Exhibit 4
To: Counsel for Janssen


Dear [Counsel]:

I write on behalf of Celltrion, Inc. ("Celltrion") in response to the letter dated December 26, 2014, REDACTED on behalf of Janssen Biotech, Inc. ("Janssen"), the reference product sponsor for Remicade®. 1

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F. The '083 Patent

The '083 patent, titled "Chemically Defined Media Compositions," issued on October 6, 2009. Its listed inventors are David Epstein, Roger Monsell, Joseph Horwitz, Susan Lenk, Sadettin Ozturk, and Christopher Marsh. The patent was assigned to Centocor, Inc. The '083 patent resulted from Appl. No. 11/260,788, filed October 27, 2005, and claims priority to Provisional Application No. 60/623,718, filed on October 29, 2004. The patent expires February 9, 2026.

Generally, the '083 patent is directed to a specific soluble composition suitable for producing a final volume of cell culture media.

The claims read:

1. A soluble composition, suitable for producing a final volume of cell culture media, wherein the composition comprises the following components in the following amounts per liter of the final volume of cell culture media:
   anhydrous CaCl₂, 5-200 mg;
   anhydrous MgCl₂, 15-50 mg;
   anhydrous MgSO₄, 20-80 mg;
   FeSO₄.7H₂O, 0.05-0.50 mg;
   Fe(NO₃)₃.9H₂O, 0.01-0.08 mg;
   ZnSO₄.7H₂O, 0.40-1.20 mg;
   ferric ammonium citrate, 0.04-200 mg;
   KCl, 280-500 mg;
   NaCl, 5000-7500 mg;
   NaH₂PO₄.H₂O, 30-100 mg;
   Na₃HPO₄, 30-100 mg;
   CuSO₄.5H₂O, 0.001-0.005 mg;
   CoCl₂.6H₂O, 0.001-0.10 mg;
   (NH₄)₆Mo₇O₂₄.4H₂O, 0.001-0.005 mg;
   MnSO₄.H₂O, 0.000070-0.0080 mg;
   NiSO₄.6H₂O, 0.000025-0.0005 mg;
   Na₂SeO₃, 0.004-0.07 mg;
   Na₂SiO₃.9H₂O, 0.02-0.4 mg;
   SnCl₂.2H₂O, 0.000025-0.0005 mg;
   NH₄VO₃, 0.0001-0.0025 mg;
   D-Glucose, 500-8000 mg;
   sodium pyruvate, 0.0-1000 mg;
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sodium hypoxanthine, 0.0-20.0 mg;  
glycine, 0.0-150 mg;  
L-alanine, 0.0-150 mg;  
L-arginine.HCl, 200-5000 mg;  
L-asparagine.H₂O, 40-250 mg;  
L-aspartic acid, 20-1000 mg;  
L-cysteine.HCl H₂O, 25.0-250 mg;  
L-cystine.2HCl, 15-150 mg;  
L-glutamic acid, 0-1000 mg;  
L-histidine.HCl.H₂O, 100-500 mg;  
L-isoleucine, 50-1000 mg;  
L-leucine, 50-1000 mg;  
L-lysine.HCl, 100-1000 mg;  
L-methionine, 50-500 mg;  
L-ornithine.HCl, 0-100 mg;  
L-phenylalanine, 25-1000 mg;  
L-proline, 0-1000 mg;  
L-serine, 50-500 mg;  
L-taurine, 0-1000 mg;  
L-threonine, 50-600 mg;  
L-tryptophan, 2-500 mg;  
L-tyrosine.2Na.2H₂O, 25-250 mg;  
L-valine, 100-1000 mg;  
d-biotin, 0.04-1.0 mg;  
D-calcium pantothenate, 0.1-5.0 mg;  
choline chloride, 1-100 mg;  
folic acid, 1-10 mg;  
i-Nonitol, 10-1000 mg;  
nicotinamide, 0.5-30 mg;  
p-aminobenzoic acid, 0.1-20 mg;  
riboflavin, 0.05-5.0 mg;  
thiamine.HCl, 0.5-20 mg;  
thymidine, 0-3.0 mg;  
vitamin B₁₂, 0.05-5.0 mg;  
linoleic acid, 0.01-2.0 mg;  
DL-α-lipoic acid, 0.03-1.0 mg;  
pyridoxine.HCl, 0.5-30 mg;  
putrescine.2HCl, 0.025-0.25 mg; and  
ethanalamine.HCl, 2-100 mg.

2. The soluble composition of claim 1 further comprising a buffering molecule with a pKₐ between 5.9 and 7.8 and a cell protectant.
3. The soluble composition of claim 2 wherein the buffering molecule consists of MOPS in the amount of 1047-5230 mg per liter of final media volume and the cell protectant consists of Pluronic-F68 in the amount of 250-1500 mg per liter of final media volume.

