CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

208083Orig1s000

MICROBIOLOGY/VIROLOGY REVIEW(S)

Division of Anti-Infective Products
Office of Antimicrobial Products
Clinical Microbiology Review

NDA: 208083 (SDN-005)
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Reviewer: Jalal U. Sheikh

APPLICANT

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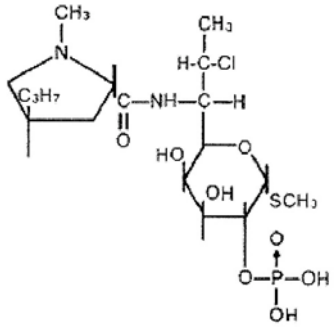
DRUG PRODUCT NAME

Proprietary Name:	N/A
Non-Proprietary Name:	Clindamycin in 0.9% Saline Injection (300 mg/50 mL, 600 mg/50 mL, and 900 mg/50 mL) in a GALAXY plastic container
Established Name:	Clindamycin
Chemical Name:	Clindamycin Phosphate, USP; L-*threo*-α-D-*galacto*-Octopyranoside, methyl-7-chloro-6,7,8-trideoxy-6-[[(1-methyl-4- propyl-2-pyrrolidinyl)carbonyl]amino]-1-thio-, 2-(dihydrogen phosphate), (2*S*-*trans*)-
Molecular Weight:	504.97 g/mol
Molecular Formula:	$C_{18}H_{34}ClN_2O_8PS$
Structural Formula:	

DRUG CATEGORY
Anti-bacterial

PROPOSED INDICATION(S)
Clindamycin is a lincosamide antibacterial indicated for the treatment of serious infections caused by susceptible anaerobic bacteria and also the following infections:

- Infections Due to Susceptible Strains of Streptococci, Pneumococci and Staphylococci.
- Lower Respiratory Tract Infections.
- Skin and Skin Structure Infections.
- Gynecological Infections.
- Intra-abdominal Infections.
- Septicemia.
- Bone and Joint Infections.

The proposed indications for the Applicant's product will be the same as the currently approved Referenced Listed Drug (RLD), CLEOCIN PHOSPHATE (Clindamycin Injection in 5% Dextrose, manufactured by Pfizer, formerly Pharmacia Upjohn) under NDA# 050639. It is important to note that the Applicant's product is IV formulation whereas the RLD has both IV and IM formulations.

PROPOSED DOSAGE FORM, STRENGTH, ROUTE OF ADMINISTRATION AND DURATION OF TREATMENT

Dosage Form	Injectable; sterile premixed solution
Route of Administration	Intravenous (IV) infusion
Dose Strength, and Duration	The concentration of clindamycin in diluent for infusion will not exceed 18 mg per mL. Infusion rates should not exceed 30 mg per minute. The usual infusion dilutions and rates are as follows: Dose / Diluent / Time 300 mg / 50 mL / 10 minutes 600 mg / 50 mL / 20 minutes 900 mg / 50 (b) (4) / 30 minutes 1200 mg / (b) (4) / (b) (4) Administration of more than 1200 mg (b) (4) infusion will not be recommended.

DISPENSED
Prescription Product

RELATED DOCUMENTS
NDA# 050639, Cleocin Phosphate (RLD)

REMARKS and CONCLUSIONS

The applicant submitted a NDA for approval of its proposed clindamycin injection by the 505(b)(2) regulatory pathway. The proposed indications for the applicant's formulation are same as the reference listed drug (RLD), CLEOCIN PHOSPHATE (Clindamycin Injection in 5% Dextrose, manufactured by Pfizer. The difference in the formulation between the Applicant's product and the RLD is the diluent; in 0.9% saline was used instead on 0.5% dextrose (for more details see Appendix-1).

No new microbiology data or information was included in this NDA. The microbiology section of the labeling for the Applicant's formulation is same as the RLD labeling (for details see Appendix-2). The RLD's labeling was last updated in (b) (4) 2016. The applicant's proposal is appropriate.

