The commercial relevance of micro-mineral nutrition for monogastrics
In spite of all the things we know and understand about nutrition we don’t really know the actual mineral requirements of the animals we feed.

“Thus there is a great deal of literature concerning the calcium and phosphorus requirements of the broiler and minimal research concerning requirements for trace elements” (NRC, 1994)

Many nutritionists don’t worry much since they believe that, by using “safely high” levels of Zn, Cu and Mn with inorganic sources, they maximize performance.
Many nutritionists believe that using organic minerals is a luxury and can ONLY be used if the use reduces total feed cost, generally done by using lower mineral levels.

Many nutritionists don’t think much about the differences between inorganic and organic mineral molecules and treat them as equivalents.
Mineral sources available for commercial animal nutrition

- **Inorganic sources of micro minerals**
  - Sulphates
  - Oxides
  - TBCC’s
  - ETC

- **Organic sources of micro minerals**
  - True Chelates (Mintrex, Glycinates)
  - Non-Chelates (many)
Comparing Organic Trace Mineral Ligands

- Ligands are ions or neutral molecules that bond to a central metal atom or ion.
- *Zinc is Zinc, Copper is Copper, Manganese is Manganese*
- The only reason to feed an organic trace mineral (OTM) over a mineral salt is to deliver minerals to the blood
- The only point of **differentiation** among OTMs is their **ligand**.
- **Structure definition** is critical to determine physical and chemical characteristics as well as consistency from lot to lot
- Chemical and physical **stability** is critical to performance.
- If the molecule disassociates prior to reaching intestinal receptor sites, antagonists can bind the mineral, causing it to precipitate out of solution rendering it unavailable to the animal.
- Receptor site proteins will absorb the soluble mineral and “pass” it to specific “chaperone,” or transport, proteins or enzymes
## Organic Trace Minerals: Non chelates

<table>
<thead>
<tr>
<th>AAFCO CLASS OF LIGAND*</th>
<th>MOLECULAR REPRESENTATION</th>
<th>SCHEMATIC MODEL</th>
<th>CHARACTERISTICS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metal (Amino Acid) Complex</td>
<td><img src="image1" alt="Metal (Amino Acid) Complex" /></td>
<td><img src="image2" alt="Metal (Amino Acid) Complex" /></td>
<td>- Many of them do not have a defined structure, i.e., there can be changes in the ligand (different AAs, protein chains or carbohydrates)</td>
</tr>
<tr>
<td>Metal (Specific Amino Acid) Complex</td>
<td><img src="image3" alt="Metal (Specific Amino Acid) Complex" /></td>
<td><img src="image4" alt="Metal (Specific Amino Acid) Complex" /></td>
<td>- Therefore it is not possible to determine the bond strength, the number of bonds, molecular size and the amount of ligands in the product.</td>
</tr>
<tr>
<td>Metal Proteinate</td>
<td><img src="image5" alt="Metal Proteinate" /></td>
<td><img src="image6" alt="Metal Proteinate" /></td>
<td>- The composition can vary and the amount of chelated mineral is uncertain.</td>
</tr>
<tr>
<td>Metal Polysaccharide Complex</td>
<td><img src="image7" alt="Metal Polysaccharide Complex" /></td>
<td><img src="image8" alt="Metal Polysaccharide Complex" /></td>
<td>- Even when the ligand is well known, the protection to the metal is partial since the ligand covers only one side of it.</td>
</tr>
</tbody>
</table>
## Organic Trace Minerals: True chelates

<table>
<thead>
<tr>
<th>AAFCO CLASS OF LIGAND*</th>
<th>MOLECULAR REPRESENTATION</th>
<th>SCHEMATIC MODEL</th>
<th>CHARACTERISTICS</th>
</tr>
</thead>
</table>
| Chelate Metal Amino acid | ![Molecular Representation](image1.png) | ![Schematic Model](image2.png) | • Are true chelates  
• They have defined structure, composition and sizes |
| Chelate metal-HMTBA | ![Molecular Representation](image3.png) | ![Schematic Model](image4.png) | |

*AAFCO CLASS OF LIGAND: Chelate Metal Amino acid and Chelate metal-HMTBA.
Minerals in the Gastric Environment (pH 2 - 5)

