# THE SUSCEPTIBILITY PATTERNS OF EIGHT ANTIMICROBIAL AGENTS FOR POTENTIAL TREATMENT OF *RHODOCOCCUS EQUI* PNEUMONIA IN FOALS

A Thesis

by

STEVEN ANTONN DANIELS

Submitted to the Office of Graduate Studies of
Texas A&M University
in partial fulfillment of the requirements for the degree of

MASTER OF SCIENCE

December 2003

Major Subject: Veterinary Microbiology

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Approved as to style and content by:

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## ABSTRACT


The Susceptibility Patterns of Eight Antimicrobial Agents for Potential Treatment of *Rhodococcus equi* Pneumonia in Foals. (December 2003)

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Chair of Advisory Committee: Dr. Russell B. Simpson

*Rhodococcus equi* is a common cause of severe pneumonia in foals, and is an opportunistic pathogen in immunocompromised humans. In combination, erythromycin and rifampin are the most commonly used antimicrobials in treating *R. equi* in foals. To provide reliable treatment, it is imperative to determine the mean inhibitory concentrations (MICs) of other antimicrobial agents in the event that certain strains of *R. equi* develop resistance to the current treatment. Several strains of *R. equi* have developed resistance to various antibiotics. In this study, *R. equi* strain 288 was completely resistant to rifampin with a MIC > 256ug/ml. The MICs of ethambutol, clarithromycin, azithromycin, isoniazide, ethionamide, rifampin, erythromycin, and linezolid of ninety-five *R. equi* isolates were also determined in this study. These isolates were obtained from the lungs and transtracheal washes of foals. In addition to these strains, three National Committee for Laboratory Clinical Standards (NCCLS) quality control strains were also tested: *R. equi* ATCC 6939, *R. equi* ATCC 33701, and *S. pneumoniae* 49619. Each drug was tested in triplicate and the MIC 50's and MIC 90's were determined for each drug. Ethambutol, isoniazide, and ethionamide were completely ineffective against *R. equi.* with MICs > 250ug/ml. *Rhodococcus equi* strains

were more susceptible to clarithromycin (MIC 90 = 0.23 ug/ml) than to azithromycin (MIC 90 = 2.33 ug/ml), rifampicin (MIC 90 = 0.67ug/ml), erythromycin (MIC 90 = 1.2ug/ml), and linezolid (MIC 90 = 4ug/ml).

# DEDICATION

This thesis is dedicated to my nephews and niece demonstrating the importance of a higher education and achieving projected goals.

# ACKNOWLEDGMENTS

I would like to take this opportunity to thank my saviour, Jesus, who provided me with the strength, courage, and patience to overcome all obstacles in the path of completing this degree. I would like to thank my family for supporting my decisions and lending me their shoulders in time of desperation. I would like to give my appreciation to the committee members, and the staff of the veterinary microbiology lab for their time and the knowledge they have instilled in me. And last but certainly not least, I would like to thank Kim DuBose for her help and time initiating and preparing this research project.

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# CHAPTER I

# INTRODUCTION

*Rhodococcus equi (formerly Corynebacterium equi)* is a common cause of severe bacterial pneumonia in foals (Barton and Hughes, 1980), and is of emerging importance in humans. Controlling *R. equi* pneumonia of foals can be demoralizing, difficult, expensive, and frustrating (Hooper-McGrevy and Prescott, 2001b). The organism was first reported to cause disease in horses in the 1920s and humans in the 1960s (Beaman et al., 1995). Since then, researchers have identified *R. equi* in a variety of animals, including cattle, goats, swine, buffalo, sheep, (Weinstock and Brown, 2002) and a host of other mammals. *R. equi* is a facultative intracellular (Nordmann and Ronco, 1992) soil-borne organism with the ability to survive in lung macrophages and other tissues in the presence or absence of oxygen (Carter et al.,1995). Although the lung is the primary organ affected by *R. equi,* this pathogen has been cultured from other tissues such as the prostate, spleen, and kidney (Weinstock and Brown, 2002). In addition, intestinal manifestations, non-septic polysynovitis, septic arthritis and osteomyelitis may occur in infected foals (Giguere and Prescott, 1997). In humans, this disease is commonly seen in immunocompromised individuals that are infected with the human immunodeficiency virus, HIV (Bowersock et al., 2000).

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This thesis follows the style and format of Veterinary Microbiology.

Young foals, during the first few weeks of life, are particularly vulnerable to *R. equi* most likely because of ineffective or inefficient immune systems. The disease in foals is most commonly diagnosed when signs are manifested between the ages of 4 and 12 weeks (Sweeney et al., 1987), but infections are thought to occur much earlier. Following infection, lesions usually develop insidiously for several weeks or months, at which time foals exhibit clinical signs of disease. Foals are refractory to infection by 3 months of age, and adult horses are rarely infected. *Rhodococcus equi* is a soil saprophyte that can propagate and survive long periods in the manure of horses (Carter et al., 1995) and other herbivores during the warm months. The fact that the organism is shed in the feces of dams and the dry environment on the farms is thought to play a very important role in the initial colonization of *R. equi* in foals (Takai et al., 1987).

Virulence of *R. equi* in foals is strongly associated with the presence of an 85-to 90-kilobase (kb) plasmid and expression of a 15- to 17-kilodalton (kd) virulence associated protein antigen (VapA) encoded by that plasmid (Takai et al., 1991a; Takai et al., 1991b). Infection in foals causes high mortality rates because the disease is difficult to recognize during its early stages, when therapy is most effective, and the organism is resistant to many antimicrobial drugs. In the United States, it has been estimated that approximately 3% of foal deaths are caused by *R. equi* (Madigan et al., 1991).

Treating infected foals with inappropriate antimicrobial drugs may also contribute to high mortality rates. Designing antimicrobial therapeutic schemes for use in infected foals requires information on the susceptibility of the organism to antimicrobial agents (Prescott, 1981). Minimum Inhibitory Concentrations (MIC) of several antimicrobial agents have been determined in an effort to develop aggressive antimicrobial drug therapy combinations (Prescott and Sweeney, 1985). The MIC values are divided into fifty and ninety percentiles. An MIC 50 indicates that 50% of the isolates tested are inhibited at a given value and an MIC 90 indicates that 90% of the isolates tested are inhibited at a given value. These values indicate the drug concentrations required to kill or inhibit the growth of an organism and are used to monitor the levels of resistance in a population tested. Antimicrobial MIC data, in conjunction with pharmacokinetic data for the target species, are crucial for the development of therapeutic regimens. Successful treatment of *R. equi* infections requires antibiotics that penetrate and concentrate in infected cells. Two such antibiotics, erythromycin and rifampin are commonly used to treat *R. equi* infections in the United States (Hillidge, 1987). Resistant isolates of *R. equi* to erythromycin and rifampin have been identified (Takai et al., 1997). Several, orally active, synthetic antimicrobial agents (Bowersock et al., 2000), which are similar in activity to erythromycin and rifampin, have been developed. The properties of azithromycin and clarithromycin suggest that they may be an alternative to erythromycin for the therapy of *R. equi* pneumonia in foals (Davis et al., 2002). There are currently no effective vaccines available for the prevention of *R. equi* infections. Studies have shown that the administration of *R. equi* hyperimmune plasma has a protective effect if given before infection (Martens et al., 1989; Madigan et al., 1991; Higuchi et al., 1999). However, this strategy is expensive, labor intensive, and not universally effective.