4. A composition comprising a cell culture media made by the steps comprising:
   a) selecting a final media volume;
   b) providing the soluble composition of claim 2 or claim 3;
   c) solubilizing the soluble composition in a volume of water less than the final media volume;
   d) adding 1.022 g of L-glutamine per liter of final media volume;
   e) adding a bicarbonate ion providing substance sufficient to produce a bicarbonate ion concentration of between 0.020 M and 0.030 M in the final media volume;
   f) optionally adding at least one substance selected from the group consisting of mycophenolic acid, hypoxanthine, xanthine, and soy hydrolysate;
   g) adding a quantity of base sufficient to adjust the pH of the solution to between pH 5.9 and pH 7.8; and
   h) adding water sufficient to bring the volume of the composition to the selected final media volume.

5. The composition of claim 4 where the bicarbonate ion providing substance sufficient to produce a bicarbonate ion concentration of between 0.020 M and 0.030 M in the final media volume is 2.1 g of NaHCO₃ per liter of final media volume.

6. A soluble composition, suitable for producing a final volume of cell culture media, wherein the composition comprises the following components in the following amounts per liter of the final volume of cell culture media:
   CaCl₂, 100.95 mg;
   MgCl₂, 24.77 mg;
   MgSO₄, 42.24 mg;
   FeSO₄.7H₂O, 0.3607 mg;
   Fe(NO₃)₃.9H₂O, 0.0432 mg;
   ZnSO₄.7H₂O, 0.6225 mg;
   ferric ammonium citrate, 43.25 mg;
   KCl, 386.9 mg;
   NaCl, 5866.0 mg;
   NaH₂PO₄.H₂O, 54.07 mg;
   Na₂HPO₄, 61.44 mg;
   CuSO₄.5H₂O, 0.003287 mg;
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CoCl₂·6H₂O, 0.0020606 mg;
(NH₄)₆Mo₇O₂₄·4H₂O, 0.000535 mg;
MnSO₄·H₂O, 0.00008571 mg;
NiSO₄·6H₂O, 0.0000514 mg;
Na₂SeO₃, 0.007489 mg;
Na₂SiO₃·9H₂O, 0.03671 mg;
SnCl₂·2H₂O, 0.0000488 mg;
NH₄VO₃, 0.0002530 mg;
D-Glucose, 3680.52 mg;
sodium pyruvate, 100 mg;
sodium hypoxanthine, 2.069 mg;
glycine, 16.23 mg;
L-alanine, 79.31 mg;
L-arginine.HCl, 674.89 mg;
L-asparagine.H₂O, 182.25 mg;
L-aspartic acid, 67.23 mg;
L-cysteine.HCl.H₂O, 57.63 mg;
L-cystine.2HCl, 106.70 mg;
L-glutamic acid, 6.36 mg;
L-histidine.HCl.H₂O, 250.55 mg;
L-isoleucine, 245.43 mg;
L-leucine, 263.42 mg;
L-lysine.HCl, 276.41 mg;
L-methionine, 85.40 mg;
L-ornithine.HCl, 2.44 mg;
L-phenylalanine, 104.23 mg;
L-proline, 14.94 mg;
L-serine, 146.36 mg;
L-taurine, 3.64 mg;
L-threonine, 199.09 mg;
L-tryptophan, 70.71 mg;
L-tyrosine.2Na·2H₂O, 195.58 mg;
L-valine, 174.34 mg;
d-biotin, 0.4359 mg;
D-calcium pantothenate, 1.9394 mg;
choline chloride, 10.8009 mg;
folic acid, 3.4329 mg;
i-inositol, 81.7965 mg;
nicotinamide, 3.1342 mg;
p-aminobenzoic acid, 2.1645 mg;
riboflavin, 0.5359 mg;
thiamine.HCl, 2.3377 mg;
thymidine, 0.316 mg;
vitamin B₁₂, 0.5887 mg;

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linoleic acid, 0.0364 mg;
DL-α-lipoic acid, 0.0909 mg;
pyridoxine.HCl, 3.0442 mg;
putrescine.2HCl, 0.0701 mg; and
ethanolamine.HCl, 14.37 mg.

7. The soluble composition of claim 6 further comprising a buffering molecule with a pKₐ of between 5.9 and 7.8 and a cell protectant.

8. The soluble composition of claim 7 wherein the buffering molecule consists of MOPS in the amount of 2709.66 mg per liter of final media volume, and the cell protectant consists of Pluronic-F68 in the amount of 865.80 mg per liter of final media volume.

