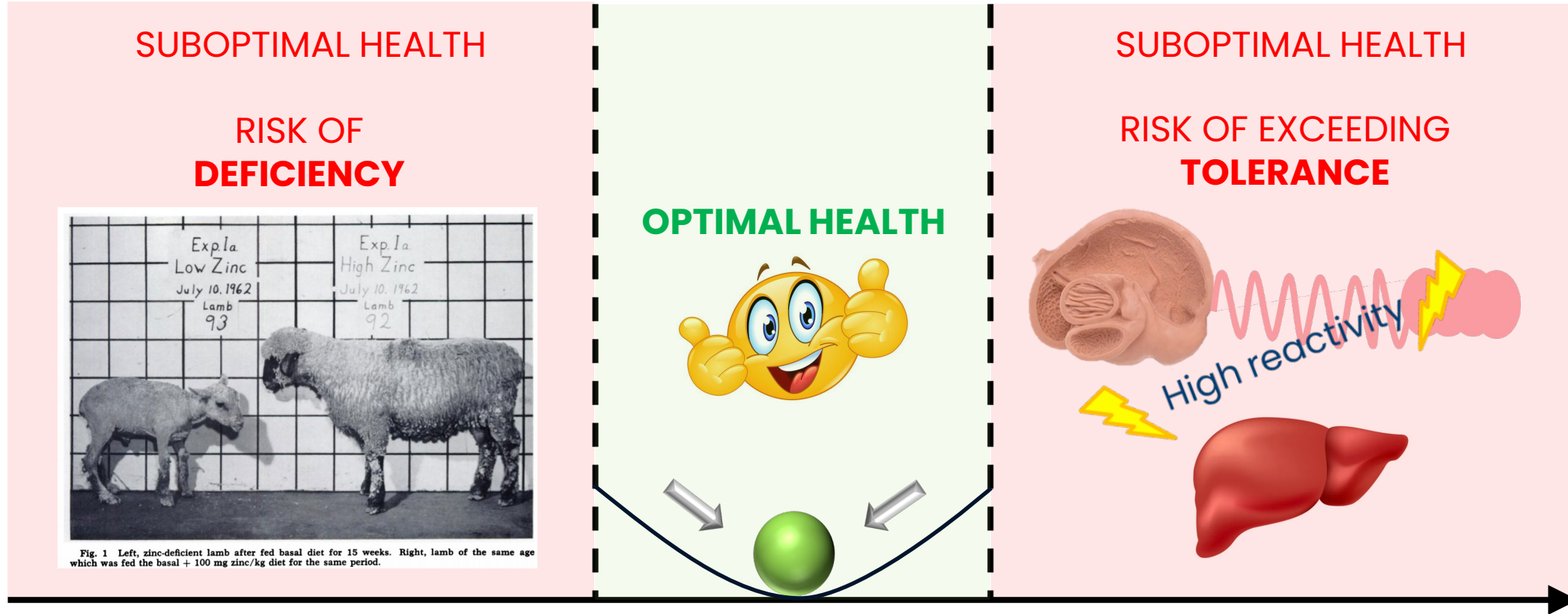




# Novel guidelines for trace metals supplementation in bovines

**Jean-Baptiste Daniel & Javier Martín-Tereso**  
R&D Ruminants

# Trace metals – Essential AND dangerous to animal physiology

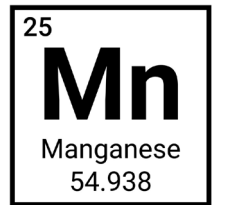
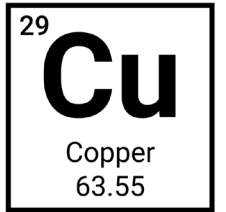
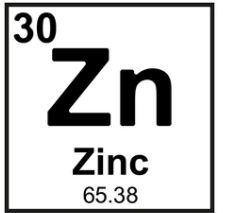


Gross trace metal supply above net requirement

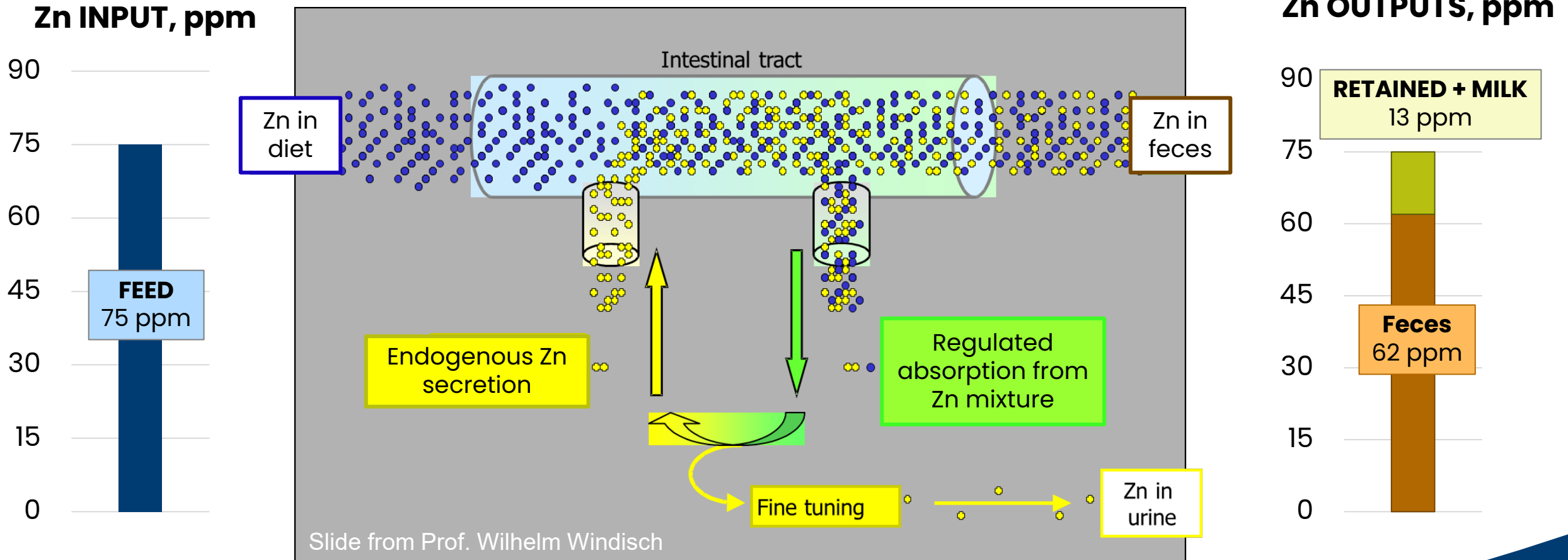
# Trace metals in bovine nutrition

## Outline

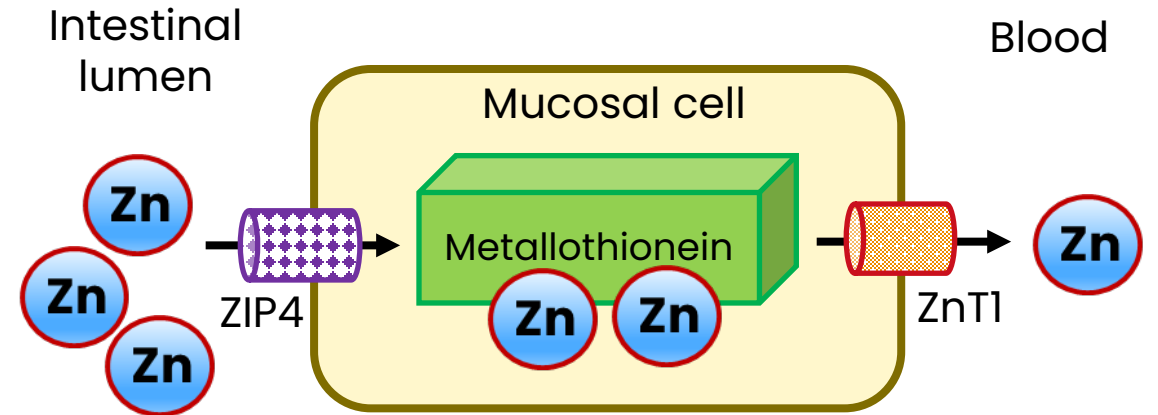
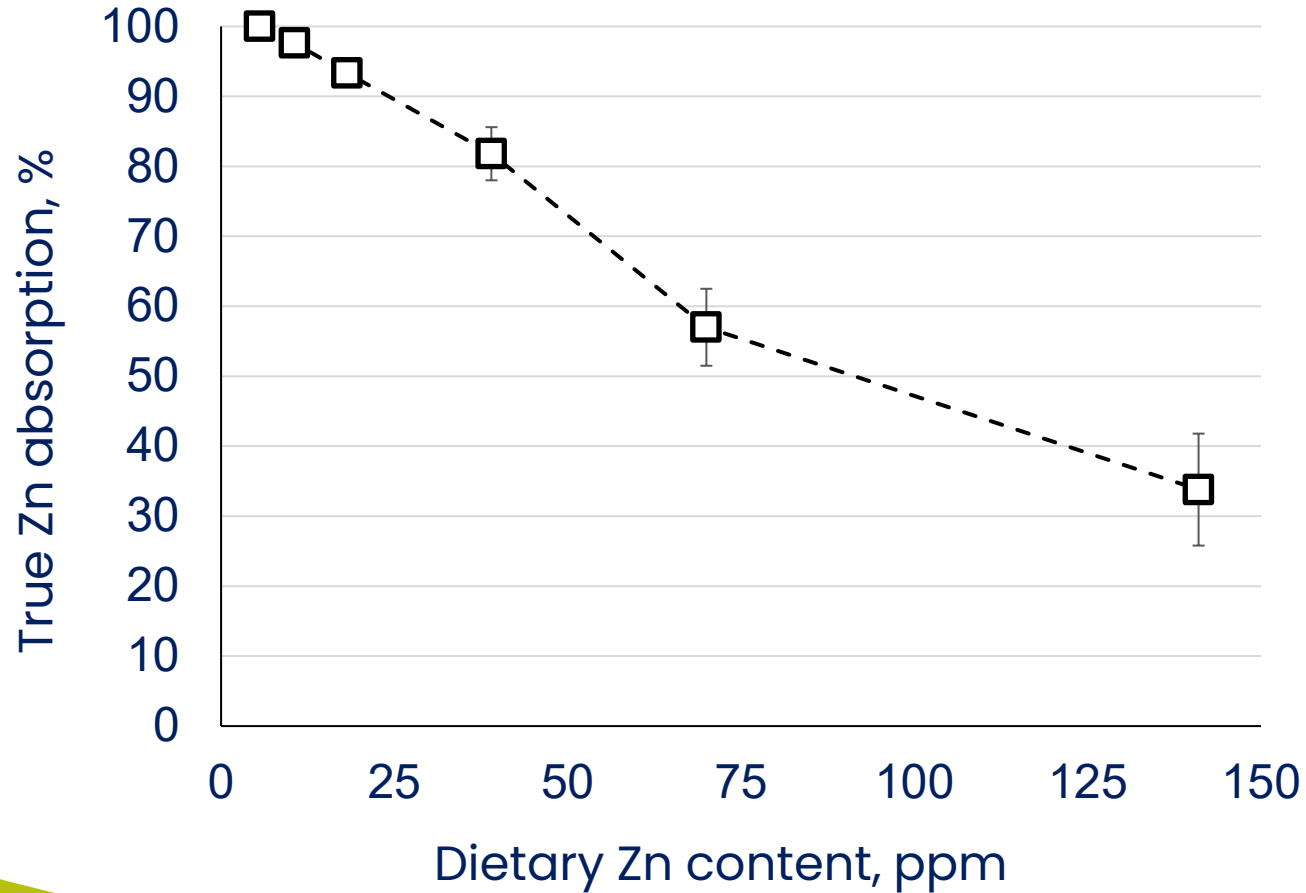
- Trace metal regulation ...
- ... and its limitations
- Novel guidelines for trace metals supplementation



# Key aspects of trace metal regulation

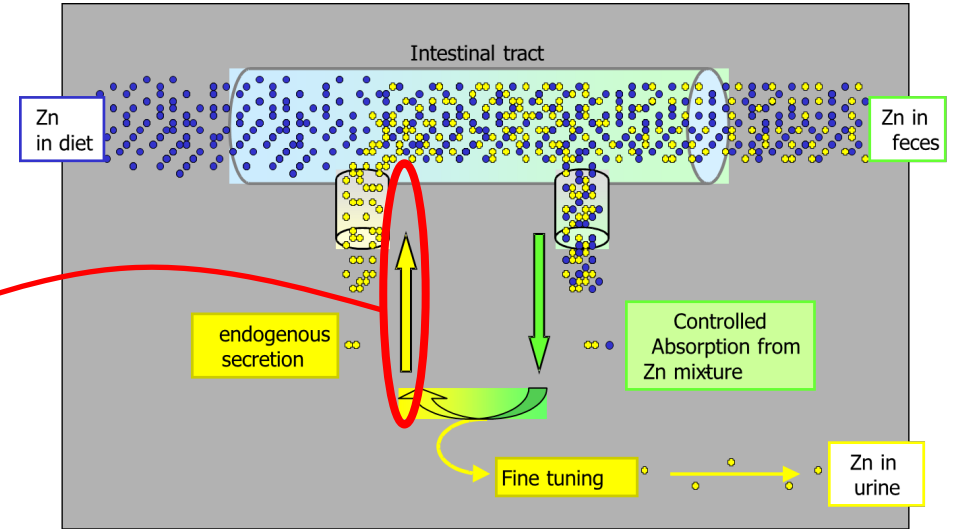
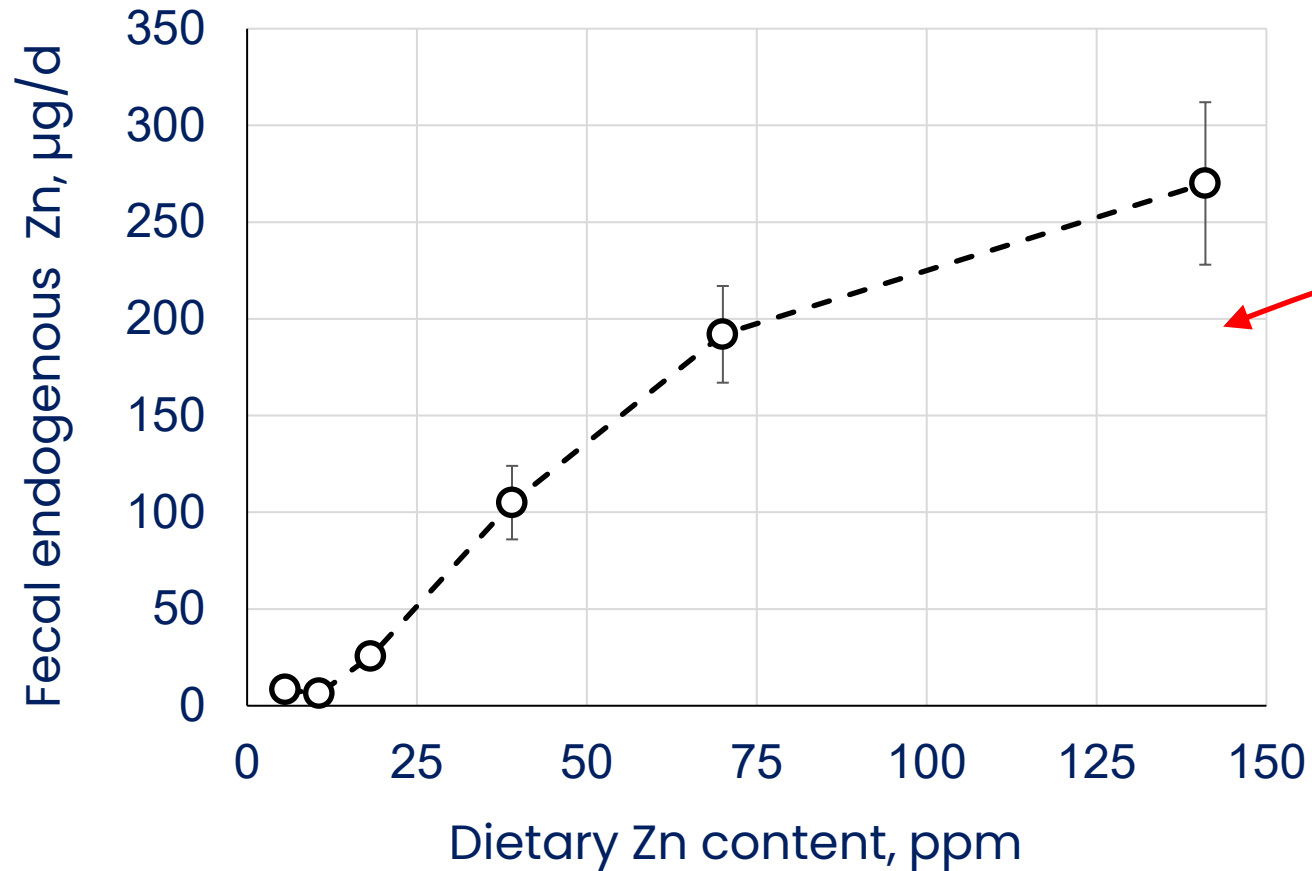