# CHAPTER II

# BACKGROUND AND SIGNIFICANCE

## 2.1 *Pathogenesis of Rhodococcus equi*

*Rhodoccocus equi* is a facultative intracellular (Nordmann and Ronco, 1992) soil-borne bacterium that can live and proliferate in foal macrophages. This organism causes pyogranulomatous lung lesions and death if not detected and treated early in the course of disease. The pathogenesis of *R. equi* pneumonia is not fully understood, but disease appears to develop after inhalation of an adequate number of virulent *R. equi* that, although effectively phagocytized by alveolar macrophages, are not killed. Failure of foal macrophages to kill *R. equi* is thought to be caused by some undefined immaturity of the immune system (Prescott and Sweeney, 1985). Therefore, *R. equi* targets alveolar macrophages, which provide a stable environment wherein the organism can survive and proliferate. In nearly all infected foals, the virulence of *R. equi* is strongly associated with a surface antigen, VapA, that is encoded by a gene on an 85-90kbp plasmid (Takai et al., 1991a; Takai et al., 1991b). Foals infected with VapA-positive isolates develop severe bronchopneumonia, whereas plasmid-cured derivatives are innocuous (Weinstock and Brown, 2002). Notable advancements in the understanding of *R. equi* pneumonia in foals have been made during the years, but satisfactory control and prevention of this disease has still not been achieved (Chaffin et al., 2003).

### 2.2 *Previous Studies on Rhodoccocus equi*

*Rhodoccocus equi* has been recognized since the early 1900s. Due to high mortality rates of foals on ranches and farms, the importance of aggressive drug therapy and preventive methods has increased. Although an effective vaccine is not yet available, passive immunization of foals with hyperimmune plasma (HIP) has become a standard and beneficial practice on many farms with endemic *R. equi* problems (Hooper-McGrevy et al., 2001a). This method has been thought to reduce the number of foals becoming infected with *R. equi* at an early age.

The combined therapy with erythromycin and rifampin has dramatically improved the survival rate of foals infected with *R. equi* (Jacks et al., 2003). Antimicrobial susceptibility patterns are an important component of the decision-making process when determining appropriate therapeutic regimens. Prescott conducted a study on the susceptibility of isolates of *R. equi* to antimicrobial drugs (Prescott, 1981). He demonstrated the MIC of both equine and porcine origin strains belonging to two different capsular serotypes, and concluded that there were no significant differences in antibiotic susceptibility patterns between source or serotype of the *R. equi* isolates tested. His study showed that *R. equi* was susceptible to erythromycin and gentamicin based upon the MIC values.

Prescott and colleagues continued their study on susceptibility of different isolates of *R. equi* (Prescott and Sweeney, 1985). The objective was to develop a therapeutic regimen that would target the site of infection and continue to penetrate infected cells for an extended period of time. Foals treated early in the course of disease respond better than do those with chronic infections (Prescott and Sweeney, 1985). Treatment, however, must be aggressive and prolonged because of the extensive lung damage, presence of large abscesses, intracellular location of the organism, and the slow response to treatment (Prescott and Sweeney, 1985). Prescott and Sweeney hypothesized that despite predictability of antibiotic susceptibility, mutants resistant to antimicrobial agents may emerge if drugs are used alone rather than in combination.

Sweeney et al (1987) reported on the response of forty-eight pneumonic foals to antimicrobial therapy. They concluded that erythromycin and rifampin constituted the most successful antimicrobial drug combination. Eighty-eight percent of the infected foals in Sweeney's study recovered with this treatment (Sweeney et al., 1987). In Japan, gentamicin and other compounds such as imipenem are used more generally, as the side effects of erythromycin can be problematic (Takai et al., 1995). Erythromycin is tolerated by most foals, but severe diarrhea, hyperthermia and depression may develop leading to dehydration and electrolyte loss that necessitate intensive fluid therapy and cessation of oral erythromycin (Giguere and Prescott, 1997). Sweeney et al (1987) also hypothesized that antimicrobial drugs should probably be directed not only against *R. equi*, but also against other organisms such as *Streptococcus zooepidemicus* that might be present.

Hillidge expanded the work of Sweeney by utilizing an erythromycin-rifampin drug combination in the treatment of foals with *R. equi* pneumonia (Hillidge, 1987). They realized that the selection of lipid-soluble antibiotics was important to successful treatment of this disease. Rifampin and to a lesser extent erythromycin, being lipid soluble, are able to penetrate caseous material (Grosset, 1980). Hillidge administered erythromycin and rifampin in combination to 89 foals from one to four months of age. All had exhibited radiographic evidence of pulmonary abscessation suggestive of *R. equi* infection, and in 57 animals this was confirmed by culture of *R. equi* from tracheal aspirates (Hillidge, 1987). The foals were observed daily for any adverse effects of the drug combination. Thoracic radiographs were examined periodically throughout the course of therapy to monitor progression or resolution of disease. When the radiographic appearance of the lungs returned to normal, drug therapy was discontinued. If the radiographs remained normal for two months, recovery from *R. equi* infection was considered complete. Of the 89 and 57 infected foals treated, 85% and 88% recovered, respectively, following therapy with erythromycin and rifampin. The duration of therapy in the survivors ranged from 28 to 63 days, with a mean of 44 days (Hillidge, 1987). This study concluded that the combination of erythromycin and rifampin was highly effective for treating *R. equi* pneumonia in foals.

As noted in the Hillidge study, it is very important to use rifampin in combination with erythromycin to reduce the chance of bacteria developing resistance to rifampin. Although rifampin is very potent against *R. equi* both in vitro and in vivo, bacterial resistance may develop if it is used alone to treat infections. During that study, *R. equi* resistance to rifampin or erythromycin was not detected (Hillidge, 1987). However, acquired resistance among *R. equi* isolates has been reported after treatment with multiple antibiotics, including doxycycline, penicillin, erythromycin, vancomycin, cotrimoxazole, and rifampin (Fierer et al., 1987; Verville et al., 1994; Ferruzzi et al., 1997). Considering the limited number of reported cases, varying degrees of host immune competence, vast geographic distribution of disease, and diverse clinical manifestations, it comes as no surprise that standard treatments for *R. equi* infection have not been established (Weinstock and Brown, 2002).

Clarithromycin is considered to be a potential alternative to erythromycin for the treatment of *R. equi*. In a study by Jacks et al. (2002), six healthy foals were treated and observed after an intragastric administration of clarithromycin at a dose of 10 mg/kg body weight (Jacks et al., 2002). The foals selected for this study were of different breeds and sex ranging from 10 to 13 weeks of age. They were kept with their dams in individual stalls throughout the study. Tablets of clarithromycin (250mg) were dissolved in 100ml of water and administered by nasogastric tube (Jacks et al., 2002). Blood samples were taken at different intervals prior to and after administration of clarithromycin. Jacks et al. (2002) concluded from this study that there were no adverse reactions after the administration of clarithromycin. They also stated that the half-life of clarithromycin was longer than reported for erythromycin, and an oral dose of 7.5 mg/kg given every 12 h based on MIC 90 and other properties, would appear appropriate for the treatment of *R. equi* infections in foals (Jacks et al., 2002).

In addition, Jacks et al. (2003) conducted a study to determine in vitro susceptibilities of *R. equi* and other common equine pathogens to azithromycin, clarithromycin, and twenty other antimicrobials. Jacks examined a total of 201 bacterial isolates from various equine sources. All bacterial isolates were cultured from tracheobronchial aspirates or postmortem specimens from pneumonic foals. The gram-positive isolates studied included *R. equi* (n=64), beta-hemolytic streptococci (*Streptococcus equi* subspecies *zooepidemicus* [n=35], *Streptococcus equi* subspecies *equi* [n=6], *Streptococcus dysgalactiae* subspecies *equisimilis* [n=6]), *Enterococcus* spp. (n=4), and coagulase-positive *Staphylococcus* spp. (n=18) (Jacks et al., 2003). Gram-negative isolates included *Salmonella enterica* (n=23), *Escherichia coli* (n=16), *Pasteurella* spp. (n=11), *Klebsiella* spp. (n=10), *Pseudomonas* spp. (n=4), *Enterobacter* spp. (n=2), and *Bordetella bronchiseptica* (n=2) (Jacks et al., 2003).

Jacks et al. (2003) demonstrated the importance of developing an alternative therapy in treating *R. equi* by comparing the MICs of the antimicrobials for the various bacterial isolates. The rational use of azithromycin and clarithromycin for the treatment of bacterial bronchopneumonia in foals has been precluded in part by the lack of in vitro susceptibility studies for equine bacterial pathogens (Jacks et al., 2003). It was shown in that study that clarithromycin was at least as active as erythromycin against *R. equi* in vitro, whereas azithromycin was eightfold less active (Jacks et al., 2003).

