

## EUCAST form for General Consultation

Consultation on: **Breakpoints for anaerobic bacteria** (ending on 15 November 2021)  
EUCAST responses to consultation comments.

Comment from (name, contact details)	Comments	EUCAST Response
NZ NAC (Juliet.Elvy@medlabsouth.co.nz)	<p>Any suggested additional species? Suggest additional Clostridium sp (tertium, septicum) and Peptostreptococcus.</p> <p>Any additional agents? Suggest ceftriaxone, cefazolin, amoxicillin</p> <p>Method looks straightforward!</p>	<p>EUCAST has decided to extend the panel of agents and species.</p> <p>In answer to several similar comments, EUCAST decided to further develop the guidance document on "<a href="#">When there are no breakpoints</a>" and to include specific advice on anaerobic bacteria not part of the current revision.</p> <p>Currently amoxicillin, amoxicillin-clavulanic acid and imipenem are discussed, and we will consider adding ceftriaxone, at least for some species. Cefazoline has not been discussed.</p> <p>Other species were discussed and ranked in order of importance and frequency. These are now for future development.</p>
Barbara Holzkecht on behalf of the Danish NAC (DANRES-M)	DANRES-M welcomes the development of a EUCAST disk diffusion methodology for selected rapidly growing anaerobic bacteria and appreciates the great work being done.	The EUCAST Steering Committee has already decided to prioritize extending the list of agents - see above.

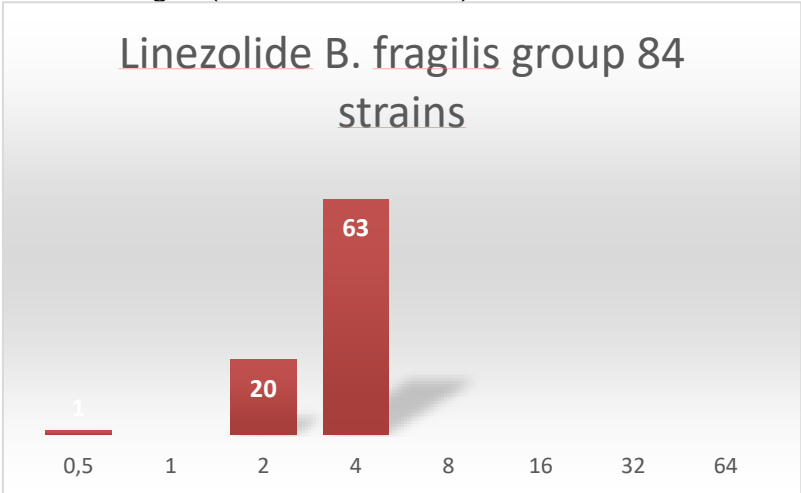
## EUCAST form for General Consultation

<p>barbara.juliane.holzknacht@regionh.dk</p>	<p>We notice that some of the distributions, on which the presumptive ECOFFs are based are rather small and some breakpoints are set conservatively, only one dilution step above the mode MIC, for example <i>F. necrophorum</i>/ benzylpenicillin and meropenem. Is this a potential problem which could result in mis-categorization of wildtype isolates due to technical variation?</p> <p>Regarding future development of clinical breakpoints for anaerobes, we request breakpoints for amoxicillin. These are relevant e.g. with regards to p.o. treatment of <i>C. acnes</i> prosthetic joint infections. MIC-distributions from available studies suggest low MIC<sub>90</sub> for amoxicillin of 0,12 mg/L<sup>1</sup> and amoxicillin p.o. treatment is suggested in international treatment guidelines <sup>2,3</sup>. Amoxicillin breakpoints will also be relevant for <i>Actinomyces</i> spp. and Gram-positive anaerobic cocci.</p> <p>We suggest that species to be prioritized for breakpoint development in the future include <i>Actinomyces</i> spp., Gram-positive anaerobic cocci and <i>Clostridium</i> species other than <i>C. perfringens</i>.</p> <p><sup>1</sup>Foster AL et al. Cutibacterium acnes in shoulder surgery: a scoping review of strategies for prevention, diagnosis, and treatment. J Shoulder Elbow Surg. 2021 Jun;30(6):1410-1422.</p> <p><sup>2</sup>W. Zimmerli and P. Sendi: Orthopedic Implant–Associated Infections; in: Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases, 9<sup>th</sup> ed. 2019.</p> <p><sup>3</sup>Osmon DR et al. Diagnosis and management of prosthetic joint infection: clinical practice guidelines by the Infectious Diseases Society of America. Clin Infect Dis. 2013 Jan;56(1):e1-e25.</p>	<p>Inhibition zone diameters on MIC distributions (<a href="#">similar to those already on the website for other species</a> and always part of any new development) were constructed for all of the agents and species which were part of the consultation. However, these were not posted at the time of the consultation but will be made available in January 2022. They will strengthen the EUCAST proposed clinical breakpoints and the ECOFFs used for the development.</p> <p>A discussion as to which anaerobic species to include in further development of the methodology is ongoing.</p> <p>We would welcome statistics where the frequency of isolation of other anaerobic species are listed in relation to the 5 now included.</p> <p>EUCAST aims to develop methods only for species which will grow well on FAA in 16-20h.</p> <p>We have discussed other species (see comment above).</p> <p><b>Actinomyces</b> is a large and heterogenous group and we encourage colleagues to submit their interest to help put together a well-defined collection of isolates to be used</p>
--	--	---

## EUCAST form for General Consultation

		<p>for the development of MIC distributions, defining of ECOFFs, testing of methodology and the setting of breakpoints.</p> <p>In answer to several similar comments, EUCAST decided to further develop the guidance document on "<a href="#">When there are no breakpoints</a>" and to include specific advice on anaerobic bacteria not part of the current revision.</p>
<p>CA-SFM lucdubreui4@gmail.com</p>	<p>Required suggestion by EUCAST for Extension of study</p> <p>Needs are: Antibiotics to add: Amoxicillin clavulanic acid most used anti-anaerobic agent Amoxicillin (most used antibiotic both orally or IV for gram positive anaerobes and can separates <math>\beta</math>-lactamase + <i>Prevotella</i> from <math>\beta</math>-lactamase neg <i>Prevotella</i> Imipenem Ertapenem not very useful</p> <p>Bacteria to add Gram positive cocci and clostridia other than <i>C. perfringens</i> and <i>C. difficile</i> including resistant <i>Enterocoster spp.</i>(previously clostridia of the RIC group) are very frequent among anaerobic infections.</p>	<p>Thank you for these proposals. They are in line with other proposals, and we shall look into the feasibility of determining breakpoints and disk diffusion 16-20h correlates. Our development is restricted to species that show good growth on FAA in 16-20h.</p> <p>With the experience of the CA-SFM committee could you provide a frequency table of anaerobic species frequently isolated from relevant infections? This would help us prioritise extensions and we will invest efforts only where the return is proportional to the money and work that are needed.</p>
<p>CA-SFM</p>	<p>As linezolid is used in bone infection, diabetic foot infections and in case of multidrug resistance (including resistance to metronidazole and carbapenems and clindamycin) a breakpoint for all anaerobes (even without a diameter) is needed and easy to set up : 4mg/L</p>	<p>Linezolid may be considered for <i>Cutibacterium acnes</i> and other grampositive species.</p>