# Key aspects of trace metal regulation



**Absorption efficiency**  
decrease with higher Zn supply !

# Key aspects of trace metal regulation

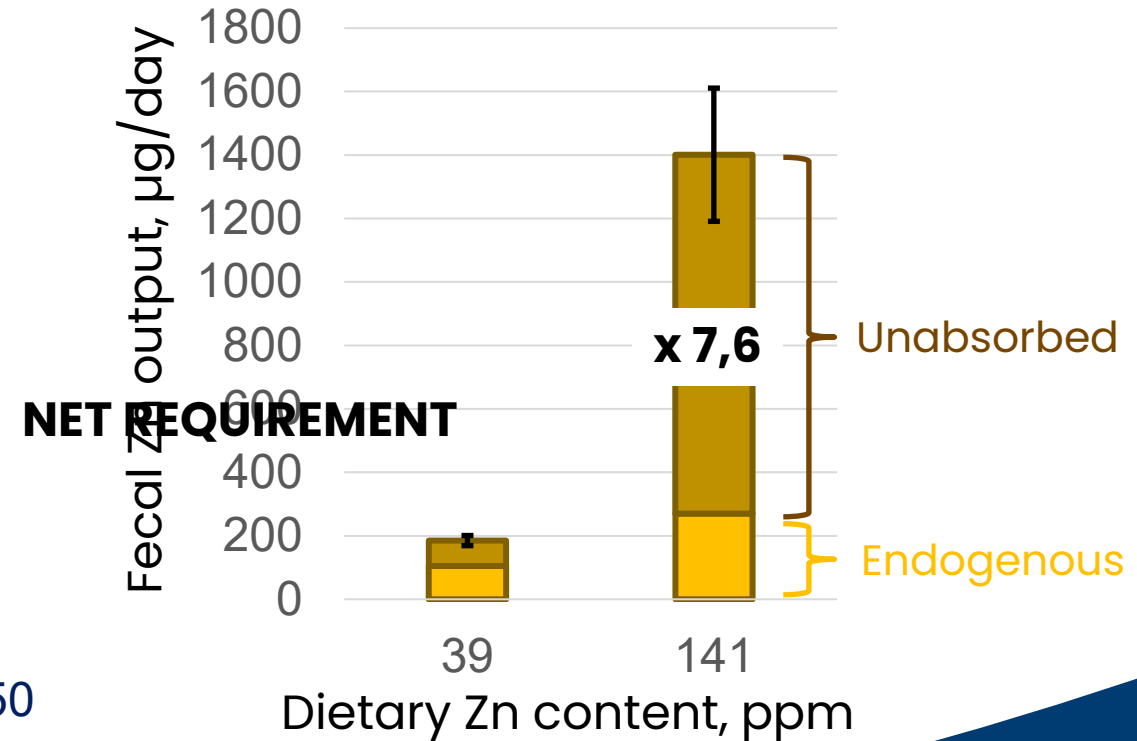
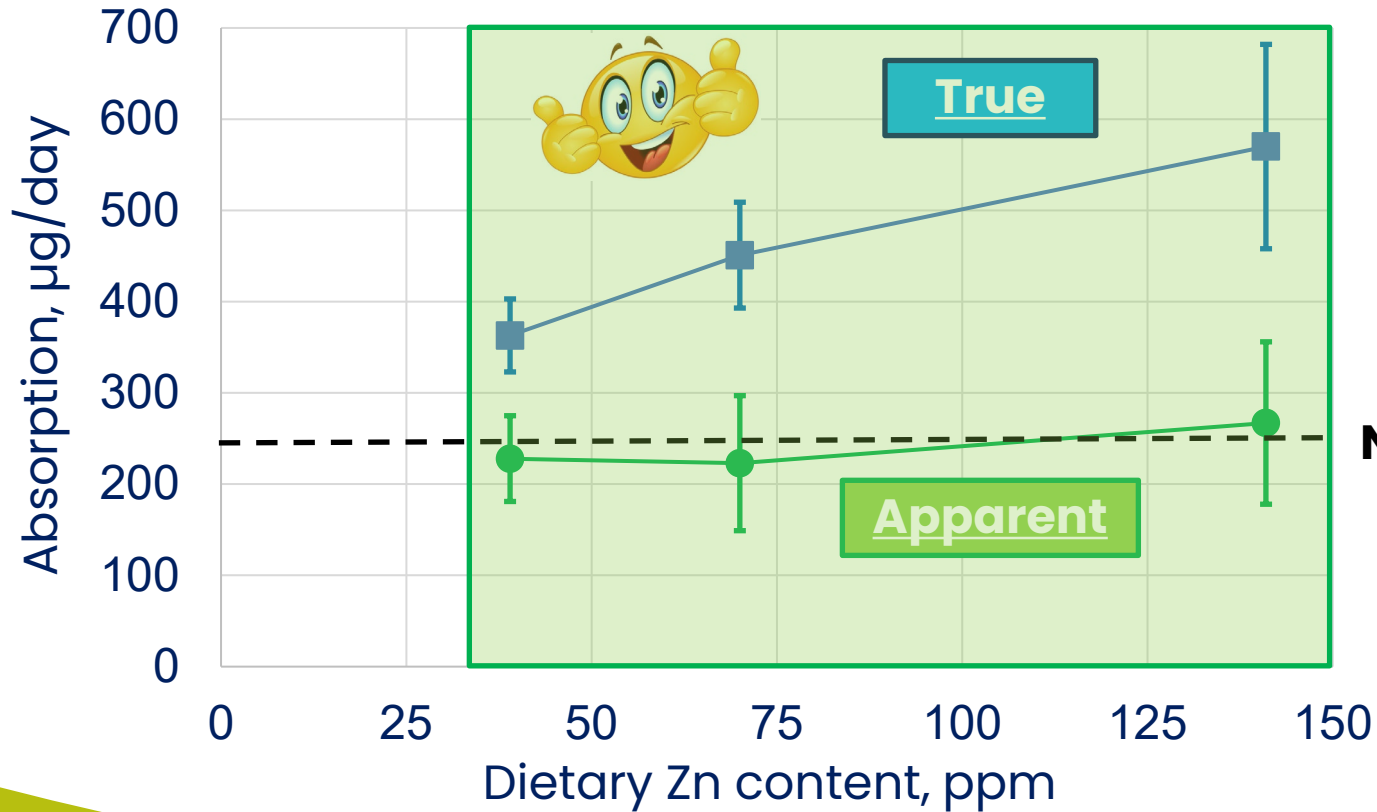


**Fecal endogenous Zn losses**  
increase with higher Zn supply !

# Key aspects of trace metal regulation



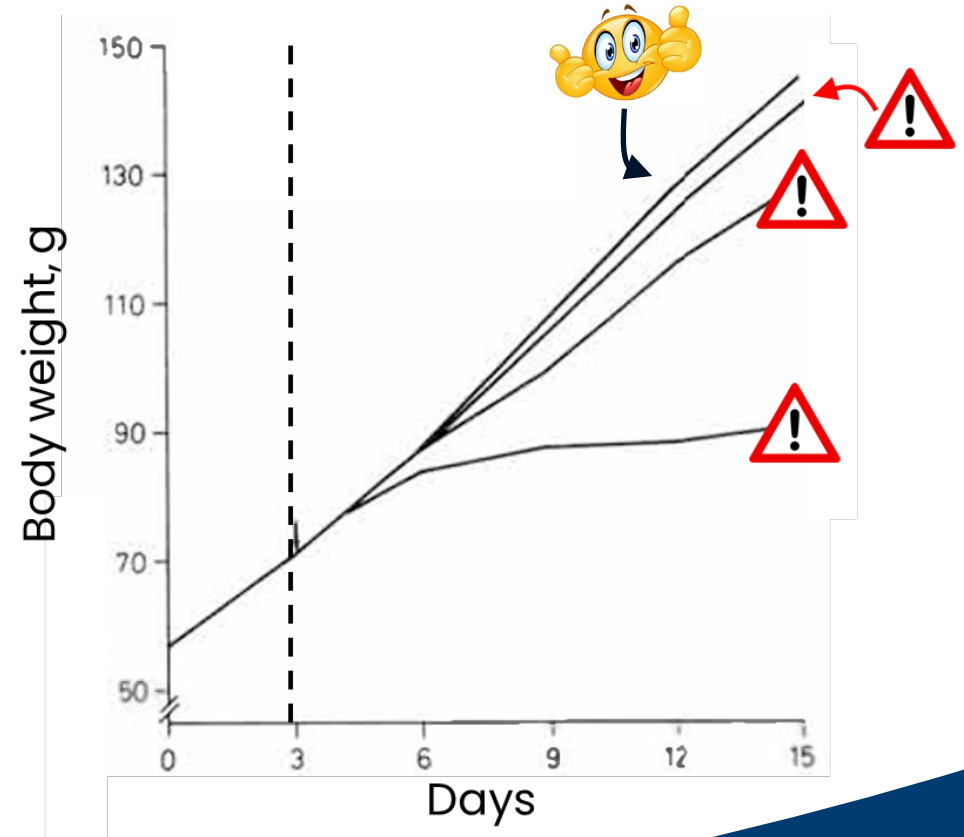
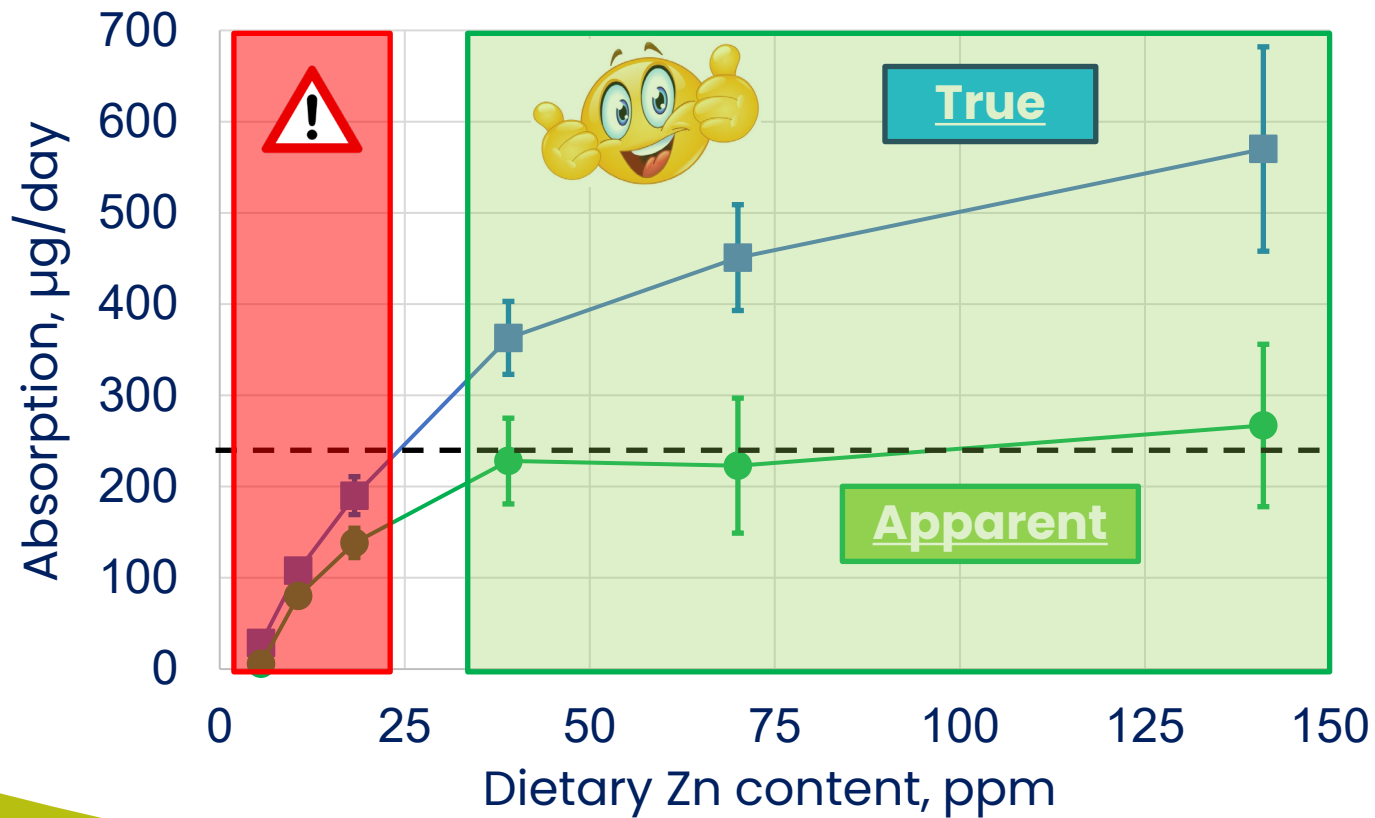
**A TIGHTLY REGULATED process ... where apparent absorption = net requirement**



# Key aspects of trace metal regulation

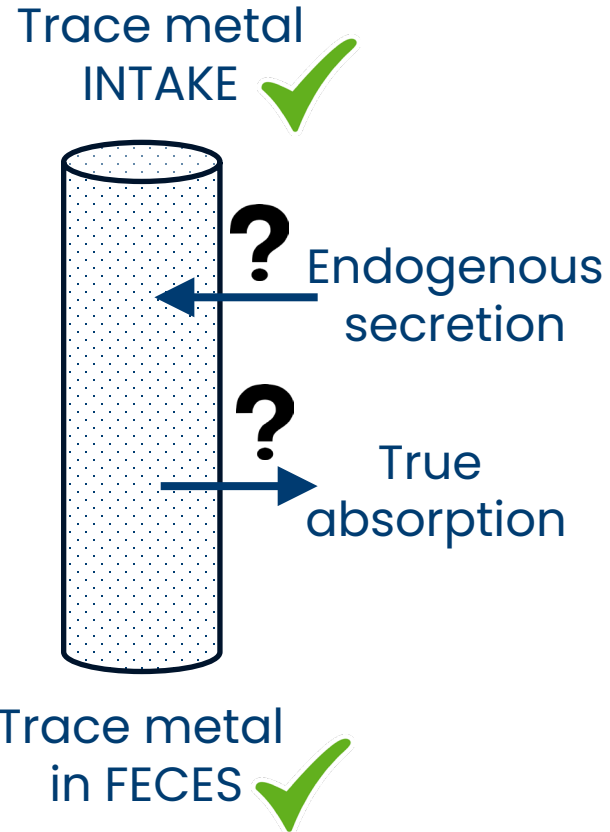


... until AVAILABLE SUPPLY IS LIMITED and apparent absorption < net requirement



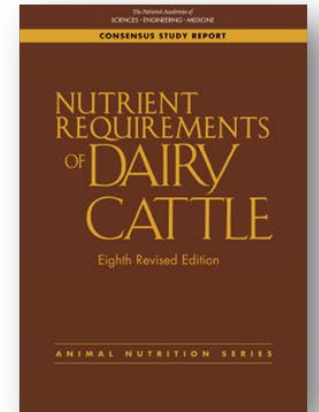


# Current approach to dietary recommendations



## Example with Zn in NASEM 2021

- **Faecal endogenous losses** = 5 x kg DMI ?  
+
- **Gestation** = 0.017 x kg BW (last trimester)  
+
- **Growth** = 24 x kg ADG  
+
- **Lactation** = 4 x kg milk



All in mg/day

÷ **True absorption = 20% ?**

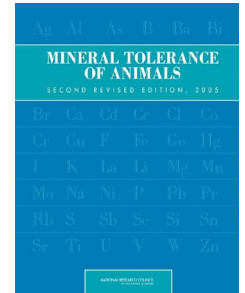
# Feeding practices exceed reference recommendations ...

... but not maximum tolerable limit

100 eastern Canadian commercial dairies, Duplessis et al., 2021



in ppm	NASEM 2021 (32 kg MY)	Average ± SD	Centile 1	Centile 99
Copper	11	17 ± 5	10	34
Manganese	27	65 ± 18	27	123
Zinc	56	76 ± 21	33	144



**MTL**  
(NRC, 2005)

40 ppm **Cu**  
2000 ppm **Mn**  
500 ppm **Zn**

39 Californian commercial dairies, Castillo et al., 2013



in ppm	NASEM 2021 (32 kg MY)	Median	Centile 10	Centile 90
Copper	11	18	10	31
Manganese	27	73	48	106
Zinc	56	74	51	103

# Trace metal balance in dairy cows

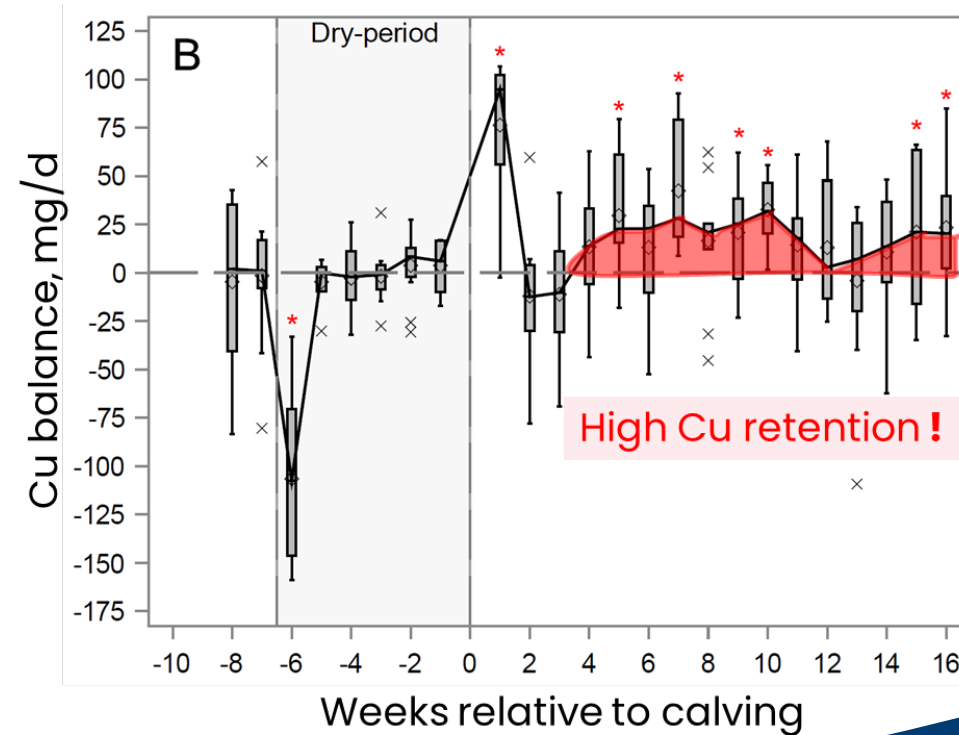
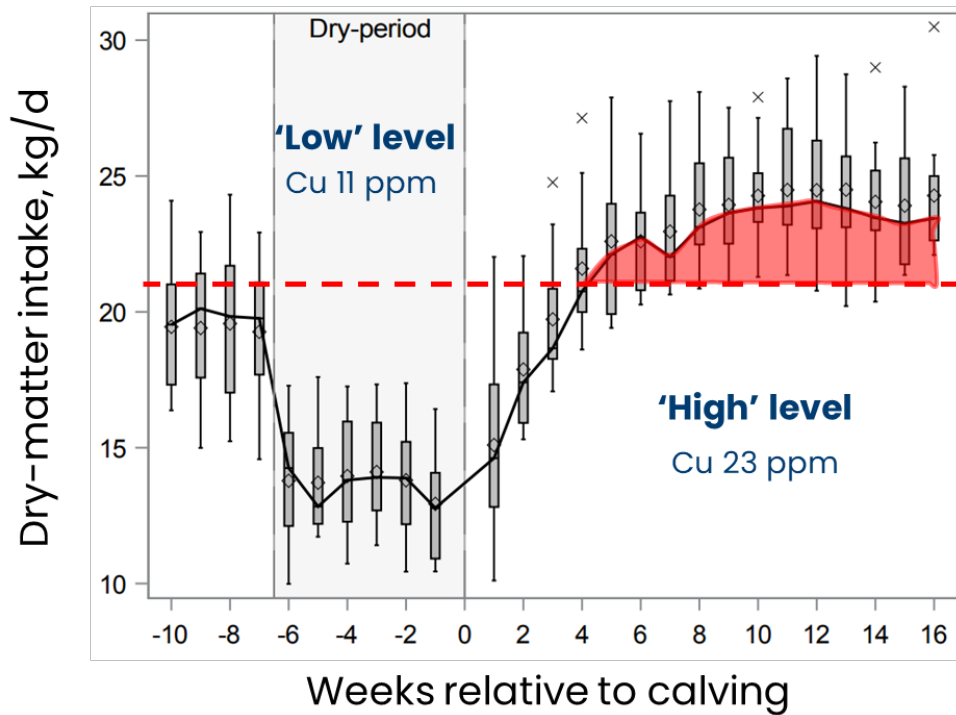
- 24 weekly periods of 48h total collection of feces and urine
- 12 dairy cows

Nutrient Physiology, Metabolism, and Nutrient-Nutrient Interactions

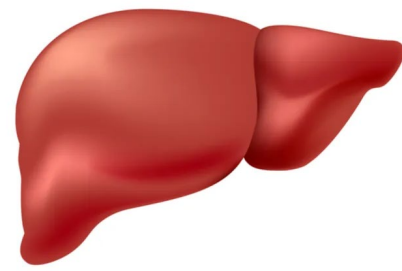
## Zinc, Copper, and Manganese Homeostasis and Potential Trace Metal Accumulation in Dairy Cows: Longitudinal Study from Late Lactation to Subsequent Mid-Lactation


Jean-Baptiste Daniel<sup>1,\*</sup>, Daniel Brugger<sup>2</sup>, Saskia van der Drift<sup>3</sup>, Deon van der Merwe<sup>3,4</sup>, Nigel Kendall<sup>5</sup>, Wilhelm Windisch<sup>6</sup>, John Doelman<sup>1</sup>, Javier Martín-Tereso<sup>1</sup>