9. The soluble composition of claim 7 further comprising the following components in the following amounts per liter of final media volume:
   0.5 mg mycophenolic acid;
   2.5 mg hypoxanthine; and
   50 mg xanthine.

10. A composition comprising a cell culture media made by the steps comprising:
      a) selecting a final media volume;
      b) providing the soluble composition of claim 7 or claim 8;
      c) solubilizing the soluble composition in a volume of water less than the final media volume;
      d) adding 1.022 g of L-glutamine per liter of final media volume;
      e) adding a bicarbonate ion providing substance sufficient to produce a bicarbonate ion concentration of between 0.020 M and 0.030 M in the final media volume;
      f) optionally adding at least one substance selected from the group consisting of mycophenolic acid, hypoxanthine, xanthine and soy hydrolysate;
      g) adding a quantity of base sufficient to adjust the pH of the solution to between pH 5.9 and pH 7.8; and
      h) adding water sufficient to bring the volume of the composition to the selected final media volume.

11. The composition of claim 10 where the bicarbonate ion providing substance sufficient to produce a bicarbonate ion concentration of between 0.020 M and 0.030 M in the final media volume is 2.1 g of NaHCO₃ per liter of final media volume.

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2. Even if Celltrion’s Use Took Place Inside the United States, Claims 1-11 Are Not Infringed.

Even if Celltrion used the media cell cultures inside the United States (which has not happened), Celltrion’s use still would not infringe the ’083 patent. As mentioned above, Celltrion purchases and uses three cell culture media from Hyclone: HyQ ADCF Growth medium, HyQ ADCF Production medium, and FMC002 Feeding medium. None of the three media supplied to or used by Celltrion infringes the ’083 patent because each lacks certain expressly claimed components, or lacks them in the ranges required by Claims 1 and 6—the two independent claims of the ’083 patent.

First, HyQ ADCF Growth medium includes at least a dozen components at concentrations outside the range claimed in the ’083 patent, including but not limited to Na₂HPO₄, CuSO₄·5H₂O, SnCl₂·2H₂O, and L-asparagine·H₂O, as exemplified in the following table:

<table>
<thead>
<tr>
<th>Component</th>
<th>Concentration in Claim 1 of the ’083 patent (mg/L)</th>
<th>Concentration in Claim 6 of the ’083 patent (mg/L)</th>
<th>Concentration in HyQ ADCF Growth medium (mg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Na₂HPO₄</td>
<td>30-100</td>
<td>61.44</td>
<td>374</td>
</tr>
<tr>
<td>CuSO₄·5H₂O</td>
<td>0.001-0.005</td>
<td>0.003287</td>
<td>0.000536</td>
</tr>
<tr>
<td>SnCl₂·2H₂O</td>
<td>0.000025-0.0005</td>
<td>0.0000488</td>
<td>7.92E-06</td>
</tr>
<tr>
<td>L-asparagine·H₂O</td>
<td>40-250</td>
<td>182.25</td>
<td>3.2</td>
</tr>
</tbody>
</table>

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Similarly, HyQ ADCF Production medium includes at least a dozen components at a concentration outside the range claimed in the ‘083 patent, including, but not limited to: Na$_2$HPO$_4$, SnCl$_2$.2H$_2$O, NH$_4$VO$_3$, and L-asparagine.H$_2$O, as shown in the following table:

<table>
<thead>
<tr>
<th>Component</th>
<th>Concentration in Claim 1 of the ‘083 patent (mg/L)</th>
<th>Concentration in Claim 6 of the ‘083 patent (mg/L)</th>
<th>Concentration in HyQ ADCF Production medium (mg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Na$_2$HPO$_4$</td>
<td>30-100</td>
<td>61.44</td>
<td>433</td>
</tr>
<tr>
<td>SnCl$_2$.2H$_2$O</td>
<td>0.000025-0.0005</td>
<td>0.0000488</td>
<td>9.18E-06</td>
</tr>
<tr>
<td>NH$_4$VO$_3$</td>
<td>0.0001-0.0025</td>
<td>0.0002530</td>
<td>5.32E-05</td>
</tr>
<tr>
<td>L-asparagine.H$_2$O</td>
<td>40-250</td>
<td>182.25</td>
<td>3.7</td>
</tr>
</tbody>
</table>

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Accordingly, none of the formulations infringe Claims 1 and 6.

Because the three formulations do not infringe independent Claims 1 and 6, and because no part of Celltrion’s use involves formulations satisfying these claims, Celltrion does not infringe any other ‘083 patent claims. Nor does Celltrion infringe any claim by the doctrine of equivalents, as the media it uses contain components in sufficiently and materially different volumes.

Sincerely,

[Counsel for Celltrion]