

3rd European Conference on Copper in Plant Protection

15th-16th November in Berlin, Germany



Human health risk assessment of copper compounds across different regulatory areas

European Conference on Copper 2018

Dr. Jens Schubert

BfR tasks - overview



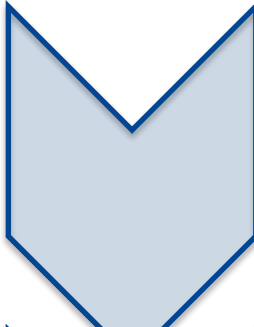
Chemical safety




Chemical safety




Plant Protection Products




REGULATION (EC) No 1107/2009 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL
of 21 October 2009
concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC



REGULATION (EC) NO 396/2005 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL
of 23 February 2005
on maximum residue levels of pesticides in or on food and feed of plant and animal origin and amending Council Directive 91/414/EEC



Council Regulation (EC) No 834/2007
of 28 June 2007
on organic production and labelling of organic products and repealing Regulation (EEC) No 2092/91



COMMISSION REGULATION (EC) No 889/2008
of 5 September 2008
laying down detailed rules for the implementation of Council Regulation (EC) No 834/2007 on organic production and labelling of organic products with regard to organic production, labelling and control

Background levels

➤ Food of plant origin:

nuts (13-37 mg/kg), cocoa powder (38 mg/kg),
oilseeds (12-17 mg/kg), pulses (6-8 mg/kg),
wheat germs (17 mg/kg), wheat bran (13 mg/kg)



www.zentrum-der-gesundheit.de



www.welt.de

➤ Food of animal origin:

liver (calf's liver: 55 mg/kg), kidney (4-8 mg/kg),
prawns (11 mg/kg), cheese (13 mg/kg)



<http://tagebuch.allesrohkost.de>

➤ Drinking water

limit: 2 mg/L



<http://www.umwelt-energie-report.de>

Derivation of reference values

essential human intake:	≈ 1 mg/day
daily intake via drinking water and food:	≈ 2 mg/day
maximum intake via drinking water and food:	≈ 10 mg/day
dose not affecting the homeostatic mechanism:	≈ 10 mg/day
dose without harmful effects after copper supplementation in humans:	≈ 10 mg/day
toxic effects after repeated ingestion:	≈ 30 mg/day

Derivation of reference values

- ADI (EFSA 2008, EFSA 2018): 0.15 mg Cu / kg bw per day, based on human data, supported by 90-day, rat, oral (NOAEL: 16 mg/kg bw/day)
- ✓ 10 mg per day / 60 kg \approx 0.17 mg Cu / kg bw per day
- ✓ 10 mg per day / 70 kg \approx 0.14 mg Cu / kg bw per day

- EFSA Journal 2018;16(1):5152:

*“...it was noted that an upper limit for copper as a nutrient had been established in an opinion of the EU Scientific Committee for Food (SCF, 2003), based on a NOAEL of 10 mg Cu/day value but adding an uncertainty factor of 2, resulting in a **proposed tolerable upper intake level of 5 mg Cu/day for adults** (corresponding to half of the ADI currently set in the pesticides area).”*

*“This approach was considered by the Peer Review in 2008 as inadequate for setting an ADI in the area of pesticides (France, 2007a,b). [...] **During the current Peer Review, the experts have confirmed the previous assessment, and no changes in the ADI are proposed.**”*

Derivation of reference values

➤ **Acceptable Daily Intake (ADI):**

- 0.15 mg Cu/kg bw/day

EFSA Scientific Report (2008) 187, 1-101, doi: 10.2903/j.efsa.2008.187r
EFSA Journal 2018;16(1):5152, 1-25, doi: 10.2903/j.efsa.2018.5152

➤ **Tolerable Upper Intake (TUI):**

- children 1-3 years: 1 mg/day
- children 4-6 years: 2 mg/day
- children 7-10 years: 3 mg/day
- adolescents 11-17 years: 4 mg/day
- adults: 5 mg/day

Scientific Committee for Food (SCF) der EFSA, 2006: Tolerable upper intake levels for Vitamins and Minerals, www.efsa.europa.eu/de/ndatopics/docs/ndatolerableuil.pdf