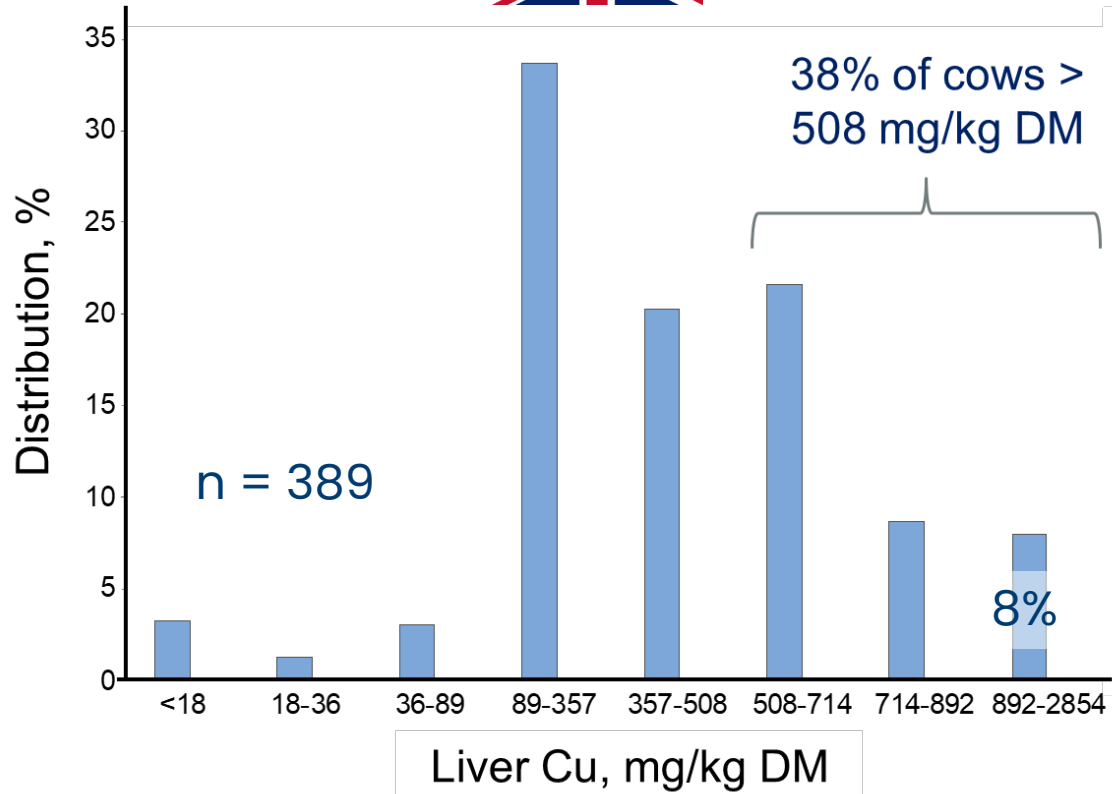
<sup>1</sup> Trouw Nutrition R&D, Amersfoort, the Netherlands; <sup>2</sup> Institute of Animal Nutrition and Diagnostics, Vetsuisse-Faculty, University of Zurich, Zurich, Switzerland; <sup>3</sup> Royal GD, Deventer, the Netherlands; <sup>4</sup> Department of Physiological Sciences, College of Veterinary Medicine, Oklahoma State University, Stillwater, Oklahoma, USA; <sup>5</sup> School of Veterinary Medicine and Science, University of Nottingham, Loughborough, UK; <sup>6</sup> Animal Nutrition, TUM School of Life Sciences Weihenstephan, Technical University of Munich, Freising, Germany




# High level of Cu in liver of dairy cattle





Kendall et al., 2015 



Strickland et al., 2019 

Adult Holstein cows ( $\geq 2$  yr of age)  
Michigan State, 2012 - 2015

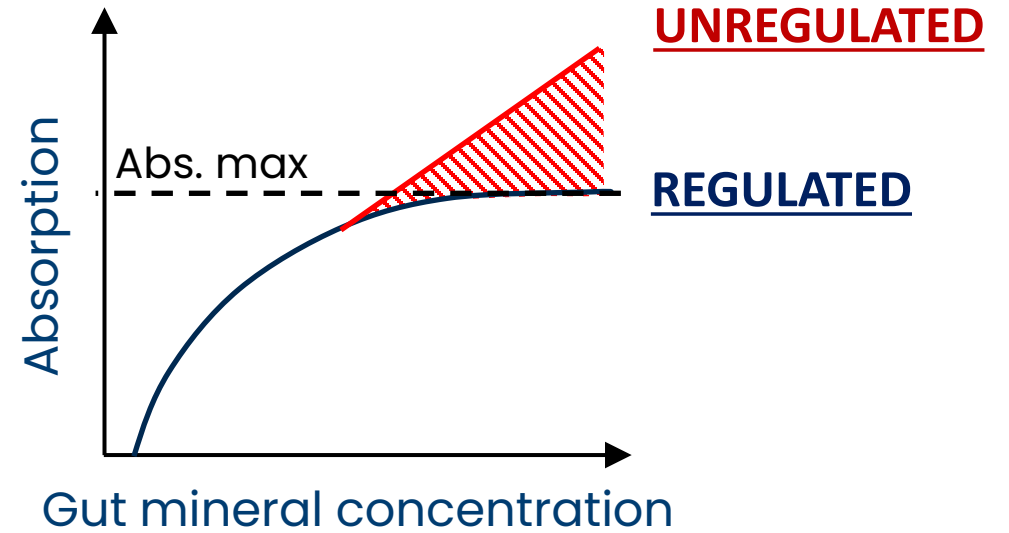
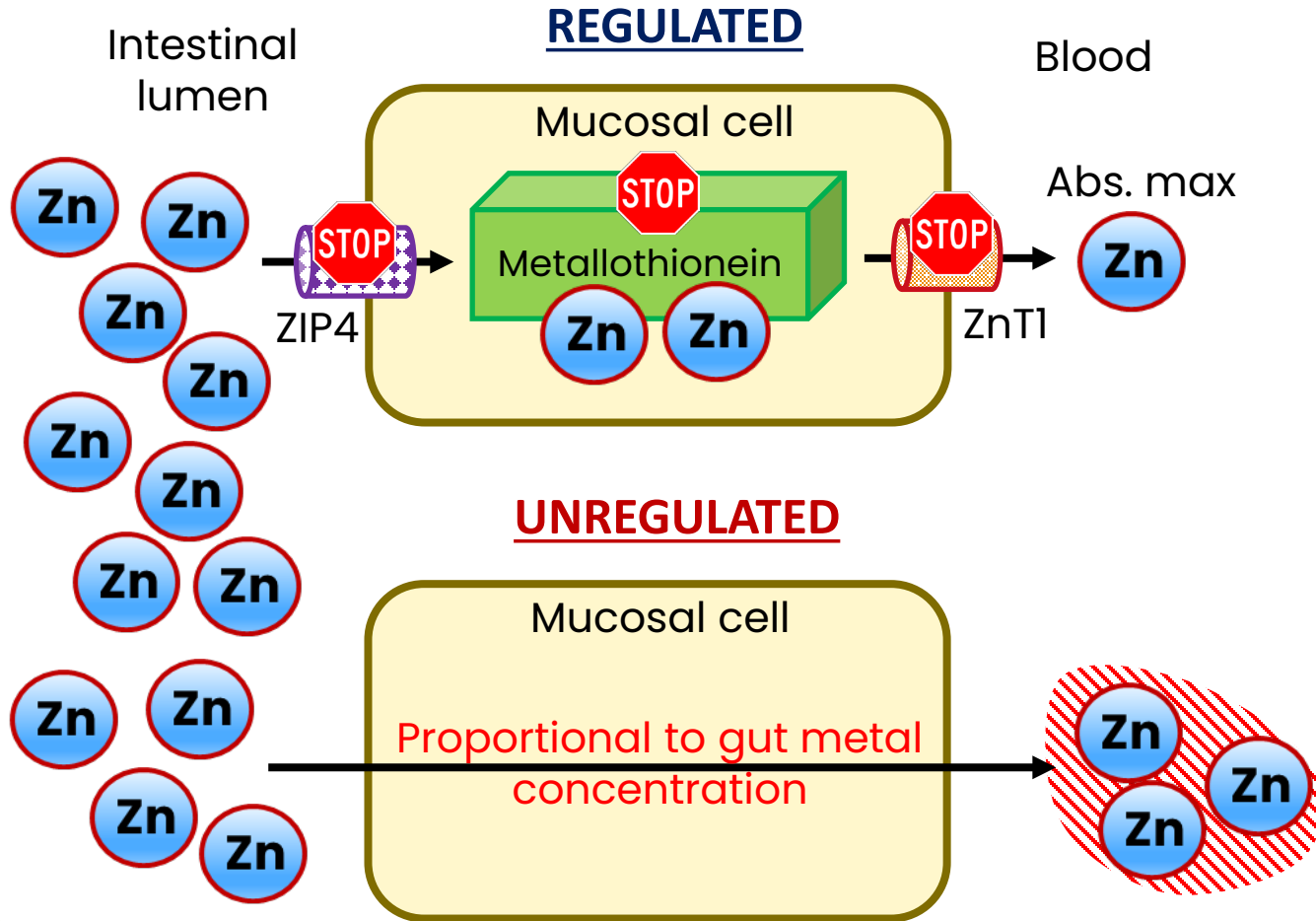
- 31 to 44% > 500 mg/kg DM
  - 5 to 12,2% > 850 mg/kg DM
- n = 562

Counotte et al., 2019   


Cattle  $\geq 2$  yr of age

- 10% > 1066 mg/kg DM

# Limitation to down-regulation upon high GIT metal content



# The neglected role of voluntary dry matter intake



	Growing heifers	Medium MY (36 kg)	High MY (50 kg)
Body weight, kg	345	600	600
Dry matter intake, kg/day	7,9	19,2	25,0
• In % BW	2,3 %	3,2 %	4,2 %
Cu intake, mg/day	120	+ 170 mg/day	+ 85 mg/day
Net Cu requirements, mg/day	1,3	+ 2,3 mg/day	+ 0,6 mg/day

Cu intake – Net Cu requirements,  
mg/day/kg BW

**0,34**

**0,48**

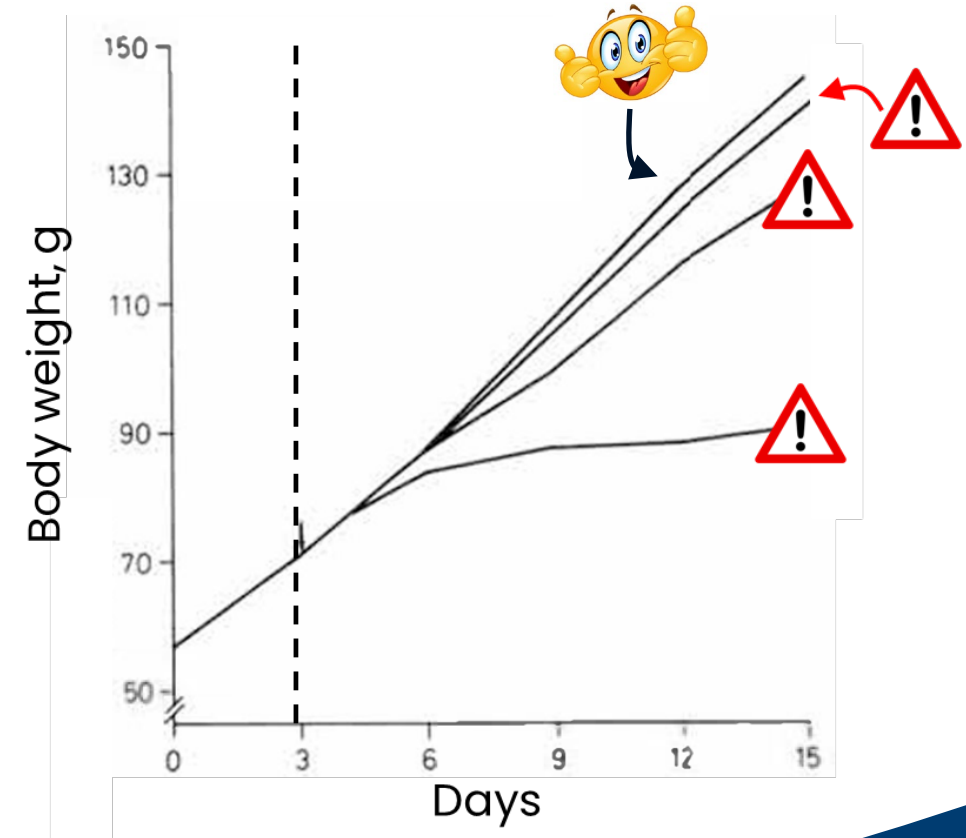
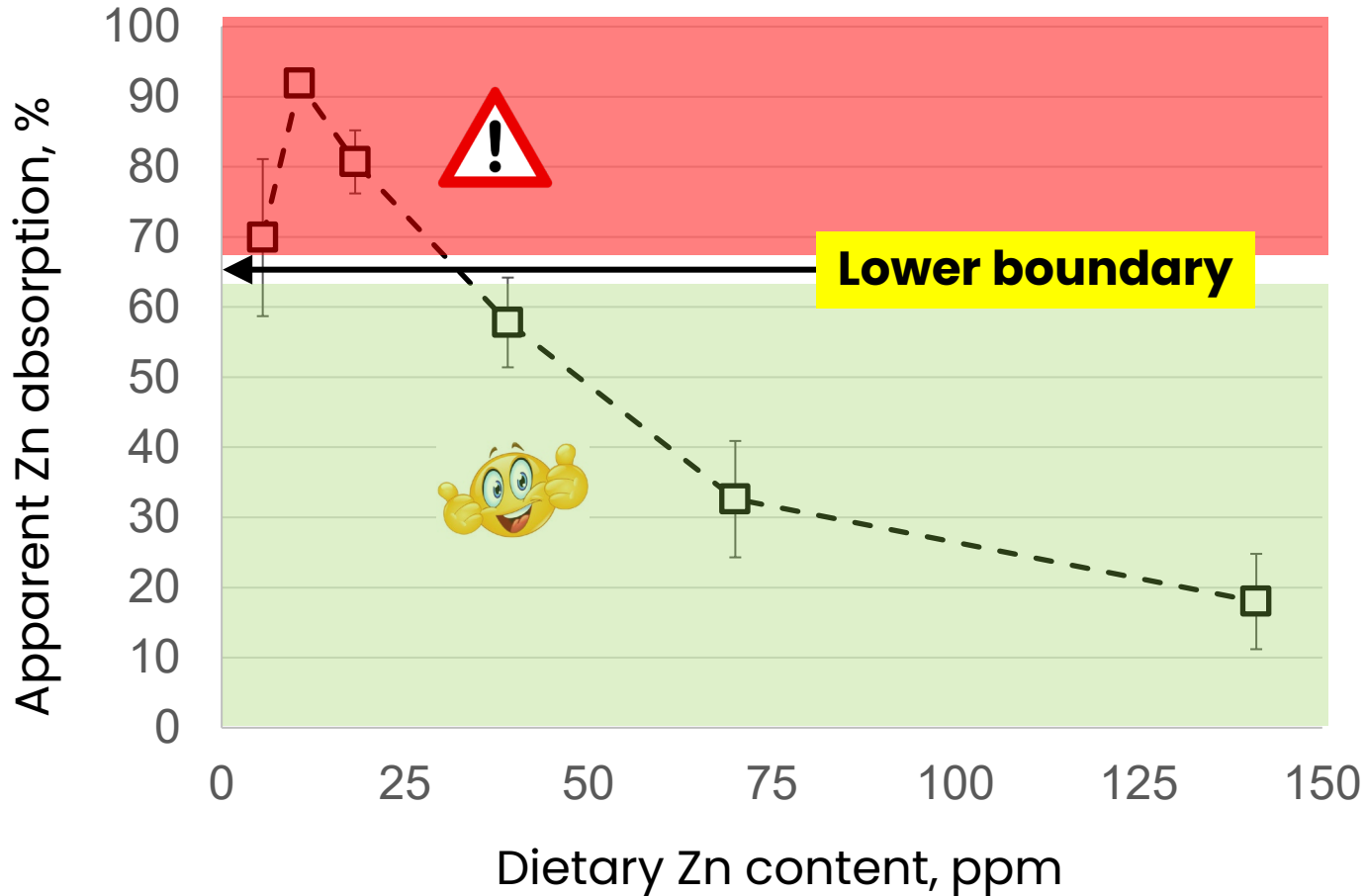
**0,62**

# Novel guidelines for trace metals supplementation

- **Lower and Upper boundaries** of regulation
- Quantification of **probability density functions**
  - For gross native supply of trace metal
  - For animal net trace metal requirements
- Defining **confidence interval of supplementation**



# Defining lower boundaries of regulation





# Estimating maximal apparent absorption for lower boundary



**Cu:** 75 dietary treatments

**Zn:** 34 dietary treatments

**Mn:** 32 dietary treatments

## Eligibility of study

Experimentally induced changes in available supply

Reported DMI and performance

Minimum duration of 50 days

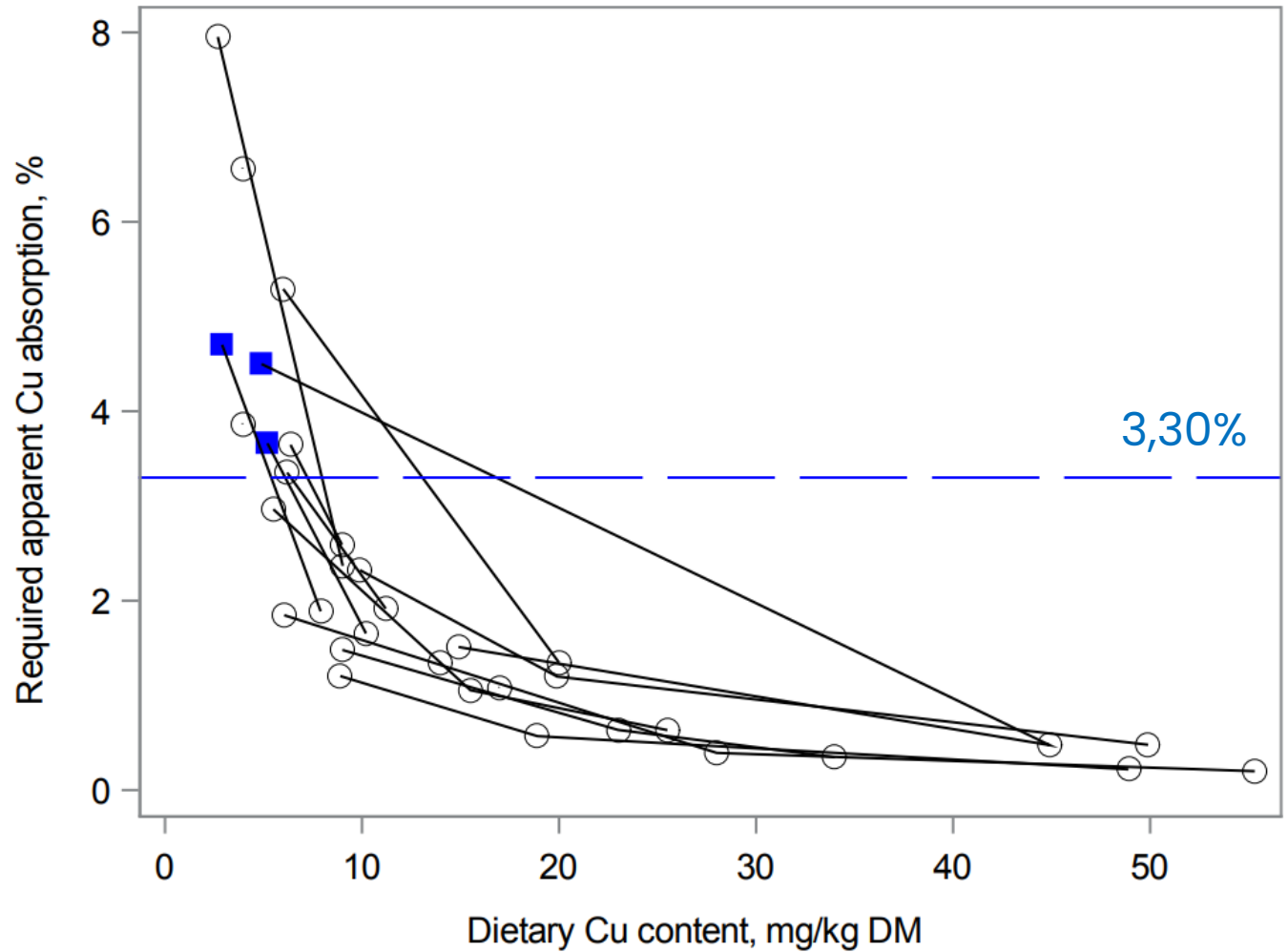
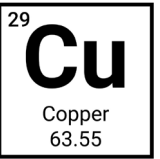
## Standard set of calculations

