Multidrug resistance has been detected in the animal and zoonotic human pathogen Rhodococcus equi after mass macrolide/rifampin antibioprophylaxis in endemically affected equine farms in the United States. Multidrug-resistant (MDR) R. equi emerged upon acquisition of pRErm46, a conjugative plasmid conferring resistance to macrolides, lincosamides, streptogramins, and, as we describe, tetracycline. Phylogenomic analyses indicate that the increasing prevalence of MDR R. equi since it was first documented in 2002 is caused by a clone, R. equi 2287, attributable to coselection of pRErm46 with a chromosomal rpoB<sup>S531F</sup> mutation driven by macrolide/rifampin therapy. pRErm46 spillover to other R. equi genotypes has given rise to a novel MDR clone, G2016, associated with a distinct rpoB<sup>S531Y</sup> mutation. Our findings illustrate that overuse of antimicrobial prophylaxis in animals can generate MDR pathogens with zoonotic potential. MDR R. equi and pRErm46-mediated resistance are currently disseminating in the United States and are likely to spread internationally through horse movements.

Rhodococcus equi is a soilborne facultative intracellular actinobacterium that causes pyogranulomatous infections in multiple animal species, including humans. Rhodococcal infection is particularly severe in young foals and immunocompromised persons, in whom it typically manifests as a life-threatening purulent bronchopneumonic disease (1–3). R. equi is able to colonize equids, pigs, and ruminants through 3 different host-specific virulence plasmid types (designated pVAPA, pVAPB, and pVAPN) (4). Analysis of the virulence plasmids carried by the isolates and comparison of genomic profiles indicate that human R. equi infections originate from animals (4–6).

R. equi is highly prevalent in horse-breeding farms worldwide (7). For decades, the standard treatment for R. equi pneumonia in foals has been a combination macrolide/rifampin therapy (8). In the absence of effective preventive methods, many horse-breeding farms rely on early ultrasonographic detection of infected foals and initiation of macrolide/rifampin prophylaxis before clinical manifestation of the disease (9). In the United States, where foal rhodococcosis is often endemic, implementation of this practice has been linked to the emergence of dual macrolide/rifampin-resistant (MR<sup>R</sup>) R. equi (10–12). First detected in the late 1990s, R. equi MR<sup>R</sup> isolates are increasingly prevalent (11–14), posing a substantial problem because no clinically proven therapeutic alternative is currently available for the treatment of affected foals (8). The MR<sup>R</sup> isolates also represent a potential hazard to human health because of the risk for zoonotic transmission.

We recently determined that the emerging MR<sup>R</sup> phenotype among R. equi isolates was linked to a novel methyltransferase gene, erm(46), which confers cross-resistance to macrolides, lincosamides, and streptogramins (MLS<sup>B</sup> phenotype) (13). erm(46) is part of a 6.9-kb transposable element, TnRErm46, which is carried by the conjugative resistance plasmid pRErm46 (15). Upon pRErm46 acquisition, TnRErm46 stabilizes itself in R. equi by transposing to the host genome, including the conjugative virulence plasmid pVAPA. Despite its high potential for horizontal spread, we found that pRErm46/TnRErm46 was restricted to a specific R. equi clone, designated 2287, likely because of co-selection with a chromosomal rifampin-resistance rpoB<sup>S531F</sup> mutation in response to macrolide/rifampin therapy (15).

We identified the multidrug-resistant (MDR) R. equi 2287 clone by analyzing isolates collected during 2002–2011 (15). Here, we investigate the spread of the erm(46) determinant in a contemporary sample...
of macrolide-resistant isolates and horizontal spread of pRErm46/TnRErm46, leading to emergence of a further MDR \textit{R. equi} clone associated with a novel \textit{rpoB}^{SSYV} mutation.

**Materials and Methods**

**Bacteria**

We sequenced the genomes of a random selection of 30 macrolide-resistant and 18 macrolide-susceptible \textit{R. equi} equine clinical strains recovered from pneumonic foals in 5 US states (Florida, Kentucky, Louisiana, New York, and Texas) during 2012–2017 (Appendix Table 1, https://wwwnc.cdc.gov/EID/article/27/2/20-3030-App1.pdf). Whenever possible, at least 1 strain from each category was chosen for each year and US state. The strains from Louisiana were a random collection of 10 convenience-sampled isolates from a single farm. All strains were routinely grown in brain-heart infusion medium (BD, https://www.bd.com) for 48 h at 37°C. Detection of the \textit{erm}(46) gene by PCR was performed as previously described (13,15).

**Antimicrobial Susceptibility Testing**

Susceptibility tests were performed at the Hagyard Equine Medical Institute diagnostic laboratory (Lexington, Kentucky, USA), Texas A&M Veterinary Medical Diagnostic Laboratory (College Station, Texas, USA), and University of Georgia Veterinary Diagnostic Laboratory (Athens, Georgia, USA) according to Clinical and Laboratory Standards Institute (CLSI) guidelines (https://clsi.org). In the absence of specific disk susceptibility interpretive criteria for \textit{R. equi}, CLSI guidelines for \textit{Staphylococcus aureus} were used in accordance with routine practices in veterinary diagnostic laboratories (11,16). MICs were determined in tryptone soy agar medium by using Etest strips (bioMérieux, https://www.biomerieux.com) according to the manufacturer’s recommendations (16). \textit{Staphylococcus aureus} ATCC 29213 was used as a control in all susceptibility tests.