RECOMMENDATIONS

From microbiology standpoint, the NDA is approvable. Minor changes are recommended in the microbiology section of the labeling to be consistent with the current Division practice and the FDA's draft guidance document: "Microbiological Data for Systemic Antibacterial Drug Products-Development, Analysis and Presentation".

AGENCY'S PROPOSED LABELING

(Only sections 12.1 and 12.4 are shown below; addition to the Applicant's proposal are shown in red, and deletions as strikethrough)

12.1 Mechanism of Action

Clindamycin is an antibacterial drug [*see* (b) (4) ~~*Microbiology (12.4)*~~].

12.4 Microbiology

Mechanism of Action

Clindamycin inhibits bacterial protein synthesis by binding to the 23S RNA of the 50S subunit of the ribosome. Clindamycin is bacteriostatic.

Resistance

Resistance to clindamycin is most often caused by modification of specific bases of the 23S ribosomal RNA. Cross-resistance between clindamycin and lincomycin is complete. Because the binding sites for these antibacterial drugs overlap, cross-resistance is sometimes observed among lincosamides, macrolides and streptogramin B. Macrolide-inducible resistance to clindamycin occurs in some isolates of macrolide-resistant bacteria. Macrolide-resistant isolates of staphylococci and beta-hemolytic streptococci should be screened for induction of clindamycin resistance using the D-zone test.

Antimicrobial Activity

Clindamycin has been shown to be active against most of the isolates of the following microorganisms, both *in vitro* and in clinical infections [*see Indications and Usage (1)]*.

Aerobic bacteria

Gram-positive ~~Bacteria~~bacteria

Staphylococcus aureus (methicillin-susceptible strains)
Streptococcus pneumoniae (penicillin-susceptible strains)
Streptococcus pyogenes

Anaerobic bacteria

Gram-positive ~~Bacteria~~bacteria

Clostridium perfringens
Peptostreptococcus anaerobius

Gram-negative bacteria

Fusobacterium necrophorum
Fusobacterium nucleatum
Prevotella melaninogenica

The following *in vitro* data are available, but their clinical significance is unknown. At least 90~~%~~ percent of the following bacteria exhibit an *in vitro* minimum inhibitory concentration (MIC) less than or equal to the susceptible breakpoint for clindamycin against isolates of similar genus or organism group. However, the efficacy of clindamycin in treating clinical infections caused by these bacteria has not been established in adequate and well-controlled clinical trials.

Aerobic bacteria

Gram-positive ~~Bacteria~~bacteria

Staphylococcus epidermidis (methicillin-susceptible strains)
Streptococcus agalactiae
Streptococcus anginosus
Streptococcus mitis
Streptococcus oralis

Anaerobic ~~Bacteria~~bacteria

Gram-positive bacteria

Actinomyces israelii
Clostridium clostridioforme
Eggerthella lenta
Finegoldia (Peptostreptococcus) magna
Micromonas (Peptostreptococcus) micros
Propionibacterium acnes

Gram-negative bacteria

Prevotella bivia
Prevotella intermedia

Susceptibility Test [redacted] Methods

When available, the clinical microbiology laboratory should provide cumulative reports of *in vitro* susceptibility test results for antimicrobial drugs used in local hospitals and practice areas as periodic reports that describe the susceptibility profile of nosocomial and community-acquired pathogens. These reports should aid [redacted] in the selection of [redacted] an appropriate antibacterial drug for treatment.

Dilution Techniques

Quantitative methods are used to determine antimicrobial [redacted] MICs. These MICs provide estimates of the susceptibility of bacteria to antimicrobial compounds. The MICs should be determined using a standardized test method[2,3] (broth and/or agar). The MIC values should be interpreted according to [redacted] criteria provided in Table 2.

Diffusion Techniques

Quantitative methods that require the measurement of zone diameters can also provide reproducible estimates of the susceptibility of bacteria to antimicrobial compounds. The zone size should be determined using a standardized test method[2,5]. This procedure uses paper disks impregnated with 2 mcg of clindamycin to test the susceptibility of bacteria to clindamycin. The disk diffusion breakpoints are provided in Table 2.

