Performance concerns?

There is hardly anything in the world that some man can't make a little worse and sell a little cheaper, and the people who consider price only are this man's lawful prey.

John Ruskin 1819-1900

ENRADIN® is a step above common enramycins.

ENRADIN® is a proven way to increase feed efficiency. At recommended levels in poultry feed, ENRADIN provides excellent control of bacteria that cause necrotic enteritis and growth depression.

Our advanced manufacturing process delivers a product that is safe, stable, homogenous and highly efficacious for your flock.

Strictly regulated production.

ENRADIN is manufactured by a highly skilled workforce under the Good Manufacturing Practice (GMP), including strict regulatory and MSD Animal Health oversights. Our manufacturing facility is inspected and approved by regulatory authorities from the following countries and regions:

US (FDA)	Australia (TGA)
EU (EDQM)	Japan (PMDA)
Germany (BfArM)	South Korea (KFDA)
UK (MRHA)	China (SFDA, MOA)

Common questions and answers.

The story behind ENRADIN: What makes it so different from generic enramycin?

With generic enramycins entering the market, we'd like to take this opportunity to answer some common questions about the superior value of ENRADIN.

Q. Where does ENRADIN come from?

A. ENRADIN is produced from fermentation products of *Streptomyces fungidicus*, isolate B5477 developed in 1966 by Japan Takeda and registered in Japan in 1974.

The specific master seed stock and the accompanying manufacturing technology were transferred to production facilities at Zhejiang Hisun Pharmaceutical Co., Ltd. (Zhejiang Hisun Pharmaceutical) in China.

Japan Takeda Animal Health (now a part of MSD Animal Health) and Zhejiang Hisun Pharmaceutical Company are the only authorized manufacturers of enramycin from the original Takeda B5477 master seed stock.

Rigorous control and monitoring of ENRADIN production ensures the product's potency and consistency.

Q. Why is it important to use this MSD specific seed stock?

A. Japan Takeda spent more than 10 years developing the *S. fungidicus* B5477 seed culture breeding, separation, purification and storage technology. The seed culture was developed to maintain a stable hereditary character. Carefully developed storage technology maintains the original seed culture, ensuring a prolonged life span and no degradation.

This unique seed culture is essential to the production of enramycin of high potency and consistent molecular quality.

Q. How is the production technique of ENRADIN unique?

A. Fermentation is a dynamic, changing process of microorganism metabolism. During fermentation, three aspects – mycelia growth, fermentation control parameters and formulation speed of the target product – have been dynamically changed and correlated.

These processes are automated in the production of ENRADIN, with online sensors to monitor the fermentation growth curve and to optimize key fermentation parameters in three categories:

Physical: temperature, pressure, agitation speed, airflow, turbidity, viscosity
Chemical: pH and dissolved oxygen
Biological: mycelia concentration

MSD Animal Health

Q. Once enramycin is produced, isn't it just enramycin? What makes ENRADIN unique?

A. All enramycin is not produced equally. Unlike a chemically synthesized product, a fermentation product like ENRADIN contains mycelia cells, culture broth, metabolism by-products and impurities, potentially including heavy metals.

The final product is a large, polypeptide macromolecule with two distinct active components, A and B. The A and B molecules differ in molecular weight due to the number of carbon and hydrogen molecules present in their structure.

An advanced extraction process is required to ensure the end product is safe, stable, homogenous and highly efficacious. The processes for ENRADIN have been carefully developed and are tested at each step.

Spray-drying of the final product ensures that ENRADIN does not remain in contact with heat for a prolonged period, as may occur with fluid bed ("roller") drying methods.

Figure 1: Color and consistency of ENRADIN vs. two generic enramycin products

ENRADIN is a state-of-the-art form of enramycin.

Longer contact with heat results in a darker color and potentially lower potency. **See Figure 1 above.**

The premix is tested to ensure homogeneity and good consistency for mixing in feeds.