**Genome Sequencing and Phylogenetic Analysis**

We extracted bacterial genomic DNA by using DNeasy UltraClean Microbial Kit (QIAGEN, https://www.qiagen.com) following the manufacturer’s instructions. DNA quality (optical density 260/280, ratio 1.8:2) and concentration (>1 µg) of each gDNA sample were verified by using a NanoDrop apparatus (Thermo Fisher Scientific, https://www.thermofisher.com). Single-molecule real-time long-read DNA sequencing was performed at Duke Center for Genomic and Computational Biology (Duke University, Durham, North Carolina, USA). SMRTbell Template Prep Kit 2.0 was used for library preparation of 4–6-kb insert for 8 multiplexed bacterial samples. Samples were run on a PacBio Sequel II system (Pacific Bioscience, https://www.pacb.com). Genomes were assembled de novo by using Canu version 1.9 (17). Whole-genome phylogenetic analysis was performed with ParSNP in the Harvest suite, designed for single-nucleotide polymorphism analysis between closely related species or strains (≥97% average nucleotide identity) (18). The program uses FastTree 2 (19) to build approximately maximum-likelihood trees from core-genome single-nucleotide polymorphisms. Trees were visualized in FigTree 1.4.4 (http://tree.bio.ed.ac.uk/software/figtree). Principal component analysis was performed by feeding VCF files extracted from ParSNP alignments to ggfortify package in R software version 3.6.1 (https://cran.r-project.org/web/packages/ggfortify/index.html).

**Statistical Analysis**

Statistical significance of tetracycline susceptibility data was determined by χ² test and Student t-test. All tests were conducted using Prism software version 8 (https://www.graphpad.com).

**Results**

The 30 macrolide-resistant \textit{R. equi} genome sequences determined in this study were subjected to phylogenetic analysis alongside a sample of 18 susceptible isolates from the same period and geographic origins to examine their relationships. The macrolide-resistant isolates had previously tested positive to \textit{erm}(46) by PCR and most (n = 22, 73%) were also resistant to rifampin (MR³ phenotype). Of note, 8 of the 2012–2017 \textit{R. equi} isolates examined here were macrolide-only–resistant (Appendix Table 1); to date, dual MR³ resistance had been invariably observed (10,11,13,15). We also included in our analysis Illumina whole-genome assemblies from 22 equine isolates characterized in our earlier study (n = 16 belonging to the 2287 clone, n = 6 control susceptible isolates) and 23 macrolide-susceptible strains representative of the global genomic diversity of \textit{R. equi} (20). Figure 1 shows the core-genome phylogeny of the 93 \textit{R. equi} strains.

**Clonal Spread of MDR \textit{R. equi} 2287**

Of 22 in total, 20 (91%) of the new MR³ isolates clustered together at short genetic distances with the previously characterized MDR 2287 isolates, indicating
they correspond to the same clonal population (Figure 1). Accordingly, all of the newly sequenced MR strains possessed the rpoB S531F mutation unique to the 2287 clone. Of those, 2 had lost the pRErm46 plasmid and only carried the TnRErm46 transposon (Figure 1), as previously observed in 1 of the 18 isolates from the 2002–2011 series (15). Collection times and locations encompassed the entire 2012–2017 period and the 5 US states for the MDR 2287 clonal population. The lack of spatial-temporal circumscription of MDR 2287 in the analyzed sample is illustrated by a principal components analysis in which the only grouping factor for the 93 _R. equi_ isolates included in this study is the genetic background of the 2287 clone (Figure 2).

We repeated the phylogenomic analysis with the 36 _R. equi_ 2287 sequences from 2002–2017 to assess the microevolution of the clone. This analysis
revealed that MDR 2287 had diversified into 3 major radiations (Figure 3), consistent with the clonal structure of R. equi evolution (20). Of note, 1 of these subclades gathered 11 of the 16 older isolates from 2002–2011, all originating from Florida or Kentucky. The remaining 5 older isolates were distributed in the 2 other subclades in which strains were grouped independently of year of collection or geographic origin. This distribution suggests a pattern of spread defined by the diversification of MDR 2287 into subclonal lineages and increasing exchange between horse farms of a progressively diverse clonal population.

Dissemination of pRErm46 and Emergence of Novel MDR R. equi Clone

Ten macrolide-resistant isolates also carried pRErm46 but did not belong to the MDR 2287 clone and were genetically diverse. Most appeared as singletons interspersed among the different lines of descent in the R. equi tree (Figure 1). In this group, 8 strains corresponded to the previously mentioned macrolide-only-resistant isolates (i.e., rifampin susceptible, no rpoB mutation; MIC <0.125–1.25 μg/mL). All but 1 of these isolates originated from the same farm in Louisiana in which an MDR 2287 isolate (no. 171) was recovered during the same period. This circumstance suggests a scenario in which the entry of MDR 2287 into this farm resulted in the conjugal spread of pRErm46 to different members of the heterogeneous R. equi populations that are typically found colonizing horse-breeding environments, or even individual animals within the same farm (21,22).

Of interest, 2 of the non-2287 macrolide-resistant isolates, numbers 155 (recovered in Kentucky in 2017) and 183 (recovered in Kentucky in 2016), were also resistant to rifampin (MIC>32 μg/mL) (Figure 1). These 2 nearly genomically identical MR^R strains carried the pRErm46 plasmid and a chromosomal rpoB mutation, Ser531Tyr (Escherichia coli numbering), distinct from that in MDR 2287 and novel in R. equi. Both MR^R isolates constitute a new emerging MDR R. equi clone, first detected in 2016, which we designated G2016.

Collectively, these data indicate that the pRErm46 macrolide-resistance plasmid, until now unique to the 2287 clone, has recently undergone horizontal transfer events to multiple R. equi genotypes. These transfers gave rise to novel MDR clones when associated with an rpoB mutation.

pRErm46 Variability and Tetracycline Resistance

pRErm46 also harbors a class 1 integron (C1I) with a tetR-tetA cassette encoding a putative tetracycline efflux pump homologous to TetA(33) from the co-ronobacterial plasmid pTET3 (15,23). TetA efflux pumps are often carried by transposons and are one of the most prevalent tetracycline-resistance mechanisms (24). Both the C1I and tetRA determinant from pRErm46 are virtually identical to those from pTET3, including flanking IS6100 insertion sequences (15). Blast alignments revealed that the C1I-tetRA(33) region was deleted in 17 of the 43 (40%) pRErm46
plasmids (Figures 1, 3), presumably because of recombination between the duplicated IS6100s (Figure 4). Similar rearrangements have been reported in other integrons carrying directly repeated IS6100 copies (25,26). Confirming the predicted functionality of pRErm46’s tetRA(33) determinant, pRErm46-positive isolates were resistant to tetracycline, in contrast to those carrying the ΔC1I-tetRA(33) form of the resistance plasmid (Table). However, all R. equi isolates were susceptible to the semisynthetic tetracycline derivative doxycycline, regardless of pRErm46 plasmid carriage (Table). This finding is consistent with previous data on Corynebacterium glutamicum showing that TetA(33) does not confer substantial cross-resistance to doxycycline (23).