Anaerobic Techniques

For anaerobic bacteria, the susceptibility to clindamycin can be determined by a standardized test method[2,4]. The MIC values obtained should be interpreted according to the criteria provided in Table 2.

Table 2. Susceptibility Test Interpretive Criteria for Clindamycin

Pathogen	Susceptibility Interpretive Criteria					
	[redacted] Minimum Inhibitory Concentrations ([redacted]-mcg/mL)			Disk Diffusion (~~Zone~~ zone ~~Diameters~~ diameters in mm)		
	S	I	R	S	I	R
Staphylococcus spp.	≤ 0.5	1–2	≥4	≥21	15–20	≤14
Streptococcus pneumoniae and other *Streptococcus* spp.	≤0.25	0.5	≥1	≥19	16–18	≤15
Anaerobic Bacteria	≤2	4	≥8	NA	NA	NA

NA = not applicable

A report of *Susceptible (S)* indicates that the antimicrobial drug is likely to inhibit growth of the pathogen if the antimicrobial drug reaches the concentration usually achievable at the site of infection. A report of *Intermediate (I)* indicates that the result should be considered equivocal, and, if the microorganism is not fully susceptible to alternative, clinically feasible drugs, the test should be repeated. This category implies possible clinical applicability in body sites where the drug is physiologically concentrated or in situations where high dosage of drug can be used. This category also provides a buffer

zone that prevents small, uncontrolled technical factors from causing major discrepancies in interpretation. A report of *Resistant (R)* indicates that the antimicrobial drug is not likely to inhibit growth of the pathogen if the antimicrobial drug reaches the concentration usually achievable at the infection site; other therapy should be selected.

Quality Control

Standardized susceptibility test procedures require the use of laboratory controls to monitor and ensure the accuracy and precision of the supplies and reagents used in the assay, and the techniques of the individuals performing the test[2,3,4,5]. Standard clindamycin powder should provide the following range of MIC (b) (4) values noted in Table 3. For the (b) (4) diffusion technique using the 2 mcg clindamycin disk, the criteria (b) (4) in Table 2 should be achieved.

Table 3. Acceptable Quality Control Ranges for Clindamycin

QC Strain	(b) (4)	
	Minimum Inhibitory Concentrations (b) (4) (mcg/mL)	**Disk Diffusion (b) (4) (~~Zone~~ zone ~~Diameters~~ diameters in mm)**
*Enterococcus faecalis** ATCC 29212	4–16	NA
Staphylococcus aureus ATCC 29213	0.06–0.25	NA
Staphylococcus aureus ATCC 25923	NA	24–30
Streptococcus pneumoniae ATCC 49619	0.03–0.12	19–25
Bacteroides fragilis ATCC 25285	0.5–2	NA
Bacteroides thetaiotaomicron ATCC 29741	2–8	NA
Clostridium difficile† ATCC 700057	2–8	NA
Eggerthella lenta ATCC 43055	0.06–0.25	NA

NA=Not applicable
ATCC® is a registered trademark of the American Type Culture Collection
* *Enterococcus faecalis* has been included in this table for quality control purposes only.
† Quality control for *C. difficile* is performed using the agar dilution method only, all other obligate anaerobes may be tested by either broth microdilution or agar dilution methods.

REFERENCES

2. CLSI. *Performance Standards for Antimicrobial Susceptibility Testing:* 27th ed. CLSI supplement M100S. Wayne, PA: Clinical and Laboratory Standards Institute; 2017.
3. CLSI. *Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria that Grow Aerobically; Approved Standard* - Tenth Edition. CLSI document M07-A10. Wayne, PA: Clinical and Laboratory Standards Institute; 2015.
4. CLSI. *Methods for Antimicrobial Susceptibility Testing of Anaerobic Bacteria; Approved Standard-Eighth Edition.* CLSI document M11-A8. Wayne, PA: Clinical and Laboratory Standards Institute; 2012.
5. CLSI. *Performance Standards for Antimicrobial Disk Susceptibility Tests; Approved Standard - Twelfth Edition*. CLSI document M02-A12. Wayne, PA: Clinical and Laboratory Standards Institute; 2015.