- Proventriculus (pH 2 – 5)
  - CuO
  - CuSO₄
  - Phytate

- Small Intestine (pH 6 – 6.5)
  - Soluble Complexes
  - Insoluble Complexes
Form of copper present in the duodenum and jejunum

- Experiments done *in vivo*
- Copper Sulfate = 8 ppm Cu

**Solubility of Cu in the small intestine**

- Soluble Cu: 38%
- Insoluble Cu: 62%

**Size of the complex Cu intestine**

- Lower absorption
- Soluble portion:
  - 29%
  - 23%
  - 3%
  - > 44%

- Molecular Weight distribution:
  - < 5,000: 5%
  - 5,000 to 30,000: 25%
  - 30,000 to 100,000: 50%
  - > 100,000: 20%
Form of Zinc present in the duodenum and jejunum

- Experiments conducted *in vivo*
- Zinc Oxide = 125 ppm Zn

**Solubility of Zn in the small intestine**

- Soluble Zn: 8%
- Insoluble Zn: 92%

**Size of Zn complexes in the intestine**

- Soluble portion: 60%
- Lower absorption

- Distribution of Peso Molecular:
  - < 5.000: 15%
  - 5.000 to 30.000: 4%
  - 30.000 to 100.000: 21%
  - > 100.000: 0%

Ideas on Micro Mineral Nutrition World Few Years Ago

We don´t understand what really happens to these minerals throughout the gut, the interactions, etc
Zn as activator of α-toxin of *Clostridium perfringens*

Ca induces denaturation of α-toxin while Zn activates and makes α-toxin stable.

Sato et al., 1978
Some Biologic Functions of Zn, Cu and Mn
Connective Tissue: Essential for Function

- Bundle of Collagen Fibers
- Elastin Fibers
Dietary Cu above that required for optimum performance was associated with increased chick tendon lysyl oxidase activity and tendon Cu was correlated with enzyme activity ($r^2 = 0.88$).
Partial condemnations due to skin problems
Broiler Breeder Hens: Carcass Effects
Effects of Body Weight and Feed allocation During Sexual Maturation in Broiler Breeder Hens. R.A. Renema

Breast Muscle Percentage At Sexual Maturity

<table>
<thead>
<tr>
<th>Source</th>
<th>Weight (g)</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Feed³</td>
<td></td>
<td></td>
</tr>
<tr>
<td>AL</td>
<td>489.7a</td>
<td>14.59b</td>
</tr>
<tr>
<td>RF</td>
<td>446.7b</td>
<td>16.20a</td>
</tr>
<tr>
<td>SEM</td>
<td>7.7</td>
<td>0.23</td>
</tr>
<tr>
<td>Size⁴</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LOW</td>
<td>442.2b</td>
<td>15.47</td>
</tr>
<tr>
<td>STD</td>
<td>469.6a</td>
<td>15.13</td>
</tr>
<tr>
<td>HIGH</td>
<td>492.8a</td>
<td>15.59</td>
</tr>
<tr>
<td>SEM</td>
<td>9.5</td>
<td>0.28</td>
</tr>
</tbody>
</table>

Source of variation
Feed: 0.0002 0.0001
Size: 0.002 0.48


Lameness (Bone Health) is currently the 4th most prevalent health issue in US broiler Industry

<table>
<thead>
<tr>
<th>Rank</th>
<th>Condition</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Enteric</td>
</tr>
<tr>
<td>2</td>
<td>Respiratory</td>
</tr>
<tr>
<td>3</td>
<td>Skin</td>
</tr>
<tr>
<td>4</td>
<td>Lameness</td>
</tr>
<tr>
<td>5</td>
<td>Chicks</td>
</tr>
</tbody>
</table>

Financial loss estimated at $120,000,000/year in USA (Cook, 2000)

All top 4 issues associated with Barrier Health
Catalytic properties of enzymes involved in maintaining egg shell/membrane quality and supporting embryogenesis

- **Zn- Carbonic anhydrase**
  - Activity of carbonic anhydrase, an essential enzyme for eggshell formation, has been directly related to zinc status of the hen
  - Zn functions in collagen synthesis

- **Cu- lysyl oxidase**
  - Cu is involved in collagen cross linking
  - Second most common metalloenzyme constituent (after zinc)

