Prevention Works in Managing Swine Disease

Ingelvac Circo
Ingelvac Myco
FLEX®
FLEX combo®
FLEX®
Ingelvac PRRS®
Enterisol Ileitis®

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follow label directions.

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Boehringer Ingelheim Vetmedica, Inc., St. Joseph, MO.

Boehringer Ingelheim Vetmedica, Inc.
2621 North Belt Highway
St. Joseph, Missouri 64506-2002
1-800-325-9167
www.bi-vetmedica.com

Because every herd is unique
The **FLEX Family™** of swine vaccines puts you in control

**CUSTOMIZED CONTROL FOR MANAGING MAJOR RESPIRATORY DISEASES IN YOUR SWINE HERD**

- Porcine Circovirus Type 2 (PCV2) vaccine
- *Mycoplasma hyopneumoniae* (*M. hyo*) vaccine
- Porcine Reproductive & Respiratory Syndrome (PRRS) Modified Live Virus vaccine
- PCV2 + *M. hyo* vaccine
- PCV2 + *M. hyo* + PRRS MLV vaccine

No other vaccine company provides you more solutions and the ability to customize the control of major swine respiratory diseases within your system than Boehringer Ingelheim Vetmedica, Inc. (BIVI). With **five effective single-dose** vaccines, you can select the right **monovalent or combination vaccine** that best fits your herd and disease management program.

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**Ingelvac CircoFLEX®**

**Ingelvac MycoFLEX®**

**FLEXcombo®**

**3FLEX®**

**Ingelvac PRRS® MLV**

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**THE INDUSTRY’S LEADING PRRS VACCINE**

BIVI study number: 6131-0852-06P-072

The effect of Ingelvac PRRS® MLV on lung lesions in pigs challenged with a 1-8-4 field strain of PRRS virus

85% Reduction

40%

30%

20%

10%

0%

No - Vaccinated

Vaccinated

P<0.05

32.9%

4.5%
The FLEX Family™ of swine vaccines puts you in control for managing major respiratory diseases in your swine herd.

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**Ingelvac CircoFLEX®** is available in 50, 100 and 250-dose presentations.

**Ingelvac PRRS® MLV** vaccine is proven safe in pigs as well as gilts and sows during any production stage. The vaccine aids in the reduction of both the reproductive and respiratory forms of PRRS virus (PRRSV). Duration of immunity is at least 4 months post-vaccination, which protects pigs through market. In breeding age females, revaccination can occur every 3–4 months and can be administered during any stage of production.

Ingelvac PRRS® MLV has demonstrated cross protection against heterologous (including Lelystad virus) and homologous challenges. Boehringer Ingelheim, Vetmedica Inc. (BIVI) Research and Development group continually researches the effectiveness of Ingelvac PRRS® MLV against current PRRS field virus strains. The graph below shows the percentage of lung lesions in both vaccinated and non-vaccinated groups of pigs challenged with a recent 1-8-4 field strain of PRRSV. Vaccinated pigs had a significant reduction in lung lesions compared to non-vaccinated pigs.

Ingelvac PRRS® MLV has become a trusted tool to help control PRRSv in swine herds. It is safe to use throughout production systems in both pigs and breeding age females. It has been proven efficacious in both homologous and heterologous challenges in susceptible pigs. No PRRS vaccine on the market has been researched more than Ingelvac PRRS® MLV and BIVI is committed to continue being an industry leader in PRRS research.

**Ingelvac CircoFLEX®** is the industry's leading PCV2 vaccine for protection in a single injection.

Ingelvac CircoFLEX® was the first in the FLEX Family™ of swine vaccines and one of the most revolutionary PCV2 vaccines on the market. As a result, it has built a reputation for providing safe, effective control of porcine circovirus associated disease (PCVAD) in pigs three weeks of age or older from a single dose.