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Appendix-1

Comparison of RLD and Applicant's clindamycin drug products

The following key points are important when comparing the package inserts of RLD Clindamycin in 0.5% Dextrose and Applicant's Clindamycin in 0.9% Sodium Chloride (for more details see Table A):

- Applicant's product is only for IV formulation not for intramuscular injection, RLD has both IV and IM formulations;
- Both RLD (Cleocin Phosphate) and Applicant's (Clindamycin in 0.9% Sodium Chloride) products are indicated in the treatment of serious infections caused by susceptible anaerobic bacteria. However, both products are also indicated in the treatment of serious infections due to susceptible strains of streptococci, pneumococci, and staphylococci.

Table A. Comparison of Pfizer and Applicant's Clindamycin formulation (300 mg, 600 mg, and 900 mg/50 mL) Drug Products

Applicant	Pfizer (Reference Listed Drug)	Applicant (Proposed Drug)
Product	CLEOCIN PHOSPHATE IV Solution in a GALAXY plastic container is a sterile solution of clindamycin phosphate with 5% dextrose.	Clindamycin in 0.9% Saline Injection in a GALAXY plastic container is a sterile solution of clindamycin phosphate with 0.9% saline.
Active Ingredient	Clindamycin Phosphate, USP	Clindamycin Phosphate, USP
Total Drug Content	300 mg (as Clindamycin) 600 mg (as Clindamycin) 900 mg (as Clindamycin)	300 mg (as Clindamycin) 600 mg (as Clindamycin) 900 mg (as Clindamycin)
Diluent	5% w/v Hydrous Dextrose, USP (50 mg/mL)	0.9% w/v Sodium Chloride, USP (9 mg/mL)
Other Inactive Ingredients	Edetate Disodium Dihydrate, USP 2 mg/50 mL (0.04 mg/mL)	Edetate Disodium Dihydrate, USP 2 mg/50 mL (b) (4)
	pH Adjusted with Sodium Hydroxide and/or Hydrochloric Acid	pH Adjusted with Sodium Hydroxide and/or Hydrochloric Acid
	(b) (4)	Water for Injection, USP
Volume	50 mL in a GALAXY plastic container	50 mL in a GALAXY plastic container
Concentration	300 mg/50 mL (6 mg/mL) 600 mg/50 mL (12 mg/mL) 900 mg/50 mL (18 mg/mL)	300 mg/50 mL (6 mg/mL) 600 mg/50 mL (12 mg/mL) 900 mg/50 mL (18 mg/mL)
Dosage Form	Injectable; sterile solution (premixed)	Injectable; sterile solution (premixed)
Container Closure	Single-use plastic container (GALAXY), premixed sterile solution	Single-use plastic container (GALAXY), premixed sterile solution
Route of Administration	Injection: IV infusion	Injection: IV infusion
Dosing Regimen	The concentration of clindamycin in diluent for infusion should not exceed 18 mg per mL. Infusion rates should not exceed 30 mg per minute. The usual infusion rate for the 300 mg/50 mL dose is 10 minutes, 600 mg/50 mL dose is 20 minutes and 900 mg/50 mL is 30 minutes.	The concentration of clindamycin in diluent for infusion should not exceed 18 mg per mL. Infusion rates should not exceed 30 mg per minute The usual infusion rate for the 300 mg/50 mL dose is 10 minutes, 600 mg/50 mL dose is 20 minutes and 900 mg/50 mL is 30 minutes.