Although many antimicrobials are active against *R. equi* in vitro, they do not provide the same response systemically or intracellularly. In one study, all 17 foals with *R. equi* pneumonia treated with a combination of penicillin and gentamicin died despite all isolates being susceptible to gentamicin and 83% being susceptible to penicillin (Sweeney, et al., 1987).

The oxazolidinones, eperezolid and linezolid, are representatives of a new class of orally active, synthetic antimicrobial agents that were determined to be effective in vitro against *R. equi* (Bowersock et al., 2000). Bowersock et al. conducted a study to determine the MICs of linezolid, eperezolid, premafloxacin, and several other antimicrobial agents against strains of *R. equi* isolated from humans and animals. He concluded that linezolid was more active against *R. equi* strains than was eperezolid with MIC 90 of 2.0 ug/ml and 16.0 ug/ml respectively. The study also stated that there were no differences in antimicrobial activity, of the agents tested, against *R. equi* strains from human and equine sources (Bowersock et al., 2000).

The purpose of this study was to determine the susceptibility patterns of eight antimicrobial agents against various strains of *R. equi. Rhodococcus equi* pneumonia in foals, and miliary tuberculosis in children caused by *Mycobacterium tuberculosis,* exhibit similar lung lesions. Thus, the choice of these drugs is based upon their lipid solubility and their ability to penetrate macrophages in caseous abscess cavities of the lung. The MIC values were analyzed to determine if *R. equi* is susceptible or resistant to the antimicrobial agents. Ninety-five *R. equi* strains were analyzed. MIC 50's and 90's were determined for each drug tested. VapA-positive and VapA-negative *R. equi* isolates were compared to determine if significant differences between the two existed.

# CHAPTER III

## RESEARCH DESIGN AND MATERIALS

The focus of this study was to determine and evaluate the MIC values of selected antimicrobials.

### 3.1 *Sources of Isolates*

The 95 *R. equi* isolates were collected from the lungs and transtracheal washes of foals in different areas of the United States. These isolates were maintained at the Equine Infectious Disease Laboratory, College of Veterinary Medicine, Texas A&M University.

### 3.2 *Quality Control Strains*

*R. equi* ATCC 6939, *R. equi* ATCC 33701, and *S. pneumoniae* ATCC 49619 are the NCCLS (National Committee for Clinical Laboratory Standards) quality control strains that were used to validate susceptibility media batch to batch, to ensure proper handling, storage and use of strips and the correct selection of MIC end points.

### 3.3 *Eight Antimicrobial Agents*

The eight antimicrobials used in this study were erythromycin, azithromycin, clarithromycin, rifampin, isoniazide, linezolid, ethambutol, and ethionamide. Erythromycin, azithromycin, and clarithromycin are classified as macrolides. The macrolides inhibit protein synthesis by binding to subunits of the 50S ribosome which inhibits the translocation step (Prescott et al., 2000). Rifampin is a synthetically modified member of the family rifamycins, isoniazide is the hydrazide of isonicotinic acid, ethambutol is the derivative of ethylenediamine, and ethionamide is a member of the thioamides. These four drugs are used to treat tuberculosis in humans. Isoniazide is considered to be more potent than rifampin (Prescott et al., 2000). Linezolid, a member of the oxazolidinones, is most active against gram-positive organisms including methicillin-resistant *Staphylococcus aureus,* vancomycin-resistant *Enterococcus* spp., and *Streptococcus* spp. (Bowersock et al., 2000).

3.4 *Antimicrobial MIC Determination*

A procedure known as an Epsilometer test (E-test)[1] was performed on each isolate in triplicate to determine its MIC value. The E-test provides values that represent the minimum concentration (ug/ml) of a given antibiotic that inhibits the growth of a particular bacterium. The E-test strips[1] contain the antibiotic of choice and an MIC calibrated scale. The E-test strips are 5mm wide and 60mm long, and provide data points that represent a continuous antimicrobial gradient with 15 concentrations. These values are more precise in comparison to conventional MICs which provide discontinuous twofold serial dilutions (AB Biodisk, 1997).

Baker et al. (1991) conducted a study to show the reliability of the E-test by predicting the MICs and interpretative categories of susceptibility as compared with three conventional methods, disk diffusion, broth microdilution, and agar dilution. On the basis of that study, it was concluded that comparison of the E-test to other conventional methods produced very good agreement of the MIC values obtained when testing the susceptibility of a particular bacterium.

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[1] AB Biodisk

The E-test was used because its stable antibiotic gradient provided more precise MIC values. Also, the E-test is superior in determining MIC values for fastidious and slow growing bacteria such as *R. equi* because of its continuous gradient. Conventional methods, such as broth or agar dilution procedures are technically more difficult to perform, especially when testing fastidious organisms with long generation times (Brown and Brown, 1991). The versatility and ease of use of the E-test make the method an attractive alternative to conventional dilution tests (Brown and Brown, 1991).

The procedure used in determining the values for each *R. equi* strain is as follows: First, a Mueller-Hinton agar[2] plate supplemented with 5% sheep blood, two sterile swabs, inoculum suspension medium (0.85% NaCl), forceps, and colorimeter were obtained. Using a sterile swab, an appropriate amount of isolate was removed from a blood agar plate that had been incubated overnight. The swab was placed into the inoculum suspension dispersing isolate with gentle agitation. The swab was pulled from the suspension and pressed against the inner wall of the test tube to remove excess fluid.

The suspension was visually calibrated with a 1.0 McFarland equivalence turbidity standard[3], confirmed and verified in a colorimeter. After calibrating the suspension, the second sterile, non-toxic cotton swab was dipped into the inoculum and pressed against the glass to remove excess fluid. A Mueller-Hinton blood agar plate was streaked in a manner that allowed even distribution of inoculum. The plate was set aside

[2] Remel, Inc.
[3] BBL Becton Dickinson

for 15 to 20 minutes to allow the excess inoculum to dry before placing the E-test strips. The strips were allowed to adjust at room temperature to reduce moisture.

Using forceps, four different E-test strips containing the antimicrobial drug of choice were placed onto the inoculated plate symmetrically with the MIC scale facing upward. Each strip was gently pressed starting at the bottom moving upward to remove air bubbles to allow even distribution of the antimicrobial and ensuring stability of the strip. The plate was covered and incubated at 37 C for 16 to 20 hours. After incubation, the MIC values where the inhibition ellipse intersects the scale at the edge of the strip were read and recorded.

# CHAPTER IV

## RESULTS

The MIC values of the 95 *R. equi* strains were determined after 16 to 20 hours of incubation to acquire visible growth. Each antimicrobial MIC value was analyzed and recorded. The MIC values of the 3 quality control strains selected for this study were in the expected range.

The MIC values of the selected antimicrobials for *R. equi* are presented in the Appendix. All *R. equi* strains in this study showed resistance to ethambutol (EB), ethionamide (ET) and isoniazide (IZ). Of the 95 isolates presented in this study, only 7 were VapA-negative (non-virulent). There was no significant difference between the antimicrobial susceptibility patterns of the virulent and avirulent strains of *R. equi* in this study. The MIC 50 and MIC 90 were determined by microsoft excel spreadsheet for each antimicrobial tested. The MIC 50 is the concentration to which 50% of the organisms tested are susceptible and the MIC 90 is the concentration at which 90% of the organisms tested are susceptible. Detailed data on these MICs are presented in Table 1 for all antimicrobials in this study.