**PCA™ AND IMPRANFLEX®**

Unlike all other PCV2 vaccines on the market, Ingelvac CircoFLEX® contains the unique combination of Purified Circovirus Antigen (PCA™) and ImpranFLEX®. PCA™ is the Ingelvac CircoFLEX® antigen in which extraneous baculovirus from the virus-like particle (VP) is removed, resulting in a highly refined vaccine. ImpranFLEX® is a proprietary water-based polymer adjuvant found in all adjuvanted FLEX Family™ vaccines. These two innovative vaccine technologies work together to generate a strong immune response and low risk of adverse reactions in vaccinated pigs.
INGELVAC CIRCOFLEX® VACCINE OVERVIEW

TIMING OF VACCINATION

Single-dose, 1 mL vaccine approved for pigs 3 weeks of age or older.

LONG DURATION OF IMMUNITY

Ingelvac CircoFLEX® provides at least 4 months of immunity, long enough to last through the critical grow-finish stage.

RAPID ONSET OF IMMUNITY

Unlike two-dose products, it provides effective immune response within 2 weeks after single dose vaccination.

Ingelvac CircoFLEX® Timeline

**CIRCOFLEX SINGLE DOSE VACCINATION**

- Birth
- Weaning
- 2 weeks
- Finishing

**IMMUNITY WITH CIRCOFLEX**

EXCELLENT SAFETY PROFILE

Because it contains both PCA™ and ImpranFLEX®, Ingelvac CircoFLEX® provides a strong immune response with low risk of injection site or other adverse reactions in pigs.

PQA PLUS® AND LABOR-SAVING BENEFITS

Single-dose administration reduces pig handling and stress by reducing labor and number of injections.

EFFECTIVELY DIAGNOSING PCVAD

The American Association of Swine Veterinarians has adopted the following criteria for confirming a diagnosis of PCVAD

CLINICAL SIGNS

Progressive weight loss, Porcine Dermatitis Nephropathy Syndrome (PDNS), pneumonia, diarrhea, and/or reproductive disease.

INCREASED MORTALITY RATES

Doubling of historical death loss due to acute disease infection.

HISTOLOGIC LESIONS

Lymphoid depletion with or without granulomatous inflammation.

DIAGNOSTIC RESULTS

PCV2 detection in lesions via PCV2 immunohistochemistry (IHC) when associated with characteristic lung lesions or in fetal myocarditis lesions in reproductive PCVAD.

| Percent of Pigs with Palpable Injection Site Lesions at Peak Time of Reactions |
|---------------------------------|-------------------------------|-------------------------------|
| Saline                          | Ingelvac CircoFLEX®          | Competitor                    |
| 0.9%*                           | 0.0%*                        | 10.1%*<sup>a</sup>            |
| 0.0%*                           | 0.8%*                        | 12.1%<sup>b</sup>             |
| N/A                             | 0.0%*                        | 17.3%<sup>c</sup>             |
| P<0.05                          | P<0.05                       | P<0.0001<br>P<0.05<sup>d</sup>|<sup>e</sup> |

In Trial 1 and 2 Ingelvac CircoFLEX® was as safe as saline as measured by injection site lesions. The competitor vaccines induced a significantly greater amount of injection site lesions compared to Ingelvac CircoFLEX®<sup>a</sup>.

Ingelvac MycoFLEX®

GIVES YOU THE FREEDOM TO VACCINATE FOR *M. HYO* WHEN IT IS APPROPRIATE

*Mycoplasma hyopneumoniae* (*M. hyo*) is a leading cause of respiratory disease throughout the entire swine industry. Controlling *M. hyo* infection within the entire production chain provides optimum results.

**M.hyo Infection Chain™**

Understanding the Infection Chain™ and utilizing the Prevention Chain™ can help you obtain the most from your Ingelvac MycoFLEX® vaccination program.
Vaccinating pigs at three weeks of age, including replacement gilts and sows, will help break the *M. hyo Infection Chain™* within a production system and decrease vertical and horizontal transmission of the disease to susceptible pigs. Understanding the Infection Chain™ and utilizing the Prevention Chain™ can help you get the most from your Ingelvac MycoFLEX® vaccination program.