Appendix-2

Applicant's Annotated Labeling Comparison with RLD, Cleocin Phosphate(Only sections 12.4 Microbiology and Section 15 References are shown)

Microbiology	1	**12.3 Microbiology**
Mechanism of Action	1	*Mechanism of Action*
Clindamycin inhibits bacterial protein synthesis by binding to the 23S RNA of the 50S subunit of the ribosome. Clindamycin is bacteriostatic.		Clindamycin inhibits bacterial protein synthesis by binding to the 23S RNA of the 50S subunit of the ribosome. Clindamycin is bacteriostatic.
Resistance	1	*Resistance*
Resistance to clindamycin is most often caused by modification of specific bases of the 23S ribosomal RNA. Cross-resistance between clindamycin and lincomycin is complete. Because the binding sites for these antibacterial drugs overlap, cross-resistance is sometimes observed among lincosamides,		Resistance to clindamycin is most often caused by modification of specific bases of the 23S ribosomal RNA. Cross-resistance between clindamycin and lincomycin is complete. Because the binding sites for these antibacterial drugs overlap, cross-resistance is sometimes observed among lincosamides,

1 Celerity's product insert was updated per FDA labeling guidance and PLR format
4 Removed RLD's intramuscular injection information as Celerity is not pursuing intramuscular injection indication
6 Replaced "IV" to "intravenous" per FDA's labeling guidance

RLD Prescribing Information	Code	Proposed Celerity Pharmaceuticals' Prescribing Information
macrolides and streptogramin B. Macrolide-inducible resistance to clindamycin occurs in some isolates of macrolide-resistant bacteria. Macrolide-resistant isolates of staphylococci and beta-hemolytic streptococci should be screened for induction of clindamycin resistance using the D-zone test.		macrolides and streptogramin B. Macrolide-inducible resistance to clindamycin occurs in some isolates of macrolide-resistant bacteria. Macrolide-resistant isolates of staphylococci and beta-hemolytic streptococci should be screened for induction of clindamycin resistance using the D-zone test.
Antimicrobial Activity	1	*Antimicrobial Activity*
Clindamycin has been shown to be active against most of the isolates of the following microorganisms, both *in vitro* and in clinical infections, as described in the **INDICATIONS AND USAGE** section.	1	Clindamycin has been shown to be active against most of the isolates of the following microorganisms, both *in vitro* and in clinical infections, as described in the *INDICATIONS AND USAGE (1)* section.
Gram-positive Bacteria	1	• **Gram-positive Bacteria**
Staphylococcus aureus (methicillin-susceptible strains) *Streptococcus pneumoniae* (penicillin-susceptible strains) *Streptococcus pyogenes*		*Staphylococcus aureus* (methicillin-susceptible strains) *Streptococcus pneumoniae* (penicillin-susceptible strains) *Streptococcus pyogenes*
Anaerobic Bacteria	1	• **Anaerobic Bacteria**
Clostridium perfringens *Fusobacterium necrophorum* *Fusobacterium nucleatum* *Peptostreptococcus anaerobius* *Prevotella melaninogenica*		*Clostridium perfringens* *Fusobacterium necrophorum* *Fusobacterium nucleatum* *Peptostreptococcus anaerobius* *Prevotella melaninogenica*
At least 90% of the microorganisms listed below exhibit *in vitro* minimum inhibitory concentrations (MICs) less than or equal to the clindamycin susceptible MIC breakpoint for organisms of a similar type to those shown in Table 2. However, the efficacy of clindamycin in treating clinical infections due to these microorganisms has not been established in adequate and well-controlled clinical trials.		At least 90% of the microorganisms listed below exhibit *in vitro* minimum inhibitory concentrations (MICs) less than or equal to the clindamycin susceptible MIC breakpoint for organisms of a similar type to those shown in Table 2. However, the efficacy of clindamycin in treating clinical infections due to these microorganisms has not been established in adequate and well-controlled clinical trials.