Whereas a ΔC1I-tetRA(33) plasmid deletion was detected in only 1 of the older (2002–2011) MDR 2287 isolates, the deletion was found in 10 of the 18 pRErm46-positive clonal isolates recovered during 2012–2017 (Figure 1). Deleted pRErm46s are observed in each of the clonal radiations of the MDR 2287 population and coexist with complete plasmids in more basal branches (Figure 3), indicating increasing occurrence because of repeated independent deletion events. The deletion was detected in all of the genetically heterogeneous macrolide-only–resistant R. equi isolates and the MDR 2287 (isolate no. 171) recovered from the Louisiana farm during the same period. This finding supports the notion that the latter was the source from which pRErm46 had spread to other locally prevalent R. equi genotypes in that particular farm.

**Discussion**

This study demonstrates that the increasing prevalence of MR R. equi since its emergence in the late 1990s–early 2000s in equine farms in the United States (11–14) is primarily caused by the spread of the recently identified MDR 2287 clone (15). The oldest characterized MDR 2287 isolate dates from 2002 and was recovered in Kentucky (15) (Figure 1), where the clone likely emerged after the implementation of mass macrolide/rifampin antibiotic prophylaxis in foals (10). Since then, R. equi MDR 2287 has been frequently transferred between geographically distant farms, presumably through carrier horses. Active exchange of R. equi populations, previously noted in our earlier study (20), is evident in the United States.
Despite the diversity of R. equi genotypes that typically circulate in farms (21, 22), the highly horizontally transferable  
\( \text{erm}(46) \) (TnRErm46) determinant remains largely confined to MDR 2287. This paradoxical clonal restriction is the probable consequence of the simultaneous requirement for  
\( \text{erm}(46) \) and the \( rpoB \) mutation under dual macrolide/rifampin pressure. More specifically, the clonal restriction is likely determined by the low odds of pRErm46/TnRErm46 and a high-resistance \( rpoB \) mutation (such as Ser531Phe in MDR 2287 or Ser531Tyr in MDR G2016) being acquired concurrently, and the latter effectively linking the mobile  
\( \text{erm}(46) \) determinant to a specific chromosomal background (15).

This interpretation implies several predictions. First, under dual macrolide/rifampin pressure, spread of an existing MR\(^R\) strain through horse movements is more likely to contribute to the bulk of resistance than the generation of new MR\(^R\) strains (15). Second, continued macrolide/rifampin therapy might eventually lead to the emergence of new MR\(^R\) clones, such as G2016 identified in this study, detected in 2016 in Kentucky and characterized by a novel \( rpoB(S33Y) \) mutation. Third, and importantly, if dual macrolide/rifampin selection ceases, unrestricted pRErm46/TnRErm46 horizontal transfer to other R. equi strains might occur. Our data appear to support these 3 possibilities.

The first and second scenarios are expected in horse-breeding areas such as Kentucky, Texas, or Florida, where R. equi is endemic and macrolide/rifampin antibiotic prophylaxis has been commonly practiced (10, 27, 28). Less intensive and more targeted antibiotic therapy is more likely in areas with smaller horse populations such as Louisiana (29), where pRErm46 spillover outside the MDR 2287 clone was detected (the third scenario). We hypothesize that a less intensive antibiotic

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### Table. Effect of absence of tetRA(33) determinant from pRErm46 plasmid on R. equi susceptibility to tetracycline and doxycycline, determined on macrolide-resistant isolates collected during 2012–2017*

| Antibiotic     | pRErm46 Phenotype† | pRErm46 MIC, µg/mL‡ | pRErm46ΔC1I-tetRA(33) Phenotype | pRErm46ΔC1I-tetRA(33) MIC, µg/mL‡ |
|----------------|--------------------|---------------------|---------------------------------|----------------------------------|
| Tetracycline   | Resistant (100)§   | 21.33 (8–48)¶       | Susceptible (100)§              | 1.97 (0.38–3)¶                   |
| Doxycycline    | Susceptible (100)  | 3.35 (0.75–6)**     | Susceptible (100)               | 1.06 (0.25–3)**                  |

*Susceptibility data to other relevant antimicrobials are shown in Appendix Table 2 (https://wwwnc.cdc.gov/EID/article/27/2/20-3030-App1.pdf).
†Determined by disk diffusion technique. Isolate percentage shown in parenthesis. Zone diameter susceptibility breakpoints based on Clinical and Laboratory Standards Institute interpretive criteria for \( \text{Staphylococcus aureus} \), routinely used for R. equi susceptibility testing in the absence of specific approved criteria for this species (11, 16).
‡Minimal inhibitory concentration determined using Etest strips. Mean value (range in parenthesis).
§p<0.001 by \( \chi^2 \) test.
¶p<0.001 by \( t \) test.
**p<0.001 by \( t \) test. Presence of TetRA(33) appears to induce a small, statistically significant MIC increase, but MIC remains below the Clinical and Laboratory Standards Institute susceptibility breakpoint for doxycycline (susceptible ≤4 µg/mL, intermediate 8 µg/mL, resistant ≥16 µg/mL).
pressure, perhaps involving macrolide monotherapy or a macrolide in combination with non-rifampin antibiotic drugs, disrupted the linkage between \textit{erm}(46) and \textit{rpoB}^{S531F} in the MDR 2287 strain found in the Louisiana farm, enabling the transfer of the plasmid to other locally prevalent \textit{R. equi} strains (Figure 1).