Ingelvac MycoFLEX® is a *non-viscous, highly syringeable, one-dose*, 1 mL mycoplasma vaccine that aids in the reduction of enzootic pneumonia caused by *M. hyo* when administered to pigs 3 weeks of age or older. It also contains the unique ImpranFLEX® water-based polymer adjuvant that improves the immune response in pigs.

**INGELVAC MYCOFLEX® VACCINE OVERVIEW**

**TIMING OF VACCINATION**

Single-dose, 1 mL vaccination can be given to pigs 3 weeks of age or older to best fit your program.

**LONG DURATION OF IMMUNITY**

Ingelvac MycoFLEX® provides at least 26 weeks of immunity to last through marketing.

**RAPID ONSET OF IMMUNITY WITH FEWER REACTIONS**

It contains the innovative ImpranFLEX® adjuvant technology that provides rapid onset of immunity as well as a low risk of adverse reactions in pigs.
FLEXcombo®

SINGLE-DOSE CUSTOMIZED CONTROL FOR BOTH PCV2 AND M. HYO

FLEXcombo® is the **first single-dose** vaccine that controls two of the most important respiratory diseases in swine: PCVAD and M. hyo.

In addition, FLEXcombo® combines the immunizing power and all the benefits of the individual Ingelvac CircoFLEX® and Ingelvac MycoFLEX® vaccines into a single 2 mL injection that is approved for administration for pigs 3 weeks of age or older. Because both vaccines contain the unique ImpranFLEX® adjuvant technology, they are **highly compatible** and provide a **rapid, long lasting immune response**, with **low risk of adverse reactions**.

The FLEXcombo® 50-dose package contains one 50 mL bottle of Ingelvac CircoFLEX® and 50 mL of Ingelvac MycoFLEX® vaccine in a 100 mL headspace bottle (HSB). The FLEXcombo® 250-dose package contains one 250 mL bottle of Ingelvac CircoFLEX® and 250 mL of Ingelvac MycoFLEX® vaccine in a 500 mL headspace bottle (HSB) for the ease and convenience of mixing both vaccines together to create a single vaccine.

**Headspace Bottle (HSB) Technology**

1/2 bottle volume for mixing with Ingelvac CircoFLEX®

1/2 bottle volume filled with Ingelvac MycoFLEX®
FLEXCOMBO® OVERVIEW

CUSTOMIZED CONTROL OF TWO DISEASES WITH ONE INJECTION
FLEXcombo® provides effective control of both PCV2 and M. hyo when administered at 3 weeks of age or older. Exact timing of vaccination will depend on your herd’s pattern of disease exposure.

FEWER INJECTIONS, LESS HANDLING AND STRESS ON PIGS AND PEOPLE
Vaccinating pigs against two diseases in a single injection reduces stress on pigs and reduces the labor needed compared to a two-dose protocol.

HEADSPACE BOTTLE BENEFIT
The Ingelvac MycoFLEX® headspace bottle technology provides a convenient way to mix the vaccines prior to administration.

FLEXcombo® Mixing Sequence

Aseptically combine the contents of the Ingelvac CircoFLEX® bottle into the Ingelvac MycoFLEX® bottle (2 & 3). Shake well (4). Administer a 2 mL dose to pigs (5).

Percent of Pigs with Palpable Injection Site Lesions at Peak Time of Reactions

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Number of Animals</th>
<th>Average Lung Lesion Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Controls—Strict</td>
<td>6</td>
<td>0.0</td>
</tr>
<tr>
<td>Controls—Challenged</td>
<td>19</td>
<td>14.3^</td>
</tr>
<tr>
<td>Ingelvac MycoFLEX®</td>
<td>18</td>
<td>5.5^</td>
</tr>
<tr>
<td>Ingelvac® CircoFLEX-MycoFLEX®</td>
<td>19</td>
<td>3.9^</td>
</tr>
</tbody>
</table>

Lack of Interference: Mycoplasma hyopneumoniae

In Trial 1 and 2 Ingelvac® CircoFLEX-MycoFLEX® was as safe as saline as measured by injection site lesions. The competitor vaccines induced a significantly greater amount of injection site lesions compared to Ingelvac® CircoFLEX-MycoFLEX®.