TABLE 1. MICs of eight antimicrobial agents against 95 *R. equi* isolates.

| | MIC (ug/ml) | | |
|---|---|---|---|
| Antimicrobial | 90% | 50% | Range (All strains) |
| Erythromycin | ≤1 | ≤1 | ≤0.17-1.5 |
| Clarithromycin | ≤0.23 | ≤0.19 | ≤0.06-0.32 |
| Azithromycin | ≤2.3 | ≤2 | ≤0.67-2.7 |
| Rifampin | ≤0.67 | ≤0.42 | ≤0.02-0.92 |
| Linezolid | ≤4 | ≤3.3 | ≤2-4.7 |
| Isoniazide | >256 | >256 | >256 |
| Ethambutol | >256 | >256 | >256 |
| Ethionamide | >256 | >256 | >256 |

# CHAPTER V

# DISCUSSION

Many studies have determined in vitro susceptibilities of equine pathogens using disk diffusion methods, but few studies have reported MICs (Adamson et al., 1985). In this study, the MICs of rifampin (RI), clarithromycin (CH), erythromycin (EM), linezolid (LZ), azithromycin (AZ), isoniazide (IZ), ethambutol (EB), and ethionamide (ET) to *R. equi* were determined utilizing the E-test method. Isoniazide, ethambutol, ethionamide and one rifampin-resistant strain, 288, did not inhibit the growth of *R. equi* isolates with MICs > 256ug/ml. MIC 90s for erythromycin, clarithromycin, and azithromycin, which are members of the macrolide group, against 95 *R. equi* isolates were 1.2 ug/ml, 0.23 ug/ml, and 2.3 ug/ml respectively. All three were highly effective against *R. equi*, but clarithromycin demonstrated the lowest minimum inhibitory concentration in vitro.

Clarithromycin is a semi-synthetic derivative of erythromycin, consisting of a 14-membered lactone ring with substitution of a methoxy group from the C-6 hydrozyl group of erythromycin (Alvarez-Elcoro and Enzler, 1999). This structural difference gives clarithromycin several advantages over erythromycin (Jacks et al., 2002). Azithromycin and clarithromycin have been proposed as alternatives to erythromycin for the treatment of *R. equi* (Jacks et al., 2003), because they are more chemically stable, have a greater bioavailability, and achieve higher concentrations in phagocytic cells and tissues than erythromycin (Whitman and Tunkel, 1992).

Rifampin and linezolid are both in a different class of antimicrobials. Rifampin is the most important synthetically modified member of the family rifamycins (Prescott et al., 2000) and is combined with erythromycin in treating *R. equi*. Rifampin should never be used alone due to the high bacterial mutation rate (Prescott et al., 2000). Resistance to rifampin results from the substitution of a limited number of highly conserved amino acids of the RNA polymerase beta subunit encoded by the *rpoB* gene (Fines et al., 2001). Linezolid is a representative of a new class of orally active, synthetic antimicrobial agents, the oxazolidinones (Bowersock et al., 2000) for potential use in *R. equi* therapy. In this study, the MIC 90s for rifampin and linezolid were 0.67 ug/ml and 4 ug/ml, respectively, against the 95 *R. equi* isolates tested. Overall, of the five active drugs, linezolid was least active and clarithromycin (MIC 90 = 0.23 ug/ml) was most active against all *R. equi* strains tested.

# CHAPTER VI

# CONCLUSION

This study revealed that although clarithromycin was shown to be the most active against *R. equi* in vitro, more research is needed in vivo before initiating treatment with clarithromycin in infected foals. This study also indicated that rifampin (MIC 90 = 0.67ug/ml) was more active than erythromycin (MIC 90 = 1.2 ug/ml) against at least 90% of the *R. equi* isolates in vitro. Both are still highly active against *R. equi* and should continue to be the primary drug therapy for treating this infection until further studies have been performed on the MICs and oral disposition of clarithromycin, azithromycin, linezolid and other antimicrobials. The rifampin-resistant strain shown in this study, validates the reasoning for investigating new antimicrobial agents for potential treatment of *R. equi*.

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# APPENDIX

Data for the eight antimicrobial agents against 95 *R. equi* isolates.

| Antibiotics | RI | EB | CH | EM | IZ | ET | LZ | AZ |
|---|---|---|---|---|---|---|---|---|
| **Controls** | | | | | | | | |
| 6939 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 33701 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 49619 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

| Antibiotics | RI | EB | CH | EM | IZ | ET | LZ | AZ |
|---|---|---|---|---|---|---|---|---|
| **R. Equi. Strains** | | | | | | | | |
| 99-244 | 0.500 | >256 | 0.125 | 0.750 | >256 | >256 | 4.000 | 2.000 |
| | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| | 1.000 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| **Average MIC** | 0.667 | >256 | 0.168 | 0.917 | >256 | >256 | 4.000 | 2.000 |
| 99-243 | 0.190 | >256 | 0.094 | 0.500 | >256 | >256 | 4.000 | 2.000 |
| | 0.380 | >256 | 0.125 | 0.750 | >256 | >256 | 3.000 | 2.000 |
| | 0.500 | >256 | 0.094 | 0.750 | >256 | >256 | 3.000 | 1.500 |
| **Average MIC** | 0.357 | >256 | 0.104 | 0.667 | >256 | >256 | 3.333 | 1.833 |
| 99-240 | 0.047 | >256 | 0.125 | 0.750 | >256 | >256 | 3.000 | 2.000 |
| | 0.047 | >256 | 0.190 | 0.750 | >256 | >256 | 4.000 | 2.000 |
| | 0.047 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| **Average MIC** | 0.047 | >256 | 0.168 | 0.833 | >256 | >256 | 3.333 | 2.000 |
| 99-239 | 0.750 | >256 | 0.190 | 0.750 | >256 | >256 | 4.000 | 2.000 |
| | 0.500 | >256 | 0.125 | 0.750 | >256 | >256 | 3.000 | 2.000 |
| | 0.500 | >256 | 0.190 | 0.750 | >256 | >256 | 3.000 | 1.500 |
| **Average MIC** | 0.583 | >256 | 0.168 | 0.168 | >256 | >256 | 3.333 | 1.833 |
| 99-237 | 0.500 | >256 | 0.125 | 0.750 | >256 | >256 | 4.000 | 1.500 |
| | 0.750 | >256 | 0.125 | 0.750 | >256 | >256 | 3.000 | 1.500 |
| | 0.380 | >256 | 0.125 | 1.000 | >256 | >256 | 4.000 | 1.500 |
| **Average MIC** | 0.543 | >256 | 0.125 | 0.833 | >256 | >256 | 3.667 | 1.500 |
| 99-236 | 0.500 | >256 | 0.190 | 0.750 | >256 | >256 | 4.000 | 1.500 |
| | 0.750 | >256 | 0.125 | 0.750 | >256 | >256 | 4.000 | 2.000 |
| | 0.500 | >256 | 0.125 | 0.750 | >256 | >256 | 4.000 | 2.000 |
| **Average MIC** | 0.583 | >256 | 0.147 | 0.750 | >256 | >256 | 4.000 | 1.833 |

| Antibiotics | RI | EB | CH | EM | IZ | ET | LZ | AZ |
|---|---|---|---|---|---|---|---|---|
| **Controls** | | | | | | | | |
| 6939 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 33701 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 49619 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

| Antibiotics | RI | EB | CH | EM | IZ | ET | LZ | AZ |
|---|---|---|---|---|---|---|---|---|
| **R. Equi. Strains** | | | | | | | | |
| 98-89 | 0.380 | >256 | 0.250 | 0.750 | >256 | >256 | 4.000 | 2.000 |
| | 0.500 | >256 | 0.250 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| **Average MIC** | 0.420 | >256 | 0.230 | 0.917 | >256 | >256 | 3.667 | 2.000 |
| 98-90 | 0.750 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| | 1.000 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| | 1.000 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| **Average MIC** | 0.917 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| 98-92 | 0.500 | >256 | 0.250 | 1.500 | >256 | >256 | 6.000 | 2.000 |
| | 0.500 | >256 | 0.250 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| | 0.500 | >256 | 0.250 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| **Average MIC** | 0.500 | >256 | 0.250 | 1.167 | >256 | >256 | 4.667 | 2.000 |
| 98-93 | 0.500 | >256 | 0.250 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| | 1.000 | >256 | 0.250 | 1.000 | >256 | >256 | 6.000 | 2.000 |
| | 0.500 | >256 | 0.250 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| **Average MIC** | 0.667 | >256 | 0.250 | 1.000 | >256 | >256 | 4.667 | 2.000 |
| 98-94 | 0.500 | >256 | 0.190 | 0.750 | >256 | >256 | 4.000 | 2.000 |
| | 0.750 | >256 | 0.250 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| | 0.500 | >256 | 0.250 | 1.000 | >256 | >256 | 4.000 | 1.500 |
| **Average MIC** | 0.583 | >256 | 0.230 | 0.917 | >256 | >256 | 4.000 | 1.833 |
| 98-95 | 0.380 | >256 | 0.125 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| | 0.500 | >256 | 0.125 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| **Average MIC** | 0.460 | >256 | 0.147 | 1.000 | >256 | >256 | 4.000 | 2.000 |