Our analyses show that MDR 2287 has diversified since its first documented isolation into a clonal complex with several radiations (Figure 3). We also detected signs of microevolution in pRErm46, with a substantial rate of deletion of the C1I-\textit{tetRA}\textsubscript{(33)} region in the 2012–2017 macrolide-resistant \textit{R. equi} cohort, resulting in loss of tetracycline resistance. The clinical significance of this finding is unclear because tetracyclines are not used to treat \textit{R. equi} infections in foals. An exception is doxycycline, which, because of its higher oral bioavailability in foals, greater tissue penetration, and better activity against gram-positive bacteria, might be used in cases of macrolide intolerance (or resistance) (2,8,30). However, our data indicate that the pRErm46-encoded TetA33 does not confer clinically relevant cross-resistance to this semisynthetic tetracycline derivative. Genetic dispensability due to lack of antibiotic selection or fitness advantage might therefore be the likely reason for the increasing occurrence of ΔC1I-\textit{tetRA}(33) pRErm46 plasmids in the macrolide-resistant \textit{R. equi} population.

MDR \textit{R. equi} shows resistance to several clinically relevant antibiotic drugs, including macrolides, lincosamides; streptogramins, and, in a substantial proportion, also tetracycline, all conferred by the pRErm46 conjugative plasmid; and rifampin conferred by a chromosomal \textit{rpoB}^{S531F/7} mutation. MDR \textit{R. equi} also demonstrates intrinsic resistance to chloramphenicol (Appendix Table 2), which is often observed in \textit{R. equi}. All of these antibiotic drugs are listed as critically or highly important for human medicine by the World Health Organization (31). Around 9\% of human \textit{R. equi} infections are caused by equine-derived (pVAPAP-positive) strains, and about half of human cases are caused by porcine-derived (pVAPB-positive) isolates (5), which recent in vitro data demonstrate can also acquire pRErm46 (32). Therefore, in addition to compromising the therapeutic management of equine \textit{R. equi} infection, these isolates represent a potential hazard to human health because of the risk of zoonotic transmission (or horizontal spread of the pRErm46 resistance plasmid to other pathogens, either directly or through environmental microbiota [32]).

Although our study is not systematic and therefore probably underestimates the extent of MDR \textit{R. equi} spread, our results provide valuable insight into the determinants underlying its emergence and dissemination. The data suggest a pattern of MDR \textit{R. equi} spread and evolution directly determined by antibiotic pressure in equine farms. The stable therapeutic regimen applied over years for \textit{R. equi} facilitates a unique understanding of the factors affecting the generation and evolution of MDR clones, and specifically how combination therapy might help in limiting the horizontal transfer of resistance. Although MDR \textit{R. equi} is, to our knowledge, still limited to the equine population in the United States, our data predict a scenario of international spread through horse movements, indicating the need for interventions to control its dissemination and potential zoonotic transmission.

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S.A.-N., S.G., N.C. and J.V.-B. designed the study. S.A.-N. performed the research. N.S. and N.C. collected isolates and susceptibility data. S.A.-N. and J.V.-B. analyzed and interpreted the data. J.V.-B. conceptualized the findings. S.A.-N. and J.V.-B. wrote the article.

New \textit{R. equi} genome assemblies were deposited in GenBank under the accession numbers indicated in Appendix Table 1.

**About the Author**

Dr. Álvarez-Narváez is a clinical assistant professor at the University of Georgia. Her primary research interests include antimicrobial resistance mechanisms and host-pathogen interactions at the molecular level.

**References**

1. Prescott JF. \textit{Rhodococcus equi}: an animal and human pathogen. Clin Microbiol Rev. 1991;4:20–34. https://doi.org/10.1128/CMR.4.1.20

2. Vázquez-Boland JA, Giguère S, Hapeshi A, MacArthur I, Anastasi E, Valero-Rello A. \textit{Rhodococcus equi}: the many facets of a pathogenic actinomycete. Vet Microbiol. 2013;167:9–33. https://doi.org/10.1016/j.vetmic.2013.06.016

Emerging Infectious Diseases • www.cdc.gov/eid • Vol. 27, No.2 February, 2021 535
3. Yamschikov AV, Schuetz A, Lyon GM. *Rhodococcus equi* infection. Lancet Infect Dis. 2010;10:350–9. https://doi.org/10.1016/S1473-3099(10)70068-2

4. MacArthur I, Anastasi E, Alvarez S, Scortti M, Vázquez-Boland JA. Comparative genomics of *Rhodococcus equi* virulence plasmids indicates host-driven evolution of the vap pathogenicity island. Genome Biol Evol. 2015;7:1241–7. https://doi.org/10.1093/gbe/evv557

5. Ocampo-Sosa AA, Lewis DA, Navas J, Quigley F, Callejo R, et al. Molecular epidemiology of *Rhodococcus equi* based on traA, vapA, and vapB virulence plasmid markers. J Infect Dis. 2007;196:763–9. https://doi.org/10.1086/519688

6. Vázquez-Boland JA, Meijer WG. The pathogenic actinobacterium *Rhodococcus equi*: what’s in a name? Mol Microbiol. 2019;112:1–15. https://doi.org/10.1111/mmi.14267

7. Muscatello G, Leandon DP, Klayt M, Ocampo-Sosa A, Lewis DA, Fogarty U, et al. *Rhodococcus equi* infection in foals: the science of ‘rattles’. Equine Vet J. 2007;39:470–8. https://doi.org/10.1111/j.1744-0596.2007.01822.x

8. Giguère S. Treatment of infections caused by *Rhodococcus equi*. Vet Clin North Am Equine Pract. 2017;33:67–85. https://doi.org/10.1016/j.cvne.2016.11.002