Derivation of reference values

➤ **Acceptable Operator Exposure Level (AOEL):**

- 0.08 mg/kg bw

EFSA Journal 2018;16(1):5152, 1-25, doi: 10.2903/j.efsa.2018.5152

- ✓ **operators:** risk assessment acceptable without PPE
- ✓ **workers:** risk assessment acceptable with PPE
- ✓ **bystanders and residents:** risk assessment acceptable for low application rates

... no consideration of other exposure pathways for operators, workers, bystanders and residents

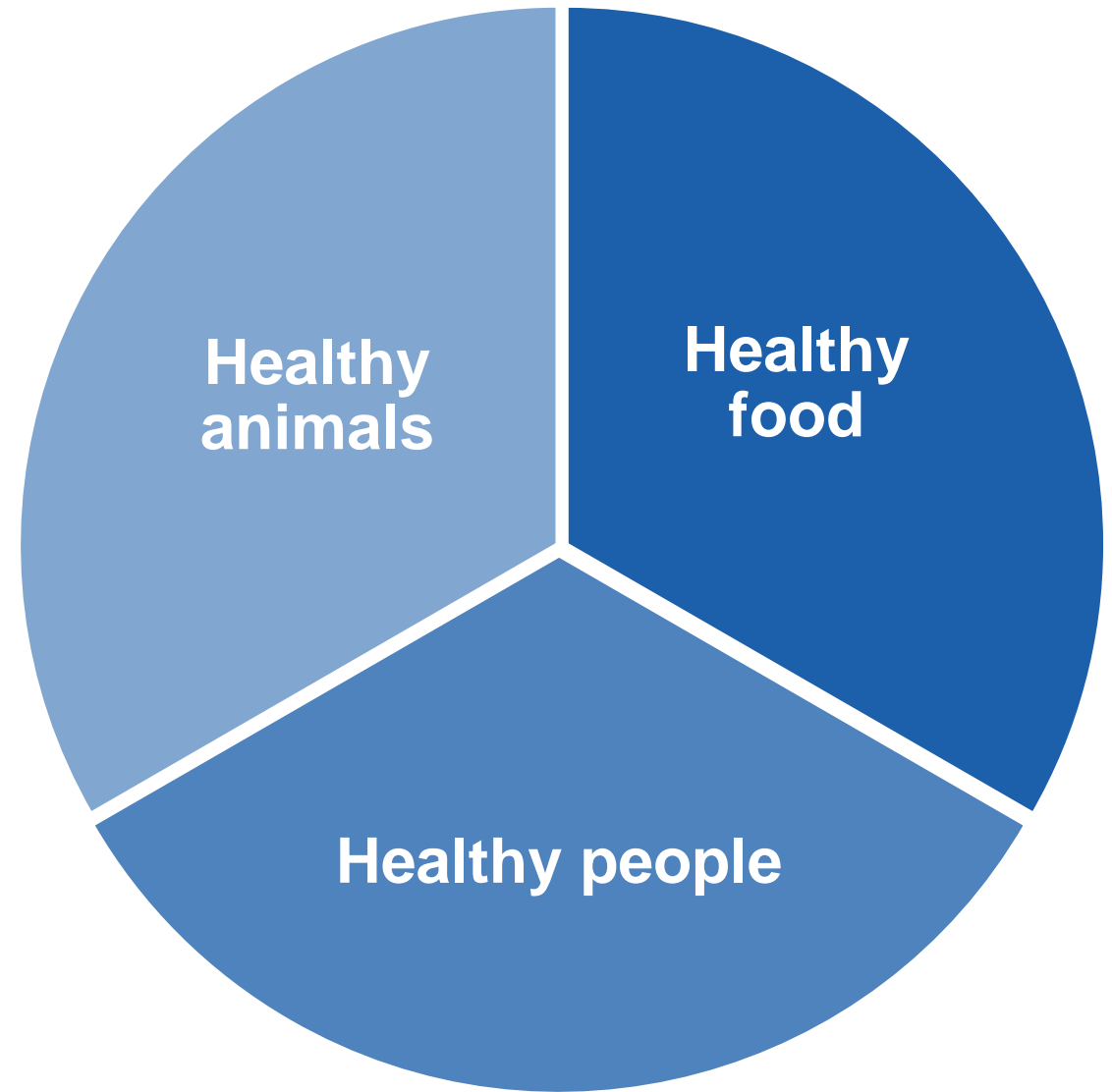
Biocidal Products

REGULATION (EU) No 528/2012 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL
of 22 May 2012
concerning the making available on the market and use of biocidal products