- **Mn - glycosyl transferases**
  - Chondroitin sulfate is the structural component of cartilage and provides much of its resistance to compression

(Leeson and Summers, 2001; Hudson et al., 2004; Bellairs & Osmond, 2005 Dibner and Richards, 2006; Dibner et al., 2007; Ferket et al., 2009)
Immune function of trace minerals

- **Zn:**
  - Macrophages activity (Ferket et Qureshi, 1992)
  - Cofactor of DNA and RNA polymerase, it influences the number of leucocytes (Gupta et al., 1985)

- **Cu:**
  - Increases the immune response in an attack (Strain, 1994).
  - Ceruloplasmina: Cu is its cofactor. It protects the membranes from the free radicals of oxygen. The amount of this protein is increased during the attack of E.coli and Salmonella

- **Mn:**
  - It acts in the activity of neutrophiles and macrophages (Underwood y Suttle, 2001).
Trace mineral support in coccidiosis control

288 male broilers, supplemented with different levels of MINTREX® Zn and challenged with *E. tenella*.

Better health and welfare status

Ref. Bun et al., 2010, Poultry Science
Immunity and oxidative stress

Maintaining oxidative balance = stronger immunity

**Immunity**
- Inflammatory process, stress hormones (adrenaline, cortisone):
  - oxygen free radicals

**Oxidative stress**
- Susceptibility to disease
- Hyper activation of immune system
- Role in auto-immune diseases

**Oxygen free radicals**
- Damages to cell membranes
Some of the benefits attributed to Organic Trace Minerals

1. Catalyse Enzyme activity
   - Hundreds of enzymes depend on Zn, Cu y Mn

2. Ensure tissue and structural health.
   - Collagen, keratine, elastine and bone formation.
   - Bone and feather structure, tendons, eggshell, gut and skin structure, wound healing, etc...

3. Optimize Immune function.
   - Ig titters.
   - B Cells, T Cells.

4. Reduce the impact of oxidative stress.
   - Micro-minerals are cofactors of enzymes such as Superoxide dismutase and Gluthation peroxidase

5. Lower impact to the environment and safety of use
   - Lower fecal excretion
   - Dioxins, etc.
PARADIGM TO BREAK: MINTREX CAN HAVE A DIRECT IMPACT IN PRODUCTION PARAMETERS

• At practical levels of supplementation and by using commercially available sources of minerals, economically important parameters can be optimized:
  • Feed Conversion
  • Weight gain
  • Carcass yield
  • Chick quality
  • Egg production per housed hen,
  • Piglet weight at birth
  • ETC..

• AND, in spite of the economic importance of this topic, many nutritionists know relatively little about Zn, Cu, and Mn nutrition
Every Mineral Source Has a Unique Potential to optimize animal performance

- Inorganics
  - Sulphates
  - Oxides
  - TBCC’s
  - ETC

- Organics
  - True Chelates (Mintrex, Glycinates)
  - Non-Chelates (many)

Every source of mineral has its own unique characteristics and peculiarities
Their peculiarities can produce unique and distinctive animal responses
Copper improved piglet performance in its sulfate form. Copper when supplemented in its oxide form was ineffective, even at high concentrations. This makes CuSO4 an IRREPLACEABLE source of copper vs. CuO, to achieve optimal piglet performance.

Important Questions to ask?

ARE ALL ORGANIC MINERALS IRREPLACEABLE VS. INORGANIC MINERALS?

FOR PRODUCTION PARAMETERS?
DO ALL ORGANIC MINERALS SHOW THE SAME IMPROVEMENTS ON THE SAME PRODUCTION PARAMETERS?
Dose-response of animals fed graded mineral concentrations

Adapted from Underwood and Suttle, 1999
MINTREX® is more bioavailable than other mineral sources.. BUT, What does that really mean?

