0 |
| > 5 cm | 3 (1.4%) | 84 (39.2%) | 0 |
| Total Animals | 214 | 214 | 212 |

Region 3

| | Prior to 1st vacc | 1 day following 1st vacc | 3 weeks post 1st vacc |
|---|---|---|---|
| No swelling | 192 (96%) | 27 (13.5%) | 162 (86.2%) |
| < 1.5 cm | 7 (3.5%) | 91 (45.5%) | 26 (13.8%) |
| 1.5 - 5.0 cm | 1 (0.5% | 81 (40.5%) | 0 |
| > 5 cm | 0 | 1 (0.5%) | 0 |
| Total Animals | 200 | 200 | 188 |

Region 4*

| | Prior to 1st vacc | 1 day following 1st vacc | 3 weeks post 1st vacc |
|---|---|---|---|
| No swelling | 198 (94.3%) | 182 (87.1%) | 179 (86.9%) |
| < 1.5 cm | 8 (3.8%) | 21 (10%) | 23 (11.2%) |
| 1.5 - 5.0 cm | 4 (1.9%) | 6 (2.9%) | 4 (1.9%) |
| > 5 cm | 0 | 0 | 0 |
| Total Animals | 210 | 209 | 206 |

*Two heifers had labored breathing /systemic reaction within 4 hours at the Region 4 dairy after 1st vaccination. One heifer was 13 months of age, and the other 11 months of age at the time of vaccination. Both heifers were treated immediately with flunixin meglumine. The 11 month old heifer fully recovered, and the 13 month old heifer died 24 hours post-vaccination due to anaphylaxis.

**Tables show the number of cattle with injection site reactions after the 2nd vaccination**

Region 1*

| | Prior to 2nd vacc | 1 day following 2nd vacc | 3 weeks post 2nd vacc |
|---|---|---|---|
| No swelling | 160 (78.8%) | 136 (67.3%) | 199 (100%) |
| < 1.5 cm | 3 (1.5%) | 5 (2.5%) | 0 |
| 1.5 - 5.0 cm | 35 (17.2%) | 37 (18.3%) | 0 |
| > 5 cm | 5 (2.5%) | 24 (11.9%) | 0 |
| Total Animals | 203 | 202 | 199 |

* Two 19-month old gestating heifers died at the Region 1 dairy after 2nd vaccination due to systemic reactions. One heifer died approximately 6 hours post-vaccination, and one heifer died approximately 24 hours post-vaccination.

Region 2

| | Prior to 2nd vacc | 1 day following 2nd vacc | 3 weeks post 2nd vacc |
|---|---|---|---|
| No swelling | 199 (93.9%) | 92 (43.4%) | 212 (100%) |
| < 1.5 cm | 5 (2.35%) | 4 (1.9%) | 0 |
| 1.5 - 5.0 cm | 5 (2.35%) | 21 (9.9%) | 0 |
| > 5 cm | 3 (1.4%) | 95 (44.8%) | 0 |
| Total Animals | 212 | 212 | 212 |

Region 3

| | Prior to 2nd vacc | 1 day following 2nd vacc | 3 weeks post 2nd vacc |
|---|---|---|---|
| No swelling | 186 (99%) | 32 (17%) | 136 (73.9%) |
| < 1.5 cm | 1 (0.5%) | 131 (69.7%) | 47 (25.6%) |
| 1.5 - 5.0 cm | 1 (0.5%) | 25 (13.3%) | 1 (0.5%) |
| > 5 cm | 0 | 0 | 0 |
| Total Animals | 188 | 188 | 184 |

Region 4*

| | Prior to 2nd vacc | 1 day following 2nd vacc | 3 weeks post 2nd vacc |
|---|---|---|---|
| No swelling | 193 (93.7%) | 136 (66%) | 193 (93.7%) |
| < 1.5 cm | 10 (4.8%) | 52 (25.2%) | 13 (6.3%) |
| 1.5 - 5.0 cm | 3 (1.5%) | 18 (8.8%) | 0 |
| > 5 cm | 0 | 0 | 0 |
| Total Animals | 206 | 206 | 206 |

*Five heifers, all < 22 months of age, had labored breathing/systemic reactions within 3 hours at the Region 4 dairy after the 2nd vaccination. All five heifers were treated with Flunixin Meglumine and epinephrine. All five heifers recovered by 24 hours post-vaccination.