Net requirement

Required apparent absorption efficiency

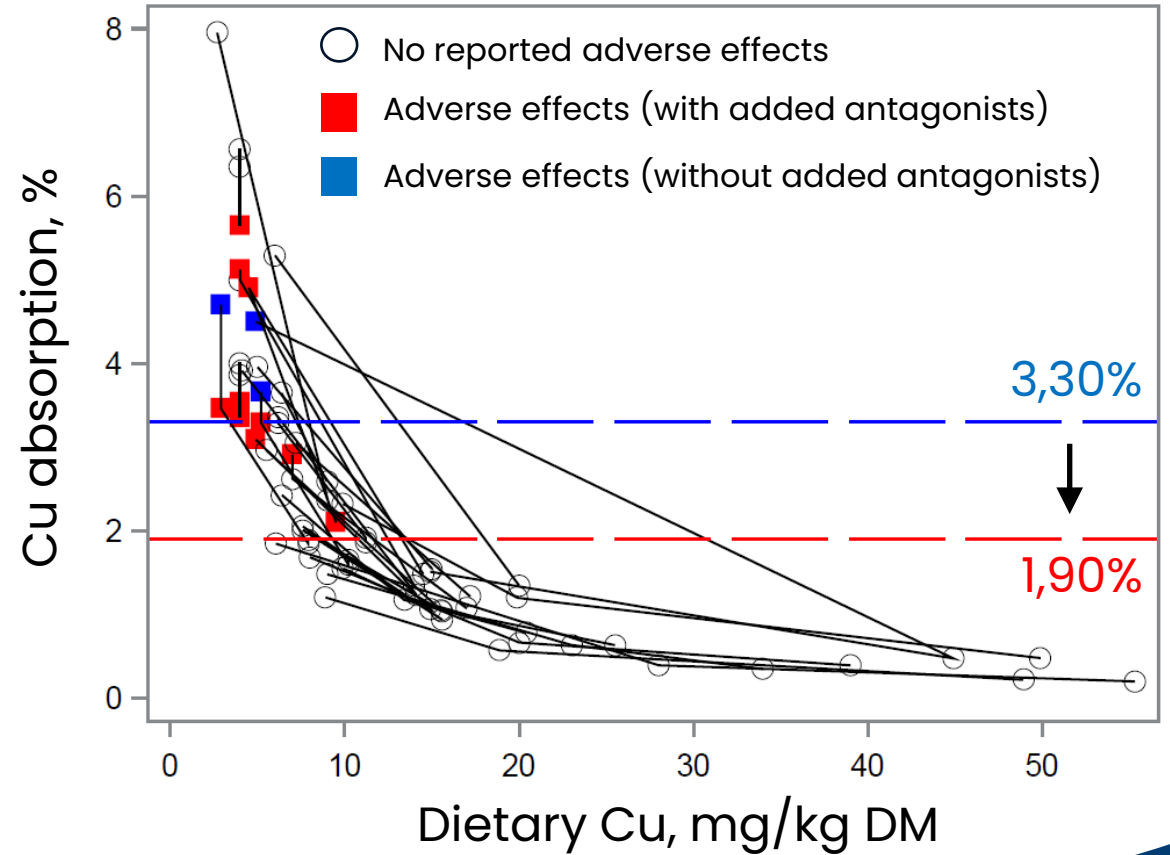
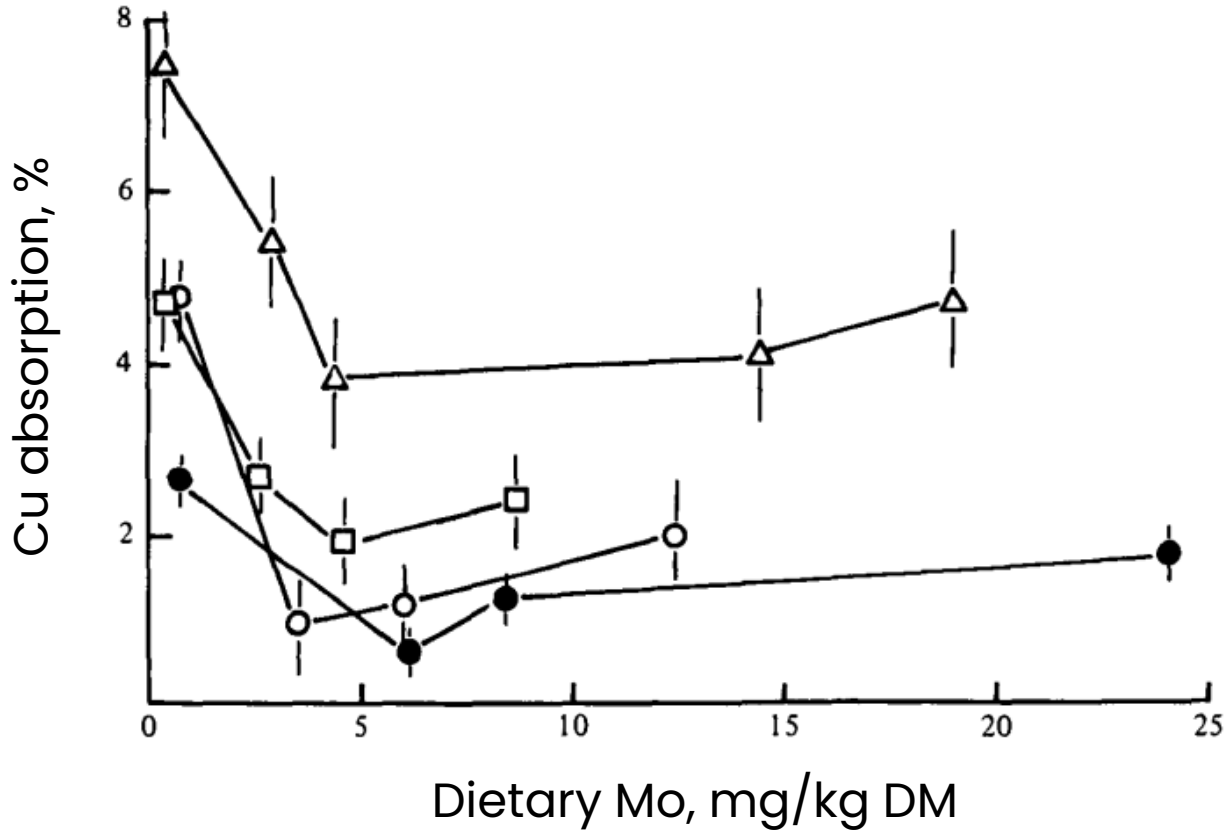
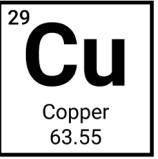
Presence/Absence of adverse effects

# Highest Cu absorption compatible with optimal performance



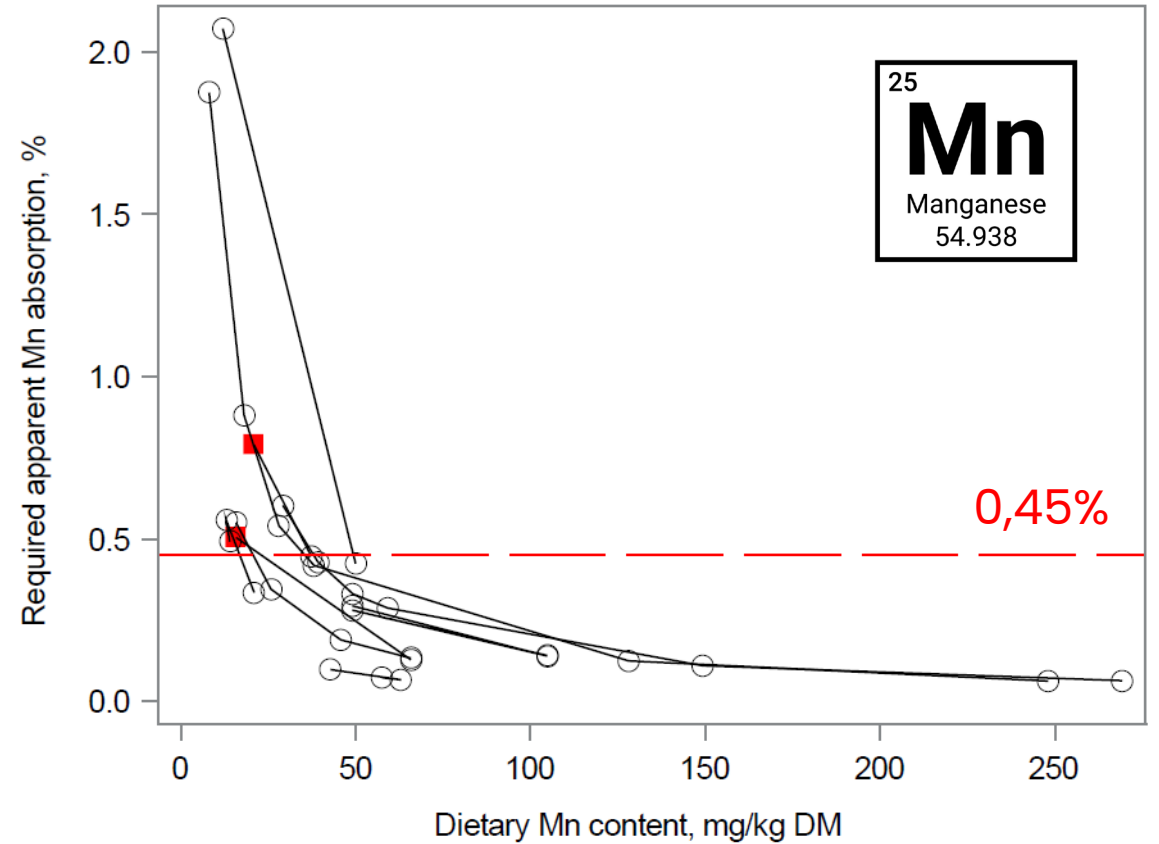
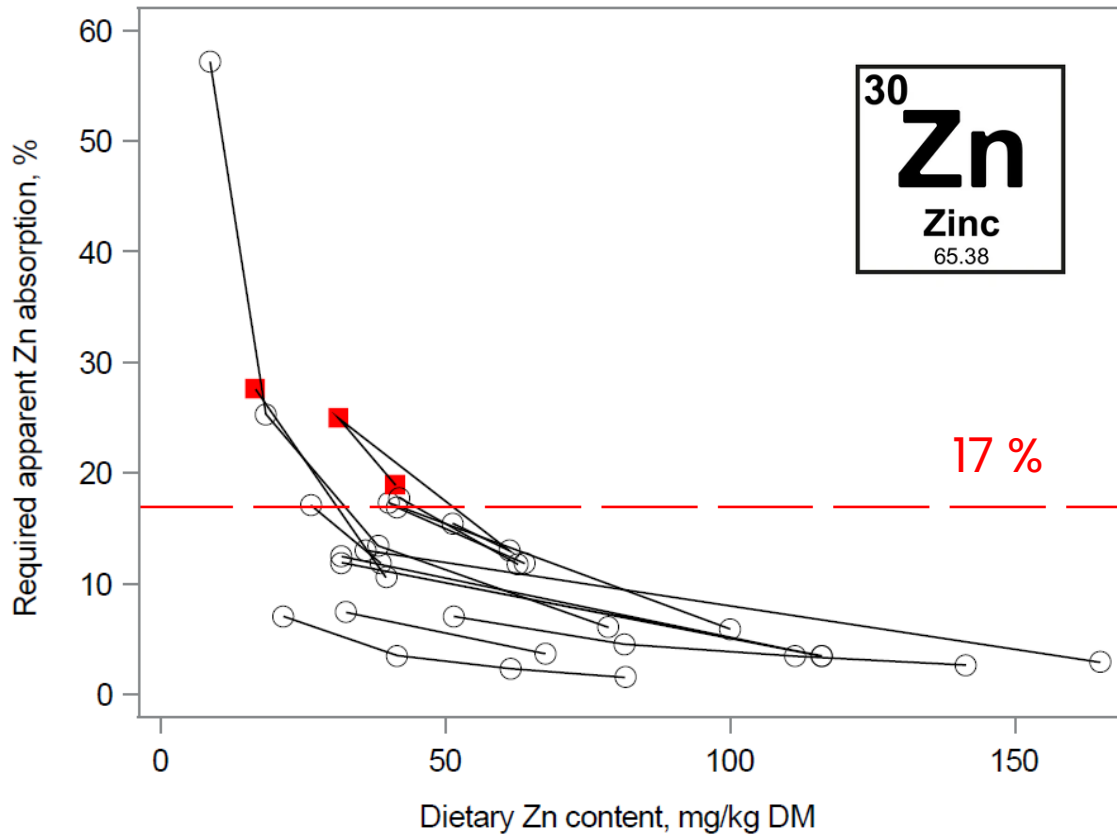
- Reduced DMI and/or ADG
- No reported adverse effects

# Coping with exceptions – High level of dietary Mo



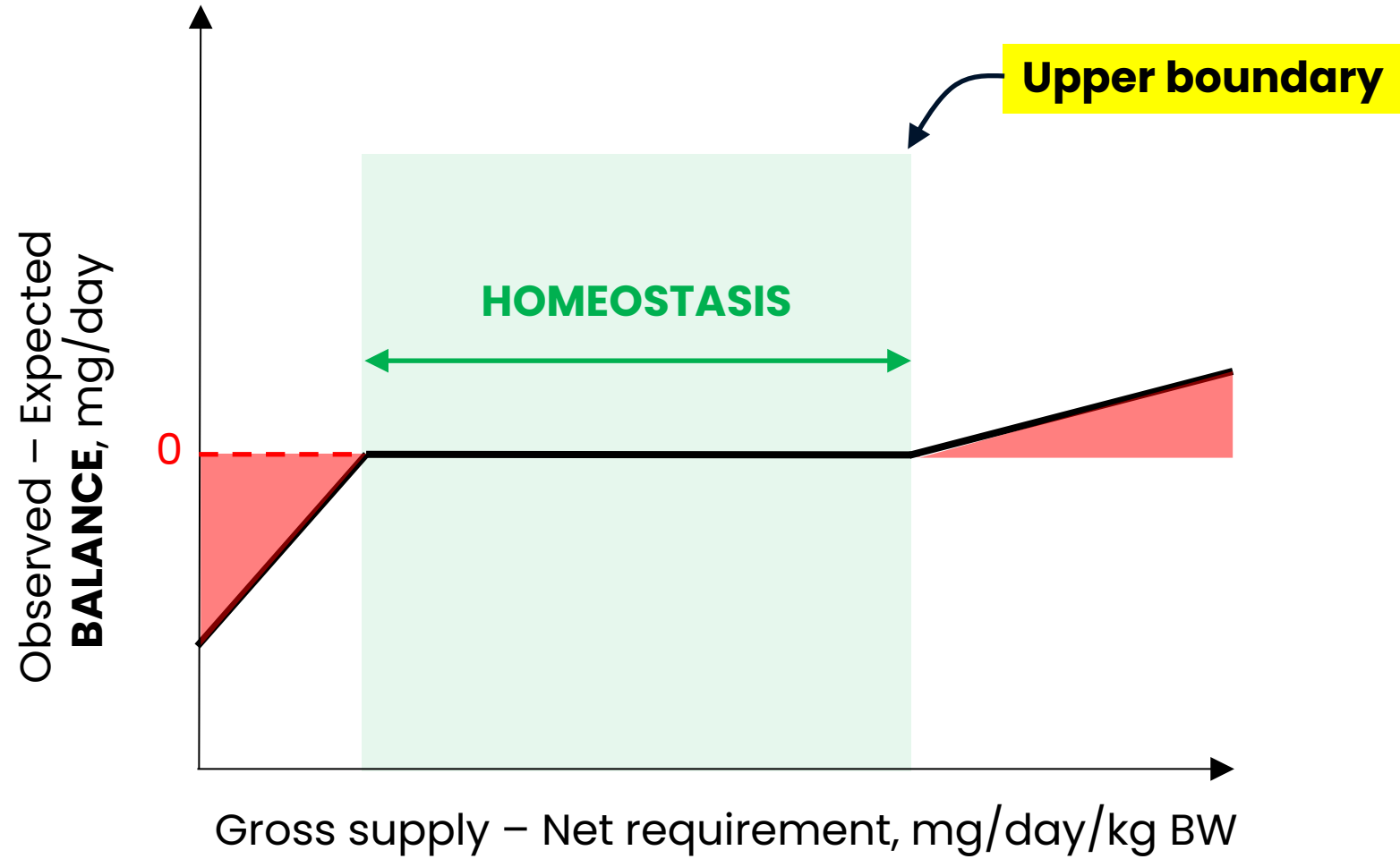
Left Figure from Suttle, 1983

# Highest Zn and Mn absorption compatible with optimal performance

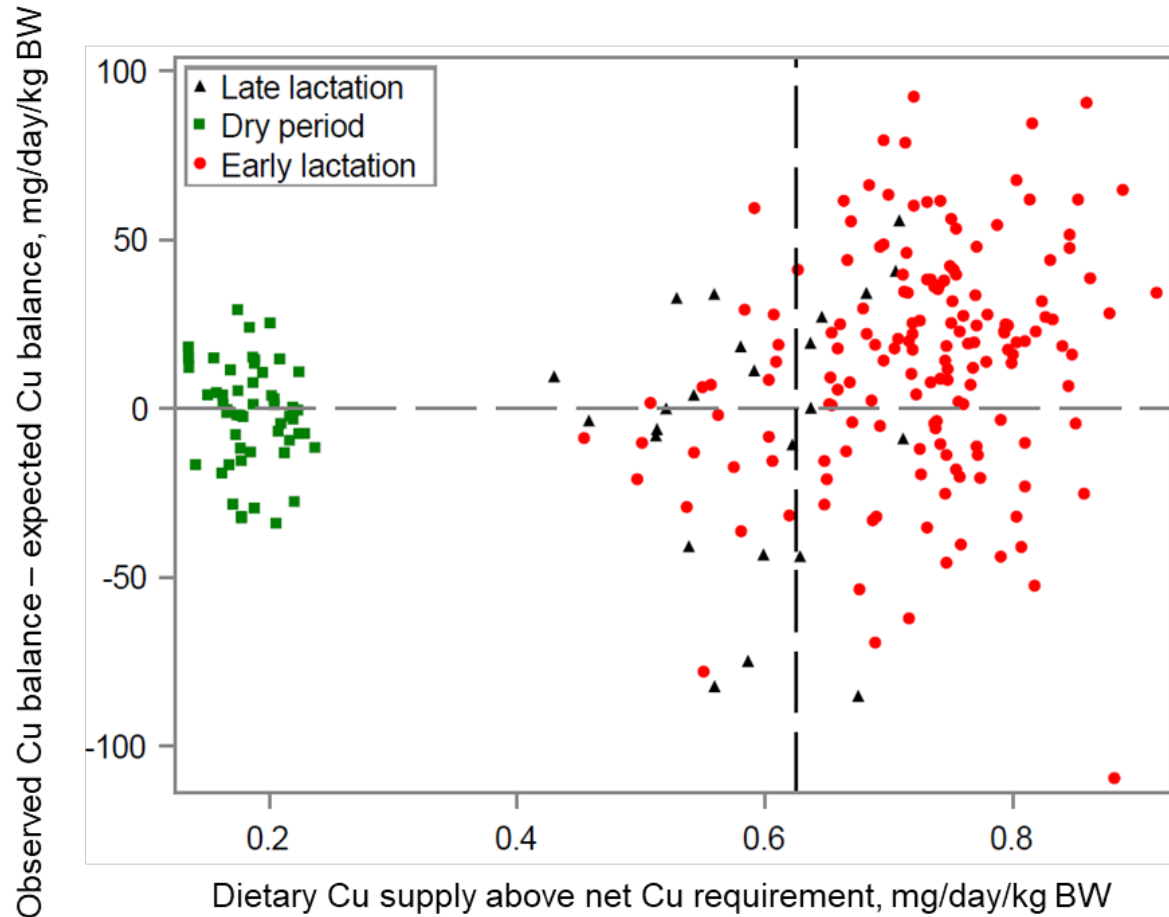


- No reported adverse effects
- Adverse effects

# Defining upper boundaries of regulation



# The upper boundaries for Cu



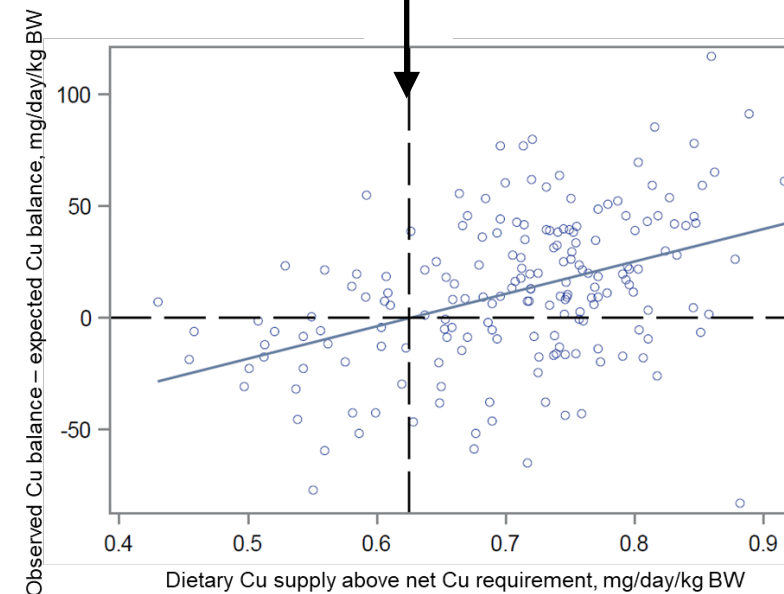
Nutrient Physiology, Metabolism, and Nutrient-Nutrient Interactions