9. Giguère S, Cohen ND, Chaffin MK, Slovis NM, Hondalus MK, Hines SA, et al. Diagnosis, treatment, control, and prevention of infections caused by *Rhodococcus equi* in foals. J Vet Intern Med. 2011;25:1209–20. https://doi.org/10.1111/j.1939-1676.2011.00835.x

10. Burton AJ, Giguère S, Sturgill TL, Berghaus LJ, Slovis NM, Whitman JL, et al. Macrolide- and rifampin-resistant *Rhodococcus equi* on a horse breeding farm, Kentucky, USA. Emerg Infect Dis. 2013;19:282–5. https://doi.org/10.3201/eid1902.121210

11. Giguère S, Lee E, Williams E, Cohen ND, Chaffin MK, Halbert N, et al. Determination of the prevalence of antimicrobial resistance to macrolides or rifampin in *Rhodococcus equi* isolates and treatment outcome in foals infected with antimicrobial-resistant isolates of *R. equi*. J Am Vet Med Assoc. 2010;237:74–81. https://doi.org/10.2460/javma.237.1.74

12. Huber L, Giguère S, Slovis NM, Carter CN, Barr BS, Cohen ND, et al. Emergence of resistance to macrolides and rifampin in clinical isolates of *Rhodococcus equi* from foals in central Kentucky, 1995 to 2017. Antimicrob Agents Chemother. 2018;63:e01714-18. https://doi.org/10.1128/AAC.01714-18

13. Anastasi E, Giguère S, Berghaus LJ, Hondalus MK, Willingham-Lane JM, MacArthur I, et al. Novel transferable *erm*(46) determinant responsible for emerging macrolide resistance in *Rhodococcus equi*. J Antimicrob Chemother. 2015;70:3184–90.

14. Erol E, Locke S, Saied A, Cruz Penn MJ, Smith J, Fortner J, et al. Antimicrobial susceptibility patterns of *Rhodococcus equi* from necropsied foals with rhodoccosis. Vet Microbiol. 2020;242:108568. https://doi.org/10.1016/j.vetmic.2019.108568

15. Álvarez-Narváez S, Giguère S, Anastasi E, Hearn J, Scortti M, Vázquez-Boland JA. Clonal confinement of a highly mobile resistance element driven by combination therapy in *Rhodococcus equi*. MBio. 2019;10:e02260-19. https://doi.org/10.1128/mBio.02260-19

16. Berghaus LJ, Giguère S, Guldbech K, Warner E, Ugorji U, Berghaus RD. Comparison of Etest, disk diffusion, and broth macrodilution for in vitro susceptibility testing of *Rhodococcus equi*. J Clin Microbiol. 2015;53:314–8. https://doi.org/10.1128/JCM.02673-14

17. Koren S, Walenz BP, Berlin K, Miller JR, Bergman NH, Phillippy AM. Canu: scalable and accurate long-read assembly via adaptive k-mer weighting and repeat separation. Genome Res. 2017;27:722–36. https://doi.org/10.1101/gr.215087.116

18. Treangen TJ, Ondov BD, Koren S, Phillippy AM. The Harvest suite for rapid core-genome alignment and visualization of thousands of intraspecific microbial genomes. Genome Biol. 2014;15:524. https://doi.org/10.1186/s13059-014-0524-x

19. Price MN, Dehal PS, Arkin AP. FastTree 2—a maximum-likelihood tree for large alignments. PLoS One. 2010;5:e9490. https://doi.org/10.1371/journal.pone.0009490

20. Anastasi E, MacArthur I, Scortti M, Alvarez S, Giguère S, Vázquez-Boland JA. Pangenome and phylogenomic analysis of the pathogenic actinobacterium *Rhodococcus equi*. Genome Biol Evol. 2016;8:3140–8. https://doi.org/10.1093/gbe/evw222

21. Cohen ND, Smith KE, Ficht TA, Takai S, Libal MC, West BR, et al. Epidemiologic study of results of pulsed-field gel electrophoresis of isolates of *Rhodococcus equi* obtained from horses and horse farms. Am J Vet Res. 2003;64:153–61. https://doi.org/10.2460/ajvr.2003.64.153

22. Morton AC, Begg AP, Anderson GA, Takai S, Lämmler C, Browning GF. Epidemiology of *Rhodococcus equi* strains on Thoroughbred horse farms. Appl Environ Microbiol. 2001;67:2167–75. https://doi.org/10.1128/AEM.67.7.2167-2175.2001

23. Tauch A, Götter S, Phüler A, Kalinowski J, Thierbach G. The 27.8-kb R-plasmid pTET3 from *Corynebacterium glutamicum* encodes the aminoglycoside adenylation transferase gene cassette aadA9 and the regulated tetracycline efflux system Tet 33 flanked by active copies of the widespread insertion sequence IS6100. Plasmid. 2002;48:117–29. https://doi.org/10.1016/S1047-619X(02)00120-8

24. Chopra I, Roberts M. Tetracycline antibiotics: mode of action, applications, molecular biology, and epidemiology of bacterial resistance. Microbiol Mol Biol Rev. 2001;65:232–60. https://doi.org/10.1128/MMBR.65.2.232-260.2001

25. Targant H, Doublet B, Aarestrup FM, Cloeckaert A, Madec JY. IS6100-mediated genetic rearrangement within the complex class I integron In104 of the *Salmonella* genomic island 1. J Antimicrob Chemother. 2010;65:1543–5. https://doi.org/10.1038/jac.2010.161

26. Partridge SR, Secchella GD, Stokes HW, Hall RM. Family of class 1 integrons related to Inc4 from *Tn1696*. Antimicrob Agents Chemother. 2001;45:3041–20. https://doi.org/10.1128/AAC.45.11.3041-3020.2001

27. Huber L, Giguère S, Cohen ND, Slovis NM, Hanafi A, Schuckert A, et al. Prevalence and risk factors associated with emergence of *Rhodococcus equi* resistance to macrolides and rifampin in horse-breeding farms in Kentucky, USA. Vet Microbiol. 2019;235:243–7. https://doi.org/10.1016/j.vetmic.2019.07.010

28. Álvarez-Narváez S, Berghaus LJ, Morris ERA, Willingham-Lane JM, Slovis NM, Giguere S, et al. A common practice of widespread antimicrobial use in horse production promotes multi-drug resistance. Sci Rep. 2020;10:911. https://doi.org/10.1038/s41598-020-57479-9

29. Kilby ER. The demographics of the US equine population. In: Salem DJ, Rowan AN, editors. The state of the animals. Washington (DC): Human Society Press; 2007. p. 175–205.