## EUCAST form for General Consultation

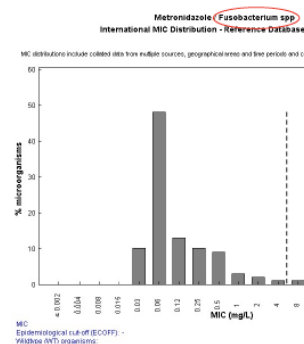
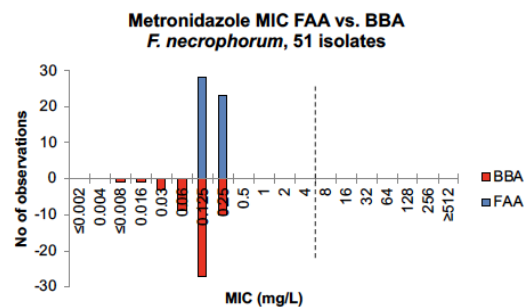
	<p>All anaerobes are inhibited by 4mg/l of linezolid. Only <i>C. ramosum</i> had MIC of 8mg/L (intrinsic resistance)</p>  <table border="1"> <caption>Linezolid MIC distribution for B. fragilis group (n=84)</caption> <thead> <tr> <th>MIC (mg/L)</th> <th>Number of Strains</th> </tr> </thead> <tbody> <tr> <td>0,5</td> <td>1</td> </tr> <tr> <td>2</td> <td>20</td> </tr> <tr> <td>4</td> <td>63</td> </tr> </tbody> </table>	MIC (mg/L)	Number of Strains	0,5	1	2	20	4	63	<p>Thank you for contributing MICs (see query below) for linezolid and suggesting a breakpoint. We will certainly consider this during 2022.</p> <p>An ECOFF of 4 mg/L seems very reasonable – 2 or 4 mg/L are the ECOFFs and clinical breakpoints of almost all species relevant to linezolid.</p> <p>Linezolid MIC-values – how were the MIC-values determined? We would appreciate knowing the methodology and agar used.</p>
MIC (mg/L)	Number of Strains									
0,5	1									
2	20									
4	63									
<p>CA-SFM (lucdubreui4@gmail.com)</p>	<p>Microbiologists tell us that EUCAST leads to <b>too many subdivisions</b> in species</p> <p>1 - For anaerobes probably a separation in two groups will fit well either Gram + and Gram - or <i>B. fragilis</i> and other anaerobes Metronidazole at 4 mg/L breakpoint will be ok for all anaerobic strains, backed by clinical data. TECOFF for <i>F. necrophorum</i> 0.5 mg/L will not fit with other fusobacteria such as <i>F. varium</i> for which the EUCAST data shows a different distribution see below. Proposal 4mg/L for fusobacteria (it has been done for Vibrio)</p>	<p>The EUCAST Steering Committee decided early in the review of breakpoints for anaerobic bacteria to base breakpoints on MIC distributions and ECOFFs of each species and for commonly isolated species which will grow in 16-20h on FAA the medium. Our experience over the years with developing methodology and breakpoints for other species has been not to lump species without first having studied each species to make sure this is possible. We have had unfortunate experience (now righted) with <i>Corynebacterium</i> spp, <i>Enterococcus</i> spp, <i>Staphylococcus</i> spp, to mention a few.</p>								

## EUCAST form for General Consultation

Antimicrobial agent*	Bacteroides spp.	Prevotella spp.	F. necrophorum	C. perfringens	C. ac
Metronidazole	4/4 E 4	4/4 E 4	0.5/0.5 E 0.5	4/4 E 4	

# Metronidazole

**Proposed breakpoints: 0.5/0.5 mg/L**



**Proposal 4 mg/l for all anaerobes**

We strive to avoid wide gaps between WT organisms and the clinical breakpoint. We thereby avoid having resistance development go undetected. Many of the current EUCAST breakpoints for anaerobes are from the early 2000 and several are “high” in relation to (a) revised breakpoints for other species and (b) wild type distributions of the most important anaerobic species and in some cases (c) also in relation to PK/PD breakpoints.

The discrepancy between the F. necrophorum metronidazole ECOFF of 0.5 and a clinical breakpoint of 4 mg/L leaves room for uncontrolled resistance development, which is why (see above) EUCAST decided to favour a specific clinical breakpoint of 0.5 for this species.

In recent years microbiologists have improved their ability to assign a correct species diagnosis by using MALDI-TOF, also for anaerobic bacteria. So today EUCAST sees little reason not to respect the individuality of the different species.

CA-SFM

2- **Simplification** and grouping of species on a common breakpoint will not change the face of the world  
In red no change needed

When embarking on the revision of breakpoints for anaerobic bacteria, the steering committee decided to primarily honour the wild type distributions of each

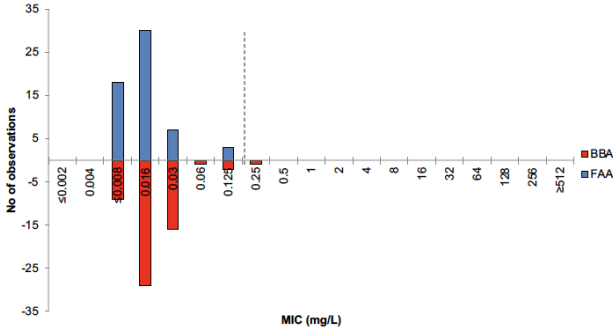
## EUCAST form for General Consultation

	Antimicrobial agent <sup>1</sup>	<i>Prevotella</i> spp.	<i>F. necrophorum</i>	<i>C. perfringens</i>	<i>C. acnes</i>	CA-SFM proposed common breakpoint	
	Benzylpenicillin	0.5/0.5 E 0.5	0.06/0.06 E 0.06	0.5/0.5 E 0.5	0.06/0.06 E 0.06		
Piperacillin-tazobactam	0.5/0.5 E 0.5	0.5/0.5 E 0.12	0.5/0.5 E 0.5	0.25/0.25 E 0.06	0.5		
Meropenem	0.25/0.25 E 0.25	0.03/0.03 E 0.03	0.12/0.12 E 0.06	0.12/0.12 E 0.12	0.25		
Vancomycin	-	-	2/2 E pending	2/2 E pending	2		
Clindamycin	0.25/0.25 E 0.06	0.25/0.25 E 0.12 – 0.25	0.25/0.25 E 0.25	0.25/0.25 E 0.25	0.25		
Metronidazole	4/4 E 4	0.5/0.5 E 0.5	4/4 E 4	-	4		
CA-SFM	<p><b>B. fragilis group</b></p> <p>Ok for clindamycin and metronidazole Piperacillin tazobactam may be 8/16 mg/L is possible. Higher dosage and continuous infusion (high exposure) may authorizes a breakpoint of 8/16 according to dosage. B . <i>fragilis</i> group 8 mg/L</p>					EUCAST found no evidence to favour a breakpoint of 16 mg/L. For other species EUCAST has abandoned 16 mg/L as a reasonable breakpoint. For Enterobacterales the breakpoint is today 8/8 mg/L and for other species even lower. EUCAST aimed to	