## Zinc, Copper, and Manganese Homeostasis and Potential Trace Metal Accumulation in Dairy Cows: Longitudinal Study from Late Lactation to Subsequent Mid-Lactation

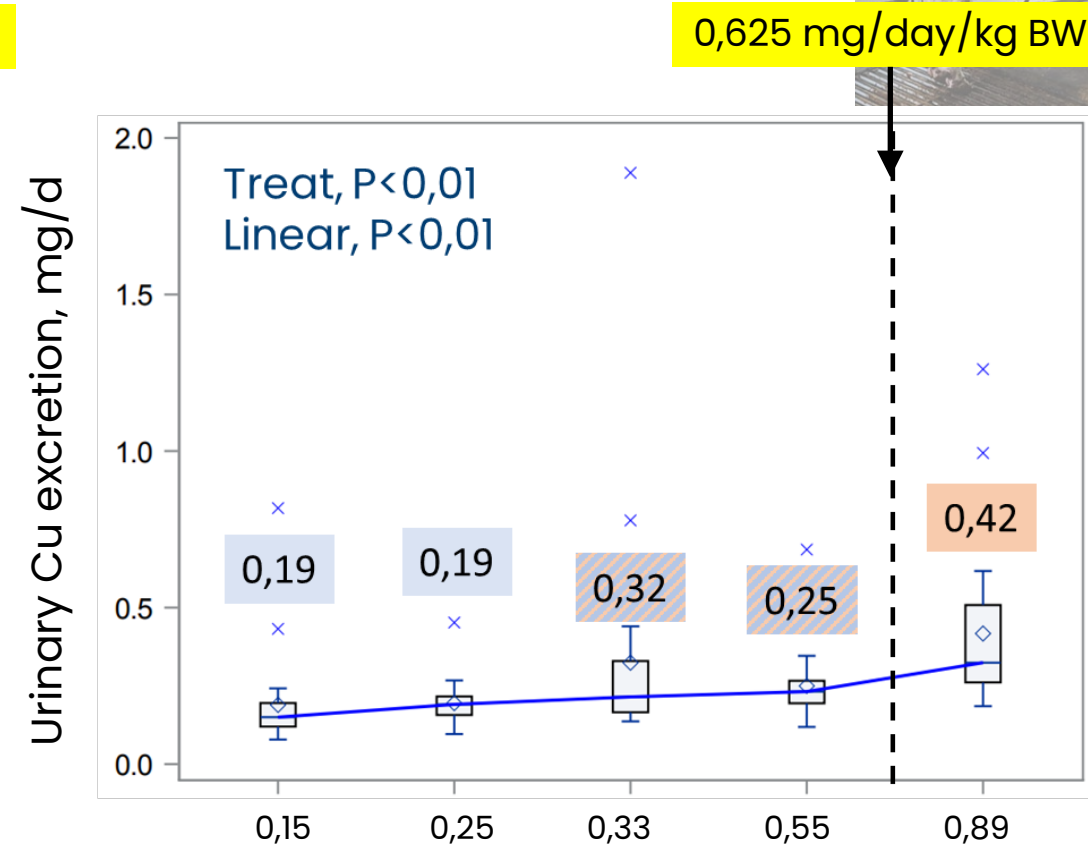
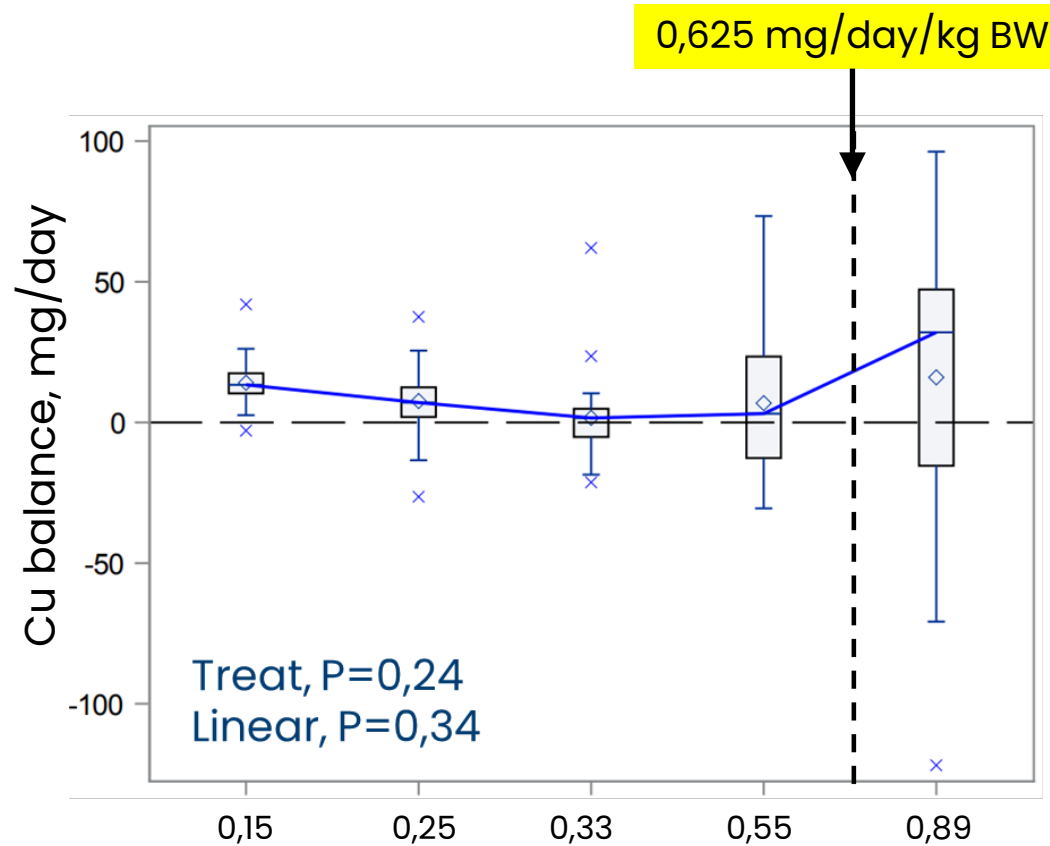
Jean-Baptiste Daniel<sup>1,\*</sup>, Daniel Brugger<sup>2</sup>, Saskia van der Drift<sup>3</sup>, Deon van der Merwe<sup>3,4</sup>, Nigel Kendall<sup>5</sup>, Wilhelm Windisch<sup>6</sup>, John Doelman<sup>1</sup>, Javier Martín-Tereso<sup>1</sup>

<sup>1</sup> Trouw Nutrition R&D, Amersfoort, the Netherlands; <sup>2</sup> Institute of Animal Nutrition and Diagnostics, Vetsuisse-Faculty, University of Zurich, Zurich, Switzerland; <sup>3</sup> Royal GD, Deventer, the Netherlands; <sup>4</sup> Department of Physiological Sciences, College of Veterinary Medicine, Oklahoma State University, Stillwater, Oklahoma, USA; <sup>5</sup> School of Veterinary Medicine and Science, University of Nottingham, Loughborough, UK; <sup>6</sup> Animal Nutrition, TUM School of Life Sciences Weihenstephan, Technical University of Munich, Freising, Germany

0,625 mg/day/kg BW

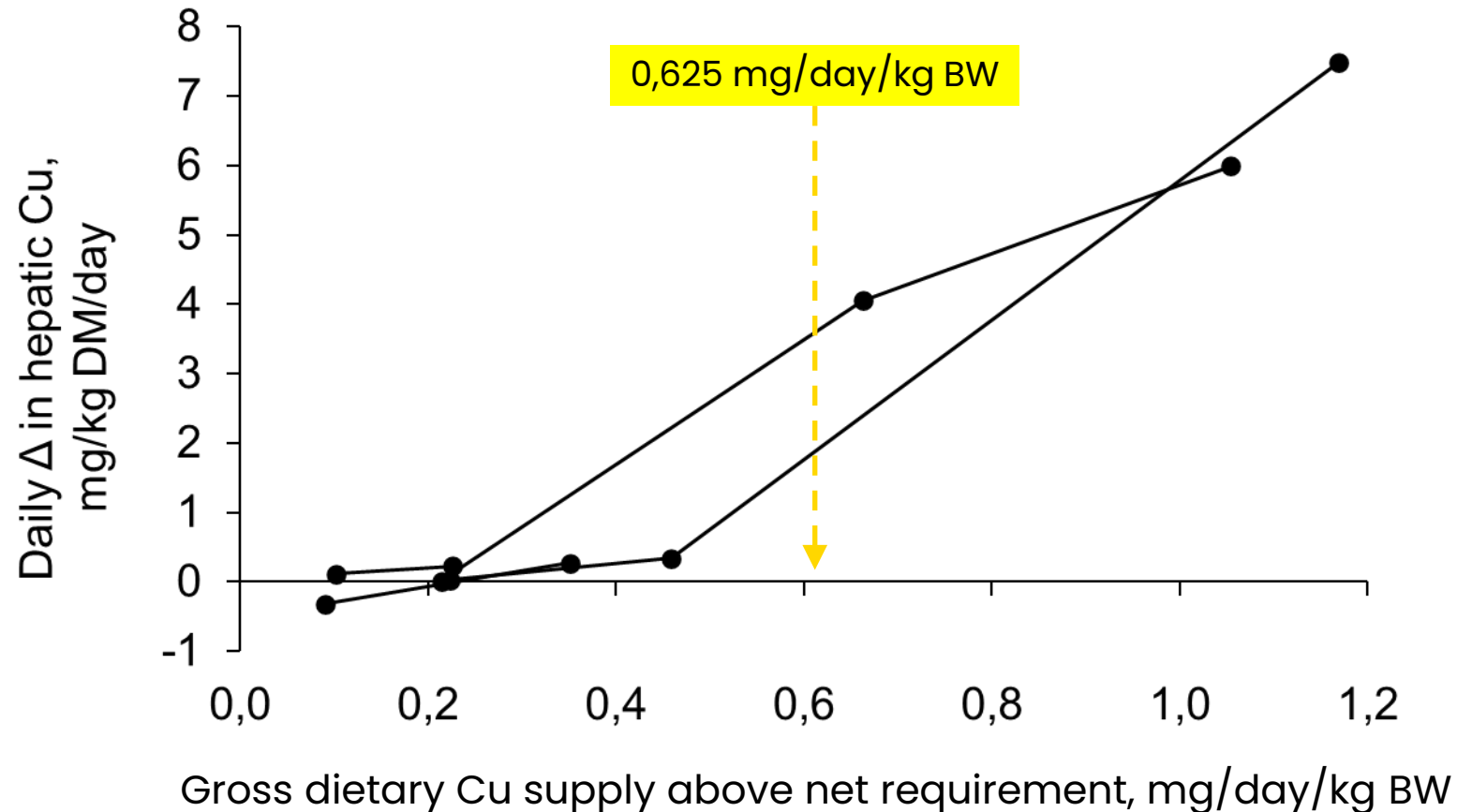


# Substantiation of upper limit of adequacy for Cu supply



Gross dietary Cu supply above net requirement, mg/day/kg BW

# Substantiation of upper limit of adequacy for Cu supply



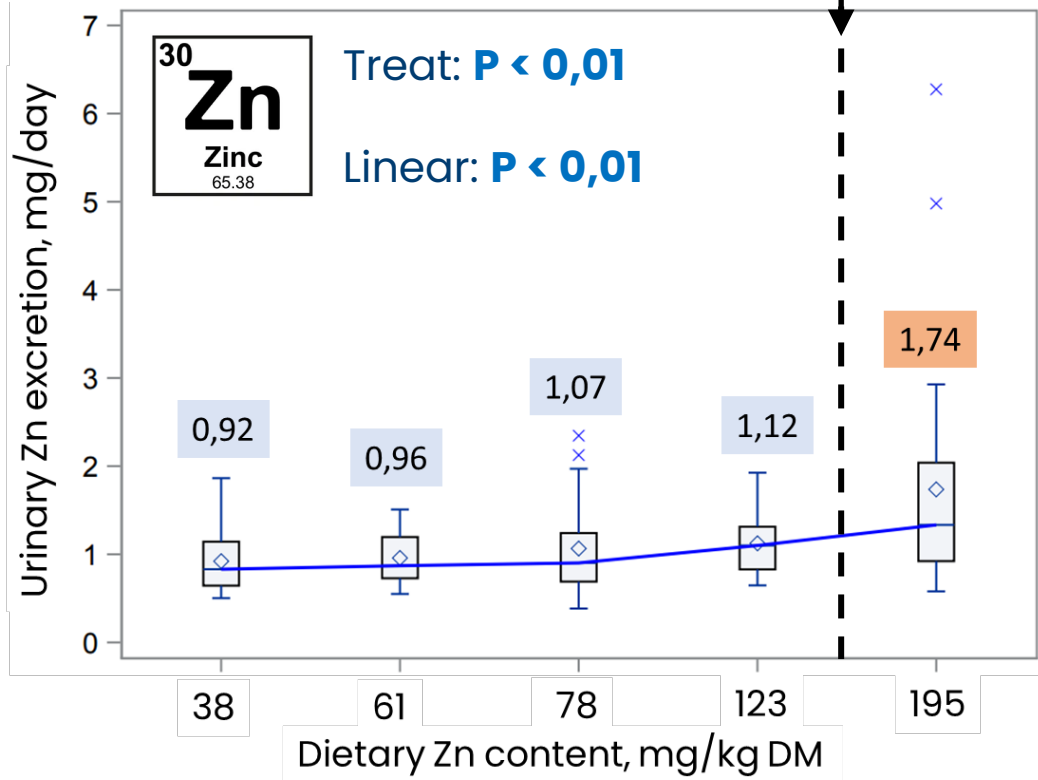
## Publications used

- Ward and Spears, 1997 (n=2)
- Engle et al., 2000 (n=3)
- Engle and Spears, 2000 (n=3)
- Balemi et al., 2010 (n=2)