30. Womble A, Giguère S, Lee EA. Pharmacokinetics of oral doxycycline and concentrations in body fluids and bronchoalveolar cells of foals. J Vet Pharmacol Ther. 2007;30:187–93. https://doi.org/10.1111/j.1365-2885.2007.00887.x
31. Collignon PJ, Conly JM, Andremont A, McEwen SA, Aidara-Kane A, Agerso Y, et al.; World Health Organization Advisory Group, Bogotá Meeting on Integrated Surveillance of Antimicrobial Resistance. World Health Organization ranking of antimicrobials according to their importance in human medicine: a critical step for developing risk management strategies to control antimicrobial resistance from food animal production. Clin Infect Dis. 2016;63:1087–93. https://doi.org/10.1093/cid/ciw475

32. Álvarez-Narváez S, Giguère S, Berghaus LJ, Dailey C, Vázquez-Boland JA. Horizontal spread of Rhodococcus equi macrolide resistance plasmid pRErm46 across environmental Actinobacteria. Appl Environ Microbiol. 2020;86:e00108–20. https://doi.org/10.1128/AEM.00108-20

33. Letek M, González P, Macarthur I, Rodríguez H, Freeman TC, Valero-Rello A, et al. The genome of a pathogenic Rhodococcus: cooptive virulence underpinned by key gene acquisitions. PLoS Genet. 2010;6:e1001145. https://doi.org/10.1371/journal.pgen.1001145

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- US CDC Real-Time Reverse Transcription PCR Panel for Detection of Severe Acute Respiratory Syndrome Coronavirus 2
- Investigation and Serologic Follow-Up of Contacts of an Early Confirmed Case-Patient with COVID-19, Washington, USA
- Characteristics and Outcomes of Coronavirus Disease Patients under Nonsurge Conditions, Northern California, USA, March–April 2020
- Tuberculosis in Internationally Displaced Children Resettling in Harris County, Texas, USA, 2010–2015
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- Rise in Babesiosis Cases, Pennsylvania, USA, 2005–2018
- Sporadic Creutzfeldt-Jakob Disease among Physicians, Germany, 1993–2018
- Population Genomic Structure and Recent Evolution of Plasmodium knowlesi, Peninsular Malaysia
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- Factors Associated with Prescription of Antimicrobial Drugs for Dogs and Cats, United Kingdom, 2014–2016
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### Appendix