1 Celerity's product insert was updated per FDA labeling guidance and PLR format

RLD Prescribing Information	Code	Proposed Celerity Pharmaceuticals' Prescribing Information
Gram-positive Bacteria *Staphylococcus epidermidis* (methicillin-susceptible strains) *Streptococcus agalactiae* *Streptococcus anginosus* *Streptococcus mitis* *Streptococcus oralis*	1	• **Gram-positive Bacteria** *Staphylococcus epidermidis* (methicillin-susceptible strains) *Streptococcus agalactiae* *Streptococcus anginosus* *Streptococcus mitis* *Streptococcus oralis*
Anaerobic Bacteria *Actinomyces israelii* *Clostridium clostridioforme* *Eggerthella lenta* *Finegoldia (Peptostreptococcus) magna* *Micromonas (Peptostreptococcus) micros* *Prevotella bivia* *Prevotella intermedia* *Propionibacterium acnes*	1	• **Anaerobic Bacteria** *Actinomyces israelii* *Clostridium clostridioforme* *Eggerthella lenta* *Finegoldia (Peptostreptococcus) magna* *Micromonas (Peptostreptococcus) micros* *Prevotella bivia* *Prevotella intermedia* *Propionibacterium acnes*
Susceptibility Testing Methods When available, the clinical microbiology laboratory should provide cumulative *in vitro* susceptibility test results for antimicrobial drugs used in local hospitals and practice areas to the physician as periodic reports that describe the susceptibility profile of nosocomial and community-acquired pathogens. These reports should aid the physician in selecting an antibacterial drug for treatment.	1	*Susceptibility Test* (b) (4) *Methods* When available, the clinical microbiology laboratory should provide cumulative *in vitro* susceptibility test results for antimicrobial drugs used in local hospitals and practice areas (b) (4) as periodic reports that describe the susceptibility profile of nosocomial and community-acquired pathogens. These reports should aid the physician in selecting an antibacterial drug for treatment.
Dilution Techniques Quantitative methods are used to determine antimicrobial minimum inhibitory concentrations (MICs). These MICs provide estimates of the	1	*Dilution Techniques* Quantitative methods are used to determine antimicrobial (b) (4) (b) (4) MICs (b) (4) These MICs provide estimates of the

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RLD Prescribing Information	Code	Proposed Celerity Pharmaceuticals' Prescribing Information
susceptibility of bacteria to antimicrobial compounds. The MICs should be determined using a standardized test method[2,3] (broth and/or agar). The MIC values should be interpreted according to the criteria provided in Table 2.		susceptibility of bacteria to antimicrobial compounds. The MICs should be determined using a standardized test method[2,3] (broth and/or agar). The MIC values should be interpreted according to (b) criteria provided in Table 2.
Diffusion Techniques Quantitative methods that require the measurement of zone diameters can also provide reproducible estimates of the susceptibility of bacteria to antimicrobial compounds. The zone size should be determined using a standardized method[2,5]. This procedure uses paper disks impregnated with 2 mcg of clindamycin to test the susceptibility of bacteria to clindamycin. The disk diffusion breakpoints are provided in Table 2.	1	*Diffusion Techniques* Quantitative methods that require the measurement of zone diameters can also provide reproducible estimates of the susceptibility of bacteria to antimicrobial compounds. The zone size should be determined using a standardized method[2,5]. This procedure uses paper disks impregnated with 2 mcg of clindamycin to test the susceptibility of bacteria to clindamycin. The disk diffusion breakpoints are provided in Table 2.
Anaerobic Techniques For anaerobic bacteria, the susceptibility to clindamycin can be determined by a standardized test method[2,4]. The MIC values obtained should be interpreted according to the criteria provided in Table 2.	1	*Anaerobic Techniques* For anaerobic bacteria, the susceptibility to clindamycin can be determined by a standardized test method[2,4]. The MIC values obtained should be interpreted according to the criteria provided in Table 2.

Table 2. Susceptibility Interpretive Criteria for Clindamycin

Pathogen	Susceptibility Interpretive Criteria: Minimal Inhibitory Concentrations (MIC in mcg/mL)			Susceptibility Interpretive Criteria: Disk Diffusion (Zone Diameters in mm)		
	S	I	R	S	I	R
Staphylococcus spp.	≤ 0.5	1–2	≥4	≥21	15–20	≤14
Streptococcus pneumonia and other *Streptococcus* spp.	≤0.25	0.5	≥1	≥19	16–18	≤15
Anaerobic Bacteria	≤2	4	≥8	NA	NA	NA