## EUCAST form for General Consultation

	<p>breakpoint for S (corresponding to T &gt; MIC 40% at 4g/8h) is ok. If we have and R breakpoint at 16 mg/L to avoid splitting the distribution a higher dosage of 4g/6h allows PTA of &gt;90% for 16 mg/L</p> <p>Remind that MONTE CARLO simulations do not take account the intrinsic activity of tazobactam on anaerobes in synergy with piperacillin independently of <math>\beta</math>-lactamase production like for <i>C. perfringens</i> and GPAC</p> <p><b>Another way is 0,0001/16 mg/L for fragilis group to reach higher dosage</b></p>	<p>handle Bacteroides in the same way as Enterobacterales. Infections with Bacteroides are often in combinations with infections with Enterobacterales and dosing and exposure should be the same for both.</p>
CA-SFM	<p>4 - Meropenem and <i>C. perfringens</i> Breakpoints are used to reach a clinical categorisation. <u>Values are independent of any reference method, microbroth dilution, agar dilution.</u> Using 0.125 mg/L as breakpoints lead to some resistant strains using Brucella agar (CLSI ). Breakpoints may not be the highest value of MIC determined on FAA on a limited number of strains. Proposal: <b>a 0.5 mg/L breakpoint will be a simplification for all anaerobes except the B. fragilis group</b></p>	<p>EUCAST disagrees with the statement that values are independent of method. Many factors influence the MIC, the MIC distributions, the ECOFF and thus also the clinical MIC breakpoints (media, media manufacturer, pH, cations etc). We are confident that the distributions produced as part of (and later checked and double checked) the recently concluded 17-clinical laboratory-trial represent the correct MICs for FAA medium, which was used throughout the development. MICs on FAA and BBA were very similar, as was shown in the material submitted for consultation, provided the organisms grew well on BBA, which was not always the case. Having looked at BBA from</p>