**Appendix Table 1.** *R. equi* genomes used in study of multidrug–resistant *Rhodococcus equi*, United States

| Isolate   | Host | Isolation year | Origin | Resistance phenotype | Accession No. | Source (reference) |
|-----------|------|----------------|--------|----------------------|---------------|--------------------|
| PAM 2274  | Horse| 2011           | Kentucky | S                     | LWTV00000000  | (1)                |
| PAM 2276  | Horse| 2005           | Florida  | MR^R                 | MULW00000000  | (1)                |
| PAM 2277  | Horse| 2004           | Florida  | MR^S                 | MUMB00000000  | (1)                |
| PAM 2278  | Horse| 2002           | Florida  | MR^S                 | MUMA00000000  | (1)                |
| PAM 2279  | Horse| 2001           | Florida  | S                    | LWTS00000000  | (1)                |
| PAM 2280  | Horse| 2009           | Florida  | MR^R                 | MULW00000000  | (1)                |
| PAM 2281  | Horse| 2005           | Florida  | MR^R                 | MULT00000000  | (1)                |
| PAM 2282  | Horse| 2011           | Kentucky | S                    | LWTT00000000  | (1)                |
| PAM 2283  | Horse| 2002           | Florida  | MR^R                 | MULY00000000  | (1)                |
| PAM 2284  | Horse| 2005           | Florida  | MR^R                 | MUL20000000   | (1)                |
| PAM 2285  | Horse| 2005           | Florida  | MR^R                 | LWTU00000000  | (1)                |
| PAM 2286  | Horse| 2010           | Kentucky | MR^R                 | LWTV00000000  | (1)                |
| PAM 2287  | Horse| 2010           | New York | S                    | LWTW00000000  | (1)                |
| PAM 2288  | Horse| 2010           | Kentucky | MR^R                 | MUXK00000000  | (1)                |
| PAM 2289  | Horse| 2010           | Texas    | MR^R                 | MVDT00000000  | (1)                |
| PAM 2292  | Horse| 2011           | Kentucky | MR^R                 | MVDJ00000000  | (1)                |
| PAM 2293  | Horse| 2011           | Kentucky | MR^R                 | MVDV00000000  | (1)                |
| PAM 2294  | Horse| 2011           | Kentucky | MR^R                 | MVDQ00000000  | (1)                |
| PAM 2295  | Horse| 2011           | Kentucky | MR^R                 | MVDR00000000  | (1)                |
| PAM 2296  | Horse| 2011           | Florida  | MR^R                 | MUXJ00000000  | (1)                |
| CL_s145   | Horse| 2017           | Kentucky | S                    | SAMN13392178  | Current study      |
| CL_mdr146 | Horse| 2017           | Kentucky | MR^R                 | SAMN13392179  | Current study      |
| CL_mdr147 | Horse| 2017           | Kentucky | MR^R                 | SAMN13392180  | Current study      |
| CL_mdr148 | Horse| 2017           | Kentucky | MR^R                 | SAMN13392181  | Current study      |
| CL_s149   | Horse| 2017           | Kentucky | S                    | SAMN13392182  | Current study      |
| CL_s150   | Horse| 2017           | Kentucky | S                    | SAMN13392183  | Current study      |
| CL_s151   | Horse| 2017           | Kentucky | S                    | SAMN13392184  | Current study      |
| CL_mdr152 | Horse| 2017           | Kentucky | MR^R                 | SAMN13392185  | Current study      |
| CL_s153   | Horse| 2017           | Kentucky | S                    | SAMN13392186  | Current study      |
| CL_s154   | Horse| 2017           | Kentucky | S                    | SAMN13392187  | Current study      |
| CL_mdr155 | Horse| 2017           | Kentucky | MR^R                 | SAMN13392188  | Current study      |
| CL_mdr156 | Horse| 2017           | Kentucky | MR^R                 | SAMN13392189  | Current study      |
| CL_s157   | Horse| 2017           | Kentucky | S                    | SAMN13392190  | Current study      |
| CL_s158   | Horse| 2017           | Kentucky | S                    | SAMN13392191  | Current study      |
| CL_s159   | Horse| 2012           | New York  | S                    | SAMN13392192  | Current study      |
| CL_mdr160 | Horse| 2012           | New York  | MR^R                 | SAMN13392193  | Current study      |
| CL_mdr161 | Horse| 2013           | New York  | MR^R                 | SAMN13392194  | Current study      |
| CL_mdr162 | Horse| 2014           | New York  | MR^R                 | SAMN13392195  | Current study      |
| CL_mdr163 | Horse| 2014           | New York  | MR^R                 | SAMN13392196  | Current study      |
| CL_mdr164 | Horse| 2015           | Texas     | MR^R                 | SAMN13392197  | Current study      |
| CL_s166   | Horse| 2015           | Texas     | S                    | SAMN13392199  | Current study      |
| CL_s167   | Horse| 2015           | Texas     | R^S                  | SAMN13392200  | Current study      |
| CL_mdr168 | Horse| 2015           | Texas     | MR^R                 | SAMN13392201  | Current study      |
| CL_mdr169 | Horse| 2015           | Florida   | MR^R                 | SAMN13392202  | Current study      |
| CL_mdr170 | Horse| 2015           | Louisiana | M^R                 | SAMN13392203  | Current study      |
| CL_mdr171 | Horse| 2015           | Louisiana | MR^R                 | SAMN13392204  | Current study      |
| CL_mdr172 | Horse| 2015           | New York  | MR^R                 | SAMN13392205  | Current study      |
| CL_mdr173 | Horse| 2015           | New York  | MR^R                 | SAMN13392206  | Current study      |
| CL_mdr174 | Horse| 2015           | New York  | MR^R                 | SAMN13392207  | Current study      |
| CL_s175   | Horse| 2015           | Kentucky  | S                    | SAMN13392208  | Current study      |
| CL_s177   | Horse| 2015           | Kentucky  | S                    | SAMN13392210  | Current study      |
### Appendix Table 2. Susceptibility of macrolide–resistant (pRErm46/TnRErm46–carrying) *R. equi* isolates (2012–2017) to clinically relevant antimicrobials in equine medicine*  

