药业先锋 信赖所在

LEADING ANIMAL PHARMACY ORIGIN OF RELIANCE

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ringpu®
瑞普生物

ONE IMMUNIZATION DOUBLE PROTECTION

RINVAC ND+IBD

Newcastle Disease and Infectious Bursal Disease Vaccine, Inactivated (Strain La Sota + Strain HQ)

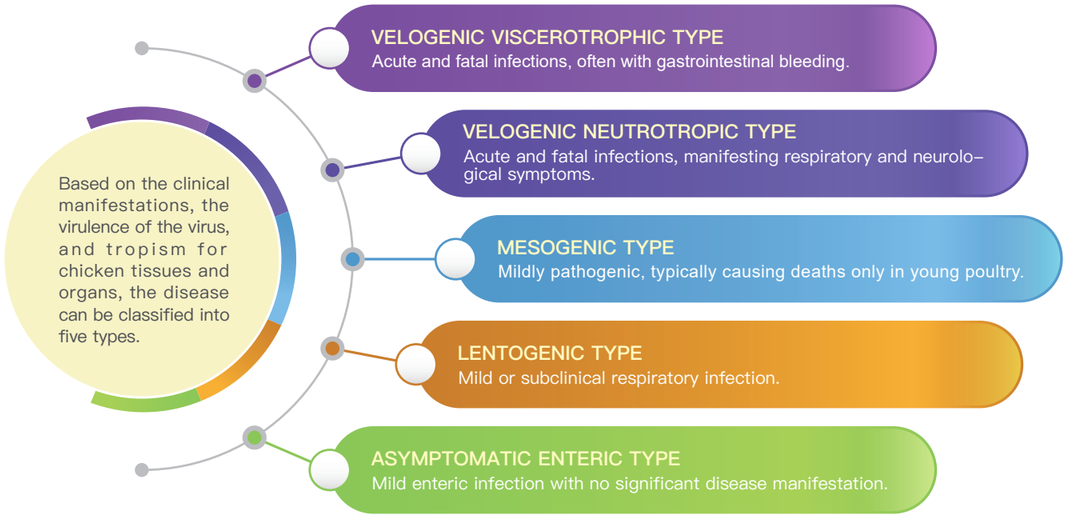
- Screened strains, broad antigenic spectrum
- High safety, can be injected at 1 day of age
- High-purity vaccine with minimal side effects
- One shot with double-prevention during the whole period
- High-quality adjuvant, easy to be absorbed

PRODUCED BY RINGPU

EPIDEMIOLOGICAL CHARACTERISTICS OF NEWCASTLE DISEASE

- **The range of susceptible hosts is continuously expanding**
  Chickens are highly susceptible, in recent years, the current host range has significantly expanded, with over 250 species of birds that can be naturally or artificially infected.
- **The seasonal nature of the disease is becoming less apparent**
  The disease is common during the transition from autumn to winter and during sudden cold weather.
- **Characteristics of the age at which the disease occurs**
  The age at onset is not clearly defined.
- **Non-typical symptoms are becoming more prevalent**
- **The shedding of NDV generally stops 5–7 days after the symptoms disappear**

CLINICAL AND NECROPSY SYMPTOMS OF NEWCASTLE DISEASE



OVERVIEW OF NEWCASTLE DISEASE

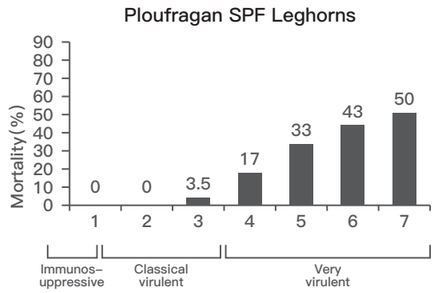
- Newcastle disease (ND) is an acute, febrile, septic, and highly contagious infectious disease of poultry caused by Newcastle disease virus.
- Its main characteristics are difficult breathing, diarrhea, neurological disorders, and bleeding of mucous membranes and serosa.
- A major infectious disease that poses a significant threat to the poultry industry.