## EUCAST form for General Consultation

	<p style="text-align: center;"><b>Meropenem</b></p> <p style="text-align: center; border: 1px solid black; padding: 2px;">Proposed breakpoints: 0.125/0.125 mg/L</p> <p style="text-align: center;">Meropenem MIC FAA vs. BBA <i>C. perfringens</i>, 58 isolates</p>  <table border="1"> <caption>Meropenem MIC Data (Estimated from Chart)</caption> <thead> <tr> <th>MIC (mg/L)</th> <th>FAA Observations</th> <th>BBA Observations</th> </tr> </thead> <tbody> <tr><td>0.002</td><td>0</td><td>0</td></tr> <tr><td>0.004</td><td>0</td><td>0</td></tr> <tr><td>0.008</td><td>18</td><td>-18</td></tr> <tr><td>0.016</td><td>30</td><td>-30</td></tr> <tr><td>0.032</td><td>10</td><td>-10</td></tr> <tr><td>0.064</td><td>2</td><td>-2</td></tr> <tr><td>0.128</td><td>2</td><td>-2</td></tr> <tr><td>0.256</td><td>0</td><td>0</td></tr> <tr><td>0.512</td><td>0</td><td>0</td></tr> <tr><td>1.024</td><td>0</td><td>0</td></tr> <tr><td>2.048</td><td>0</td><td>0</td></tr> <tr><td>4.096</td><td>0</td><td>0</td></tr> <tr><td>8.192</td><td>0</td><td>0</td></tr> <tr><td>16.384</td><td>0</td><td>0</td></tr> <tr><td>32.768</td><td>0</td><td>0</td></tr> <tr><td>65.536</td><td>0</td><td>0</td></tr> <tr><td>131.072</td><td>0</td><td>0</td></tr> <tr><td>262.144</td><td>0</td><td>0</td></tr> <tr><td>524.288</td><td>0</td><td>0</td></tr> <tr><td>1048.576</td><td>0</td><td>0</td></tr> <tr><td>2097.152</td><td>0</td><td>0</td></tr> <tr><td>4194.304</td><td>0</td><td>0</td></tr> <tr><td>8388.608</td><td>0</td><td>0</td></tr> <tr><td>16777.216</td><td>0</td><td>0</td></tr> <tr><td>33554.432</td><td>0</td><td>0</td></tr> <tr><td>67108.864</td><td>0</td><td>0</td></tr> <tr><td>134217.728</td><td>0</td><td>0</td></tr> <tr><td>268435.456</td><td>0</td><td>0</td></tr> <tr><td>536870.912</td><td>0</td><td>0</td></tr> <tr><td>1073741.824</td><td>0</td><td>0</td></tr> <tr><td>2147483.648</td><td>0</td><td>0</td></tr> <tr><td>4294967.296</td><td>0</td><td>0</td></tr> <tr><td>8589934.592</td><td>0</td><td>0</td></tr> <tr><td>17179869.184</td><td>0</td><td>0</td></tr> <tr><td>34359738.368</td><td>0</td><td>0</td></tr> <tr><td>68719476.736</td><td>0</td><td>0</td></tr> <tr><td>137438953.472</td><td>0</td><td>0</td></tr> <tr><td>274877906.944</td><td>0</td><td>0</td></tr> <tr><td>549755813.888</td><td>0</td><td>0</td></tr> <tr><td>1099511627.776</td><td>0</td><td>0</td></tr> <tr><td>2199023255.552</td><td>0</td><td>0</td></tr> <tr><td>4398046511.104</td><td>0</td><td>0</td></tr> <tr><td>8796093022.208</td><td>0</td><td>0</td></tr> <tr><td>17592186044.416</td><td>0</td><td>0</td></tr> <tr><td>35184372088.832</td><td>0</td><td>0</td></tr> <tr><td>70368744177.664</td><td>0</td><td>0</td></tr> <tr><td>140737488355.328</td><td>0</td><td>0</td></tr> <tr><td>281474976710.656</td><td>0</td><td>0</td></tr> <tr><td>562949953421.312</td><td>0</td><td>0</td></tr> <tr><td>1125899906842.624</td><td>0</td><td>0</td></tr> <tr><td>2251799813685.248</td><td>0</td><td>0</td></tr> <tr><td>4503599627370.496</td><td>0</td><td>0</td></tr> <tr><td>9007199254740.992</td><td>0</td><td>0</td></tr> <tr><td>18014398509481.984</td><td>0</td><td>0</td></tr> <tr><td>36028797018963.968</td><td>0</td><td>0</td></tr> <tr><td>72057594037927.936</td><td>0</td><td>0</td></tr> <tr><td>144115188075855.872</td><td>0</td><td>0</td></tr> <tr><td>288230376151711.744</td><td>0</td><td>0</td></tr> <tr><td>576460752303423.488</td><td>0</td><td>0</td></tr> <tr><td>1152921504606846.976</td><td>0</td><td>0</td></tr> <tr><td>2305843009213693.952</td><td>0</td><td>0</td></tr> <tr><td>4611686018427387.904</td><td>0</td><td>0</td></tr> <tr><td>9223372036854775.808</td><td>0</td><td>0</td></tr> <tr><td>18446744073709551.616</td><td>0</td><td>0</td></tr> <tr><td>36893488147419103.232</td><td>0</td><td>0</td></tr> <tr><td>73786976294838206.464</td><td>0</td><td>0</td></tr> <tr><td>147573952589676412.928</td><td>0</td><td>0</td></tr> <tr><td>295147905179352825.856</td><td>0</td><td>0</td></tr> <tr><td>590295810358705651.712</td><td>0</td><td>0</td></tr> <tr><td>1180591620717411303.424</td><td>0</td><td>0</td></tr> <tr><td>2361183241434822606.848</td><td>0</td><td>0</td></tr> <tr><td>4722366482869645213.696</td><td>0</td><td>0</td></tr> <tr><td>9444732965739290427.392</td><td>0</td><td>0</td></tr> <tr><td>18889465931478580854.784</td><td>0</td><td>0</td></tr> <tr><td>37778931862957161709.568</td><td>0</td><td>0</td></tr> <tr><td>75557863725914323419.136</td><td>0</td><td>0</td></tr> <tr><td>151115727451828646838.272</td><td>0</td><td>0</td></tr> <tr><td>302231454903657293676.544</td><td>0</td><td>0</td></tr> <tr><td>604462909807314587353.088</td><td>0</td><td>0</td></tr> <tr><td>1208925819614629174706.176</td><td>0</td><td>0</td></tr> <tr><td>2417851639229258349412.352</td><td>0</td><td>0</td></tr> <tr><td>4835703278458516698824.704</td><td>0</td><td>0</td></tr> <tr><td>9671406556917033397649.408</td><td>0</td><td>0</td></tr> <tr><td>19342813113834066795298.816</td><td>0</td><td>0</td></tr> <tr><td>38685626227668133590597.632</td><td>0</td><td>0</td></tr> <tr><td>77371252455336267181195.264</td><td>0</td><td>0</td></tr> <tr><td>154742504910672534362390.528</td><td>0</td><td>0</td></tr> <tr><td>309485009821345068724781.056</td><td>0</td><td>0</td></tr> <tr><td>618970019642690137449562.112</td><td>0</td><td>0</td></tr> <tr><td>1237940039285380274899124.224</td><td>0</td><td>0</td></tr> <tr><td>2475880078570760549798248.448</td><td>0</td><td>0</td></tr> <tr><td>4951760157141521099596496.896</td><td>0</td><td>0</td></tr> <tr><td>9903520314283042199192993.792</td><td>0</td><td>0</td></tr> <tr><td>19807040628566084398385987.584</td><td>0</td><td>0</td></tr> <tr><td>39614081257132168796771975.168</td><td>0</td><td>0</td></tr> <tr><td>79228162514264337593543950.336</td><td>0</td><td>0</td></tr> <tr><td>158456325028528675187087900.672</td><td>0</td><td>0</td></tr> <tr><td>316912650057057350374175801.344</td><td>0</td><td>0</td></tr> <tr><td>633825300114114700748351602.688</td><td>0</td><td>0</td></tr> <tr><td>1267650600228229401496703205.376</td><td>0</td><td>0</td></tr> <tr><td>2535301200456458802993406410.752</td><td>0</td><td>0</td></tr> <tr><td>5070602400912917605986812821.504</td><td>0</td><td>0</td></tr> <tr><td>10141204801825835211973625643.008</td><td>0</td><td>0</td></tr> <tr><td>20282409603651670423947251286.016</td><td>0</td><td>0</td></tr> <tr><td>40564819207303340847894502572.032</td><td>0</td><td>0</td></tr> <tr><td>81129638414606681695789005144.064</td><td>0</td><td>0</td></tr> <tr><td>162259276829213363391578010288.128</td><td>0</td><td>0</td></tr> <tr><td>324518553658426726783156020576.256</td><td>0</td><td>0</td></tr> <tr><td>649037107316853453566312041152.512</td><td>0</td><td>0</td></tr> <tr><td>1298074214633706907132624082305.024</td><td>0</td><td>0</td></tr> <tr><td>2596148429267413814265248164610.048</td><td>0</td><td>0</td></tr> <tr><td>5192296858534827628530496329220.096</td><td>0</td><td>0</td></tr> <tr><td>10384593717069655257060992658440.192</td><td>0</td><td>0</td></tr> <tr><td>20769187434139310514121985316880.384</td><td>0</td><td>0</td></tr> <tr><td>41538374868278621028243970633760.768</td><td>0</td><td>0</td></tr> <tr><td>83076749736557242056487941267521.536</td><td>0</td><td>0</td></tr> <tr><td>166153499473114484112975882535043.072</td><td>0</td><td>0</td></tr> <tr><td>332306998946228968225951765070086.144</td><td>0</td><td>0</td></tr> <tr><td>664613997892457936451903530140172.288</td><td>0</td><td>0</td></tr> <tr><td>1329227995784915872903807060280344.576</td><td>0</td><td>0</td></tr> <tr><td>2658455991569831745807614120560689.152</td><td>0</td><td>0</td></tr> <tr><td>5316911983139663491615228241121378.304</td><td>0</td><td>0</td></tr> <tr><td>10633823966279326983230456482242756.608</td><td>0</td><td>0</td></tr> <tr><td>21267647932558653966460912964485513.216</td><td>0</td><td>0</td></tr> <tr><td>42535295865117307932921825928971026.432</td><td>0</td><td>0</td></tr> <tr><td>85070591730234615865843651857942052.864</td><td>0</td><td>0</td></tr> <tr><td>170141183460469231731687303715884105.728</td><td>0</td><td>0</td></tr> <tr><td>340282366920938463463374607431768211.456</td><td>0</td><td>0</td></tr> <tr><td>680564733841876926926749214863536422.912</td><td>0</td><td>0</td></tr> <tr><td>1361129467683753853853498429727072845.824</td><td>0</td><td>0</td></tr> <tr><td>272225893536750770770699685945414569.168</td><td>0</td><td>0</td></tr> <tr><td>544451787073501541541399371890829138.336</td><td>0</td><td>0</td></tr> <tr><td>1088903574147003083082798743781658276.672</td><td>0</td><td>0</td></tr> <tr><td>2177807148294006166165597487563316553.344</td><td>0</td><td>0</td></tr> <tr><td>4355614296588012332331194975126633106.688</td><td>0</td><td>0</td></tr> <tr><td>8711228593176024664662389950253266213.376</td><td>0</td><td>0</td></tr> <tr><td>17422457186352049329324779900506532426.752</td><td>0</td><td>0</td></tr> <tr><td>34844914372704098658649559801013064853.504</td><td>0</td><td>0</td></tr> <tr><td>69689828745408197317299119602026129707.008</td><td>0</td><td>0</td></tr> <tr><td>139379657490816394634598239204052259414.016</td><td>0</td><td>0</td></tr> <tr><td>278759314981632789269196478408104518828.032</td><td>0</td><td>0</td></tr> <tr><td>557518629963265578538392956816209037656.064</td><td>0</td><td>0</td></tr> <tr><td>111503725992653115707678591363241807531.128</td><td>0</td><td>0</td></tr> <tr><td>223007451985306231415357182726483615062.256</td><td>0</td><td>0</td></tr> <tr><td>446014903970612462830714365452967230124.512</td><td>0</td><td>0</td></tr> <tr><td>892029807941224925661428730905934460249.024</td><td>0</td><td>0</td></tr> <tr><td>1784059615882449851322857461811868920498.048</td><td>0</td><td>0</td></tr> <tr><td>3568119231764899702645714923623737840996.096</td><td>0</td><td>0</td></tr> <tr><td>7136238463529799405291429847247475681992.192</td><td>0</td><td>0</td></tr> <tr><td>14272476927059598810582859694494951363984.384</td><td>0</td><td>0</td></tr> <tr><td>28544953854119197621165719388989902727968.768</td><td>0</td><td>0</td></tr> <tr><td>57089907708238395242331438777979805455937.536</td><td>0</td><td>0</td></tr> <tr><td>114179815416476790484662877555959610911875.072</td><td>0</td><td>0</td></tr> <tr><td>228359630832953580969325755111919221823750.144</td><td>0</td><td>0</td></tr> <tr><td>456719261665907161938651510223838443647500.288</td><td>0</td><td>0</td></tr> <tr><td>913438523331814323877303020447676887295000.576</td><td>0</td><td>0</td></tr> <tr><td>1826877046663628647754606040895353774590001.152</td><td>0</td><td>0</td></tr> <tr><td>3653754093327257295509212081790707549180002.304</td><td>0</td><td>0</td></tr> <tr><td>7307508186654514591018424163581415098360004.608</td><td>0</td><td>0</td></tr> <tr><td>14615016373309029182036848327162830196720009.216</td><td>0</td><td>0</td></tr> <tr><td>29230032746618058364073696654325660393440018