- Copper compounds approved as active substances:
 - ✓ PT 2 – Disinfectants and algacides not intended for direct application to humans or animals
 - ✓ PT 8 – Wood preservatives
 - ✓ PT 21 – Antifouling products

- Biocidal products authorized in Germany:
 - ✓ PT 8 – Wood preservatives

Germany: > 1000 registered BP



Feed additives

**REGULATION (EC) No 1831/2003 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL
of 22 September 2003
on additives for use in animal nutrition**

**COMMISSION REGULATION (EC) No 1334/2003
of 25 July 2003**

**amending the conditions for authorisation of a number of additives in feedingstuffs belonging to
the group of trace elements**

➤ **Recommendations for daily supply¹:**

- | | |
|-------------------------|------------------------------|
| ▪ cattle's, dairy cows: | 10 mg/kg feed dry matter |
| ▪ piglets | 6 mg/kg feed dry matter |
| ▪ porker | 4 – 5 mg/kg feed dry matter |
| ▪ breeding sows | 8 – 10 mg/kg feed dry matter |
| ▪ horses | 10 mg/kg feed dry matter |
| ▪ poultry | 6 – 8 mg/kg feed dry matter |

¹ Society for nutrition physiology (Gesellschaft für Ernährungsphysiologie (GfE))

SCIENTIFIC OPINION

ADOPTED: 13 July 2016

doi: 10.2903/j.efsa.2016.4563

Revision of the currently authorised maximum copper content in complete feed

EFSA Panel on Additives and Products or Substances used in Animal Feed (FEEDAP)

COMMISSION IMPLEMENTING REGULATION (EU) 2018/1039




of 23 July 2018

concerning the authorisation of Copper(II) diacetate monohydrate, Copper(II) carbonate dihydroxy monohydrate, Copper(II) chloride dihydrate, Copper(II) oxide, Copper(II) sulphate pentahydrate, Copper(II) chelate of amino acids hydrate, Copper(II) chelate of protein hydrolysates, Copper(II) chelate of glycine hydrate (solid) and Copper(II) chelate of glycine hydrate (liquid) as feed additives for all animal species and amending Regulations (EC) No 1334/2003, (EC) No 479/2006 and (EU) No 349/2010 and Implementing Regulations (EU) No 269/2012, (EU) No 1230/2014 and (EU) 2016/2261

Authorised copper compounds as additives in feedingstuff

- Copper(II) diacetate, monohydrate
- Copper(II) carbonate, dihydroxy monohydrate
- Copper(II) chloride, dihydrate
- Copper(II) oxide
- Copper(II) sulphate, pentahydrate
- Copper(II) chelate of amino acids hydrate
- Copper(II) chelate of protein hydrolysates

Maximum content of Cu in mg/kg of complete feed

- | | | |
|--------------------------------------------------------------------|--------------------|---------------------------------------------------------------------------------------|
| ➤ piglets (up to 4 weeks/ 5 th – 8 th week): | 150/100 mg/kg feed |  |
| ➤ bovines before the start of rumination: | 15 mg/kg feed | |
| ➤ other bovines: | 30 mg/kg feed |  |
| ➤ ovines: | 15 mg/kg feed | |
| ➤ caprines: | 35 mg/kg feed |  |
| ➤ other species: | 25 mg/kg feed | |