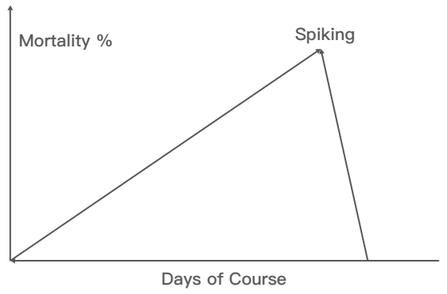
RESISTANCE OF INFECTIOUS BURSAL DISEASE

- The virus can survive for more than 100 days in contaminated poultry houses.
- Highly resistant to heat, sunlight, and ultraviolet radiation. It remains viable at 56℃ for 5 hours and at 60℃ for 30 minutes, but is rapidly inactivated at 70℃.
- Resistant to acidic conditions but sensitive to alkaline environments. The virus remains active at pH 2.0 for 1 hour, while activity is inhibited at pH 12.
- Not sensitive to ether or chloroform.
- Sensitive to routine disinfectants: 3% cresol soap solution, 0.2% peracetic acid, 2% sodium hypochlorite, 5% bleaching powder, 3% phenol, 3% formalin, and 0.1% mercuric chloride can inactivate the virus within 30 minutes.

CLINICAL SYMPTOMS OF INFECTIOUS BURSAL DISEASE

- **Typical Disease Onset:**
  - Mainly occurs in 3–6–weeks of age chickens; short disease course, around one week.
  - Sharp peak in mortality. High mortality rate.
  - Typical symptoms of IBD:
    Bursa: Enlarged, hemorrhagic, and edematous, with a “Purple grape” appearance.
    Kidneys: Swollen with mottling.
    Muscles: Hemorrhages in the breast and thigh muscles.
    Stomach: Hemorrhages at the junction between the proventriculus and gizzard.
- **Subclinical Disease Onset:**
  - Often caused by early infection due to low maternal antibodies, immune failure, or infection by variant strains.
  - Onset occurs before 20 days of age, sometimes even before 10 days of age.
  - Infected chickens show no typical symptoms or significant mortality. However, there is a decrease in egg production, and antibody levels against other diseases may also be suboptimal.
  - Upon necropsy, the bursal atrophy is observed, leading to lifelong immunosuppression.





PHYSICOCHEMICAL PROPERTIES OF INFECTIOUS BURSAL DISEASE

Temperature

- Strong heat resistance.
- Maintains activity after 5 hours at 56℃ and 30 minutes at 60℃.
- Can be completely inactivated by high temperature treatment at 70℃ for more than 30 minutes.
- Can infect healthy chicken flocks after being stored at –20℃ for three years.
- Virulence remains unaffected after being stored at –58℃ for three years.

Acidity and Alkalinity

- IBDV has strong resistance to strong acidic and alkaline conditions.
- It can survive for 1 hour in an environment with pH 2.
- It can only be inactivated after more than 30 minutes at 70℃ in an environment with pH 12.

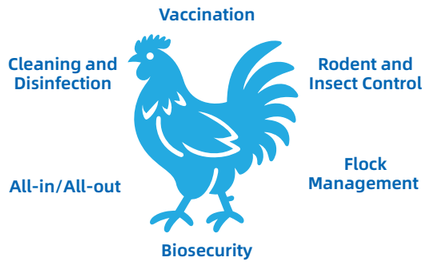
Disinfectants

- Low sensitivity to chloroform, ether, trypsin, and quaternary ammonium disinfectants.
- 0.5% formalin, 0.5% ammonium chloride for 10 minutes, 0.05% sodium hydroxide, and compound iodine disinfectants have good disinfection effects.
- Glutaraldehyde and benzalkonium bromide have good killing effects.