.432</td><td>0</td><td>0</td></tr> <tr><td>58460065493236116728147393308651320786880036.864</td><td>0</td><td>0</td></tr> <tr><td>116920130986472233456294786617302641573760073.728</td><td>0</td><td>0</td></tr> <tr><td>233840261972944466912589573234605283147520147.456</td><td>0</td><td>0</td></tr> <tr><td>467680523945888933825179146469210566295040294.912</td><td>0</td><td>0</td></tr> <tr><td>935361047891777867650358292938421132590080589.824</td><td>0</td><td>0</td></tr> <tr><td>1870722095783555735300716585876842265180161179.648</td><td>0</td><td>0</td></tr> <tr><td>3741444191567111470601433171753684530360322359.296</td><td>0</td><td>0</td></tr> <tr><td>7482888383134222941202866343507369060720644718.592</td><td>0</td><td>0</td></tr> <tr><td>14965776766268445882405732687014738121441289437.184</td><td>0</td><td>0</td></tr> <tr><td>29931553532536891764811465374029476242882578874.368</td><td>0</td><td>0</td></tr> <tr><td>59863107065073783529622930748058952485765157748.736</td><td>0</td><td>0</td></tr> <tr><td>119726214130147567059245861496117904971530315497.472</td><td>0</td><td>0</td></tr> <tr><td>239452428260295134118491722992235809943060630994.944</td><td>0</td><td>0</td></tr> <tr><td>478904856520590268236983445984471619886121261989.888</td><td>0</td><td>0</td></tr> <tr><td>957809713041180536473966891968943239772242523979.776</td><td>0</td><td>0</td></tr> <tr><td>1915619426082361072947933783937886479544485047959.552</td><td>0</td><td>0</td></tr> <tr><td>3831238852164722145895867567875772959088970095919.104</td><td>0</td><td>0</td></tr> <tr><td>7662477704329444291791735135751545918177940191838.208</td><td>0</td><td>0</td></tr> <tr><td>15324955408658888583583470271503091836355880383676.416</td><td>0</td><td>0</td></tr> <tr><td>30649910817317777167166940543006183672711760767352.832</td><td>0</td><td>0</td></tr> <tr><td>61299821634635554334333881086012367345423521534705.664</td><td>0</td><td>0</td></tr> <tr><td>122599643269271108668667762172024734690847043069411.328</td><td>0</td><td>0</td></tr> <tr><td>245199286538542217337335524344049469381694086138822.656</td><td>0</td><td>0</td></tr> <tr><td>490398573077084434674671048688098938763388172277645.312</td><td>0</td><td>0</td></tr> <tr><td>980797146154168869349342097376197877526776344555290.624</td><td>0</td><td>0</td></tr> <tr><td>1961594292288337738698684194752395755053552689110581.248</td><td>0</td><td>0</td></tr> <tr><td>3923188584576675477397368389504791510107105378221162.496</td><td>0</td><td>0</td></tr> <tr><td>784637716915335095479473677900958302021421075644234.992</td><td>0</td><td>0</td></tr> <tr><td>156927543383067019095894735580191660404284215128847.984</td><td>0</td><td>0</td></tr> <tr><td>313855086766134038191789471160383320808568430257695.968</td><td>0</td><td>0</td></tr> <tr><td>627710173532268076383578942320766641617136860515391.936</td><td>0</td><td>0</td></tr> <tr><td>1255420347064536152767157884641533283234273721030783.872</td><td>0</td><td>0</td></tr> <tr><td>2510840694129072305534315769283066566468547442061567.744</td><td>0</td><td>0</td></tr> <tr><td>5021681388258144611068631538566133132937094884123135.488</td><td>0</td><td>0</td></tr> <tr><td>10043362776516289222137263077132262658741897768246270.976</td><td>0</td><td>0</td></tr> <tr><td>20086725553032578444274526154264525317483795536492541.952</td><td>0</td><td>0</td></tr> <tr><td>40173451106065156888549052308529050634967591072985083.904</td><td>0</td><td>0</td></tr> <tr><td>80346902212130313777098104617058101269935182145970167.808</td><td>0</td><td>0</td></tr> <tr><td>160693804424260627554196209234116202539870364291940335.616</td><td>0</td><td>0</td></tr> <tr><td>321387608848521255108392418468232405079740728583880671.232</td><td>0</td><td>0</td></tr> <tr><td>642775217697042510216784836936464810159481457167761342.464</td><td>0</td><td>0</td></tr> <tr><td>1285550435394085020433569673872929620318962914335522684.928</td><td>0</td><td>0</td></tr> <tr><td>257110087078817004086713934774585924063792582867104537.856</td><td>0</td><td>0</td></tr> <tr><td>514220174157634008173427869549171848127585157344209075.712</td><td>0</td><td>0</td></tr> <tr><td>1028440348315268016346855739098343696255170314688418151.424</td><td>0</td><td>0</td></tr> <tr><td>2056880696630536032693711478196687392510340629376836302.848</td><td>0</td><td>0</td></tr> <tr><td>4113761393261072065387422956393374785020681258753672605.696</td><td>0</td><td>0</td></tr> <tr><td>8227522786522144130774845912786749570041362517507345211.392</td><td>0</td><td>0</td></tr> <tr><td>1645504557304428826154969182557349914008272503501469022.784</td><td>0</td><td>0</td></tr> <tr><td>329100911460885765230993836511469982801654500700293845.568</td><td>0</td><td>0</td></tr> <tr><td>658201822921771530461987673022939965603309001400587911.136</td><td>0</td><td>0</td></tr> <tr><td>1316403645843543060923975346045879931206618002801175822.272</td><td>0</td><td>0</td></tr> <tr><td>2632807291687086121847950692091759862413236005602351644.544</td><td>0</td><td>0</td></tr> <tr><td>5265614583374172243695901384183519724826472011204703289.088</td><td>0</td><td>0</td></tr> <tr><td>10531229</td></tr></tbody></table>	MIC (mg/L)	FAA Observations	BBA Observations	0.002	0	0	0.004	0	0	0.008	18	-18	0.016	30	-30	0.032	10	-10	0.064	2	-2	0.128	2	-2	0.256	0	0	0.512	0	0	1.024	0	0	2.048	0	0	4.096	0	0	8.192	0	0	16.384	0	0	32.768	0	0	65.536	0	0	131.072	0	0	262.144	0	0	524.288	0	0	1048.576	0	0	2097.152	0	0	4194.304	0	0	8388.608	0	0	16777.216	0	0	33554.432	0	0	67108.864	0	0	134217.728	0	0	268435.456	0	0	536870.912	0	0	1073741.824	0	0	2147483.648	0	0	4294967.296	0	0	8589934.592	0	0	17179869.184	0	0	34359738.368	0	0	68719476.736	0	0	137438953.472	0	0	274877906.944	0	0	549755813.888	0	0	1099511627.776	0	0	2199023255.552	0	0	4398046511.104	0	0	8796093022.208	0	0	17592186044.416	0	0	35184372088.832	0	0	70368744177.664	0	0	140737488355.328	0	0	281474976710.656	0	0	562949953421.312	0	0	1125899906842.624	0	0	2251799813685.248	0	0	4503599627370.496	0	0	9007199254740.992	0	0	18014398509481.984	0	0	36028797018963.968	0	0	72057594037927.936	0	0	144115188075855.872	0	0	288230376151711.744	0	0	576460752303423.488	0	0	1152921504606846.976	0	0	2305843009213693.952	0	0	4611686018427387.904	0	0	9223372036854775.808	0	0	18446744073709551.616	0	0	36893488147419103.232	0	0	73786976294838206.464	0	0	147573952589676412.928	0	0	295147905179352825.856	0	0	590295810358705651.712	0	0	1180591620717411303.424	0	0	2361183241434822606.848	0	0	4722366482869645213.696	0	0	9444732965739290427.392	0	0	18889465931478580854.784	0	0	37778931862957161709.568	0	0	75557863725914323419.136	0	0	151115727451828646838.272	0	0	302231454903657293676.544	0	0	604462909807314587353.088	0	0	1208925819614629174706.176	0	0	2417851639229258349412.352	0	0	4835703278458516698824.704	0	0	9671406556917033397649.408	0	0	19342813113834066795298.816	0	0	38685626227668133590597.632	0	0	77371252455336267181195.264	0	0	154742504910672534362390.528	0	0	309485009821345068724781.056	0	0	618970019642690137449562.112	0	0	1237940039285380274899124.224	0	0	2475880078570760549798248.448	0	0	4951760157141521099596496.896	0	0	9903520314283042199192993.792	0	0	19807040628566084398385987.584	0	0	39614081257132168796771975.168	0	0	79228162514264337593543950.336	0	0	158456325028528675187087900.672	0	0	316912650057057350374175801.344	0	0	633825300114114700748351602.688	0	0	1267650600228229401496703205.376	0	0	2535301200456458802993406410.752	0	0	5070602400912917605986812821.504	0	0	10141204801825835211973625643.008	0	0	20282409603651670423947251286.016	0	0	40564819207303340847894502572.032	0	0	81129638414606681695789005144.064	0	0	162259276829213363391578010288.128	0	0	324518553658426726783156020576.256	0	0	649037107316853453566312041152.512	0	0	1298074214633706907132624082305.024	0	0	2596148429267413814265248164610.048	0	0	5192296858534827628530496329220.096	0	0	10384593717069655257060992658440.192	0	0	20769187434139310514121985316880.384	0	0	41538374868278621028243970633760.768	0	0	83076749736557242056487941267521.536	0	0	166153499473114484112975882535043.072	0	0	332306998946228968225951765070086.144	0	0	664613997892457936451903530140172.288	0	0	1329227995784915872903807060280344.576	0	0	2658455991569831745807614120560689.152	0	0	5316911983139663491615228241121378.304	0	0	10633823966279326983230456482242756.608	0	0	21267647932558653966460912964485513.216	0	0	42535295865117307932921825928971026.432	0	0	85070591730234615865843651857942052.864	0	0	170141183460469231731687303715884105.728	0	0	340282366920938463463374607431768211.456	0	0	680564733841876926926749214863536422.912	0	0	1361129467683753853853498429727072845.824	0	0	272225893536750770770699685945414569.168	0	0	544451787073501541541399371890829138.336	0	0	1088903574147003083082798743781658276.672	0	0	2177807148294006166165597487563316553.344	0	0	4355614296588012332331194975126633106.688	0	0	8711228593176024664662389950253266213.376	0	0	17422457186352049329324779900506532426.752	0	0	34844914372704098658649559801013064853.504	0	0	69689828745408197317299119602026129707.008	0	0	139379657490816394634598239204052259414.016	0	0	278759314981632789269196478408104518828.032	0	0	557518629963265578538392956816209037656.064	0	0	111503725992653115707678591363241807531.128	0	0	223007451985306231415357182726483615062.256	0	0	446014903970612462830714365452967230124.512	0	0	892029807941224925661428730905934460249.024	0	0	1784059615882449851322857461811868920498.048	0	0	3568119231764899702645714923623737840996.096	0	0	7136238463529799405291429847247475681992.192	0	0	14272476927059598810582859694494951363984.384	0	0	28544953854119197621165719388989902727968.768	0	0	57089907708238395242331438777979805455937.536	0	0	114179815416476790484662877555959610911875.072	0	0	228359630832953580969325755111919221823750.144	0	0	456719261665907161938651510223838443647500.288	0	0	913438523331814323877303020447676887295000.576	0	0	1826877046663628647754606040895353774590001.152	0	0	3653754093327257295509212081790707549180002.304	0	0	7307508186654514591018424163581415098360004.608	0	0	14615016373309029182036848327162830196720009.216	0	0	29230032746618058364073696654325660393440018.432	0	0	58460065493236116728147393308651320786880036.864	0	0	116920130986472233456294786617302641573760073.728	0	0	233840261972944466912589573234605283147520147.456	0	0	467680523945888933825179146469210566295040294.912	0	0	935361047891777867650358292938421132590080589.824	0	0	1870722095783555735300716585876842265180161179.648	0	0	3741444191567111470601433171753684530360322359.296	0	0	7482888383134222941202866343507369060720644718.592	0	0	14965776766268445882405732687014738121441289437.184	0	0	29931553532536891764811465374029476242882578874.368	0	0	59863107065073783529622930748058952485765157748.736	0	0	119726214130147567059245861496117904971530315497.472	0	0	239452428260295134118491722992235809943060630994.944	0	0	