Q. In the photograph, Figure 1, ENRADIN from MSD appears to have a finer, more powder consistency than the other products. Is this important?

A. Yes. Mash feed formulations must undergo a lot of vibration during transportation. A coarse, heavy product can easily settle out of the mash, resulting in poor uniformity of distribution in the finished feed.

A product made of fine particles ensures a homogenous mix in the final stages before pelleting in crumble or pellet-feed forms.

Q. How is the potency and biological activity of ENRADIN certified?

A. The potency and biological activity of ENRADIN is monitored and certified using a culture method based on the only enramycin reference standard in the world: the original Japan Takeda reference standard. The reference standard used by Zhejiang Hisun Pharmaceutical has been certified using the Japan Takeda reference standard. When you buy ENRADIN, you get enramycin at the right potency, plus full MSD Animal Health support and warranty from a solid partner that has been in the molecule development and enhancement business for more than 40 years.

Q. When samples of generic products are tested against the recognized reference standard, how do they compare?

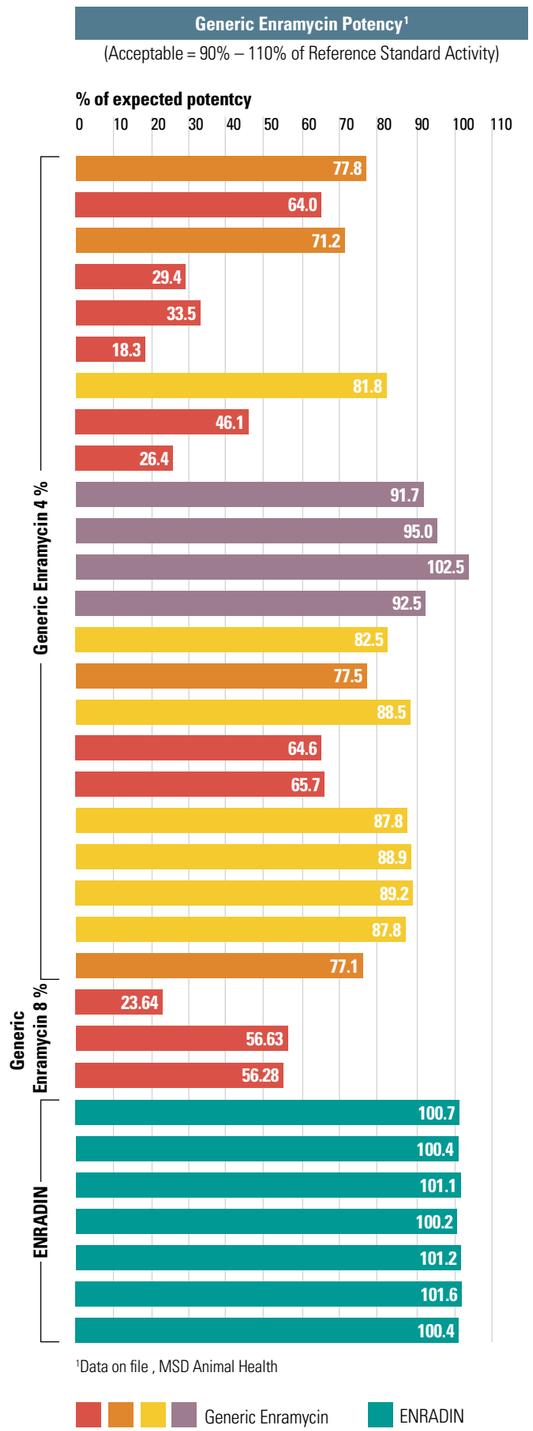
A. The samples demonstrate highly variable activity.[1]

This is why GMP manufacturing processes and automation with monitoring of intermediate steps are so important. ENRADIN is always tested against the reference standard. As a result, every batch demonstrates high potency. **See Figure 2.**

Take advantage of more than 40 years of expertise. Bring the value of our state-of-the-art production knowledge to your end products.

