

**THE USE OF HUMAN INTERFERON ALPHA FROM TWO DIFFERENT SOURCES AT TWO DIFFERENT DOSAGES FOR THE TREATMENT OF BOVINE RESPIRATORY TRACT DISEASE**

**ACC STUDY NO.:** 93AUBO08 AND 93AUBO09

**LOCATION:** Texas A&M Agricultural Research Center  
Bushland, Texas

**SUMMARY:** Two hundred (200) mixed breed calves were purchased for the study. Through a normal marketing system using an order buyer. At arrival in Bushland, Texas, calves were weighed and placed in pens with feed and water. On the next day, calves were weighed, rectal temperatures were recorded and calves were administered their respective oral treatments which consisted of placebo or natural human interferon alpha (nHuIFN $\alpha$ ) from Hayashibara Biochemical Laboratories (HBL) or Interferon Sciences Inc. (ISI). The five treatments were randomly allotted so there were 40 calves in each treatment group. The assigned treatments were given as shown: placebo, 200 IU or 400 IU of either HBL IFN $\alpha$  or ISI HuIFN $\alpha$ .

The study demonstrated that one dose of 200 IU nHuIFN $\alpha$  per calf resulted in a significant decrease ( $P > 0.05$ ) in morbid calves.

**INTRODUCTION:** Infectious bovine rhinotracheitis (IBR) is an acute respiratory disease in cattle that is highly contagious and produces high fever. The IBR virus has worldwide distribution and is one of the principal etiologic agents in the Bovine Respiratory Disease Complex (BRDC). Clinical signs usually appear in the first 14 days after cattle enter the feedlot. Virus excreted from nasal and ocular secretions is transmitted to susceptible cattle by direct contact. Infectious bovine rhinotracheitis is characterized by high fever (104-107°F), salivation, loss of appetite, rapid and shallow respiration and dyspnea. The usually low mortality rate is higher in stressed cattle; however, death is usually a result of a bacterial complication after the virus infection. The IBR virus is responsible for severe economic loss to the cattle industry. There is a need for improved methods of producing immunopotentiality in calves at arrival at feedlots. Oral interferon may offer immunopotentiality or supportive therapy during BRDC and could reduce the cost of disease.

**OBJECTIVES:** To compare 2 different interferons at 2 different concentrations administered to newly arrived feeder calves orally in a single dose for the reduction of morbidity and mortality.

#### **MATERIAL AND METHODS:**

Animals - Two hundred (200) mixed breed calves were purchased for the study through a normal marketing system using an order buyer.

Interferon - The stabilized active ingredient, (nHuIFN $\alpha$ ) natural human interferon alpha at 200 IU or 400 IU dosages was used in this study. One nHuIFN $\alpha$  was supplied by Hayashibara Biochemical laboratories, Inc. of Okayama, Japan and the other nHuIFN $\alpha$  was supplied by Interferon Sciences, Inc. of New Brunswick, New Jersey.

**EXPERIMENTAL DESIGN:** The experiment was a randomized block design with factorial arrangement of 4 treatments and a placebo with 40 head in each treatment. The cattle were blocked by weight with the heaviest to the lightest animal forming the blocks. Each 5 animals was a block. The treatments were blinded by the study representative and drug delivered to the investigators labeled number 1 through 200 in individual syringes. The blinding occurred by randomly assigning the placebo and drug levels. All treatments were administered in a 4ml oral dose. The cattle were weighed and ear tagged upon arrival and assigned to pens (20 calves/pen); their weights and ear tag numbers were recorded. The 5 treatments were randomly allotted within the blocks using a random number table. The 5 treatments of human interferon alpha from Hayashibara Biochemical laboratories, Inc. (HBL) or Interferon Sciences, Inc. (ISI) were as follows:

<u>Treatments of HuIFN<math>\alpha</math></u>	<u>Total IFN<math>\alpha</math> (IU)/Calf</u>	<u>No. of Calves</u>
Placebo (the diluent without HuIFN $\alpha$ )	0	40
50 IU/ml @ 4ml (HBL)	200	40
100 IU/ml @ 4ml (HBL)	400	40
50 IU/ml @ 4ml (ISI)	200	40
100 IU/ml @ 4ml (ISI)	400	40

The 40 placebo treated calves were randomly allotted in blocks of 2 between the HBL and ISI diluent without IFN $\alpha$ .