| Antibiotics | RI | EB | CH | EM | IZ | ET | LZ | AZ |
|---|---|---|---|---|---|---|---|---|
| **Controls** | | | | | | | | |
| 6939 | 0.380 | >256 | 0.125 | 0.750 | >256 | >256 | 3.000 | 1.500 |
| | 0.250 | >256 | 0.125 | 0.750 | >256 | >256 | 3.000 | 1.500 |
| | 0.380 | >256 | 0.125 | 0.750 | >256 | >256 | 3.000 | 1.500 |
| **Average MIC** | 0.337 | >256 | 0.125 | 0.750 | >256 | >256 | 3.000 | 1.500 |
| 33701 | 0.380 | >256 | 0.125 | 0.500 | >256 | >256 | 4.000 | 2.000 |
| | 0.380 | >256 | 0.125 | 0.500 | >256 | >256 | 4.000 | 1.500 |
| | 0.380 | >256 | 0.125 | 0.750 | >256 | >256 | 4.000 | 2.000 |
| **Average MIC** | 0.380 | >256 | 0.125 | 0.583 | >256 | >256 | 4.000 | 1.833 |
| 49619 | 0.125 | >256 | 0.047 | 0.094 | >256 | >256 | 2.000 | 0.190 |
| | 0.125 | >256 | 0.047 | 0.125 | >256 | >256 | 2.000 | 0.125 |
| | 0.125 | >256 | 0.032 | 0.094 | >256 | >256 | 1.500 | 0.190 |
| **Average MIC** | 0.125 | >256 | 0.042 | 0.104 | >256 | >256 | 1.833 | 0.168 |

| Antibiotics | RI | EB | CH | EM | IZ | ET | LZ | AZ |
|---|---|---|---|---|---|---|---|---|
| **R. Equi. Strains** | | | | | | | | |
| 98-87 | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| **Average MIC** | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.667 | 2.000 |
| 98-88 | 1.000 | >256 | 0.190 | 1.500 | >256 | >256 | 3.000 | 2.000 |
| | 1.000 | >256 | 0.380 | 1.500 | >256 | >256 | 3.000 | 3.000 |
| | 0.380 | >256 | 0.380 | 1.000 | >256 | >256 | 4.000 | 3.000 |
| **Average MIC** | 0.793 | >256 | 0.317 | 1.333 | >256 | >256 | 3.333 | 2.667 |
| 98-96 | 0.380 | >256 | 0.190 | 1.500 | >256 | >256 | 4.000 | 2.000 |
| | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| **Average MIC** | 0.380 | >256 | 0.190 | 1.167 | >256 | >256 | 4.000 | 2.000 |
| 98-97 | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 1.500 |
| | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 1.500 |
| | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| **Average MIC** | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.667 | 1.667 |
| 98-99 | 0.380 | >256 | 0.190 | 1.500 | >256 | >256 | 4.000 | 2.000 |
| | 0.380 | >256 | 0.380 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| | 0.380 | >256 | 0.190 | 1.500 | >256 | >256 | 3.000 | 1.500 |
| **Average MIC** | 0.380 | >256 | 0.253 | 1.333 | >256 | >256 | 3.667 | 1.833 |
| 98-100 | 0.500 | >256 | 0.190 | 0.750 | >256 | >256 | 4.000 | 1.500 |
| | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| **Average MIC** | 0.460 | >256 | 0.190 | 0.917 | >256 | >256 | 4.000 | 1.833 |

| **Antibiotics Controls** | **RI** | **EB** | **CH** | **EM** | **IZ** | **ET** | **LZ** | **AZ** |
|---|---|---|---|---|---|---|---|---|
| 6939 | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| **Average MIC** | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.333 | 2.000 |
| 33701 | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| **Average MIC** | 0.460 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| 49619 | 0.125 | >256 | 0.064 | 0.094 | >256 | >256 | 3.000 | 0.250 |
| | 0.125 | >256 | 0.064 | 0.094 | >256 | >256 | 4.000 | 0.250 |
| | 0.125 | >256 | 0.064 | 0.094 | >256 | >256 | 3.000 | 0.250 |
| **Average MIC** | 0.125 | >256 | 0.064 | 0.094 | >256 | >256 | 3.333 | 0.250 |

| Antibiotics | RI | EB | CH | EM | IZ | ET | LZ | AZ |
|---|---|---|---|---|---|---|---|---|
| **R. Equi. Strains** | | | | | | | | |
| 98-78 | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 6.000 | 2.000 |
| | 0.500 | >256 | 0.190 | 0.750 | >256 | >256 | 4.000 | 3.000 |
| **Average MIC** | 0.500 | >256 | 0.190 | 0.917 | >256 | >256 | 4.667 | 2.333 |
| 98-79 | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| **Average MIC** | 0.420 | >256 | 0.190 | 1.000 | >256 | >256 | 3.333 | 2.000 |
| 98-80 | 0.500 | >256 | 0.190 | 1.500 | >256 | >256 | 4.000 | 2.000 |
| | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| | 0.380 | >256 | 0.190 | 1.500 | >256 | >256 | 4.000 | 2.000 |
| **Average MIC** | 0.460 | >256 | 0.190 | 1.333 | >256 | >256 | 4.000 | 2.000 |
| 98-81 | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| | 0.500 | >256 | 0.250 | 1.500 | >256 | >256 | 4.000 | 3.000 |
| **Average MIC** | 0.420 | >256 | 0.210 | 1.167 | >256 | >256 | 4.000 | 2.333 |
| 98-84 | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| **Average MIC** | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| 98-85 | 1.000 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 3.000 |
| | 0.750 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.750 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| **Average MIC** | 0.833 | >256 | 0.190 | 1.000 | >256 | >256 | 3.667 | 2.333 |

| Antibiotics | RI | EB | CH | EM | IZ | ET | LZ | AZ |
|---|---|---|---|---|---|---|---|---|
| **Controls** | | | | | | | | |
| 6939 | 0.190 | >256 | 0.125 | 0.750 | >256 | >256 | 3.000 | 2.000 |
| | 0.190 | >256 | 0.125 | 0.750 | >256 | >256 | 2.000 | 2.000 |
| | 0.380 | >256 | 0.125 | 0.750 | >256 | >256 | 4.000 | 2.000 |
| **Average MIC** | 0.253 | >256 | 0.125 | 0.750 | >256 | >256 | 3.000 | 2.000 |
| 33701 | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| **Average MIC** | 0.460 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| 49619 | 0.125 | >256 | 0.064 | 0.094 | >256 | >256 | 4.000 | 0.250 |
| | 0.125 | >256 | 0.064 | 0.094 | >256 | >256 | 4.000 | 0.250 |
| | 0.125 | >256 | 0.064 | 0.094 | >256 | >256 | 3.000 | 0.250 |
| **Average MIC** | 0.125 | >256 | 0.064 | 0.094 | >256 | >256 | 3.667 | 0.250 |