Food supplements

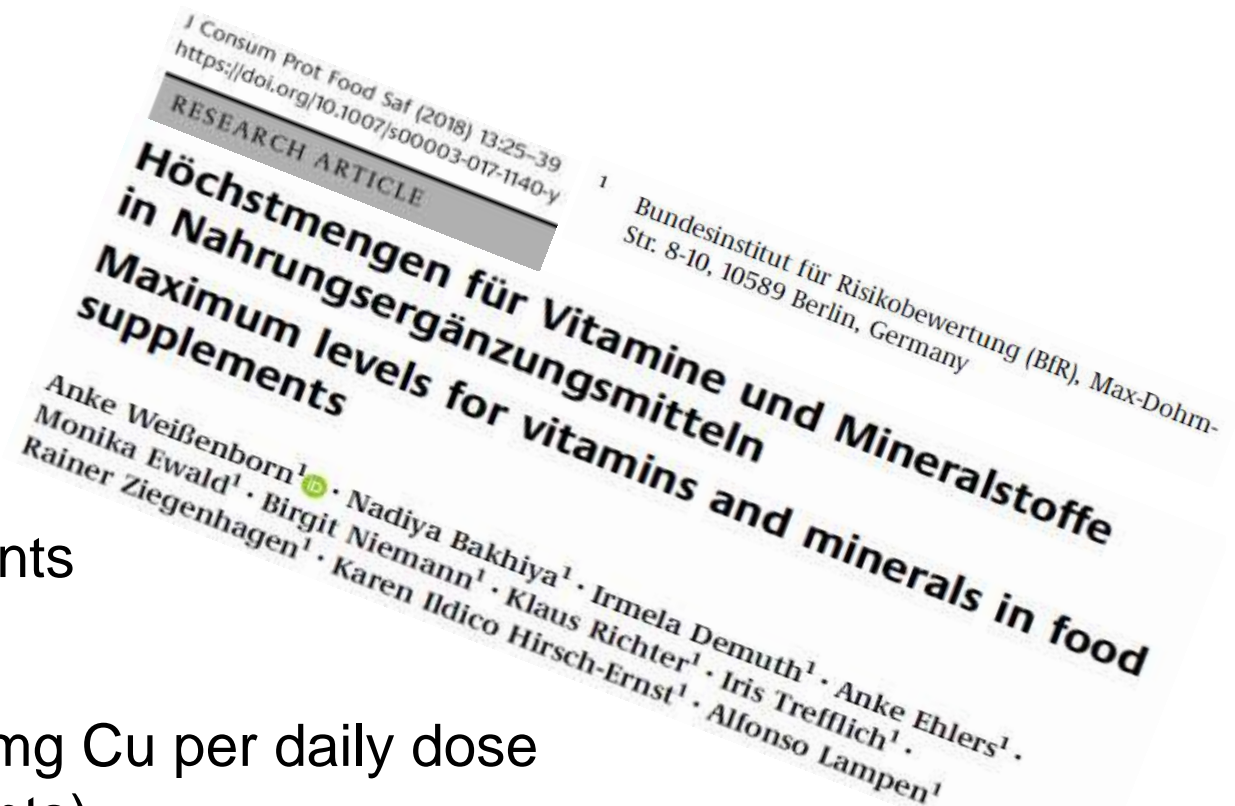
**DIRECTIVE 2002/46/EC OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL
of 10 June 2002
on the approximation of the laws of the Member States relating to food supplements**

➤ **Annex II:** Substances which may be used in the manufacture of food supplements