Lack of Interference: PCV2

<table>
<thead>
<tr>
<th>Group</th>
<th>Lymphoid Depletion</th>
<th>Lymphoid Inflammation</th>
<th>Lymphoid IHC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>20/24</td>
<td>21/24</td>
<td>22/24</td>
</tr>
<tr>
<td>Ingelvac® CircoFLEX-MycoFLEX®</td>
<td>0/24</td>
<td>1/24</td>
<td>2/24</td>
</tr>
</tbody>
</table>

BIVI study numbers: ^6127-1004-077P-187  ^6131-0981-05P-022
"Ingelvac® CircoFLEX-MycoFLEX® = FLEXcombo®"
3FLEX® is available in 50-dose presentation.

THE ULTIMATE IN CUSTOMIZATION FOR CONTROL OF THREE RESPIRATORY DISEASES IN SWINE: PCV2, M. HYO AND PRRS

3FLEX® is the only single-dose, three-way vaccine licensed by the USDA for use in swine to control PCV2, M. hyo and Porcine Reproductive & Respiratory Syndrome (PRRS).

As part of the FLEX Family™ of swine vaccines, 3FLEX® provides you the additional ability to customize a disease control program where all three diseases are present.

For most swine producers, a single 2 mL dose of 3FLEX® replaces multiple injections of monovalent vaccines; saving time, labor and the hassles and stress of handling pigs multiple times. More importantly, extensive research studies show that 3FLEX® consistently provides effective protection against disease associated with PCV2, M. hyo and PRRS.

In addition, there is no interference between the individual antigens when administered to pigs as a single injection. This means 3FLEX® effectively immunizes pigs against all three diseases and there is low risk of adverse reactions.

3FLEX®: Safety Maintained

<table>
<thead>
<tr>
<th>MEASUREMENT</th>
<th>CONTROLS</th>
<th>3FLEX®</th>
<th>P-VALUE</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 hour Abnormal Reaction</td>
<td>3/677</td>
<td>1/672</td>
<td>P=0.3724</td>
</tr>
<tr>
<td>All days combined (d 0-14)</td>
<td>43/677</td>
<td>48/672</td>
<td>P=0.6517</td>
</tr>
<tr>
<td>14 day Injection Site Reaction</td>
<td>0/677</td>
<td>0/672</td>
<td>—</td>
</tr>
</tbody>
</table>

*Abnormal Clinical Presentation included: Scours, greasy pig, gaunt, lethargy, lame, hernia, swollen joints, mortality, coughing, pneumonia. None of the clinical abnormalities observed during the 2 week post-treatment observation period were attributed to the administration of the trivalent vaccine mixture.

BIVI study number: 6131-0981-06P-086
### 3FLEX® Mixing Sequence

Each 3FLEX® package contains one bottle of Ingelvac CircoFLEX®, one bottle of Ingelvac MycoFLEX® (HSB), and one bottle of lyophilized Ingelvac PRRS® MLV.

Aseptically combine the contents of Ingelvac CircoFLEX® bottle into the Ingelvac MycoFLEX® bottle (2 & 3). Shake well (4). Empty the combined contents of the CircoFLEX and MycoFLEX into the Ingelvac PRRS® MLV bottle (5). Shake well (6). Administer a 2 mL dose to pigs (7).

### 3FLEX® VACCINE OVERVIEW

#### CUSTOMIZED CONTROL OF THREE SWINE DISEASES

3FLEX® is the only USDA-approved combination vaccine for protection against PCV2, M. hyo and PRRS in a single injection.

#### FEWER INJECTIONS

3FLEX® is easy to mix and is administered in a single 2 mL injection to pigs 3 weeks of age or older, reducing labor and stress of injecting pigs multiple times.

#### RESEARCH PROVEN EFFECTIVE

Extensive research studies show lack of interference between antigens and a high level of immunization and product efficacy against three diseases.