On Day 1, cattle were weighed, rectal temperatures were recorded and cattle were administered their respective treatments.

The cattle were checked in the morning before 9 am for nasal discharge and diarrhea on each day of the study. The daily observations were recorded. All cattle with a mucopurulent nasal discharge and rectal temperature of 104°F or greater were treated with an antibiotic (Micotil®) at the recommended dosage. Calves with watery diarrhea that did not require antibiotic for respiratory tract treatment were treated orally with neomycin sulfate at the recommended dosage. Clinical observation and treatment record were completed daily. After Micotil® administration, the cattle were maintained in a hospital pen for two days and then returned to their original pen.

Both calves that died during the study were transported to the Texas Veterinary Diagnostic Laboratory, Amarillo, Texas for a complete necropsy.

#### Experimental Plan -

<u>DAY</u>	<u>EVENT</u>
0	Calves arrived, were processed, ear tagged and individually weighed.
1	Weights and rectal temperatures were recorded and HuIFN $\alpha$ treatments were administered.
2-13	Clinical observations were made daily.
14	Clinical observations were made, weights and rectal temperatures were recorded. Study was terminated.

**STATISTICS:** Any animal that was treated with Micotil® was considered morbid and constituted a HuIFN $\alpha$  treatment failure. The number of morbid cattle within treatments were subjected to Chi square analysis. Calves which were diagnosed as morbid at the time of nHuIFN $\alpha$  treatment were judged to have illness prior to the study and were deleted from the analysis.

The rectal temperatures, weights, average daily gains, feed intake and feed to gain ratios were collected and analyzed by the following model:

$$Y_{ijkl} = \mu_i + T_j + D_k(T_j) + e_{ijkl}$$

$Y_{ijkl}$  is rectal temperature,

$\mu_i$  is the grand mean,

$T_j$  is the treatment effect,

$D_k$  is the days of trial,

$D_k(T_j)$  is treatment within day of trial, and

$e_{ijkl}$  is the experimental error.

Means were separated by Duncan's Multiple Range Test (PC SAS 6.03).

**RESULTS:** Calves with fever ( $\geq 104.0^\circ\text{F}$ ) on arrival were deleted from the study because they had illness before nHuIFN $\alpha$  treatments were given.

Compared to controls, calves treated with 200 IU ISI nHuIFN $\alpha$ /calf had significantly fewer morbid calves ( $P > 0.05$ ). Calves given 200 IU ISI nHuIFN $\alpha$  had better weight gains at 10 days (9%) and at day 13 (10%), compared to placebo treated control calves (graph 1).

More than 50% of the calves given placebo or 400 IU of either nHuIFN $\alpha$  were treated with antibiotics within 3 days of treatment. However, it took 5 days for 1/2 of the 200 IU (HBL) groups to require antibiotics. The calves given 200 IU (ISI) only had a total of 15 (45%) treated for illness.

Overall, 23 of 31 control calves (74%) were treated for BRDC, whereas only 45% of ISI - 200 IU, 53% of HBL required treatment (Table 1).