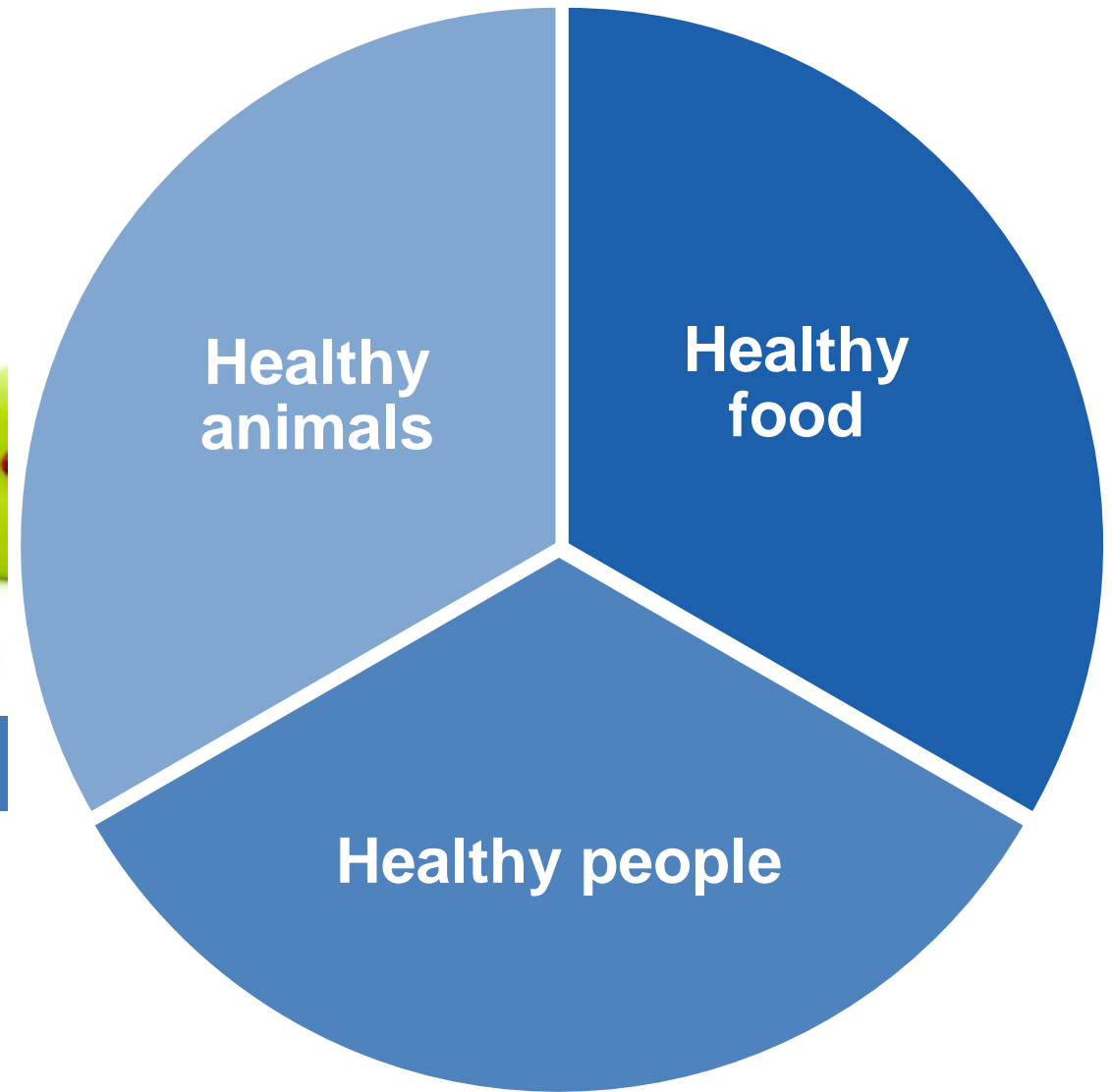
- ✓ Copper carbonate
- ✓ Copper citrate
- ✓ Copper gluconate
- ✓ Copper sulphate
- ✓ Copper lysine complex

➤ No EU-wide regulation for maximum levels in food supplements available

➤ Proposal BfR: adults maximum 1 mg Cu per daily dose (not suitable for children/adolescents)



Product safety



Cosmetics and Food Contact Materials

REGULATION (EC) No 1223/2009 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL
of 30 November 2009
on cosmetic products