NA = not applicable

Table 2. Susceptibility Interpretive Criteria for Clindamycin

Pathogen	Susceptibility Interpretive Criteria: (b) (4) Inhibitory Concentrations (b) (4) mcg/mL)			Susceptibility Interpretive Criteria: Disk Diffusion (Zone Diameters in mm)		
	S	I	R	S	I	R
Staphylococcus spp.	≤ 0.5	1–2	≥4	≥21	15–20	≤14
Streptococcus pneumonia and other *Streptococcus* spp.	≤0.25	0.5	≥1	≥19	16–18	≤15
Anaerobic Bacteria	≤2	4	≥8	NA	NA	NA

NA = not applicable

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RLD Prescribing Information	Code	Proposed Celerity Pharmaceuticals' Prescribing Information
A report of *Susceptible (S)* indicates that the antimicrobial drug is likely to inhibit growth of the pathogen if the antimicrobial drug reaches the concentration usually achievable at the site of infection. A report of *Intermediate (I)* indicates that the result should be considered equivocal, and, if the microorganism is not fully susceptible to alternative, clinically feasible drugs, the test should be repeated. This category implies possible clinical applicability in body sites where the drug is physiologically concentrated or in situations where high dosage of drug can be used. This category also provides a buffer zone that prevents small, uncontrolled technical factors from causing major discrepancies in interpretation. A report of *Reststant (R)* indicates that the antimicrobial drug is not likely to inhibit growth of the pathogen if the antimicrobial drug reaches the concentration usually achievable at the infection site; other therapy should be selected.		A report of *Susceptible (S)* indicates that the antimicrobial drug is likely to inhibit growth of the pathogen if the antimicrobial drug reaches the concentration usually achievable at the site of infection. A report of *Intermediate (I)* indicates that the result should be considered equivocal, and, if the microorganism is not fully susceptible to alternative, clinically feasible drugs, the test should be repeated. This category implies possible clinical applicability in body sites where the drug is physiologically concentrated or in situations where high dosage of drug can be used. This category also provides a buffer zone that prevents small, uncontrolled technical factors from causing major discrepancies in interpretation. A report of *Resistant (R)* indicates that the antimicrobial drug is not likely to inhibit growth of the pathogen if the antimicrobial drug reaches the concentration usually achievable at the infection site; other therapy should be selected.
Quality Control	1	*Quality Control*
Standardized susceptibility test procedures require the use of laboratory controls to monitor and ensure the accuracy and precision of the supplies and reagents used in the assay, and the techniques of the individuals performing the test[2,3,4,5]. Standard clindamycin powder should provide the MIC ranges in Table 3. For the disk diffusion technique using the 2 mcg clindamycin disk the criteria provided in Table 2 should be achieved.		Standardized susceptibility test procedures require the use of laboratory controls to monitor and ensure the accuracy and precision of the supplies and reagents used in the assay, and the techniques of the individuals performing the test[2,3,4,5]. Standard clindamycin powder should provide the MIC ranges in Table 3. For the disk diffusion technique using the 2 mcg clindamycin disk the criteria provided in Table 2 should be achieved.