| Antibiotics | RI | EB | CH | EM | IZ | ET | LZ | AZ |
|---|---|---|---|---|---|---|---|---|
| **R. Equi. Strains** | | | | | | | | |
| 98-69 | 0.750 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| **Average MIC** | 0.583 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| 98-71 | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 3.000 |
| | 0.500 | >256 | 0.190 | 0.750 | >256 | >256 | 3.000 | 2.000 |
| **Average MIC** | 0.500 | >256 | 0.190 | 0.917 | >256 | >256 | 3.000 | 2.333 |
| 98-72 | 0.230 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.230 | >256 | 0.250 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.032 | >256 | 0.190 | 0.750 | >256 | >256 | 2.000 | 2.000 |
| **Average MIC** | 0.164 | >256 | 0.210 | 0.917 | >256 | >256 | 2.667 | 2.000 |
| 98-73 | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 3.000 |
| | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| **Average MIC** | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.333 |
| 98-75 | 0.190 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| | 0.250 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| | 0.190 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| **Average MIC** | 0.210 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| 98-77 | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| **Average MIC** | 0.420 | >256 | 0.190 | 1.000 | >256 | >256 | 3.667 | 2.000 |

| Antibiotics | RI | EB | CH | EM | IZ | ET | LZ | AZ |
|---|---|---|---|---|---|---|---|---|
| **Controls** | | | | | | | | |
| 6939 | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.380 | >256 | 0.125 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| **Average MIC** | 0.380 | >256 | 0.168 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| 33701 | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| | 0.500 | >256 | 0.125 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| | 0.500 | >256 | 0.125 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| **Average MIC** | 0.460 | >256 | 0.147 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| 49619 | 0.064 | >256 | 0.032 | 1.000 | >256 | >256 | 1.500 | 0.094 |
| | 0.094 | >256 | 0.032 | 1.000 | >256 | >256 | 2.000 | 0.125 |
| | 0.094 | >256 | 0.047 | 1.000 | >256 | >256 | 2.000 | 0.125 |
| **Average MIC** | 0.084 | >256 | 0.037 | 1.000 | >256 | >256 | 1.833 | 0.115 |

| Antibiotics | RI | EB | CH | EM | IZ | ET | LZ | AZ |
|---|---|---|---|---|---|---|---|---|
| **R. Equi. Strains** | | | | | | | | |
| 98-61 | 0.750 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.750 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| **Average MIC** | 0.667 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| 98-63 | 0.750 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.750 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| **Average MIC** | 0.667 | >256 | 0.190 | 1.000 | >256 | >256 | 3.333 | 2.000 |
| 98-64 | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| **Average MIC** | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| 98-65 | 0.023 | >256 | 0.250 | 1.000 | >256 | >256 | 2.000 | 2.000 |
| | 0.023 | >256 | 0.250 | 0.750 | >256 | >256 | 3.000 | 3.000 |
| | 0.023 | >256 | 0.250 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| **Average MIC** | 0.023 | >256 | 0.250 | 0.917 | >256 | >256 | 2.667 | 2.333 |
| 98-66 | 0.500 | >256 | 0.190 | 1.500 | >256 | >256 | 4.000 | 2.000 |
| | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| **Average MIC** | 0.460 | >256 | 0.190 | 1.167 | >256 | >256 | 3.333 | 2.000 |
| 98-68 | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| | 0.500 | >256 | 0.190 | 0.750 | >256 | >256 | 4.000 | 2.000 |
| **Average MIC** | 0.460 | >256 | 0.190 | 0.917 | >256 | >256 | 4.000 | 2.000 |

| Antibiotics | RI | EB | CH | EM | IZ | ET | LZ | AZ |
|---|---|---|---|---|---|---|---|---|
| **Controls** | | | | | | | | |
| 6939 | 0.380 | >256 | 0.190 | 0.750 | >256 | >256 | 3.000 | 2.000 |
| | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| **Average MIC** | 0.460 | >256 | 0.190 | 0.917 | >256 | >256 | 3.000 | 2.000 |
| 33701 | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| **Average MIC** | 0.420 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| 49619 | 0.125 | >256 | 0.064 | 0.094 | >256 | >256 | 3.000 | 0.190 |
| | 0.125 | >256 | 0.047 | 0.094 | >256 | >256 | 2.000 | 0.125 |
| | 0.125 | >256 | 0.064 | 0.094 | >256 | >256 | 2.000 | 0.190 |
| **Average MIC** | 0.125 | >256 | 0.058 | 0.094 | >256 | >256 | 2.333 | 0.168 |

| Antibiotics<br>R. Equi. Strains | RI | EB | CH | EM | IZ | ET | LZ | AZ |
|---|---|---|---|---|---|---|---|---|
| 97-42 | 0.750 | >256 | 0.190 | 0.750 | >256 | >256 | 3.000 | 2.000 |
| | 0.750 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| | 0.750 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| **Average MIC** | 0.750 | >256 | 0.190 | 0.917 | >256 | >256 | 3.667 | 2.000 |
| 97-43 | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.500 | >256 | 0.250 | 1.000 | >256 | >256 | 3.000 | 3.000 |
| | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 3.000 |
| **Average MIC** | 0.460 | >256 | 0.210 | 1.000 | >256 | >256 | 3.333 | 2.667 |
| 97-44 | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.380 | >256 | 0.190 | 0.750 | >256 | >256 | 3.000 | 2.000 |
| **Average MIC** | 0.380 | >256 | 0.190 | 0.917 | >256 | >256 | 3.000 | 2.000 |
| 97-45 | 0.500 | >256 | 0.190 | 1.500 | >256 | >256 | 4.000 | 2.000 |
| | 0.500 | >256 | 0.190 | 1.500 | >256 | >256 | 4.000 | 2.000 |
| | 0.500 | >256 | 0.190 | 1.500 | >256 | >256 | 4.000 | 2.000 |
| **Average MIC** | 0.500 | >256 | 0.190 | 1.500 | >256 | >256 | 4.000 | 2.000 |
| 98-56 | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| **Average MIC** | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 3.667 | 2.000 |

| Antibiotics | RI | EB | CH | EM | IZ | ET | LZ | AZ |
|---|---|---|---|---|---|---|---|---|
| **Controls** | | | | | | | | |
| 6939 | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 3.000 |
| **Average MIC** | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.333 |
| 33701 | 0.500 | >256 | 0.190 | 0.750 | >256 | >256 | 4.000 | 2.000 |
| | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| **Average MIC** | 0.500 | >256 | 0.190 | 0.917 | >256 | >256 | 3.667 | 2.000 |
| 49619 | 0.094 | >256 | 0.047 | 0.064 | >256 | >256 | 2.000 | 0.190 |
| | 0.064 | >256 | 0.047 | 0.047 | >256 | >256 | 2.000 | 0.190 |
| | 0.064 | >256 | 0.047 | 0.064 | >256 | >256 | 1.500 | 0.190 |
| **Average MIC** | 0.074 | >256 | 0.047 | 0.058 | >256 | >256 | 1.833 | 0.190 |

| Antibiotics<br>R. Equi. Strains | RI | EB | CH | EM | IZ | ET | LZ | AZ |
|---|---|---|---|---|---|---|---|---|
| 97-37 | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| **Average MIC** | 0.420 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| 97-38 | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.250 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| **Average MIC** | 0.337 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| 97-39 | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 3.000 |
| | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| **Average MIC** | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.333 | 2.333 |
| 97-40 | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| **Average MIC** | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.667 | 2.000 |
| 97-41 | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| **Average MIC** | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 3.667 | 2.000 |
| 98-53 | 0.380 | >256 | 0.190 | 0.750 | >256 | >256 | 4.000 | 2.000 |
| | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| **Average MIC** | 0.380 | >256 | 0.190 | 0.917 | >256 | >256 | 3.667 | 2.000 |

| Antibiotics | RI | EB | CH | EM | IZ | ET | LZ | AZ |
|---|---|---|---|---|---|---|---|---|
| **Controls** | | | | | | | | |
| 6939 | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| **Average MIC** | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.333 | 2.000 |
| 33701 | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| **Average MIC** | 0.420 | >256 | 0.190 | 1.000 | >256 | >256 | 3.333 | 2.000 |
| 49619 | 0.094 | >256 | 0.047 | 0.064 | >256 | >256 | 2.000 | 0.190 |
| | 0.094 | >256 | 0.047 | 0.064 | >256 | >256 | 2.000 | 0.190 |
| | 0.094 | >256 | 0.047 | 0.064 | >256 | >256 | 2.000 | 0.190 |
| **Average MIC** | 0.094 | >256 | 0.047 | 0.064 | >256 | >256 | 2.000 | 0.190 |