- Metallothionein (MT) mRNA expression is a marker for Zn absorption/status in multiple species
- Mintrex Zn is 248 % more bioavailable compared to ZnSO4

b) Metallothionein (MT)

\[
Y = 0.92X_1 + 2.28X_2 + 1.82
\]

R²= 0.9974

R²= 0.8467

Supplemental Zn intake, mg/d
Dose-response of OTM vs. ITM

Adequate for OTM’s

Adequate for Sulfates

Dietary Mineral Concentration

Response

Organic Trace minerals

Sulfates

A

B
Mintrex vs Other Mineral Sources

Dietary Mineral Concentration

Adequate for Mintrex

Adequate for Sulfates
Effect of various levels of Mintrex Cu and CuSO₄ on overall nursery ADG (0~42 d)  
(Data of 6 trials)

Cu level $P < 0.05$

Cu Source $P = 0.449$

Mintrex Cu: $y = -0.0007x^2 + 0.2618x + 393.38$

$R^2 = 0.7398$

CuSO₄: $y = -0.0007x^2 + 0.2038x + 393.38$

$R^2 = 0.703$
Effect of various levels of Mintrex Cu and CuSO₄ on overall nursery G:F (0~42 d)
(Data of 6 trials)

CuSO₄: \( y = 0.0624x + 665.52 \)
\( R^2 = 0.689 \)

Mintrex Cu: \( y = 0.1425x + 665.52 \)
\( R^2 = 0.7471 \)

Cu level \( P = 0.051 \)
Cu Source \( P < 0.01 \)
80 ppm of MINTREX Cu Optimizes Carcass Parameters in swine
Initial weight 32 kg / Final weight 120 kg

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>CuSO4 160ppm</th>
<th>Mintrex Cu 80ppm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carcass weight (kg)</td>
<td>88.1 a</td>
<td>88.2 a</td>
<td><strong>90.6 b</strong></td>
</tr>
<tr>
<td>P=0.006</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Loin depth (pol.)</td>
<td>2.19 a</td>
<td>2.17 a</td>
<td><strong>2.28 b</strong></td>
</tr>
<tr>
<td>P=0.008</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>CuSO4 160ppm</th>
<th>Mintrex Cu 80ppm</th>
</tr>
</thead>
<tbody>
<tr>
<td>U$/swine</td>
<td>118.7 a</td>
<td>119.4 a</td>
<td><strong>122.8 b</strong></td>
</tr>
</tbody>
</table>
A body weight comparison between 3 sources of Cu included in swine diets

BW_70d (kg)

Control: 29.94 b
Sulphate: 30.61 b
Mintrex Cu: 32.00 a
TBCC: 30.82 b

P = 0.0084
CV = 9.77%

Orthogonal contrasts

<table>
<thead>
<tr>
<th>Contrast</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control x All</td>
<td>0.0142</td>
</tr>
<tr>
<td>Mintrex x (Sulphate + TBCC)</td>
<td>0.0139</td>
</tr>
<tr>
<td>Sulphate x TBCC</td>
<td>0.7119</td>
</tr>
</tbody>
</table>
In a trial conducted with Olive Flounder- Mintrex Cu improved weight gain when compared to CuSO₄.

### Weight gain at 14 wks

**+ 7%**

<table>
<thead>
<tr>
<th>Dietary Copper (mg/kg)</th>
<th>CuSO₄</th>
<th>MintrexCu</th>
</tr>
</thead>
<tbody>
<tr>
<td>Base 0.87 mg/kg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>d</td>
<td>c</td>
</tr>
<tr>
<td>10</td>
<td>bc</td>
<td>a</td>
</tr>
<tr>
<td>15</td>
<td>d</td>
<td></td>
</tr>
<tr>
<td>20</td>
<td>e</td>
<td>de</td>
</tr>
<tr>
<td>40</td>
<td>g</td>
<td>f</td>
</tr>
<tr>
<td>80</td>
<td></td>
<td>i</td>
</tr>
</tbody>
</table>

Semi-purified Diets; no added antagonists.
The distinctive dose-response curve of any mineral source may depend on a complex combination of unique characteristics such as:

- Bio efficacy
- Site of absorption
- Solubility
- Interaction with other components in the diet
- Oxidative balance
- Antimicrobial effect
- ???
- Etc., etc.,

To illustrate how poorly we understand this interaction, try to explain why ZnO at 2,000 ppm benefits piglets that much more compared to ZnSO4 or OTM. It’s certainly not due to higher bio efficacy...
Take home message

1. Minerals have unique and distinctive effects on animal performance
2. The performance potential of an animal may be determined by the source of mineral it is fed
3. Micro-mineral nutrition may impact economically important performance parameters and therefore deserve more attention