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RLD Prescribing Information	Code	Proposed Celerity Pharmaceuticals' Prescribing Information
Table 3. Acceptable Quality Control Ranges for Clindamycin		**Table 3. Acceptable Quality Control Ranges for Clindamycin**
QC Strain / Acceptable Quality Control Ranges: Minimum Inhibitory Concentration Range (mcg/mL) / Disk Diffusion Range (Zone Diameters in mm)		QC Strain / (b) (4) (b) (4) / Minimum Inhibitory Concentration Range (mcg/mL) / Disk Diffusion (Zone Diameters in mm)
*Enterococcus faecalis** ATCC 29212 — 4–16 — NA		*Enterococcus faecalis** ATCC 29212 — 4–16 — NA
Staphylococcus aureus ATCC 29213 — 0.06–0.25 — NA		*Staphylococcus aureus* ATCC 29213 — 0.06–0.25 — NA
Staphylococcus aureus ATCC 25923 — NA — 24–30		*Staphylococcus aureus* ATCC 25923 — NA — 24–30
Streptococcus pneumoniae ATCC 49619 — 0.03–0.12 — 19–25		*Streptococcus pneumoniae* ATCC 49619 — 0.03–0.12 — 19–25
Bacteroides fragilis ATCC 25285 — 0.5–2 — NA		*Bacteroides fragilis* ATCC 25285 — 0.5–2 — NA
Bacteroides thetaiotaomicron ATCC 29741 — 2–8 — NA		*Bacteroides thetaiotaomicron* ATCC 29741 — 2–8 — NA
Clostridium difficile† ATCC 700057 — 2–8 — NA		*Clostridium difficile*† ATCC 700057 — 2–8 — NA
Eggerthella lenta ATCC 43055 — 0.06–0.25 — NA		*Eggerthella lenta* ATCC 43055 — 0.06–0.25 — NA
NA=Not applicable ATCC® is a registered trademark of the American Type Culture Collection * *Enterococcus faecalis* has been included in this table for quality control purposes only. † Quality control for *C. difficile* is performed using the agar dilution method only, all other obligate anaerobes may be tested by either broth microdilution or agar dilution methods.		NA=Not applicable ATCC® is a registered trademark of the American Type Culture Collection * *Enterococcus faecalis* has been included in this table for quality control purposes only. † Quality control for *C. difficile* is performed using the agar dilution method only, all other obligate anaerobes may be tested by either broth microdilution or agar dilution methods.
REFERENCES	1	**15 REFERENCES**
1. Smith RB, Phillips JP: Evaluation of CLEOCIN HCl and CLEOCIN Phosphate in an Aged Population. Upjohn TR 8147-82-9122-021, December 1982. 2. CLSI. *Performance Standards for Antimicrobial Susceptibility Testing:* 26th ed. CLSI supplement M100S. Wayne, PA: Clinical and Laboratory Standards Institute; 2016. 3. CLSI. *Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria that Grow Aerobically; Approved Standard* - Tenth Edition. CLSI document M07-A10. Wayne, PA: Clinical and Laboratory Standards Institute; 2015. 4. CLSI. *Methods for Antimicrobial Susceptibility Testing of Anaerobic Bacteria; Approved Standard-Eighth Edition.* CLSI document M11-A8. Wayne, PA: Clinical and Laboratory Standards Institute; 2012.		1. Smith RB, Phillips JP: Evaluation of CLEOCIN HCl and CLEOCIN Phosphate in an Aged Population. Upjohn TR 8147-82-9122-021, December 1982. 2. CLSI. *Performance Standards for Antimicrobial Susceptibility Testing:* 26th ed. CLSI supplement M100S. Wayne, PA: Clinical and Laboratory Standards Institute; 2016. 3. CLSI. *Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria that Grow Aerobically; Approved Standard* - Tenth Edition. CLSI document M07-A10. Wayne, PA: Clinical and Laboratory Standards Institute; 2015. 4. CLSI. *Methods for Antimicrobial Susceptibility Testing of Anaerobic Bacteria; Approved Standard-Eighth Edition.* CLSI document M11-A8. Wayne, PA: Clinical and Laboratory Standards Institute; 2012.

1 Celerity's product insert was updated per FDA labeling guidance and PLR format
28 "13 NONCLINICAL TOXICOLOGY" heading was added to Celerity's product insert per FDA labeling guidance and PLR format

RLD Prescribing Information	Code	Proposed Celerity Pharmaceuticals' Prescribing Information
5. CLSI. *Performance Standards for Antimicrobial Disk Susceptibility Tests; Approved Standard - Twelfth Edition.* CLSI document M02-A12. Wayne, PA: Clinical and Laboratory Standards Institute; 2015.		5. CLSI. *Performance Standards for Antimicrobial Disk Susceptibility Tests; Approved Standard - Twelfth Edition.* CLSI document M02-A12. Wayne, PA: Clinical and Laboratory Standards Institute; 2015.

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JALAL U SHEIKH
04/10/2017

SHUKAL BALA
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