

# Review of: "A Harmless Avian Vaccine Virus Could Be Developed into an Off-the-Shelf “Antibiotic” for Viruses"

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The Infectious Bursal Disease Virus (IBDV) is a non-pathogenic, double-stranded RNA virus commonly used in poultry to enhance immune responses, which has sparked interest in its potential antiviral effects. Recently, efforts to modify IBDV as a new treatment alternative to existing vaccines have gained attention, and Bakacs and colleagues briefly summarized the clinical utility of IBDV. However, they did not point out several potential issues regarding IBDV. This commentary describes the primary challenges associated with the clinical application of IBDV and underscores the need for further research.

## 1. Potential for Viral Mutation

Viruses have the potential to mutate during replication within hosts. If IBDV mutates to become pathogenic in humans, it could introduce unexpected health risks, making it crucial to closely monitor this potential.

## 2. Lack of Dosage Determination and Indicators

The absence of established indicators for determining appropriate IBDV dosages poses a significant issue. While IBDV can activate the immune system, excessive doses might lead to adverse effects or excessive inflammatory reactions (e.g., cytokine storms). Therefore, establishing dosage indicators and guidelines is urgent, requiring further clinical trials and data accumulation.

## 3. Risk of Cytokine Storm

While IBDV exerts antiviral effects by activating the interferon pathway, the risk of triggering a cytokine storm cannot be dismissed. Patients with high viral loads or heightened immune responses could experience excessive inflammatory reactions, and a detailed investigation into this risk is warranted.

## 4. Variability in Immune Response

IBDV elicits immune responses, but reactions may vary among patients. This is especially concerning for immunocompromised patients and the elderly, for whom effects are uncertain and unpredictable side effects could arise. Research considering individual immune response differences is necessary.

## 5. Uncertainty Regarding Long-Term Safety

IBDV's safety profile is based on limited data, with insufficient information on the safety and potential side effects of long-term use. This is especially relevant in chronic viral infections, where repeated IBDV administration may be required. Research to understand its long-term impact is essential.

## **6. Interaction with Other Vaccines and Infections**

IBDV promotes the expression of interferon- $\beta$  and interferon- $\lambda$ , raising concerns about interactions with other viral infections or vaccines. For instance, using IBDV following influenza or COVID-19 vaccination may trigger unexpected immune responses, necessitating further investigation.

## **7. Regulatory Approval and Ethical Challenges**

IBDV is primarily used as a poultry vaccine and would require regulatory approval for use in humans. Its application as a treatment would also necessitate thorough safety trials and ethical approval, adding challenges to the approval process.

In conclusion, while the clinical application of IBDV as an antiviral drug is promising, it presents numerous challenges. Particularly concerning are issues of safety, long-term use, and interactions with other vaccines and infections, which all require careful scrutiny. Moving forward, large-scale clinical trials will be necessary to address these challenges and fully assess IBDV's potential as an antiviral drug.