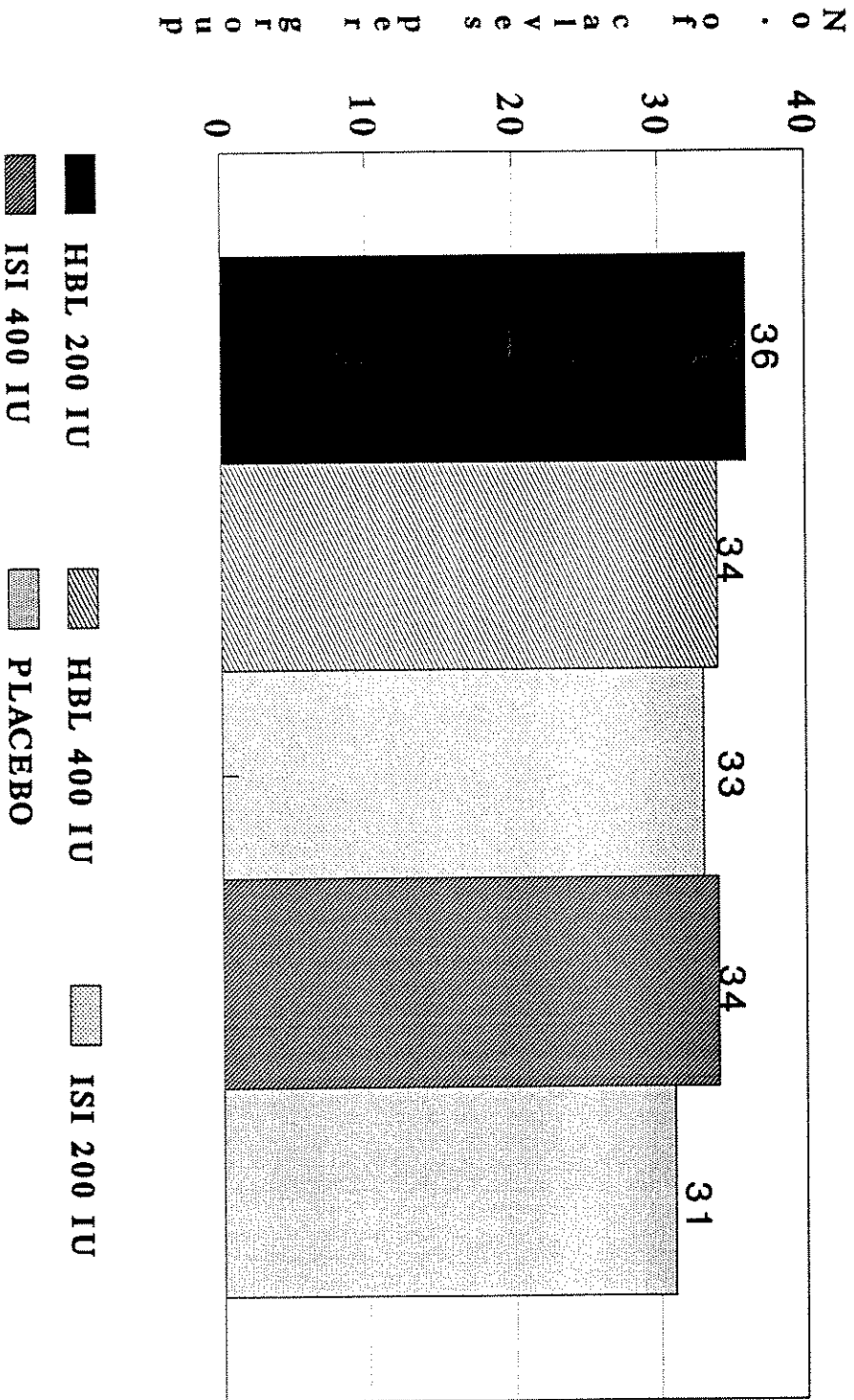
**DISCUSSION:** This study indicated that a single low dose of nHuIFN $\alpha$  reduced morbidity of calves with Bovine Respiratory Diseases Complex. Calves treated with 400 IU nHuIFN $\alpha$  once on day 1 of the study required significantly more treatments for morbid calves in the first 3 days after treatment. As the study progressed, more illness occurred in calves given 200 IU, but the number of calves requiring antibiotics for BRDC was only 34 out of 69, compared to 43 out of 68 calves given 400 IU nHuIFN $\alpha$ .

Table 1. Number of Calves Treated Each Day, by Treatment Each Group

nHuIFN $\alpha$ Group	Total No.	Days After nHuIFN $\alpha$ Treatments								Treated	
		1	2	3	4	5	6	7	8	Total	%
HBL200	36	7	1	2	5	3	1	0	0	19	53
HBL400	34	10	4	4	0	0	0	1	1	20	59
ISI200	33	5	2	4	3	0	1	0	0	15	45
ISI400	34	10	7	1	5	0	0	0	0	23	68
Placebo	31	7	7	6	1	0	1	1	0	23	74
Total	168	39	21	17	14	3	3	2	1	100	60