| Antibiotics | RI | EB | CH | EM | IZ | ET | LZ | AZ |
|---|---|---|---|---|---|---|---|---|
| **R. Equi. Strains** | | | | | | | | |
| 97-48 | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.380 | >256 | 0.250 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| **Average MIC** | 0.380 | >256 | 0.210 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| 97-47 | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| **Average MIC** | 0.460 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| 98-52 | 0.500 | >256 | 0.250 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.380 | >256 | 0.250 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.380 | >256 | 0.250 | 1.500 | >256 | >256 | 3.000 | 2.000 |
| **Average MIC** | 0.420 | >256 | 0.250 | 1.167 | >256 | >256 | 3.000 | 2.000 |
| 98-55 | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| **Average MIC** | 0.420 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| 98-57 | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| **Average MIC** | 0.460 | >256 | 0.190 | 1.000 | >256 | >256 | 3.667 | 2.000 |
| 98-58 | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 3.000 |
| | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| **Average MIC** | 0.420 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.333 |

| Antibiotics Controls | RI | EB | CH | EM | IZ | ET | LZ | AZ |
|---|---|---|---|---|---|---|---|---|
| 6939 | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| **Average MIC** | 0.460 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| 33701 | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.500 | >256 | 0.125 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| **Average MIC** | 0.420 | ≥256 | 0.168 | 1.000 | ≥256 | ≥256 | 3.333 | 2.000 |
| 49619 | 0.064 | >256 | 0.047 | 0.064 | >256 | >256 | 2.000 | 0.250 |
| | 0.094 | >256 | 0.047 | 0.064 | >256 | >256 | 1.500 | 0.250 |
| | 0.094 | >256 | 0.064 | 0.064 | >256 | >256 | 2.000 | 0.250 |
| **Average MIC** | 0.084 | >256 | 0.053 | 0.064 | >256 | >256 | 1.833 | 0.250 |

| Antibiotics | RI | EB | CH | EM | IZ | ET | LZ | AZ |
|---|---|---|---|---|---|---|---|---|
| **R. Equi. Strains** | | | | | | | | |
| 71 | 0.032 | >256 | 0.250 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.032 | >256 | 0.250 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.032 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 3.000 |
| **Average MIC** | 0.032 | >256 | 0.230 | 1.000 | >256 | >256 | 3.000 | 2.333 |
| 72 | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.380 | >256 | 0.250 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.380 | >256 | 0.250 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| **Average MIC** | 0.380 | >256 | 0.230 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| 97-35 | 0.250 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| | 0.190 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| | 0.190 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| **Average MIC** | 0.210 | >256 | 0.190 | 1.000 | >256 | >256 | 3.667 | 2.000 |
| 97-36 | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.500 | >256 | 0.250 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| **Average MIC** | 0.500 | >256 | 0.210 | 1.000 | >256 | >256 | 3.333 | 2.000 |
| 98-60 | 0.500 | >256 | 0.250 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.500 | >256 | 0.250 | 1.000 | >256 | >256 | 3.000 | 3.000 |
| | 0.500 | >256 | 0.250 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| **Average MIC** | 0.500 | >256 | 0.250 | 1.000 | >256 | >256 | 3.000 | 2.333 |
| 98-59 | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| **Average MIC** | 0.420 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |

| Antibiotics | RI | EB | CH | EM | IZ | ET | LZ | AZ |
|---|---|---|---|---|---|---|---|---|
| **Controls** | | | | | | | | |
| 6939 | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| **Average MIC** | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| 33701 | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| **Average MIC** | 0.460 | >256 | 0.190 | 1.000 | >256 | >256 | 3.667 | 2.000 |
| 49619 | 0.064 | >256 | 0.047 | 0.064 | >256 | >256 | 1.500 | 0.094 |
| | 0.064 | >256 | 0.047 | 0.064 | >256 | >256 | 1.500 | 0.125 |
| | 0.047 | >256 | 0.047 | 0.064 | >256 | >256 | 1.500 | 0.125 |
| **Average MIC** | 0.058 | >256 | 0.047 | 0.064 | >256 | >256 | 1.500 | 0.115 |

| Antibiotics | RI | EB | CH | EM | IZ | ET | LZ | AZ |
|---|---|---|---|---|---|---|---|---|
| **R. Equi. Strains** | | | | | | | | |
| 7 | 0.023 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.023 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.023 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| **Average MIC** | 0.023 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| 14 | 0.380 | >256 | 0.250 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.380 | >256 | 0.250 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.500 | >256 | 0.250 | 1.500 | >256 | >256 | 3.000 | 3.000 |
| **Average MIC** | 0.420 | >256 | 0.250 | 1.167 | >256 | >256 | 3.000 | 2.333 |
| 73 | 0.023 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| | 0.023 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.023 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| **Average MIC** | 0.023 | >256 | 0.190 | 1.000 | >256 | >256 | 3.333 | 2.000 |
| 97-36 | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.500 | >256 | 0.250 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.500 | >256 | 0.250 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| **Average MIC** | 0.500 | >256 | 0.230 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| 99-242 | 0.380 | >256 | 0.250 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.250 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| **Average MIC** | 0.377 | >256 | 0.210 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| 97-35 | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.250 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| **Average MIC** | 0.337 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |

| Antibiotics | RI | EB | CH | EM | IZ | ET | LZ | AZ |
|---|---|---|---|---|---|---|---|---|
| **Controls** | | | | | | | | |
| 6939 | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| **Average MIC** | 0.420 | >256 | 0.190 | 1.000 | >256 | >256 | 3.333 | 2.000 |
| 33701 | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 1.500 |
| **Average MIC** | 0.460 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 1.833 |
| 49619 | 0.064 | >256 | 0.032 | 0.047 | >256 | >256 | 1.000 | 0.094 |
| | 0.064 | >256 | 0.032 | 0.047 | >256 | >256 | 1.500 | 0.125 |
| | 0.064 | >256 | 0.047 | 0.064 | >256 | >256 | 1.500 | 0.125 |
| **Average MIC** | 0.064 | >256 | 0.037 | 0.053 | >256 | >256 | 1.333 | 0.115 |

| Antibiotics | RI | EB | CH | EM | IZ | ET | LZ | AZ |
|---|---|---|---|---|---|---|---|---|
| **R. Equi. Strains** | | | | | | | | |
| 65 | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 2.000 | 1.500 |
| | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| **Average MIC** | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 2.667 | 1.833 |
| 66 | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| **Average MIC** | 0.420 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| 68 | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| **Average MIC** | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.667 | 2.000 |
| 69 | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| **Average MIC** | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| 70 | 0.750 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.750 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| **Average MIC** | 0.667 | >256 | 0.190 | 1.000 | >256 | >256 | 3.333 | 2.000 |
| 19757-4 | 0.380 | >256 | 0.250 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.380 | >256 | 0.250 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| **Average MIC** | 0.380 | >256 | 0.230 | 1.000 | >256 | >256 | 3.000 | 2.000 |

| Antibiotics | RI | EB | CH | EM | IZ | ET | LZ | AZ |
|---|---|---|---|---|---|---|---|---|
| **Controls** | | | | | | | | |
| 6939 | *********** | *********** | *********** | *********** | *********** | *********** | *********** | *********** |
| Contaminated | *********** | *********** | *********** | *********** | *********** | *********** | *********** | *********** |
| | *********** | *********** | *********** | *********** | *********** | *********** | *********** | *********** |
| **Average MIC** | *********** | *********** | *********** | *********** | *********** | *********** | *********** | *********** |
| 33701 | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| **Average MIC** | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.667 | 2.000 |
| 49619 | 0.094 | >256 | 0.047 | 0.064 | >256 | >256 | 2.000 | 0.094 |
| | 0.094 | >256 | 0.047 | 0.047 | >256 | >256 | 1.500 | 0.094 |
| | 0.064 | >256 | 0.032 | 0.064 | >256 | >256 | 2.000 | 0.125 |
| **Average MIC** | 0.084 | >256 | 0.042 | 0.058 | >256 | >256 | 1.833 | 0.104 |