478904856520590268236983445984471619886121261989.888	0	0	957809713041180536473966891968943239772242523979.776	0	0	1915619426082361072947933783937886479544485047959.552	0	0	3831238852164722145895867567875772959088970095919.104	0	0	7662477704329444291791735135751545918177940191838.208	0	0	15324955408658888583583470271503091836355880383676.416	0	0	30649910817317777167166940543006183672711760767352.832	0	0	61299821634635554334333881086012367345423521534705.664	0	0	122599643269271108668667762172024734690847043069411.328	0	0	245199286538542217337335524344049469381694086138822.656	0	0	490398573077084434674671048688098938763388172277645.312	0	0	980797146154168869349342097376197877526776344555290.624	0	0	1961594292288337738698684194752395755053552689110581.248	0	0	3923188584576675477397368389504791510107105378221162.496	0	0	784637716915335095479473677900958302021421075644234.992	0	0	156927543383067019095894735580191660404284215128847.984	0	0	313855086766134038191789471160383320808568430257695.968	0	0	627710173532268076383578942320766641617136860515391.936	0	0	1255420347064536152767157884641533283234273721030783.872	0	0	2510840694129072305534315769283066566468547442061567.744	0	0	5021681388258144611068631538566133132937094884123135.488	0	0	10043362776516289222137263077132262658741897768246270.976	0	0	20086725553032578444274526154264525317483795536492541.952	0	0	40173451106065156888549052308529050634967591072985083.904	0	0	80346902212130313777098104617058101269935182145970167.808	0	0	160693804424260627554196209234116202539870364291940335.616	0	0	321387608848521255108392418468232405079740728583880671.232	0	0	642775217697042510216784836936464810159481457167761342.464	0	0	1285550435394085020433569673872929620318962914335522684.928	0	0	257110087078817004086713934774585924063792582867104537.856	0	0	514220174157634008173427869549171848127585157344209075.712	0	0	1028440348315268016346855739098343696255170314688418151.424	0	0	2056880696630536032693711478196687392510340629376836302.848	0	0	4113761393261072065387422956393374785020681258753672605.696	0	0	8227522786522144130774845912786749570041362517507345211.392	0	0	1645504557304428826154969182557349914008272503501469022.784	0	0	329100911460885765230993836511469982801654500700293845.568	0	0	658201822921771530461987673022939965603309001400587911.136	0	0	1316403645843543060923975346045879931206618002801175822.272	0	0	2632807291687086121847950692091759862413236005602351644.544	0	0	5265614583374172243695901384183519724826472011204703289.088	0	0	10531229
MIC (mg/L)	FAA Observations	BBA Observations																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
0.002	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
0.004	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
0.008	18	-18																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
0.016	30	-30																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
0.032	10	-10																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
0.064	2	-2																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
0.128	2	-2																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
0.256	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
0.512	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
1.024	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
2.048	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
4.096	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
8.192	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
16.384	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
32.768	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
65.536	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
131.072	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
262.144	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
524.288	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
1048.576	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
2097.152	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
4194.304	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
8388.608	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
16777.216	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
33554.432	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
67108.864	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
134217.728	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
268435.456	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
536870.912	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
1073741.824	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
2147483.648	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
4294967.296	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
8589934.592	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
17179869.184	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
34359738.368	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
68719476.736	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
137438953.472	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
274877906.944	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
549755813.888	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
1099511627.776	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
2199023255.552	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
4398046511.104	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
8796093022.208	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
17592186044.416	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
35184372088.832	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
70368744177.664	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
140737488355.328	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
281474976710.656	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
562949953421.312	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
1125899906842.624	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
2251799813685.248	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
4503599627370.496	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
9007199254740.992	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
18014398509481.984	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
36028797018963.968	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
72057594037927.936	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
144115188075855.872	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
288230376151711.744	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
576460752303423.488	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
1152921504606846.976	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
2305843009213693.952	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
4611686018427387.904	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
9223372036854775.808	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
18446744073709551.616	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
36893488147419103.232	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
73786976294838206.464	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
147573952589676412.928	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
295147905179352825.856	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
590295810358705651.712	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
1180591620717411303.424	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
2361183241434822606.848	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
4722366482869645213.696	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
9444732965739290427.392	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
18889465931478580854.784	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
37778931862957161709.568	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
75557863725914323419.136	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
151115727451828646838.272	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
302231454903657293676.544	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
604462909807314587353.088	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
1208925819614629174706.176	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
2417851639229258349412.352	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
4835703278458516698824.704	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
9671406556917033397649.408	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
19342813113834066795298.816	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
38685626227668133590597.632	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
77371252455336267181195.264	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
154742504910672534362390.528	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
309485009821345068724781.056	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
618970019642690137449562.112	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
1237940039285380274899124.224	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
2475880078570760549798248.448	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
4951760157141521099596496.896	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
9903520314283042199192993.792	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
19807040628566084398385987.584	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
39614081257132168796771975.168	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
79228162514264337593543950.336	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
158456325028528675187087900.672	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
316912650057057350374175801.344	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
633825300114114700748351602.688	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
1267650600228229401496703205.376	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
2535301200456458802993406410.752	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
5070602400912917605986812821.504	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
10141204801825835211973625643.008	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
20282409603651670423947251286.016	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
40564819207303340847894502572.032	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
81129638414606681695789005144.064	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
162259276829213363391578010288.128	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
324518553658426726783156020576.256	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
649037107316853453566312041152.512	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
1298074214633706907132624082305.024	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
2596148429267413814265248164610.048	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