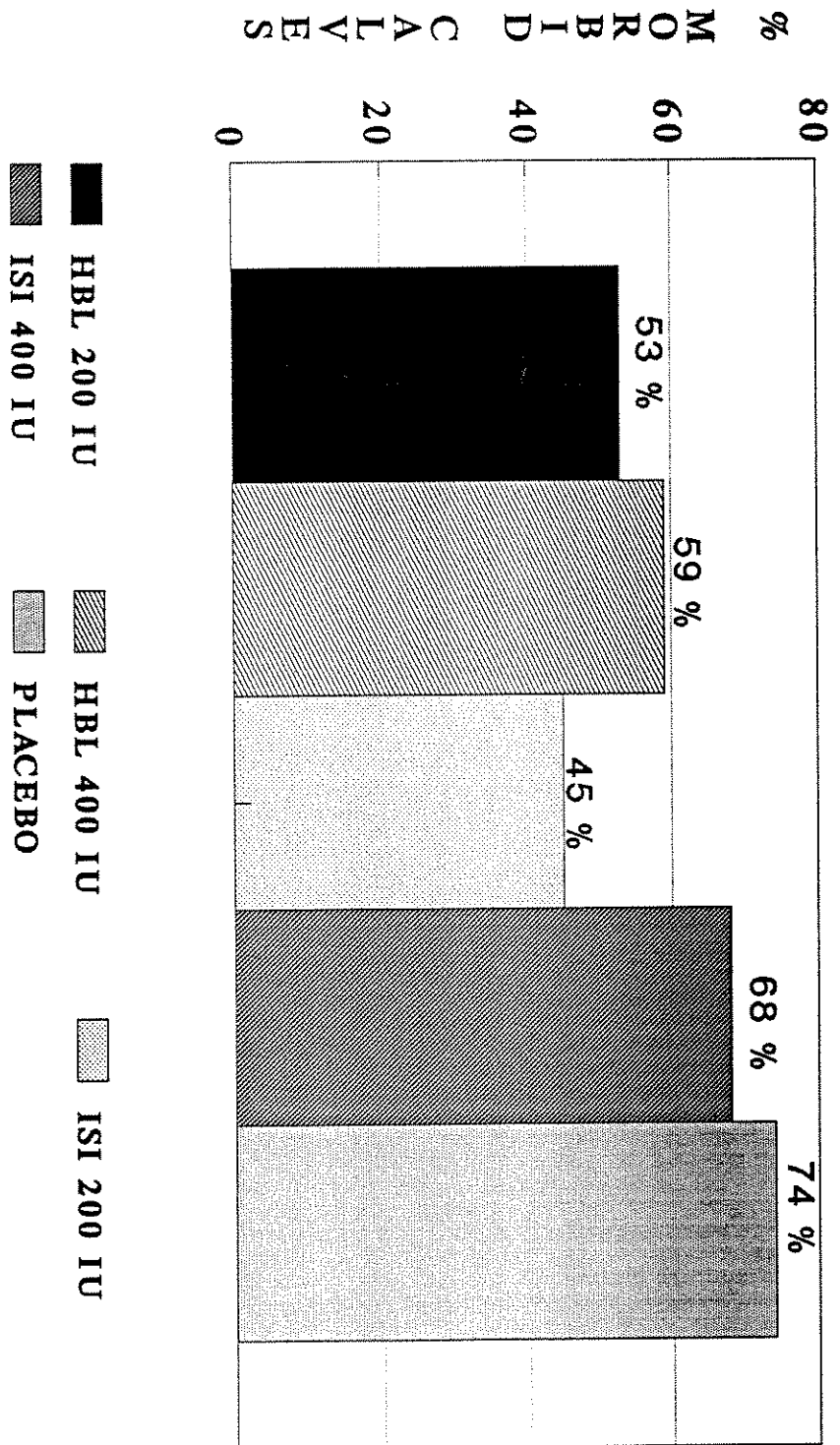
# TOTAL NUMBER OF CALVES IN EACH GROUP

CALVES WITH OUT FEVER ON DAY 1



# TOTAL % OF MORBID CALVES FROM EACH GROUP

CALVES WITH OUT FEVER ON DAY 1



# AVG. DAILY GAIN 13 DAYS