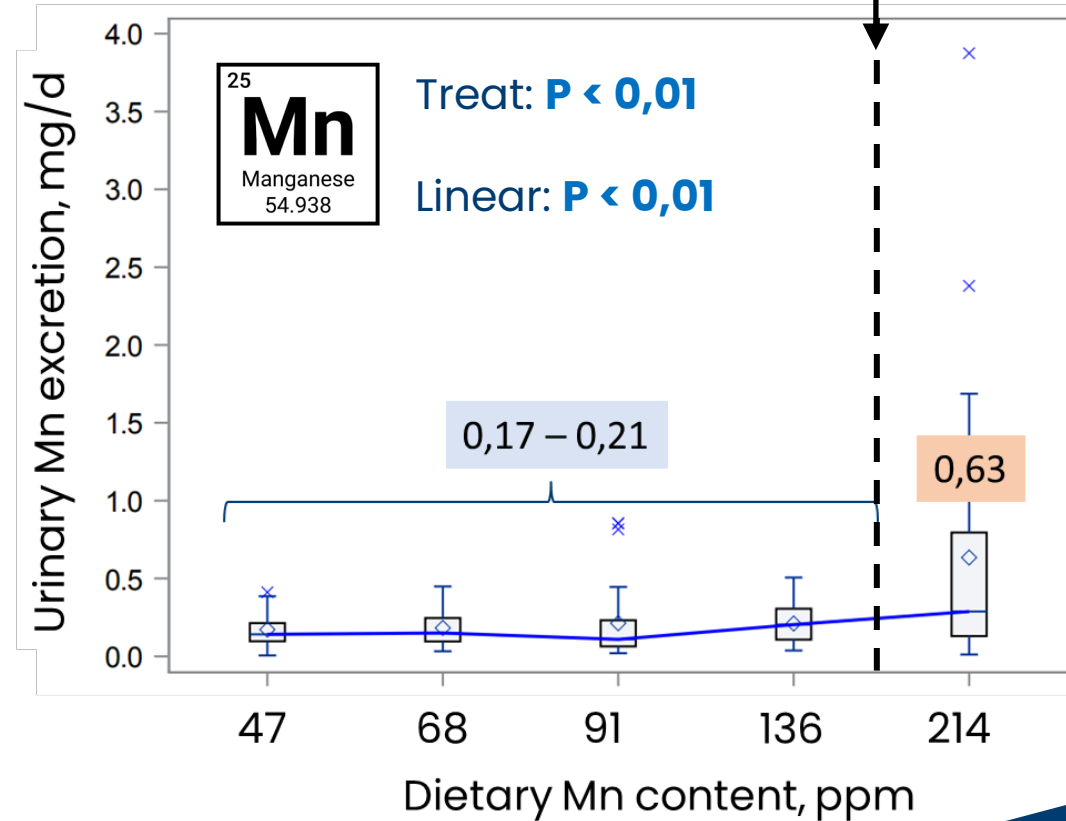


# Upper boundaries for Zn and Mn

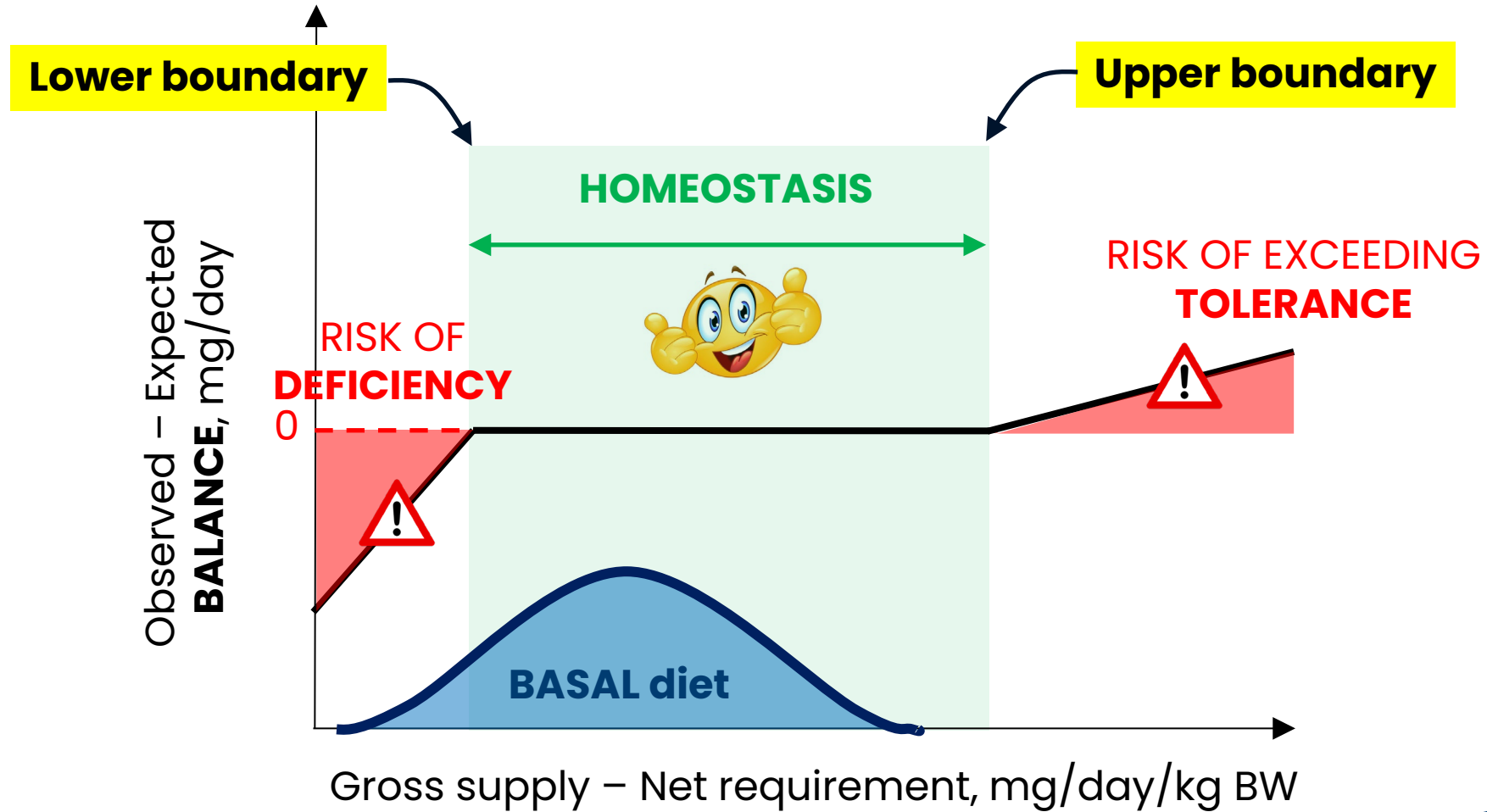
3,54 mg/day/kg BW



2,92 mg/day/kg BW



# Quantifying the risk of inadequate trace metal supply



# Simulating the probability density function of supply



## Grass forages

Cu	12,0 ± 7,0
Zn	26,5 ± 12,8
Mn	38,1 ± 20,8



## Corn silage

Cu	8,1 ± 4,4
Zn	30,8 ± 21,5
Mn	57,3 ± 40,0



## Concentrate

Cu	8,9 ± 1,0
Zn	48,7 ± 5,7
Mn	48,8 ± 7,8

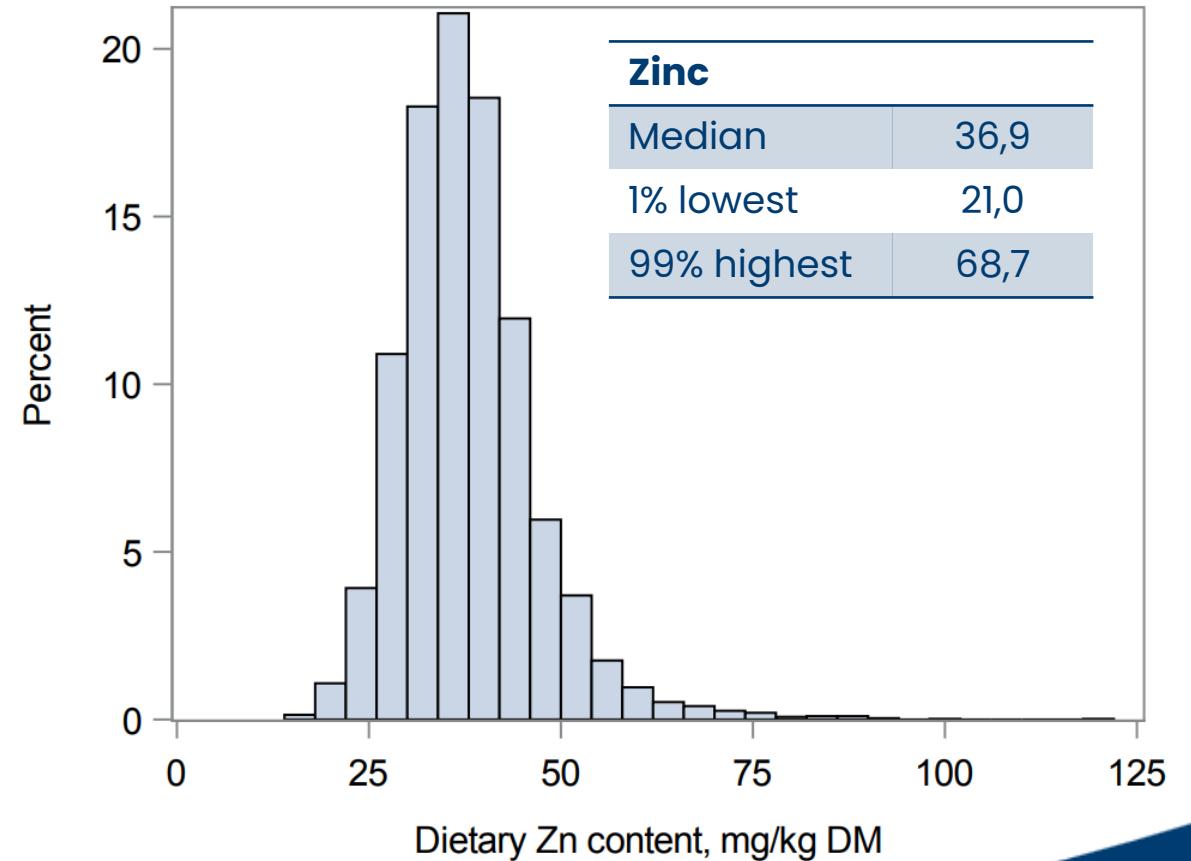
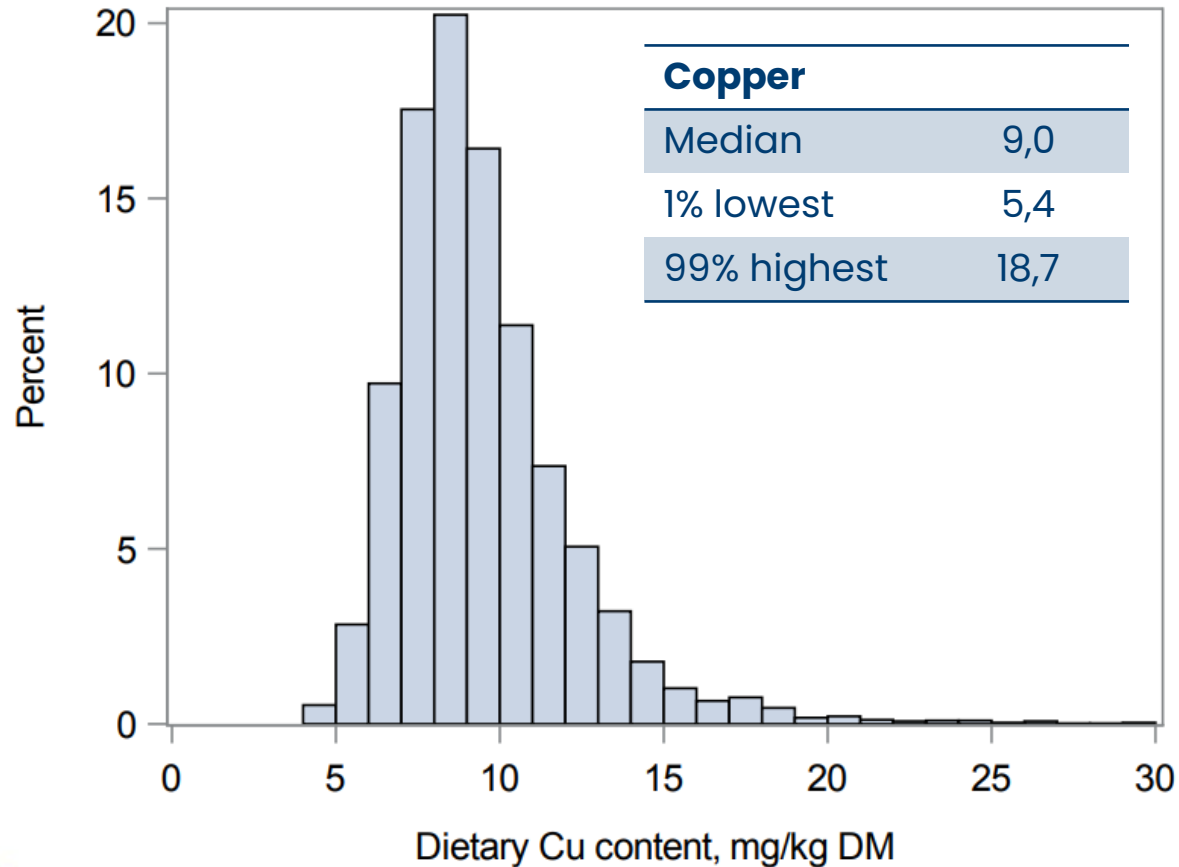
Adams et al., 1974  
Feedipedia

Remaining %DM  
Random  
(0% to 100% CS)

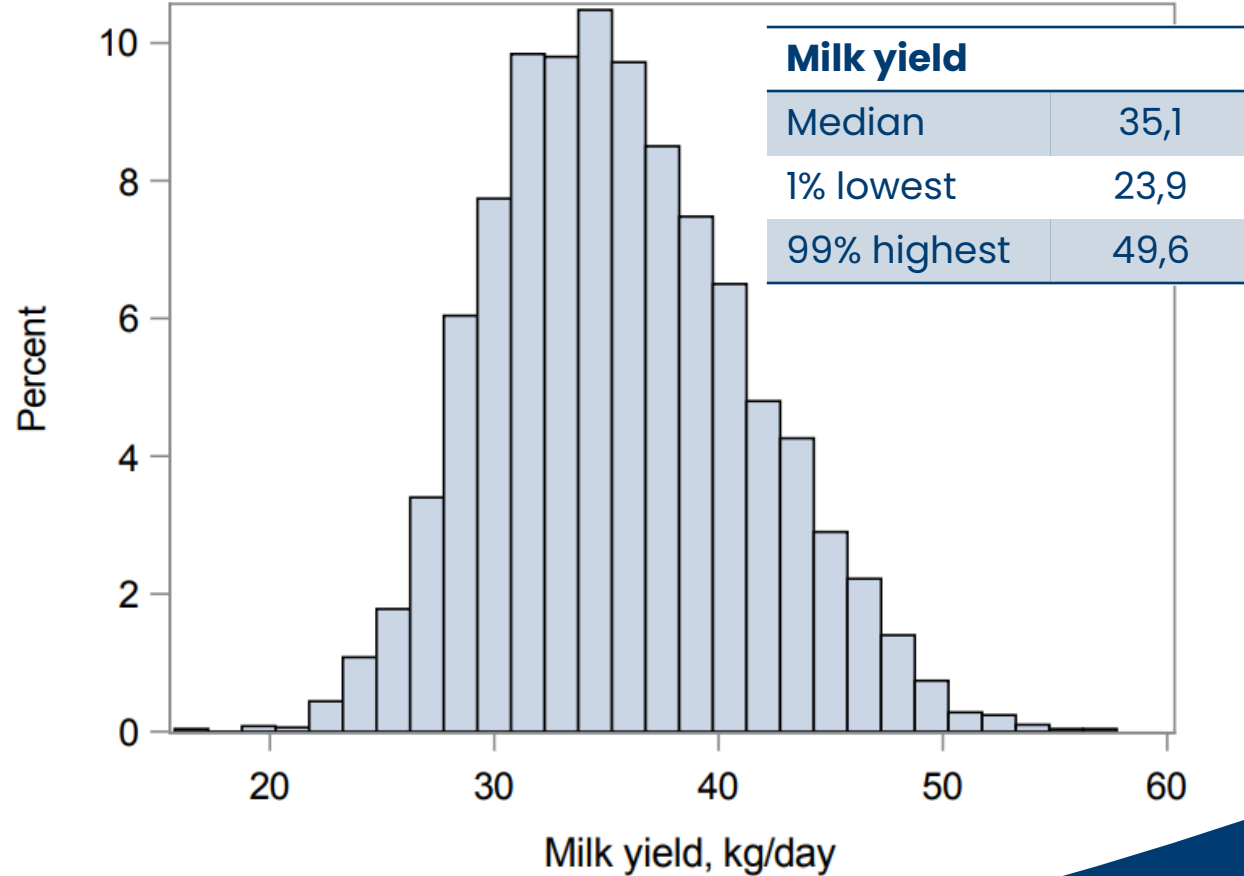
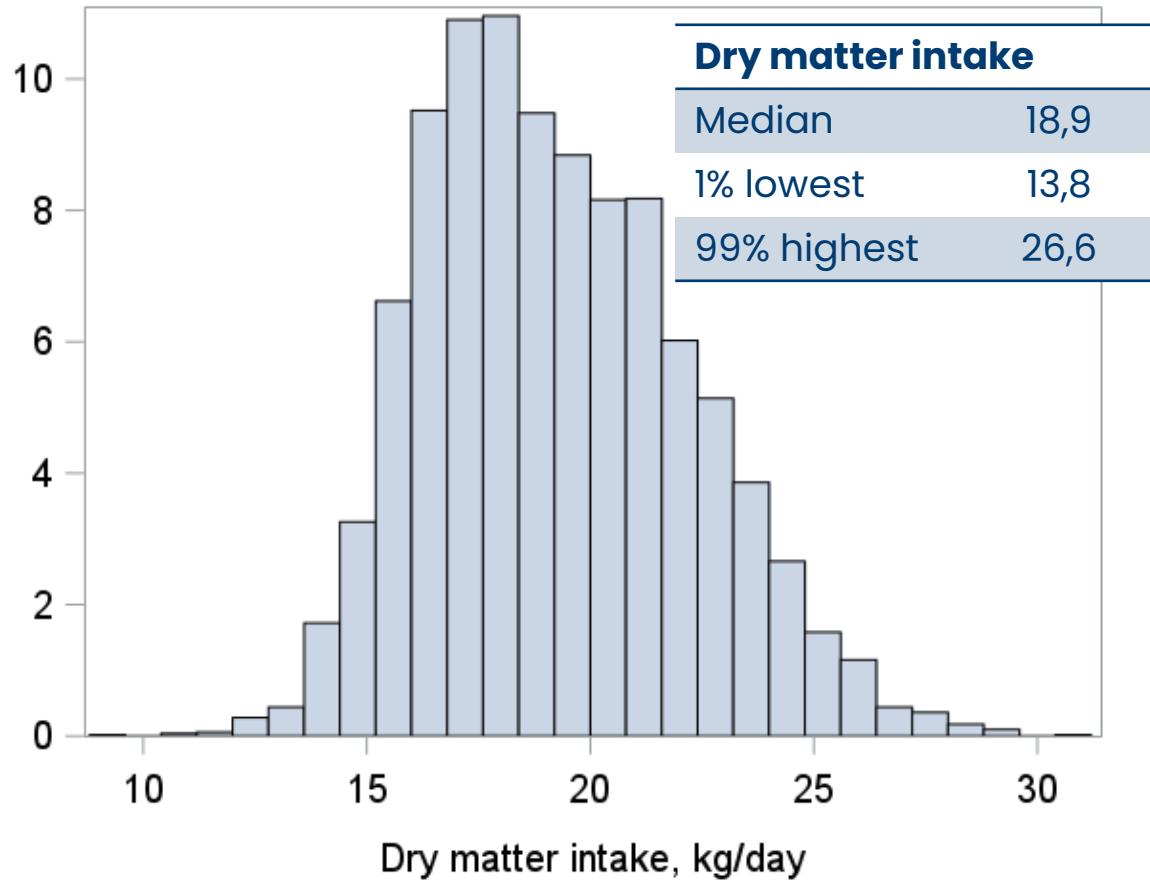
47 ± 13 % DM  
Daniel et al., 2016