5192296858534827628530496329220.096	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
10384593717069655257060992658440.192	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
20769187434139310514121985316880.384	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
41538374868278621028243970633760.768	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
83076749736557242056487941267521.536	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
166153499473114484112975882535043.072	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
332306998946228968225951765070086.144	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
664613997892457936451903530140172.288	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
1329227995784915872903807060280344.576	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
2658455991569831745807614120560689.152	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
5316911983139663491615228241121378.304	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
10633823966279326983230456482242756.608	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
21267647932558653966460912964485513.216	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
42535295865117307932921825928971026.432	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
85070591730234615865843651857942052.864	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
170141183460469231731687303715884105.728	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
340282366920938463463374607431768211.456	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
680564733841876926926749214863536422.912	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
1361129467683753853853498429727072845.824	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
272225893536750770770699685945414569.168	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
544451787073501541541399371890829138.336	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
1088903574147003083082798743781658276.672	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
2177807148294006166165597487563316553.344	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
4355614296588012332331194975126633106.688	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
8711228593176024664662389950253266213.376	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
17422457186352049329324779900506532426.752	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
34844914372704098658649559801013064853.504	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
69689828745408197317299119602026129707.008	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
139379657490816394634598239204052259414.016	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
278759314981632789269196478408104518828.032	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
557518629963265578538392956816209037656.064	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
111503725992653115707678591363241807531.128	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
223007451985306231415357182726483615062.256	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
446014903970612462830714365452967230124.512	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
892029807941224925661428730905934460249.024	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
1784059615882449851322857461811868920498.048	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
3568119231764899702645714923623737840996.096	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
7136238463529799405291429847247475681992.192	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
14272476927059598810582859694494951363984.384	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
28544953854119197621165719388989902727968.768	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
57089907708238395242331438777979805455937.536	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
114179815416476790484662877555959610911875.072	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
228359630832953580969325755111919221823750.144	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
456719261665907161938651510223838443647500.288	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
913438523331814323877303020447676887295000.576	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
1826877046663628647754606040895353774590001.152	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
3653754093327257295509212081790707549180002.304	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
7307508186654514591018424163581415098360004.608	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
14615016373309029182036848327162830196720009.216	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
29230032746618058364073696654325660393440018.432	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
58460065493236116728147393308651320786880036.864	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
116920130986472233456294786617302641573760073.728	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
233840261972944466912589573234605283147520147.456	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
467680523945888933825179146469210566295040294.912	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
935361047891777867650358292938421132590080589.824	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
1870722095783555735300716585876842265180161179.648	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
3741444191567111470601433171753684530360322359.296	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
7482888383134222941202866343507369060720644718.592	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
14965776766268445882405732687014738121441289437.184	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
29931553532536891764811465374029476242882578874.368	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
59863107065073783529622930748058952485765157748.736	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
119726214130147567059245861496117904971530315497.472	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
239452428260295134118491722992235809943060630994.944	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
478904856520590268236983445984471619886121261989.888	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
957809713041180536473966891968943239772242523979.776	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
1915619426082361072947933783937886479544485047959.552	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
3831238852164722145895867567875772959088970095919.104	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
7662477704329444291791735135751545918177940191838.208	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
15324955408658888583583470271503091836355880383676.416	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
30649910817317777167166940543006183672711760767352.832	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
61299821634635554334333881086012367345423521534705.664	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
122599643269271108668667762172024734690847043069411.328	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
245199286538542217337335524344049469381694086138822.656	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
490398573077084434674671048688098938763388172277645.312	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
980797146154168869349342097376197877526776344555290.624	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
1961594292288337738698684194752395755053552689110581.248	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
3923188584576675477397368389504791510107105378221162.496	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
784637716915335095479473677900958302021421075644234.992	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
156927543383067019095894735580191660404284215128847.984	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
313855086766134038191789471160383320808568430257695.968	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
627710173532268076383578942320766641617136860515391.936	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
1255420347064536152767157884641533283234273721030783.872	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
2510840694129072305534315769283066566468547442061567.744	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
5021681388258144611068631538566133132937094884123135.488	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
10043362776516289222137263077132262658741897768246270.976	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
20086725553032578444274526154264525317483795536492541.952	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
40173451106065156888549052308529050634967591072985083.904	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
80346902212130313777098104617058101269935182145970167.808	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
160693804424260627554196209234116202539870364291940335.616	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
321387608848521255108392418468232405079740728583880671.232	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
642775217697042510216784836936464810159481457167761342.464	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
1285550435394085020433569673872929620318962914335522684.928	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
257110087078817004086713934774585924063792582867104537.856	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
514220174157634008173427869549171848127585157344209075.712	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
1028440348315268016346855739098343696255170314688418151.424	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
2056880696630536032693711478196687392510340629376836302.848	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
4113761393261072065387422956393374785020681258753672605.696	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
8227522786522144130774845912786749570041362517507345211.392	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
1645504557304428826154969182557349914008272503501469022.784	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
329100911460885765230993836511469982801654500700293845.568	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
658201822921771530461987673022939965603309001400587911.136	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
1316403645843543060923975346045879931206618002801175822.272	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
2632807291687086121847950692091759862413236005602351644.544	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
5265614583374172243695901384183519724826472011204703289.088	0	0																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
10531229																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																										