The strong resistance to external environmental conditions is an important reason for the long-term existence of IBDV in poultry breeding environments.

PREVENTION OF INFECTIOUS BURSAL DISEASE

- Strict disinfection, biosecurity management measures, and appropriate vaccination strategies are effective in preventing Infectious Bursal Disease (IBD).
- It is very difficult to completely eliminate IBDV from farms. Studies indicate that the virus can survive in poultry houses for 122 days and in feed and drinking water for 52 days, and remain infectious.
- Therefore, Strictly implement disinfection measures are essential for IBDV control. These measures directly reduce the viral load in the environment, thereby lowering the risk of transmission.



- Some vectors that can carry the virus—such as mosquitoes, beetles, rodents, and wild birds—must be systematically controlled and eliminated.
- Since early infection with IBDV can cause severe and long-lasting immunosuppression, vaccination is an effective measure for the prevention and control of IBD.

KEYS TO SUCCESSFUL IMMUNIZATION

- High and uniform maternal antibody levels
- Vaccine selection tailored to field conditions
- Precise calculation of the optimal vaccination window
- A well-designed vaccination program
- Correct administration techniques
- Reinforced biosecurity measures

IMMUNIZATION FOR BREEDERS

By implementing a proper immunization program for breeders, a higher antibody level can be achieved during egg production, thereby providing offspring with high maternal antibodies, which ensures that the offspring are not infected by IBD wild-type virus in the early stages.

DECAY OF MATERNAL ANTIBODIES

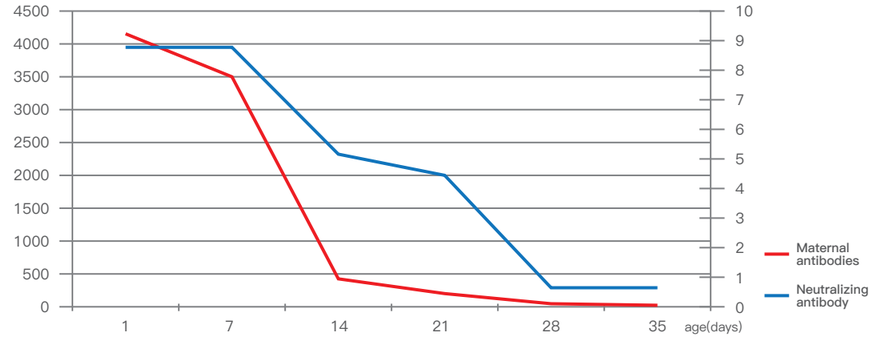
Geometric mean titers (GMT)[1] for maternal antibodies against different pathogens at dfferent ages

Pathogen[2]	Parent-flock[3]	Days of age						
		0	5	10	15	20	25	30
AEV	3,839	405	29	2	0	0	0	0
AIV	1,910	668	37	2	1	0	0	0
CAV	9,283	1,985	108	18	1	1	0	0
IBDV	35,012	21,104	16,295	10,643	3,983	546	84	2
IBV	19,472	6,706	860	15	0	0	0	0
ILTV	3,146	209	10	2	2	1	0	0
MG	3,165	1,134	365	5	1	0	0	0
MS	4,881	828	21	3	1	0	0	0
NDV	8.5	5.9	4.9	3.5	3.5	3.1	2.4	1.1
Reo	2,761	790	41	4	0	0	0	0