### 3FLEX® Family Product with ImpranFLEX®

3FLEX® is part of the FLEX Family™ of vaccines from BIVI and contains the unique ImpranFLEX® aqueous-based polymer adjuvant for strong immune response and low risk of adverse reactions.

#### 3FLEX®: Maintains Efficacy

#### 3FLEX®: Lack of Interference Study

**Figure 1. Average PRRS ELISA S/P Ratio**

No difference in serological PRRS response in 3 week old pigs vaccinated with either 3FLEX® or FLEXcombo® concurrently administered with Ingelvac PRRS® MLV.


**Figure 2. Percentage PRRS ELISA Positive**

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>3FLEX®</th>
<th>P-VALUE</th>
</tr>
</thead>
<tbody>
<tr>
<td>PVC2 Lymphoid depletion°</td>
<td>20/24 (83.3%)</td>
<td>0/24 (0.0%)</td>
<td>P&lt;0.0001</td>
</tr>
<tr>
<td>PVC2 IHC Positive (lymph node)°</td>
<td>22/24 (91.7%)</td>
<td>2/24 (8.3%)</td>
<td>P&lt;0.0001</td>
</tr>
<tr>
<td>M. hyo Lung pathology°</td>
<td>10.6%</td>
<td>3.8%</td>
<td>P&lt;0.0078</td>
</tr>
<tr>
<td>PRRS Lung pathology°</td>
<td>32.9%</td>
<td>4.5%</td>
<td>P&lt;0.0001</td>
</tr>
</tbody>
</table>

BIVI study numbers: 6131-0981-05P-022 6131-1004-08P-018 6131-0852-06P-072
ImpranFLEX®

THE ADVANCED AQUEOUS-BASED POLYMER ADJUVANT TECHNOLOGY

ImpranFLEX® is a proprietary water-based adjuvant that is utilized consistently throughout the FLEX Family™ of vaccines. ImpranFLEX® improves the immune response of the vaccine within the pig, resulting in faster, long-lasting disease protection.

ImpranFLEX® is found in monovalent Ingelvac CircoFLEX® and Ingelvac MycoFLEX® vaccines, as well as in the same products used in FLEXcombo® and 3FLEX®.
FLEX Family™ of vaccines

ONE FLEX FAMILY™, FIVE SWINE VACCINES, MULTIPLE SOLUTIONS... CUSTOMIZED TO YOUR HERD’S RESPIRATORY DISEASE PROBLEMS.

**INGELVAC CIRCOFLEX®**

Ingelvac CircoFLEX® was the first of the FLEX Family™ of swine vaccines and one of the most revolutionary PCV2 vaccines on the market. Utilizing PCA™ technology and ImpranFLEX™, Ingelvac CircoFLEX® is a leader in safe, consistent and effective control of PCVAD with a single dose.

**INGELVAC MYCOFLEX®**

Proven safety, efficacy, and quick long-lasting immunity with a single dose and provides you the freedom to vaccinate for M. hyo when it is appropriate. Mycoplasma hyopneumoniae is a leading cause of respiratory disease throughout the entire swine industry. While the disease impacts finishing pigs frequently and severely, M. hyo infection can occur at any point within the entire production system and therefore prevention at each stage is necessary.

**FLEXCOMBO®**

The first single dose combination vaccine furthering the customized control of both PCV2 and M. hyo. Consistent disease control and safety are not compromised and lack of interference is proven.

**3FLEX®**

The only licensed combination vaccine proven safe and effective in controlling three major respiratory diseases PCV2, M. hyo and PRRS. 3FLEX® provides the ability to customize a disease control program when all three diseases are present.

**INGELVAC PRRS® MLV**

The industry’s leading PRRS vaccine, with proven cross protection and long-lasting immunity. BIVI remains committed to being an industry leader in PRRS research.
Ingelvac PRRS® MLV

THE INDUSTRY’S LEADING PRRS VACCINE

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The effect of Ingelvac PRRS® MLV on lung lesions in pigs challenged with a 1-8-4 field strain of PRRS virus

BIVI study number: 6131-0852-06P-072
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