## EUCAST form for General Consultation

	<p>I calculate on a distribution on 2220 strains collected in France resistance rates will be 4.5% at 8 mg/l breakpoint and 54.9% at 1mg/L. 1mg/L does not fit the clinical situations. CA-SFM Agree on breakpoint 8/8mg/L or 8/16. But why a same consideration was not taken for clindamycin and <i>C. perfringens</i> with a trimodal distribution ? See next comment on clindamycin and <i>C. perfringens</i></p>	<p>This cannot be compared to Bacteroides and piperacillin-tazobactam where there is a host of different species involved and where the proposed breakpoint (8/8) is the same as the one decided and accepted for Enterobacterales. The proposed clindamycin breakpoint for <i>Cl.perfringens</i> is likewise on par with those for other gram-positive microorganisms in the tables.</p>
CA-SFM	<p>6 - <i>Fusobacterium clindamycin</i> In absence of <i>erm</i> gene all strains of fusobacteria are inhibited by 1mg/L of clindamycin. Why breakpoint is not 1mg/L considering the large usage of this antibiotic in the past ? Do we really need a specific breakpoint for <i>F. necrophorum</i>?</p>	<p>In the review of clindamycin breakpoints throughout the tables, breakpoints have been lowered to 0.25 or 0.5 at the most. For <i>F. necrophorum</i> we have adhered to the principle "if there is clinical data to assess outcome with wild type organisms but no robust clinical data on non-wild type organisms, we refrain from proposing a breakpoint which strays far from the ECOFF".</p> <p>Other <i>Fusobacterium</i> spp than <i>F.necrophorum</i> were not part of the development of methodology or breakpoints and will be addressed in phase 2 of the development together with one or two more <i>Clostridium</i> spp.</p>

## EUCAST form for General Consultation

	<h3 style="text-align: center;">Clindamycin</h3> <p style="text-align: center; border: 1px solid black; padding: 5px; color: red; font-weight: bold;">Proposed breakpoints: 0.25/0.25 mg/L</p> <div style="display: flex; justify-content: space-around;"> <div data-bbox="584 576 1061 858"> <p><b>Clindamycin MIC FAA vs. BBA</b> <i>F. necrophorum</i>, 51 isolates</p> </div> <div data-bbox="1128 564 1469 879"> <p style="text-align: center; font-size: small;">Clindamycin (<i>Fusobacterium spp.</i>) International MIC Distributions - <i>Esperanza</i> Database 2020-03-18</p> </div> </div>	
CA-SFM	<p>7 - benzyl penicillin and perfringens</p> <p>Only one strain of <i>C. perfringens</i> highly resistant to benzylpenicillin has been described by I. Poxton (Scotland) in the world. Strains above the ECOFF may have unknown mechanism (PBP ?) but may not be necessarily categorize as resistant. Highest value is 2mg/L for benzyl penicillin. Amoxicillin MIC are generally one dilution greater. MIC of 4 mg/L is the highest MIC value for <i>C. perfringens</i> and according to PTA</p>	<p>Almost all our <i>C. perfringens</i> isolates have MICs of 0.5 mg/L or lower. This is the case for the Cardiff study on FAA with agar dilution and this is the case for the distribution on the EUCAST website and for several papers available (although for these gradient tests were used). The current EUCAST benzylpenicillin breakpoints are 0.25/0.5. This is in the neighbourhood of what we consider the</p>

## EUCAST form for General Consultation

	<p>values this support a treatment by this drug and will prevent to use a carbapenem. <b>Proposal 2/2 mg/L for Benzyl penicillin</b></p> <p><i>C. perfringens</i> is the fastest growing bacteria; a strong Mc Farland 1 may leads to important inoculum effect. We used to decrease the inoculum to 0.5 McF to avoid this phenomon.</p> <h3 style="text-align: center;">Benzylpenicillin</h3> <div style="text-align: center; border: 1px solid black; padding: 5px; width: fit-content; margin: 0 auto;"> <p><b>Proposed breakpoints: 0.5/0.5 mg/L</b></p> </div> <div style="display: flex; justify-content: space-around;"> <div data-bbox="566 722 1055 1013"> <p><b>Benzylpenicillin MIC FAA vs. BBA</b> <i>C. perfringens</i>, 58 isolates</p> </div> <div data-bbox="1055 722 1469 1013"> <p><b>Benzylpenicillin / Clostridium perfringens</b> International MIC Distribution - Reference Database 2020-02-18</p> </div> </div>	<p>highest possible breakpoint for several other species. Only in <i>S. pneumoniae</i>, where there is abundant literature in support, do we have a breakpoint between SI and R of <math>S \leq 2</math> mg/L and then this is tied to a very high benzylpenicillin dosage.</p>
<p>CA-SFM</p>	<p><b>8 - <i>C. acnes</i> and benzyl-penicillin distribution (EUCAST search data base)</b></p> <p>Proposed Breakpoint 0,06mg/L ??</p> <p>Why split the wild type distribution ?</p>	<p>The distributions referred to were performed on BBA with a variety of methods. This is also the case for the distributions on the EUCAST MIC distribution website.</p> <p>EUCAST SC has used freshly performed agar dilution MICs on FAA media where all</p>

## EUCAST form for General Consultation

	<p>How many strains with MIC of 0,06mg/L will be at 0.12mg/L repeating testing</p> <p>In lack of any mechanism of resistance for a species, and to avoid variations in measurements why the breakpoint is not ECOFF + a dilution far from the PK/PD breakpoint</p> <table border="1" data-bbox="573 592 1458 751"> <tr> <td>0.002</td> <td>0.004</td> <td>0.008</td> <td>0.016</td> <td>0.03</td> <td>0.06</td> <td>0.125</td> <td>0.25</td> <td>0.5</td> <td>1</td> </tr> </table> <table border="1" data-bbox="573 820 1458 963"> <tr> <td>0</td> <td>0</td> <td>1</td> <td>118</td> <td>92</td> <td>62</td> <td>30</td> <td>0</td> <td>0</td> <td>0</td> </tr> </table> <p>Tentative breakpoints is the highest value of MIC determined on a weak number of strains (54)</p> <p>If you look at the EUCAST distribution on 363 strains thus 10% of <i>C. acnes</i> are resistant to benzyl penicillin !</p> <p>Strain with MIC of 0,12mg/L using Brucella agar dilution is resistant!</p> <p><b>We propose 0,12 mg/L for <i>C. acnes</i> or 0.5 mg/l for all gram positive anaerobes</b></p>	0.002	0.004	0.008	0.016	0.03	0.06	0.125	0.25	0.5	1	0	0	1	118	92	62	30	0	0	0	<p>isolates were inhibited by 0.016. The one isolate with a higher MIC was on BBA. We have invited colleagues to provide isolates with higher MICs and are expecting results from the currently ongoing phase 2 of the clinical laboratory trial. However, so far we have no evidence to suggest that a higher breakpoint than 0.06 is needed on FAA. However, the difference between 0.06 and 0.12 is one dilution and EUCAST will discuss to adjust the breakpoint.</p> <p>As a response to the comments originating from the general consultation, EUCAST has further developed the guidance document "<a href="#">When there are no breakpoints</a>" and included a section on anaerobic bacteria.</p>
0.002	0.004	0.008	0.016	0.03	0.06	0.125	0.25	0.5	1													
0	0	1	118	92	62	30	0	0	0													

## EUCAST form for General Consultation

# Benzylpenicillin

Proposed breakpoints: 0.06/0.06 mg/L