A feed conversion increase of just 0.01 kg in a 1.6 kg broiler is worth $1.94/1,000 kg of feed at U.S. $300/1,000 kg. Any measurable loss in performance, even 10 grams, is worth more than the difference in drug cost.

Figure 2



Q. Only some of the generic samples are close to the 90% standard, and many others are far below. Is that good enough?

A. Not really. Consider the risks of using products below acceptable standard activity levels.

The samples themselves show wide variability.[1] How do you know which batch you will receive? Without a reference standard for testing, automated production and careful monitoring of intermediate steps, variability can be expected from generic products.

The stability of a generic product is unknown. ENRADIN's stability has been confirmed as per VICH* guideline.

Long-term stability study:

36 months, 25 ± 2C, 60% ± 5%
Accelerated: 6 months, 40 ± 2C, 75% ± 5%

A generic enramycin might also create increased variability for a final product made with coarse particles that may not mix uniformly in the feed, or that do not remain uniformly mixed during transportation.

No other enramycin manufacturer possesses the recognized reference standard of ENRADIN. The potency and biological activity of *generic* enramycins cannot be reliably measured.

The efficacy and long-term stability of ENRADIN have been tested by decades of successful use. ENRADIN is well recognized by producers and nutritionists around the world. It is a brand built on and supported by more than 40 years of experience.

Use this advantage to enhance your profitability. ENRADIN is the brand you can trust.

*Veterinary International Conference on Harmonization

We control process and quality in every way.

So you benefit from reliability in every feed mix.

ENRADIN Quality and Process Control	
Quality Procedures	Check
GMP training	Yes
Testing of raw materials • 28 raw materials each undergo specific test regimen to ensure safety and quality	Yes
Testing of finished product • Particle size, appearance, identity, potency, contaminants	Yes
Stability monitoring	Yes
EM water system monitoring	Yes
Compressed air system monitoring	Yes
Lab equipment qualification	Yes
Validation management	Yes
Sample/retained sample management	Yes
Pharmacopeia compliance	Yes
Reference Standard management	Yes
Test skill training	Yes
Deviation and complaint procedures	Yes
Risk identification and control measures	Yes
Critical Control Point monitoring schedule	Yes
Procedure and documentation of cleaning • Facilities • Equipment • Transport vehicles	Yes
Traceability of raw materials and ingredients	Yes
Batch number and documentation	Yes

ENRADIN Quality and Process Control		
GMP Systems		Check
Quality System	Annual product review	Yes
	Auditing program • Regulatory inspection • Internal GMP audits • Audits of suppliers	Yes
	Change control	Yes
	Complaints • Product quality complaints	Yes
	GMP verification	Yes
	Deviation management	Yes
	Product release	Yes
	Quality management	Yes
	Reprocess/Rework	Yes
	SOP management	Yes
	GMP training & personnel	Yes
Facility & Equipment System	Cleaning/Housekeeping/ Maintenance	Yes
	Cleaning validation	Yes
	Environment control	Yes
	Facilities & equipment qualification	Yes
	Maintenance/Calibration utilities	Yes
Production System	Documentation	Yes
	Process controls	Yes
	Manufacturing practices	Yes
	Process validation	Yes
Packaging & Labeling System	Labeling & packaging component control	Yes
	Packaging control	Yes
Laboratory Control System	Laboratory instrumentation	Yes
	Sampling and testing	Yes
	Stability	Yes
Material Control System	Material handling	Yes
	Supplier management	Yes

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RELAX

Enjoy superior results that last

Enradin's **superior activity** for ***Clostridium perfringens*** and its **consistent efficacy** make it the **leading brand and most effective** feed medication for **Clostridial Enteritis**

ENRADIN®

SUPERIOR ACTIVITY, SUPERIOR RESULTS

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