# Modeling native dietary concentration

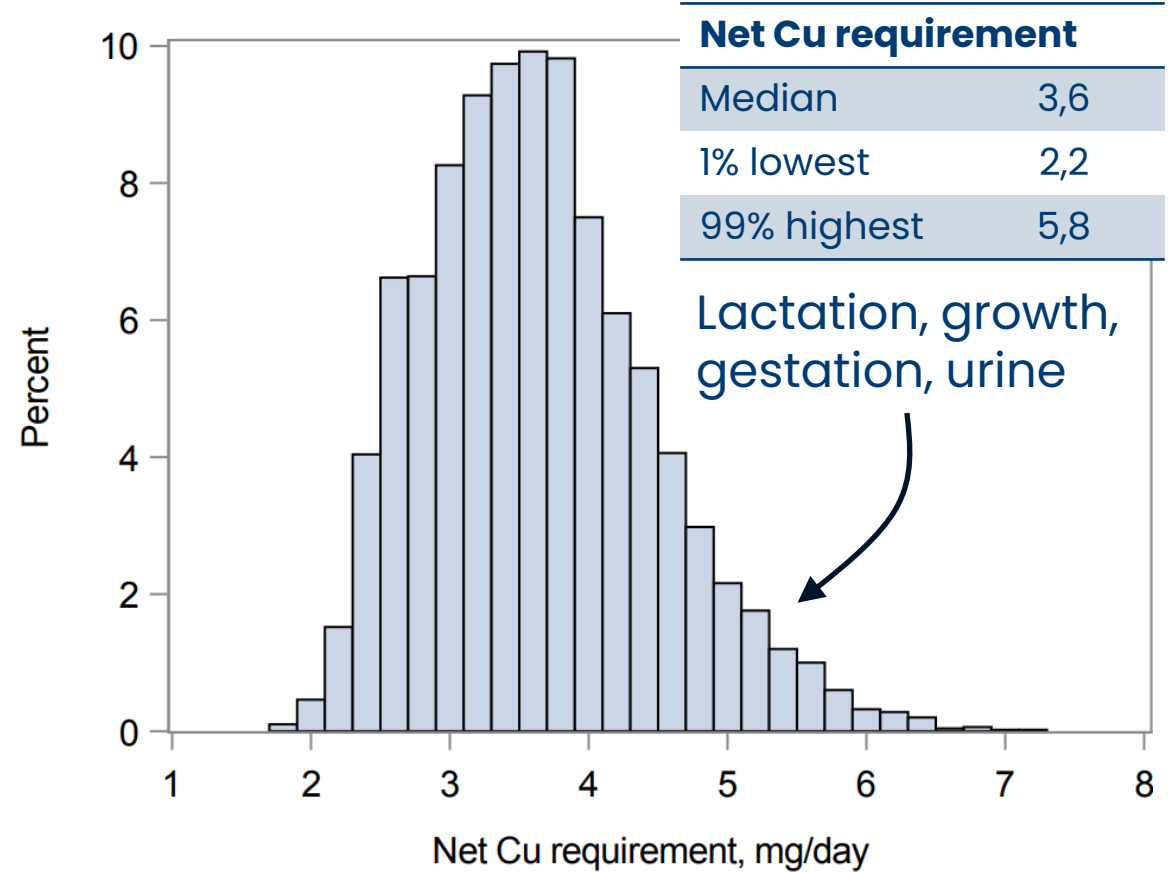
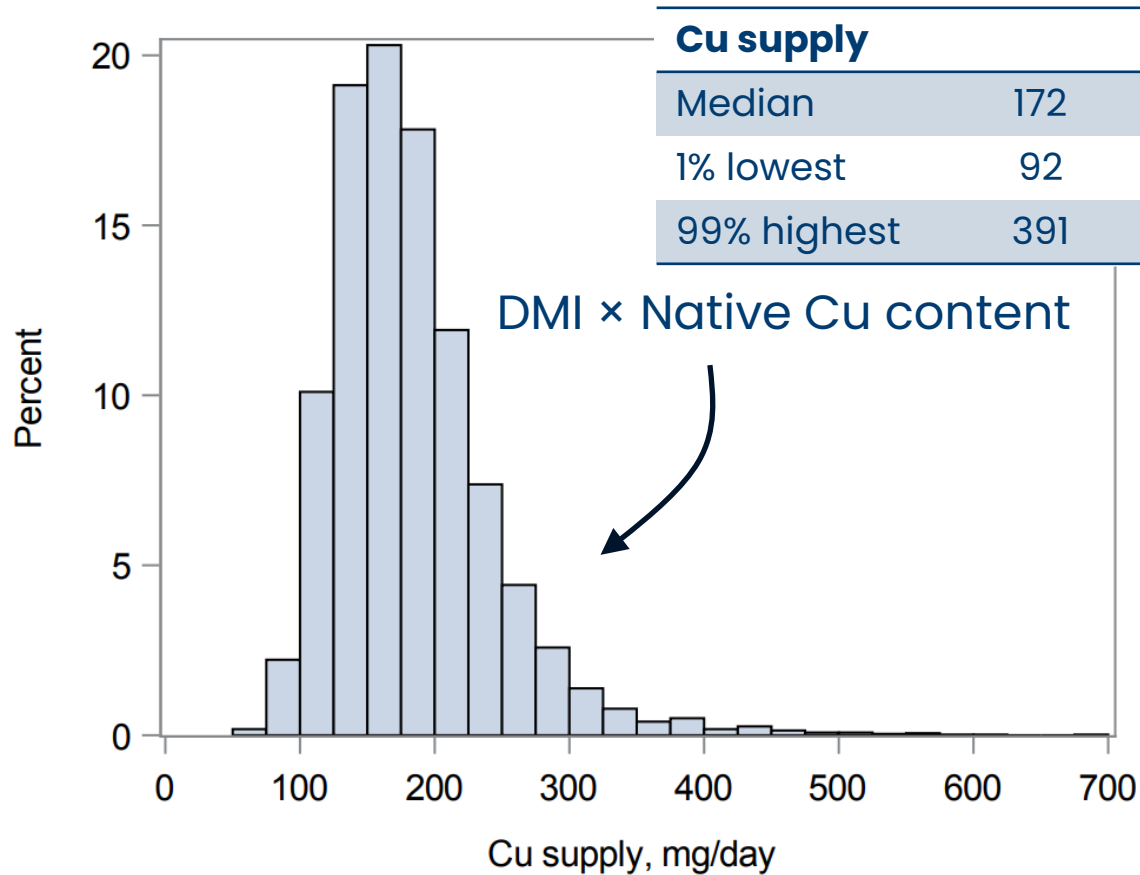


# Modeling animal diversity



30% primiparous and 70% multiparous ; Mean ( $\pm$ SD) from meta-analysis of Husnain and Santos, 2019

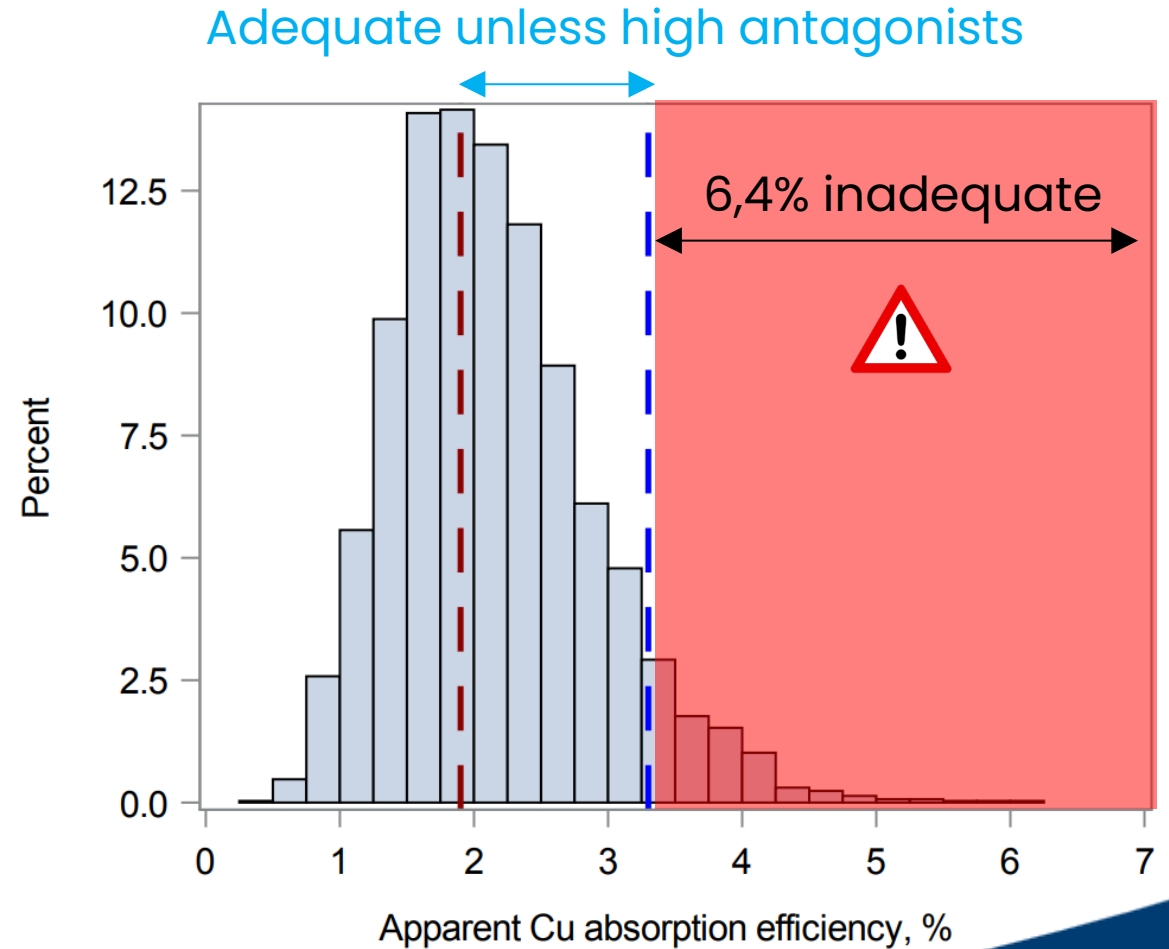
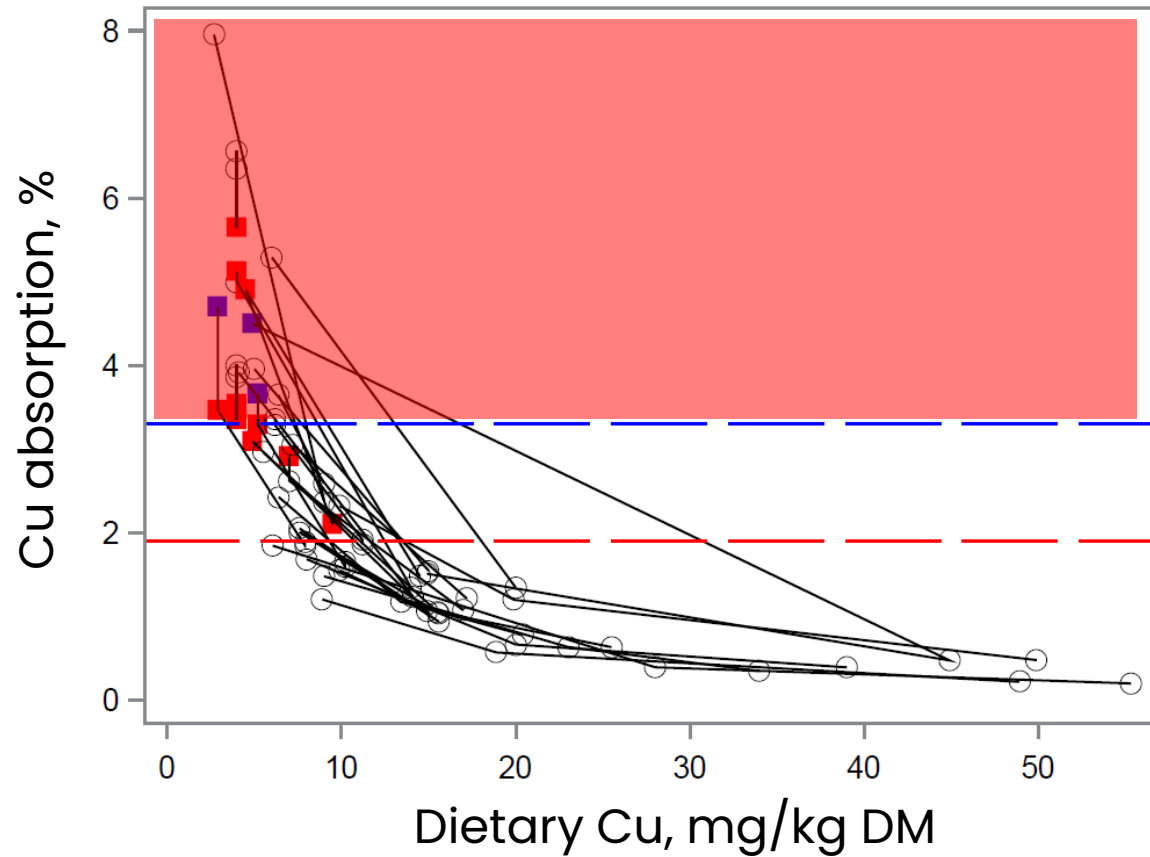
# Modeling trace metal supply and requirement



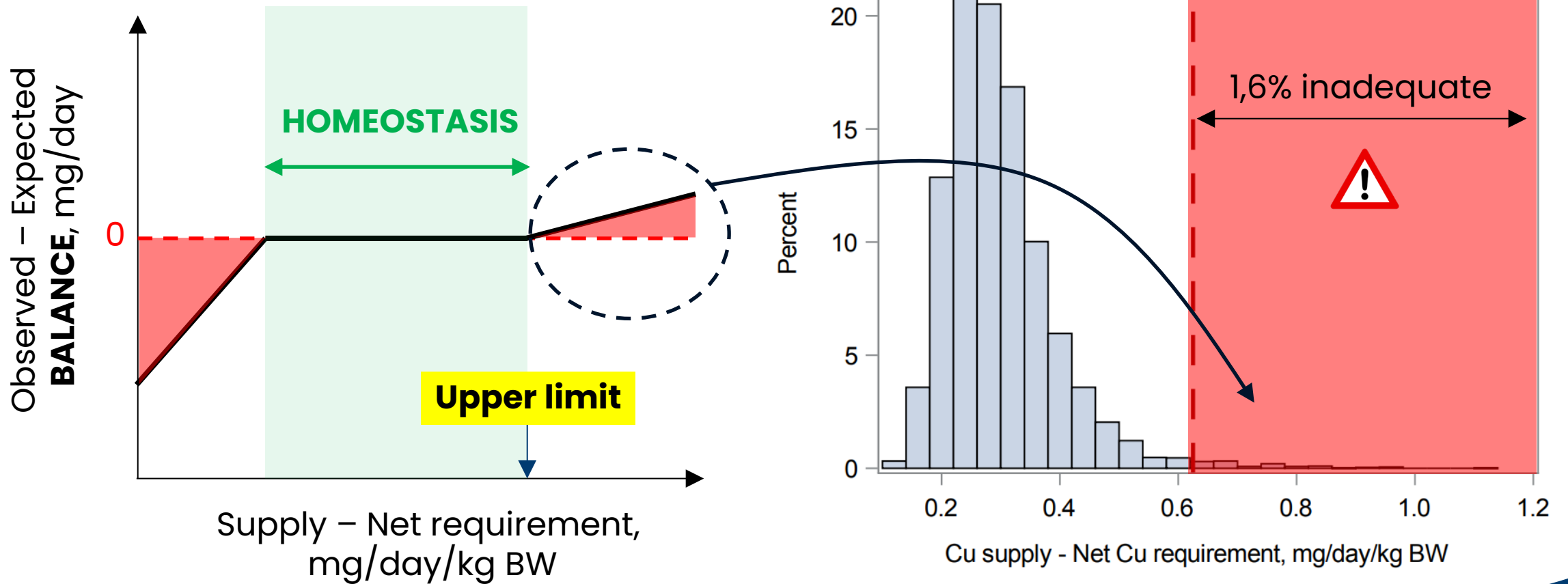
**Apparent absorption efficiency for LOWER boundary**

**Gross supply above net requirement for UPPER boundary**

# Probability that supply is below LOWER boundary



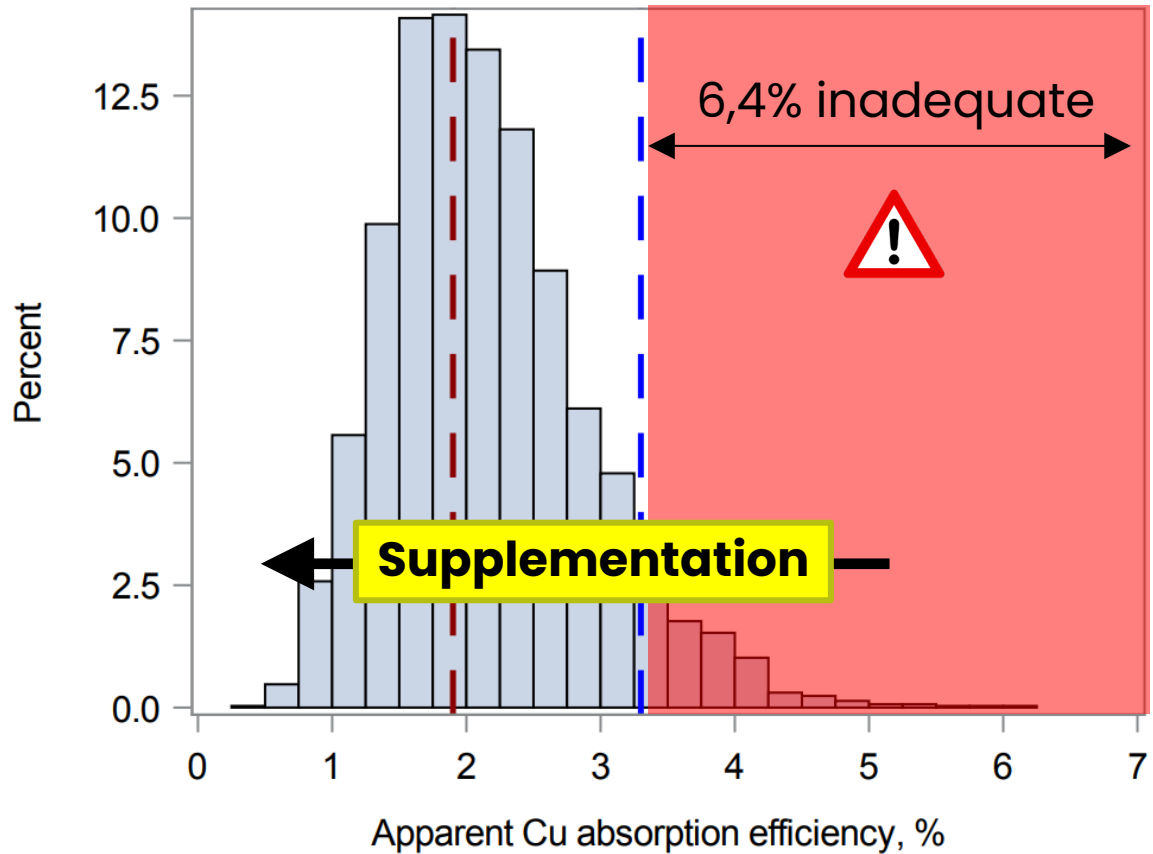
# Probability that supply is above UPPER boundary