GUMBORO DISEASE

Decline of matemal IBD antibodies

Maternal IBD antibodies in broiler Chicken

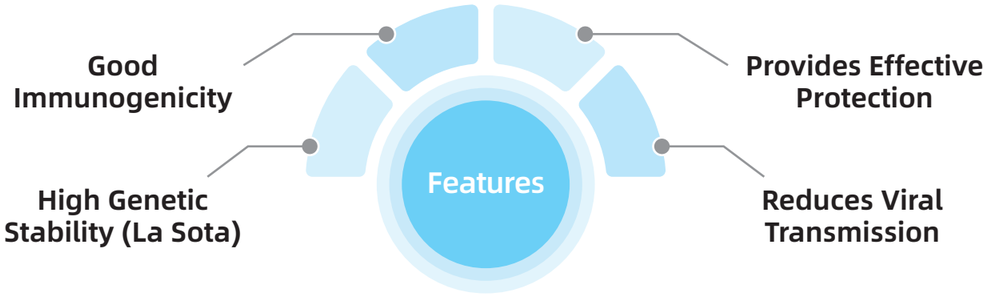


ABILITY OF LIVE VACCINE TO OVERCOME MATERNAL ANTIBODY INTERFERENCE

IN FIELD CONDITIONS

- Virulent strains can overcome virus-neutralizing antibody titers of up to VN 1:500.
- Intermediate strains can overcome virus-neutralizing antibody titers of up to VN 1:250.
- Attenuated strains can overcome virus-neutralizing antibody titers of up to VN 1:100.

TECHNOLOGY FEATURES



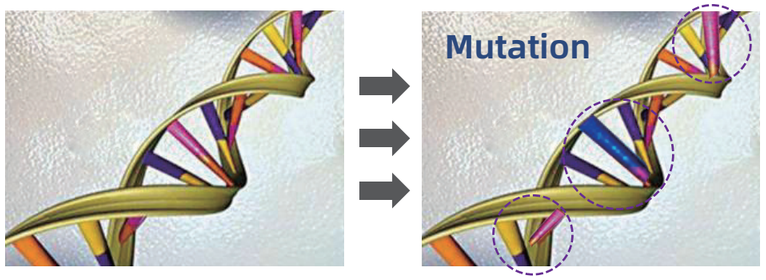
ADAPTATION OF THE STRAIN HQ

- Using a prevalent highly virulent strain, which is highly targeted.
- Developed through over 20 passages of cultivation and adaptation, resulting in an attenuated, cell-adapted virus designated as the HQ strain.

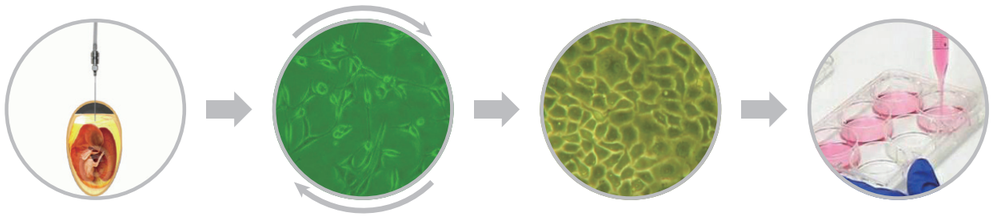
IBDV Wild-type Virus → Chicken Embryonic bursa-derived cells → Chicken Embryonic kidney cells → Chicken Embryonic fibroblast cellsv

- Primary cell culture → Passage cell culture: Cultivation time is reduced by half, and the virus titer is increased by 10 times.