| Isolate          | Host   | Isolation year | Origin | Resistance phenotype | Accession No. | Source (reference) | MIC μg/mL  | Phenotype | MIC μg/mL | Phenotype | MIC μg/mL |
|------------------|--------|----------------|--------|----------------------|---------------|-------------------|------------|-----------|-----------|-----------|-----------|
| CL_mdr178        | Horse  | 2015           | Kentucky | MR<sup>R</sup>       | SAMN13392211  | Current study     | 0.39 (0.125) | R         | 0.38 (0.19) | R         | 0.22 (0.064–0.38) |
| CL_s179          | Horse  | 2015           | Kentucky | S                    | SAMN13392212  | Current study     | –          | S         | –         | S         | –         |
| CL_mdr180        | Horse  | 2015           | Kentucky | MR<sup>R</sup>       | SAMN13392213  | Current study     | –          | R         | –         | –         | –         |
| CL_mdr181        | Horse  | 2016           | Kentucky | MR<sup>R</sup>       | SAMN13392214  | Current study     | –          | R         | –         | –         | –         |
| CL_s182          | Horse  | 2016           | Kentucky | S                    | SAMN13392215  | Current study     | –          | S         | –         | –         | –         |
| CL_mdr183        | Horse  | 2016           | Kentucky | MR<sup>R</sup>       | SAMN13392216  | Current study     | –          | R         | –         | –         | –         |
| CL_mdr184        | Horse  | 2016           | Kentucky | MR<sup>R</sup>       | SAMN13392217  | Current study     | –          | –         | –         | –         | –         |
| CL_mdr185        | Horse  | 2016           | Louisiana | M<sup>R</sup>     | SAMN13392218  | Current study     | –          | –         | –         | –         | –         |
| CL_s186          | Horse  | 2016           | Louisiana | S                    | SAMN13392219  | Current study     | 0.29 (0.19–0.38) | –         | –         | –         | –         | –         |
| CL_mdr187        | Horse  | 2016           | Louisiana | M<sup>R</sup>     | SAMN13392220  | Current study     | –          | –         | –         | –         | –         |
| CL_mdr188        | Horse  | 2017           | Louisiana | M<sup>R</sup>     | SAMN13392221  | Current study     | –          | –         | –         | –         | –         |
| CL_mdr189        | Horse  | 2017           | Louisiana | M<sup>R</sup>     | SAMN13392222  | Current study     | –          | –         | –         | –         | –         |
| CL_s190          | Horse  | 2017           | Louisiana | S                    | SAMN13392223  | Current study     | –          | S         | –         | –         | –         |
| CL_mdr191        | Horse  | 2017           | Louisiana | M<sup>R</sup>     | SAMN13392224  | Current study     | –          | –         | –         | –         | –         |
| CL_mdr192        | Horse  | 2017           | Louisiana | M<sup>R</sup>     | SAMN13392225  | Current study     | –          | –         | –         | –         | –         |
| CL_s193          | Horse  | 2017           | Louisiana | S                    | SAMN13392226  | Current study     | –          | S         | –         | –         | –         |
| CL_mdr194        | Horse  | 2017           | New York | M<sup>R</sup>      | SAMN13392227  | Current study     | –          | –         | –         | –         | –         |
| 103S             | Horse  | –              | Canada   | S                    | NCBI RefSeq   | –                 | –          | –         | –         | –         | –         |
| DSM20307<sup>T</sup> | Horse | –              | Sweden   | S                    | LWTX00000000  | (3)               | –          | –         | –         | –         | –         |
| ATCC33707        | Human  | –              | Canada   | S                    | NCBI RefSeq   | –                 | –          | –         | –         | –         | –         |
| PAM 1204         | Sheep  | –              | Canada   | S                    | LWBN00000000  | (3)               | –          | –         | –         | –         | –         |
| PAM 1216         | Horse  | –              | Mexico   | S                    | LWHS00000000  | (3)               | –          | –         | –         | –         | –         |
| PAM 1271         | Horse  | –              | Canada   | S                    | LWIC00000000  | (3)               | –          | –         | –         | –         | –         |
| PAM 1340         | Horse  | –              | France   | S                    | LWHT00000000  | (3)               | –          | –         | –         | –         | –         |
| PAM 1354         | Human  | –              | Japan    | S                    | LWHU00000000  | (3)               | –          | –         | –         | –         | –         |
| PAM 1357         | Horse  | –              | France   | S                    | LWHV00000000  | (3)               | –          | –         | –         | –         | –         |
| PAM 1413         | Human  | –              | Hungary  | S                    | LWWH00000000  | (3)               | –          | –         | –         | –         | –         |
| PAM 1422         | Horse  | –              | Hungary  | S                    | LWHX00000000  | (3)               | –          | –         | –         | –         | –         |
| PAM 1475         | Pig    | –              | Hungary  | S                    | LWYH00000000  | (3)               | –          | –         | –         | –         | –         |
| PAM 1496         | Pig    | –              | Hungary  | S                    | LWZH00000000  | (3)               | –          | –         | –         | –         | –         |
| PAM 1533         | Pig    | –              | Slovenia | S                    | LWIA00000000  | (3)               | –          | –         | –         | –         | –         |
| PAM 1557         | Bovine | –              | Ireland  | S                    | LWIB00000000  | (3)               | –          | –         | –         | –         | –         |
| PAM 1571         | Bovine | –              | Ireland  | S                    | LWTO00000000  | (3)               | –          | –         | –         | –         | –         |
| PAM 1572         | Bovine | –              | Ireland  | S                    | LXF00000000   | (3)               | –          | –         | –         | –         | –         |
| PAM 1593         | Human  | –              | Spain    | S                    | LXFH00000000  | (3)               | –          | –         | –         | –         | –         |
| PAM 1600         | Horse  | –              | Australia | S                    | LXFO00000000  | (3)               | –          | –         | –         | –         | –         |
| PAM 1637         | Horse  | –              | Australia | S                    | LWHR00000000  | (3)               | –          | –         | –         | –         | –         |
| PAM 1643         | Horse  | –              | Netherlands | S                    | LWTP00000000  | (3)               | –          | –         | –         | –         | –         |
| PAM 2012         | Bovine | –              | Germany  | S                    | LWTY00000000  | (3)               | –          | –         | –         | –         | –         |

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*MR*: macrolide resistant; *MR<sup>R</sup>*: macrolide and rifampin resistant; *R*: rifampin resistant; *S*: susceptible; –: data not available.

**Typical levels of macrolide resistance.** MICs > 64 μg/mL for clarithromycin, > 256 μg/mL for azithromycin and erythromycin; range 24 to >256 μg/mL (4). See Table (https://www4.cdc.gov/EID/article/27/3/20-2030–T1.htm) for tetracycline and doxycycline data. ND, not determined; *R*: resistant; *S*: susceptible.

<sup>T</sup>Determined by disk diffusion technique. Isolate percentage shown in parenthesis. Zone diameter susceptibility breakpoints based on Clinical and Laboratory Standards Institute interpretive criteria for *Staphylococcus aureus*, routinely used for *R. equi* susceptibility testing in the absence of specific approved criteria for this species (Table).

<sup>†</sup>Minimal inhibitory concentration determined by using Etest strips. Mean value (range in parenthesis).
References

1. Álvarez–Narváez S, Giguère S, Anastasi E, Hearn J, Scortti M, Vázquez–Boland JA. Clonal confinement of a highly mobile resistance element driven by combination therapy in *Rhodococcus equi*. MBio. 2019;10:e02260–19. PubMed https://doi.org/10.1128/mBio.02260–19

2. Letek M, González P, Macarthur I, Rodríguez H, Freeman TC, Valero–Rello A, et al. The genome of a pathogenic *Rhodococcus*: cooptive virulence underpinned by key gene acquisitions. PLoS Genet. 2010;6:e1001145. PubMed https://doi.org/10.1371/journal.pgen.1001145

3. Anastasi E, MacArthur I, Scortti M, Alvarez S, Giguère S, Vázquez–Boland JA. Pangenome and phylogenomic analysis of the pathogenic actinobacterium *Rhodococcus equi*. Genome Biol Evol. 2016;8:3140–8. PubMed https://doi.org/10.1093/gbe/evw222

4. Anastasi E, Giguère S, Berghaus LJ, Hondalus MK, Willingham–Lane JM, MacArthur I, et al. Novel transferable *erm*(46) determinant responsible for emerging macrolide resistance in *Rhodococcus equi*. J Antimicrob Chemother. 2015;70:3184–90. PubMed