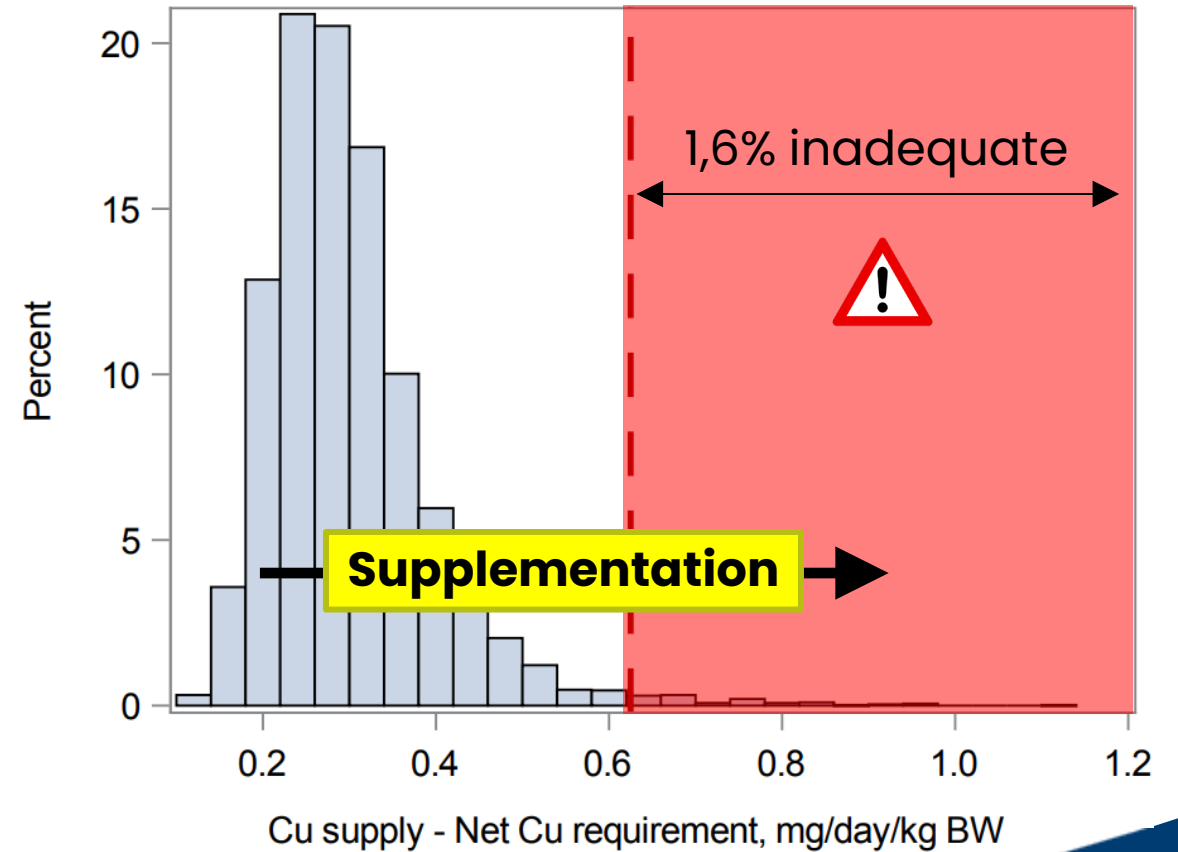


# Impact of supplemental feeding strategy

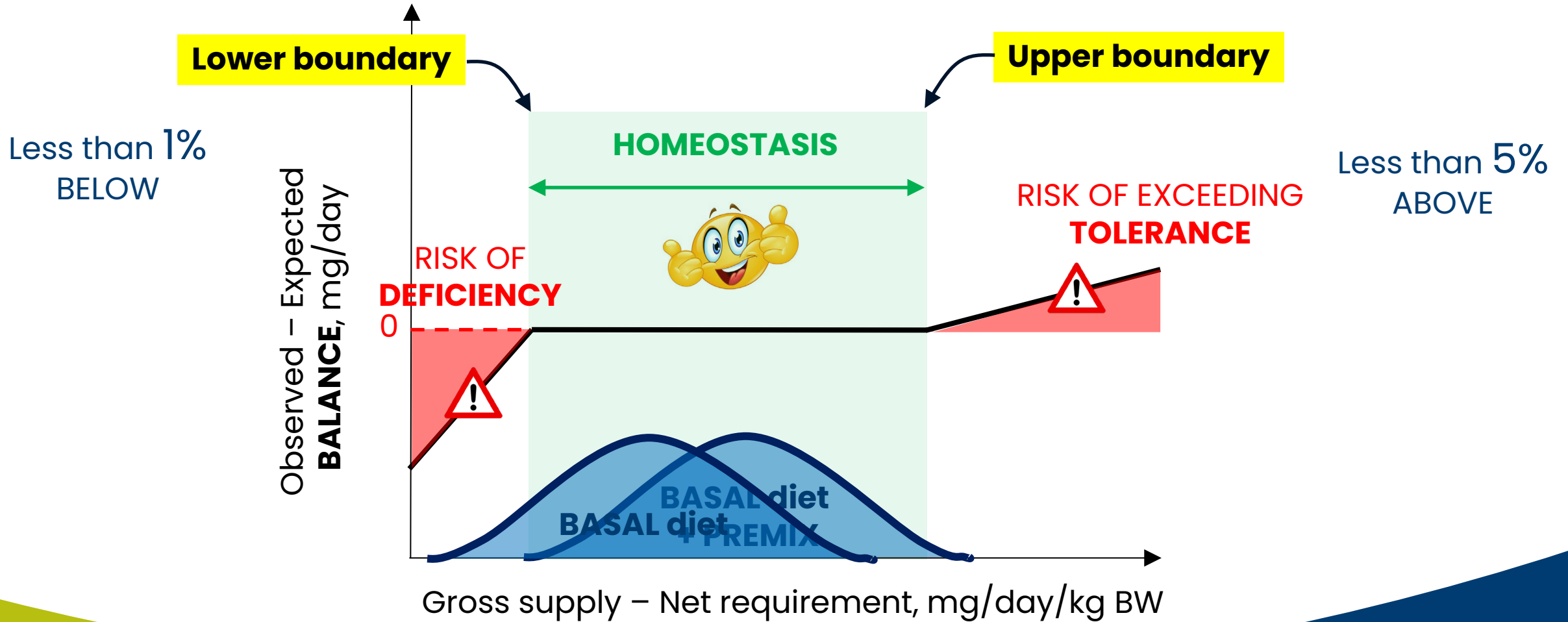
## RISK OF DEFICIENCY



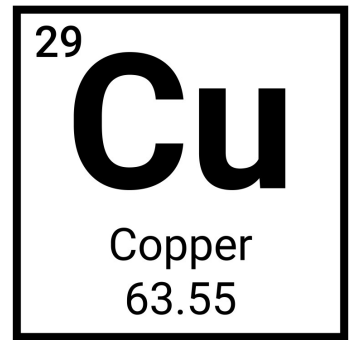
## RISK OF EXCEEDING TOLERANCE



# Defining confidence interval of supplementation



# Optimal ranges of supplemental Cu (in ppm)

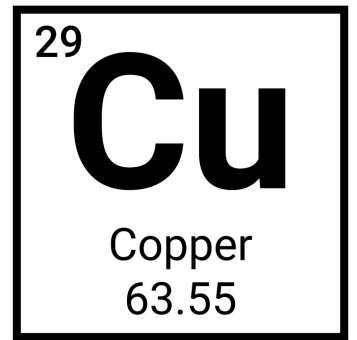


## Boundaries of adequacy, ppm

	LOWER limit	UPPER limit
Growing heifers (4 to 20 mo.)	2	8
Prepartum heifers (0 to -3 mo. prior to 1 <sup>st</sup> calving)	5	22
Lactating cows	2	4
Dry-cows (0 to -3 mo. prior to 2 <sup>nd</sup> (or >) calving)	3	17

Less than 1% < lower limit AND less than 5% > UPPER limit

# Optimal ranges of supplemental Cu (in ppm)



	Boundaries of adequacy, ppm	
	LOWER limit	UPPER limit
Growing heifers (4 to 20 mo.)	2 (8*)	8
Prepartum heifers (0 to -3 mo. prior to 1 <sup>st</sup> calving)	5 (13*)	22
Lactating cows	2 (8*)	4
Dry-cows (0 to -3 mo. prior to 2 <sup>nd</sup> (or >) calving)	3 (10*)	17

Less than 1% < lower limit AND less than 5% > UPPER limit

**\*Assuming high antagonists across ALL diets**

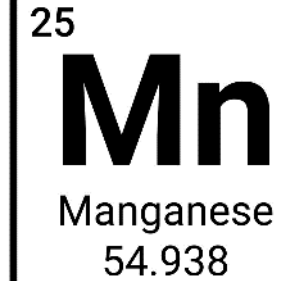
# Optimal ranges of supplemental Zn (in ppm)



	Boundaries of adequacy, ppm	
	LOWER limit	UPPER limit
Growing heifers (4 to 20 mo.)	11	82
Prepartum heifers (0 to -3 mo. prior to 1 <sup>st</sup> calving)	3	156
Lactating cows	41	57
Dry-cows (0 to -3 mo. prior to 2 <sup>nd</sup> (or >) calving)	0	128

Less than 1% < lower limit AND less than 5% > UPPER limit

# Optimal ranges of supplemental Mn (in ppm)



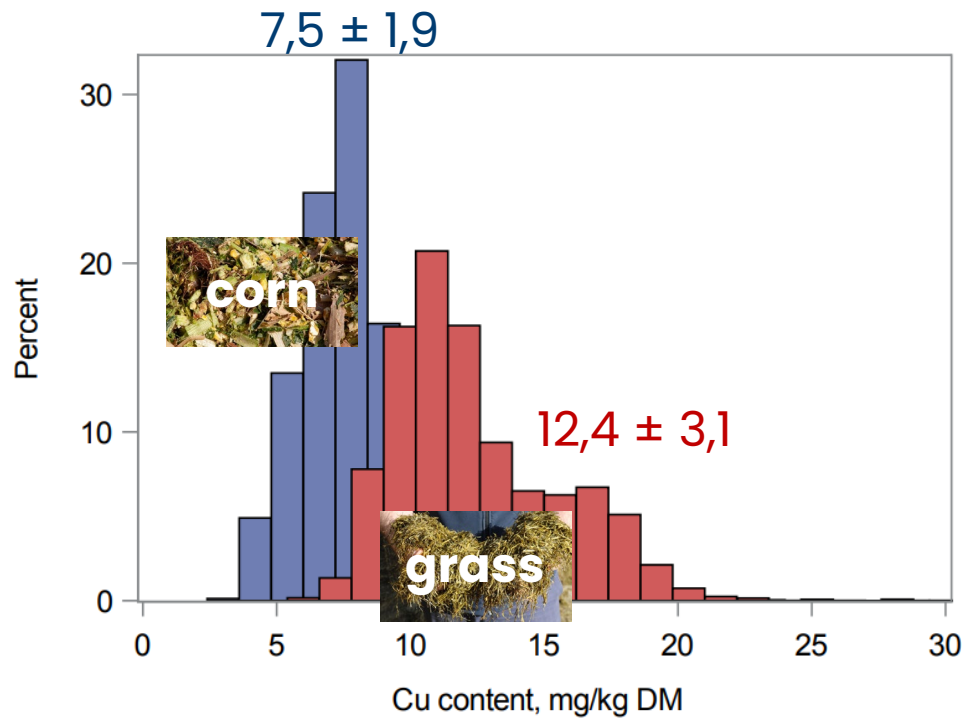
	Boundaries of adequacy, ppm	
	LOWER limit	UPPER limit
Growing heifers (4 to 20 mo.)	15	34
Prepartum heifers (0 to -3 mo. prior to 1 <sup>st</sup> calving)	1	95
Lactating cows	0	18
Dry-cows (0 to -3 mo. prior to 2 <sup>nd</sup> (or >) calving)	0	76

Less than 1% < lower limit AND less than 5% > UPPER limit

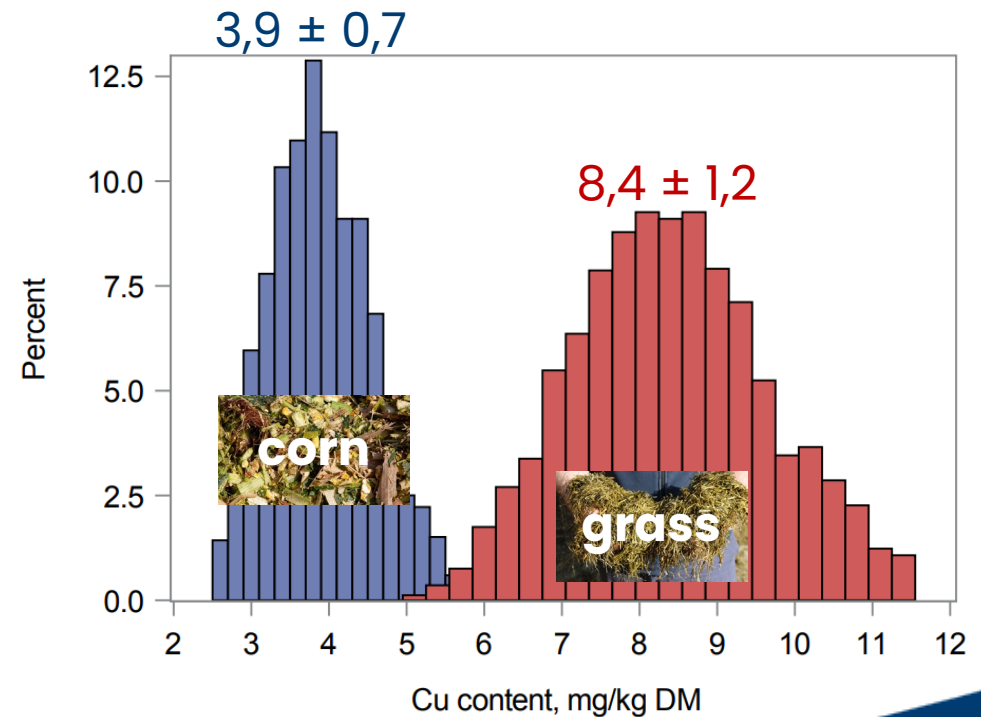
# Evaluation with local practical dataset



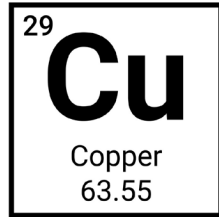
Diet composition (% DM)	
Corn silage	37,1 ± 11,9
Grass silage	32,9 ± 14,0
Concentrate	31,8 ± 10,4



Diet composition (% DM)	
Grass silage	33,4 ± 7,0
Corn silage	29,8 ± 6,2
Concentrate	29,5 ± 8,8



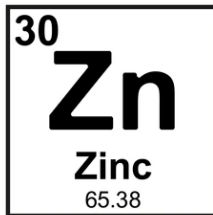
# Optimal ranges of supplemental Cu, Zn, and Mn (in ppm)



	Lower limit	Upper limit
Literature data	2 (8*)	4
Québec (1248 farms)	0 (5*)	4
Kempenshof (individual cow data)	2 (9*)	7

*Lactation*

*3 ppm Cu*



	Lower limit	Upper limit
Literature data	41	57
Québec (1248 farms)	30	57
Kempenshof (individual cow data)	34	46

*43 ppm Zn*



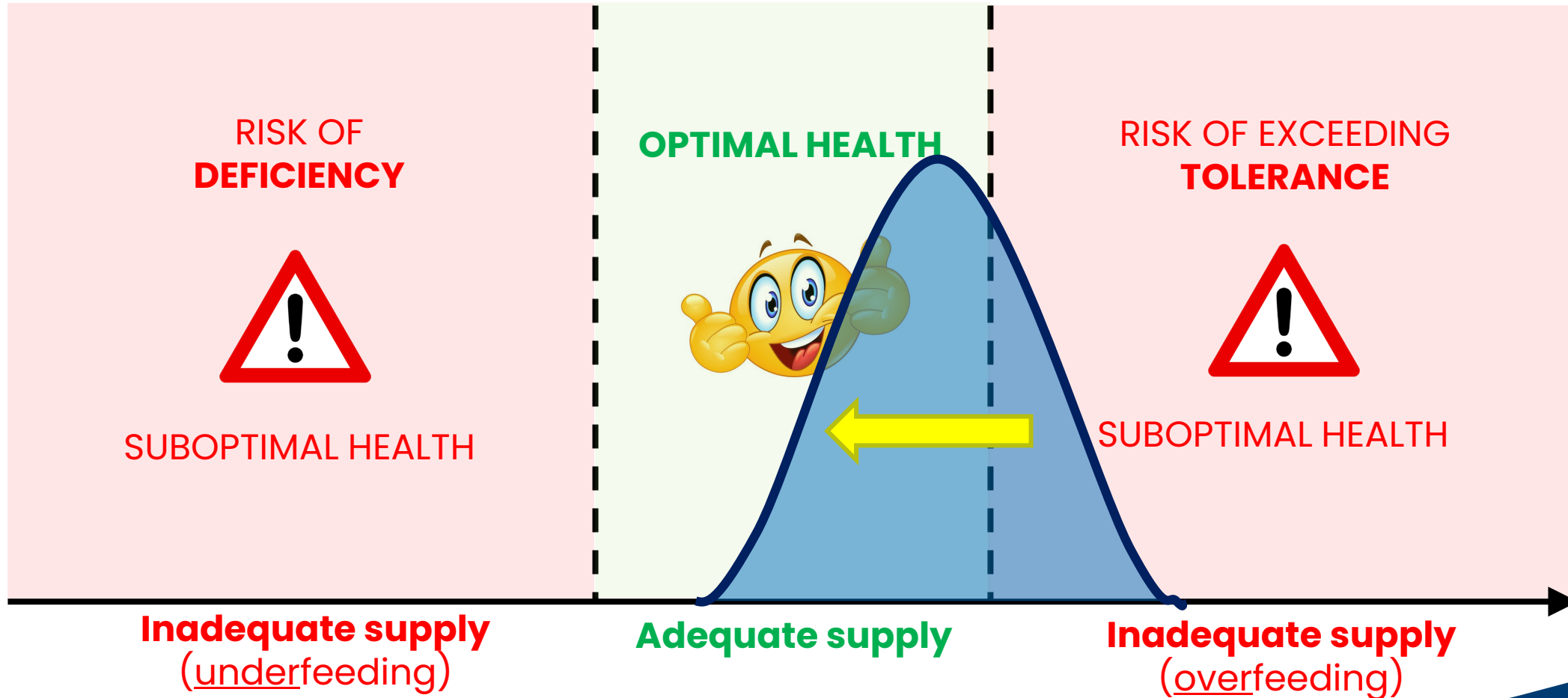
	Lower limit	Upper limit
Literature data	0	18
Québec (1248 farms)	0	19
Kempenshof (individual cow data)	0	16

*10 ppm Mn*

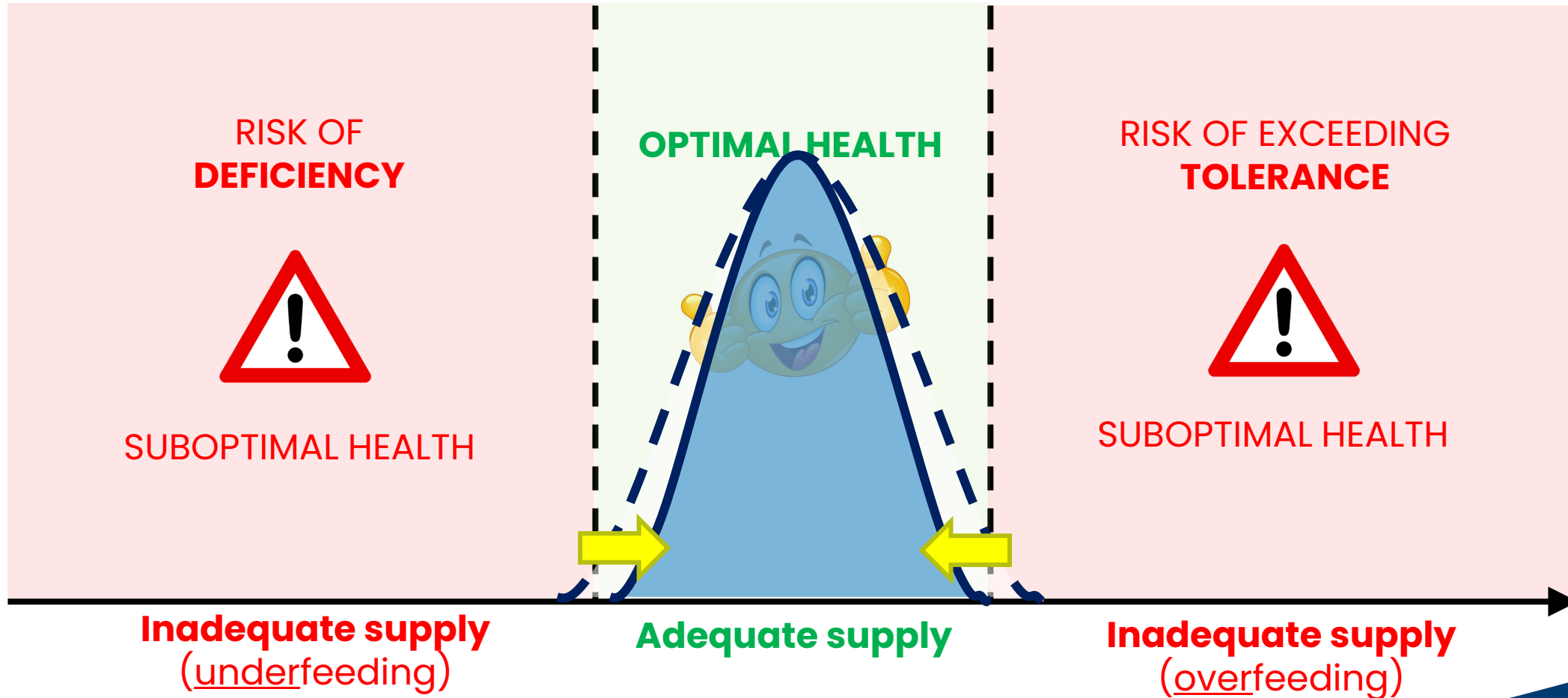
Less than 1% < lower limit AND less than 5% > UPPER limit



# Trace mineral supply and animal health



# Trace mineral quality and animal health



# Take home messages

- **Unregulated retention of trace metals** in bovines is a **biological anomaly** induced by supplementation practices and the high DMI of dairy cattle.
- Supplementation guidelines should consider:
  - **Opportunity** of **UP regulation** competence
  - **Risk** of exceeding **DOWN regulation** competence
- These novel guidelines confirm the value of supplementation BUT expose the potential risk of excess supplementation

**Adequate trace metal nutrition requires**  
an accurate definition of supplemental dose,  
and a form of supplementation that support homeostasis