- **CHICKEN EMBRYO CULTURE**
- **EMBRYO-DERIVED CELL CULTURE**
- **VIRUS CLONING AND PURIFICATION**



HQ Epidemic Strain — HQ Cell-adapted Strain

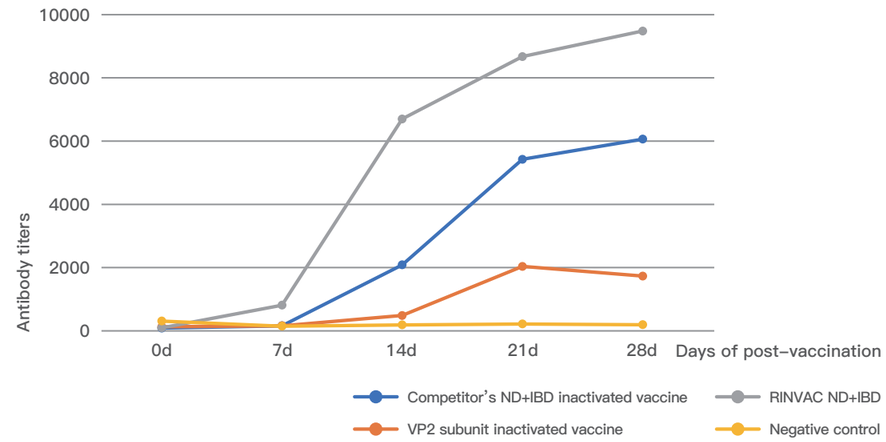


Chicken embryo — Primary cell — Passage cell — Clone purification

PRODUCT FEATURES OF
RINVAC ND+IBD

Vaccine	Days of post-vaccination					Challenge Protection
	0d	7d	14d	21d	28d	
Competitor's ND+IBD inactivated vaccine	90	160	2089	5426	6062	8/10
VP2 subunit inactivated vaccine	130	160	487	2039	1733	6/10
RINVAC ND+IBD	96	813	6699	8673	9480	10/10
Negative control	311	150	190	217	194	1/10

Antibody responses and challenge protection results in SPF chickens vaccinated with different types of inactivated IBD vaccines



Trend chart of IBD ELISA antibody in SPF chickens vaccinated with different types of inactivated IBD vaccines

TERMINATOR OF IBD

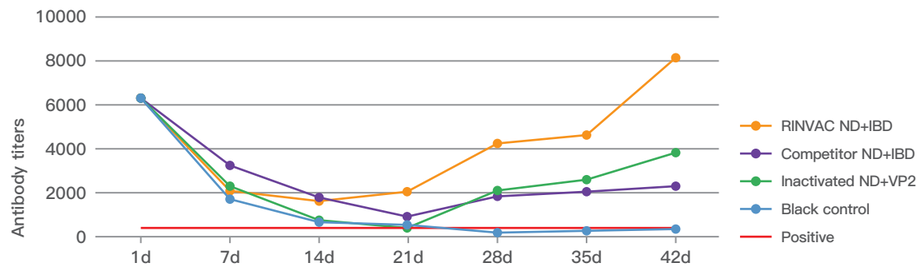
- Cultivation using passage cell line DF1 and microcarrier suspension culture technology. Virus titer is increased by 100 times.
- Antigen purification process, with two-stage filtration columns to remove impurities, enhance antigen purity, and reduce immune side effects.
- One immunization for broilers can provide protection until they are ready for market; vaccination of breeders can offer protection to their offspring for up to 21 days; no virus shedding, no immunosuppression.

Photo of Bioreactor

RAPIDLY BREAKS THROUGH MATERNAL ANTIBODIES, SHORTEN THE IMMUNE WINDOW PERIOD, A SINGLE VACCINATION IN BROILERS PROVIDES PROTECTION UNTIL MARKET AGE.

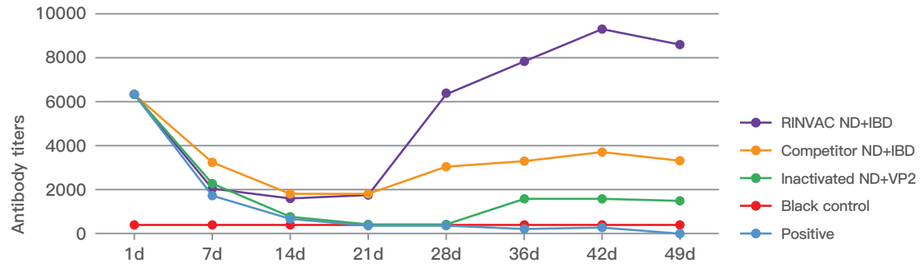
- After vaccinating 1-day-old white-feather broilers carrying maternal antibodies with RINVAC ND+IBD, antibody levels rise sharply by 15 days post-vaccination, effectively overcoming maternal-antibody interference and markedly shortening the immunity gap period.
- 100% protection against IBDV virulent challenge at 30 and 42 days of age.
- Ensuring birds remain protected until market age.