| Antibiotics | RI | EB | CH | EM | IZ | ET | LZ | AZ |
|---|---|---|---|---|---|---|---|---|
| **R. Equi. Strains** | | | | | | | | |
| 28 | 0.750 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.750 | >256 | 0.250 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.750 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| **Average MIC** | 0.750 | >256 | 0.210 | 1.000 | >256 | >256 | 3.333 | 2.000 |
| 29 | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| | 0.250 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.250 | >256 | 0.125 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| **Average MIC** | 0.293 | >256 | 0.168 | 1.000 | >256 | >256 | 3.667 | 2.000 |
| 30 | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| **Average MIC** | 0.460 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| 59 | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| | 0.380 | >256 | 0.250 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| **Average MIC** | 0.380 | >256 | 0.210 | 1.000 | >256 | >256 | 3.667 | 2.000 |
| 61 | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| **Average MIC** | 0.420 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| 62 | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| **Average MIC** | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.667 | 2.000 |

| Antibiotics Controls | RI | EB | CH | EM | IZ | ET | LZ | AZ |
|---|---|---|---|---|---|---|---|---|
| 6939 | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| **Average MIC** | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| 33701 | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| **Average MIC** | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| 49619 | 0.064 | >256 | 0.047 | 0.064 | >256 | >256 | 3.000 | 0.190 |
| | 0.064 | >256 | 0.047 | 0.064 | >256 | >256 | 2.000 | 0.190 |
| | 0.094 | >256 | 0.047 | 0.064 | >256 | >256 | 2.000 | 0.190 |
| **Average MIC** | 0.074 | >256 | 0.047 | 0.064 | >256 | >256 | 2.333 | 0.190 |

| Antibiotics | RI | EB | CH | EM | IZ | ET | LZ | AZ |
|---|---|---|---|---|---|---|---|---|
| **R. Equi. Strains** | | | | | | | | |
| 20A | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.380 | >256 | 0.125 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| **Average MIC** | 0.420 | >256 | 0.168 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| 20 | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.500 | >256 | 0.125 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| **Average MIC** | 0.500 | >256 | 0.168 | 1.000 | >256 | >256 | 3.333 | 2.000 |
| 23 | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| | 0.380 | >256 | 0.190 | 1.500 | >256 | >256 | 4.000 | 2.000 |
| **Average MIC** | 0.380 | >256 | 0.190 | 1.167 | >256 | >256 | 3.667 | 2.000 |
| 24 | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| | 0.500 | >256 | 0.125 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| **Average MIC** | 0.500 | >256 | 0.168 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| 25 | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| **Average MIC** | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.667 | 2.000 |
| 27 | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| **Average MIC** | 0.460 | >256 | 0.190 | 1.000 | >256 | >256 | 3.667 | 2.000 |

| Antibiotics | RI | EB | CH | EM | IZ | ET | LZ | AZ |
|---|---|---|---|---|---|---|---|---|
| **Controls** | | | | | | | | |
| 6939 | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.380 | >256 | 0.190 | 1.500 | >256 | >256 | 3.000 | 2.000 |
| | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| **Average MIC** | 0.380 | >256 | 0.190 | 1.167 | >256 | >256 | 3.000 | 2.000 |
| 33701 | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| **Average MIC** | 0.460 | >256 | 0.190 | 1.000 | >256 | >256 | 3.667 | 2.000 |
| 49619 | 0.064 | >256 | 0.032 | 0.047 | >256 | >256 | 2.000 | 0.125 |
| | 0.047 | >256 | 0.032 | 0.047 | >256 | >256 | 2.000 | 0.125 |
| | 0.047 | >256 | 0.032 | 0.047 | >256 | >256 | 2.000 | 0.125 |
| **Average MIC** | 0.053 | >256 | 0.032 | 0.047 | >256 | >256 | 2.000 | 0.125 |

| Antibiotics | RI | EB | CH | EM | IZ | ET | LZ | AZ |
|---|---|---|---|---|---|---|---|---|
| **R. Equi. Strains** | | | | | | | | |
| 6 | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| **Average MIC** | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 3.333 | 2.000 |
| 9 | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| **Average MIC** | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.667 | 2.000 |
| 16 | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 1.500 |
| | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.380 | >256 | 0.190 | 0.750 | >256 | >256 | 3.000 | 1.500 |
| **Average MIC** | 0.380 | >256 | 0.190 | 0.917 | >256 | >256 | 3.000 | 1.667 |
| 17 | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| **Average MIC** | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.667 | 2.000 |
| 18 | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| **Average MIC** | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| 19 | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| **Average MIC** | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |

| Antibiotics | RI | EB | CH | EM | IZ | ET | LZ | AZ |
|---|---|---|---|---|---|---|---|---|
| **Controls** | | | | | | | | |
| 6939 | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| **Average MIC** | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.333 | 2.000 |
| 33701 | ********** | ********* | ********** | ********** | ********** | ********** | ********** | ********** |
| Contaminated | ********** | ********** | ********** | ********** | ********** | ********** | ********** | ********** |
| | ********** | ********** | ********** | ********** | ********** | ********** | ********** | ********** |
| | ********** | ********* | ********** | ********** | ********** | ********** | ********** | ********** |
| 49619 | 0.0940 | >256 | 0.0320 | 0.0320 | >256 | >256 | 2.000 | 0.0940 |
| | 0.0640 | >256 | 0.0470 | 0.0470 | >256 | >256 | 1.500 | 0.0940 |
| | 0.0640 | >256 | 0.0230 | 0.0470 | >256 | >256 | 1.500 | 0.0940 |
| **Average MIC** | 0.0740 | >256 | 0.0340 | 0.0420 | >256 | >256 | 1.666 | 0.0940 |

| Antibiotics | RI | EB | CH | EM | IZ | ET | LZ | AZ |
|---|---|---|---|---|---|---|---|---|
| **R. Equi. Strains** | | | | | | | | |
| 98-101 | 0.380 | >256 | 0.125 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.380 | >256 | 0.125 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| **Average MIC** | 0.380 | >256 | 0.147 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| 99-108 | 0.094 | >256 | 0.064 | 0.500 | >256 | >256 | 3.000 | 2.000 |
| | 0.094 | >256 | 0.094 | 0.750 | >256 | >256 | 3.000 | 2.000 |
| | 0.094 | >256 | 0.125 | 0.500 | >256 | >256 | 3.000 | 2.000 |
| **Average MIC** | 0.094 | >256 | 0.094 | 0.583 | >256 | >256 | 3.000 | 2.000 |
| 99-109 | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.380 | >256 | 0.125 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 4.000 | 2.000 |
| **Average MIC** | 0.460 | >256 | 0.168 | 1.000 | >256 | >256 | 3.333 | 2.000 |
| 99-110 | 0.380 | >256 | 0.064 | 0.190 | >256 | >256 | 2.000 | 0.500 |
| | 0.380 | >256 | 0.064 | 0.190 | >256 | >256 | 2.000 | 0.750 |
| | 0.500 | >256 | 0.064 | 0.250 | >256 | >256 | 2.000 | 0.750 |
| **Average MIC** | 0.420 | >256 | 0.064 | 0.210 | >256 | >256 | 2.000 | 0.667 |
| 99-112 | 0.380 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.500 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | 0.380 | >256 | 0.125 | 0.500 | >256 | >256 | 4.000 | 2.000 |
| **Average MIC** | 0.420 | >256 | 0.168 | 0.833 | >256 | >256 | 3.333 | 2.000 |
| 288 | >256 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | >256 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| | >256 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |
| **Average MIC** | >256 | >256 | 0.190 | 1.000 | >256 | >256 | 3.000 | 2.000 |

**RI (rifampin) EB (ethambutol) CH (clarithromycin) EM (erythromycin)**

**IZ (isoniazide) ET (ethionamide) LZ (linezolid) AZ (azithromycin)**

# VITA

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