Figure-1. ELISA antibody titers in 1-day-old Ross 308 broilers vaccinated with different types of IBD vaccines



Note: For 1-day-old chickens, administer one dose via subcutaneous injection in the back of the neck, 0.2 mL/bird for oil-adjuvanted vaccines, and 1 dose/bird for other vaccines.

Figure-2. ELISA antibody titers in 7-day-old Ross 308 broilers vaccinated with different types of IBD vaccines



NO IMPAIRMENT TO BURSAL DEVELOPMENT, NO IMMUNOSUPPRESSIVE EFFECTS.

- 30 white-feathered broilers of 1 day-old age were vaccinated with different types of IBD vaccines, and 10 unvaccinated sentinel chickens were as one group. Bursal antibodies were tested on days 30 and 42 after immunization.
- The results showed that the cohabitation group with the antigen-antibody complex vaccine had an abnormal increase in antibodies at 42 days of age, indicating that the chickens were infected with IBDV, and this vaccine exhibited virus shedding.
- However, no increase in antibodies was observed in the other groups, indicating no virus shedding with those vaccines; the cohabitation group with "RINVAC ND+IBD" showed no abnormal antibody levels, and compared to the other groups, the bursa-derived antibody values in the "RINVAC ND+IBD " group were significantly higher, as shown in the table below.

Sample	Immune group	30 days of age					42 days of age				
		Antibody	Spleen-to-body ratio	Bursa-to-body ratio	SSIX	BBIX	Antibody	Spleen-to-body ratio	Bursa-to-body ratio	SSIX	BBIX
RINVAC ND+IBD	Co-habitation	120	0.70	1.85	1.00	0.89	132	0.59	1.93	1.02	1.24
	Immune	3515	0.87	2.41	1.24	1.16	4780	0.67	1.63	1.16	1.04
Competitor 1	Co-habitation	165	0.68	1.95	0.97	0.94	93	0.71	1.85	1.22	1.19
	Immune	875	0.75	2.18	1.07	1.05	2092	0.68	1.53	1.17	0.98
Competitor 2	Co-habitation	178	0.72	1.88	1.03	0.90	176	0.82	1.39	1.41	0.89
	Immune	334	0.68	2.24	0.97	1.08	1060	0.77	1.25	1.33	0.80
Competitor 3	Co-habitation	186	0.93	1.83	1.33	0.88	3717	1.01	0.67	1.74	0.43
	Immune	336	0.65	1.76	0.93	0.85	3332	0.97	0.70	1.67	0.45
Control group		95	0.70	2.08	1.00	1.00	72	0.58	1.56	1.00	1.00

Immune Organ Index = (Immune organ weight / Body weight) × 1000
BBIX = Bursa-to-Body ratio of test birds ÷ Bursa-to-body ratio of blank-control birds
SSIX = Spleen-to-body ratio of test birds ÷ Spleen-to-body ratio of blank-control birds

- When BBIX < 0.7, bursal atrophy is judged to have occurred; the lower the BBIX value, the greater the virulence of the IBDV strain.
- When SSIX > 1.3, an inflammatory reaction is considered present; the higher the SSIX value, the more severe the reaction.

A SINGLE VACCINATION OF BREEDERS CONFERS MATERNAL ANTIBODIES TO PROTECT CHICKS HATCHED WITHIN 4 MONTHS AGAINST IBDV FOR 3 WEEKS.

- Four months after vaccination with RINVAC ND+IBD, breeders still maintain a high IBD antibody level (2^{15}).
- The maternal antibody level of offspring chicks remains around 2^{10} before 21 days of age, ensuring 100% protection against challenge.
- High maternal antibodies can effectively protect chicks from IBD.

Provide 100% protection for offspring chicks up to 21 days of age.

CHALLENGE PROTECTION TEST AGAINST IBDV IN 1-4 WEEK-OLD OFFSPRING FROM SPF BREEDER CHICKENS IMMUNIZED WITHIN 1-4 MONTHS

Group of batch No.	Time after breeder immunization	Antibodies of breeder (log2)	7 days chicks		14 days chicks		21 days chicks		28 days chicks	
			Neutralizing antibody	Challenge–protection	Neutralizing antibody	Challenge–protection	Neutralizing antibody	Challenge–protection	Neutralizing antibody	Challenge–protection
11001	1.5 Months	15.6	14.3	8/8	12.3	8/8	11.4	9/9	9.1	7/9
	2.5 Months	15.4	14.1	9/9	9.1	7/7	8.9	9/9	7.9	3/9
	3 Months	15.5	13.2	10/10	12.0	10/10	10.8	10/10	9.4	7/10
	4 Months	15.1	13.1	9/9	12.2	7/7	10.9	8/8	9.3	7/9
Control	1.5 Months	1.75	1.3	0/8	1.3	0/8	1.3	0/8	1.4	0/8
	2.5 Months	1.5	2.0	0/8	1.0	0/8	1.6	0/8	1.5	0/8
	3 Months	1.5	1.3	0/8	1.0	0/9	1.4	0/10	0.4	0/10
	4 Months	2.0	1.0	0/10	0	0/3	1.0	0/3	1.0	0/4

CENTRIFUGATION AND PURIFICATION, PURE VACCINE

- The use of low–temperature continuous flow centrifugation and purification technology can effectively remove impurities such as impurity proteins, greatly reducing the side effects of vaccination. in addition high–speed centrifugation in a low–temperature environment maintains the good antigenicity of the vaccine and ensures its good immunogenicity.
- The first enterprise to propose control standards for endotoxin and impurity proteins in inactivated vaccines.

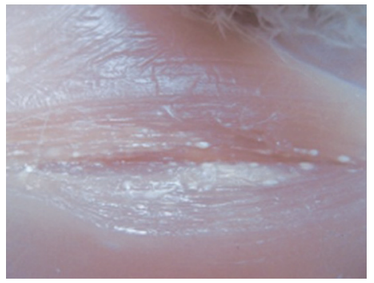
Test items	Ringpu specification for inactivate vaccines	China Standard
Endotoxin (Finished product)	< 50 EU/mL	None
Impurity protein (Finished product)	< 2.5 mg/mL	None
Residual formaldehyde	< 0.6%	< 2%

NEW AND PREMIUM ADJUVANT, EASY TO ABSORB

- A new type of premium adjuvant with low viscosity makes the vaccine easy to withdraw, injectand absorb, and to induce the body to produce good and non–specific immune responses.

Comparison of absorption of vaccines with different oil–based adjuvants

Vaccines made with the premium adju–vantsare well absorbed after injection, causingittle tissue.



Vaccines made with some general adju–vantsare poorly absorbed after injection and causesevere tissue damage.

Note: Inject intramuscular 0.3 mL into chest and observe the absorption of the vaccine after 20 days of age.

DOSAGE AND ADMINISTRATION OF RINVAC ND+IBD

Indication

It is used to prevent New–castle disease and infectious bursal disease in chickens.

Duration of immunity

- 1.5 months for chicks under 2 weeks of age
- 2 months for chickens within 2~4 weeks of age
- 4 months for adult breeders

Administration

Subcutaneous injection in the neck region or intramuscular injection.

Dosage

- For chicks under 2 weeks of age, 0.2 mL/bird
- Between 2 and 4 weeks of age, 0.3 mL/bird
- For breeders before laying and during laying, 0.5 mL/bird