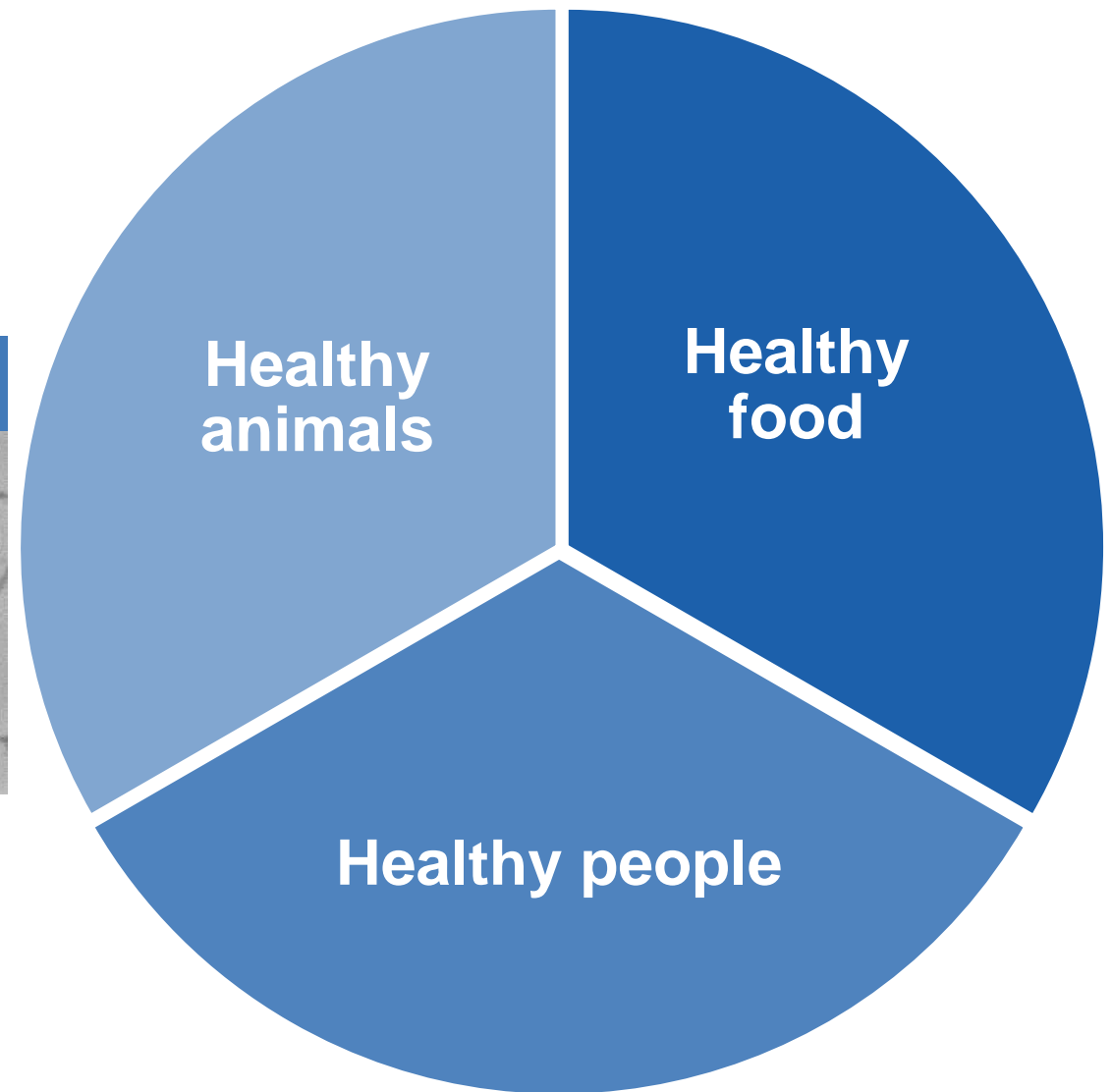
- copper compounds can be used for cosmetic purposes as colorants:
 - ✓ 74160 (29H,31H-Phthalocyaninato(2-)-N29, N30, N31, N32 copper),
 - ✓ 74260 (Polychloro copper phthalocyanine),
 - ✓ 77400 (Copper)

COMMISSION REGULATION (EU) No 10/2011
of 14 January 2011

on plastic materials and articles intended to come into contact with food

- Annex I: Union list of authorised substances:
 - ✓ Powders, flakes and fibres of brass, bronze, copper, stainless steel, tin, iron and alloy of copper, tin and iron
 - ✓ Copper iodide, Copper bromide
- Annex II: Restrictions on materials and articles:
 - ✓ Copper = 5 mg/kg food or food simulant

Biological safety



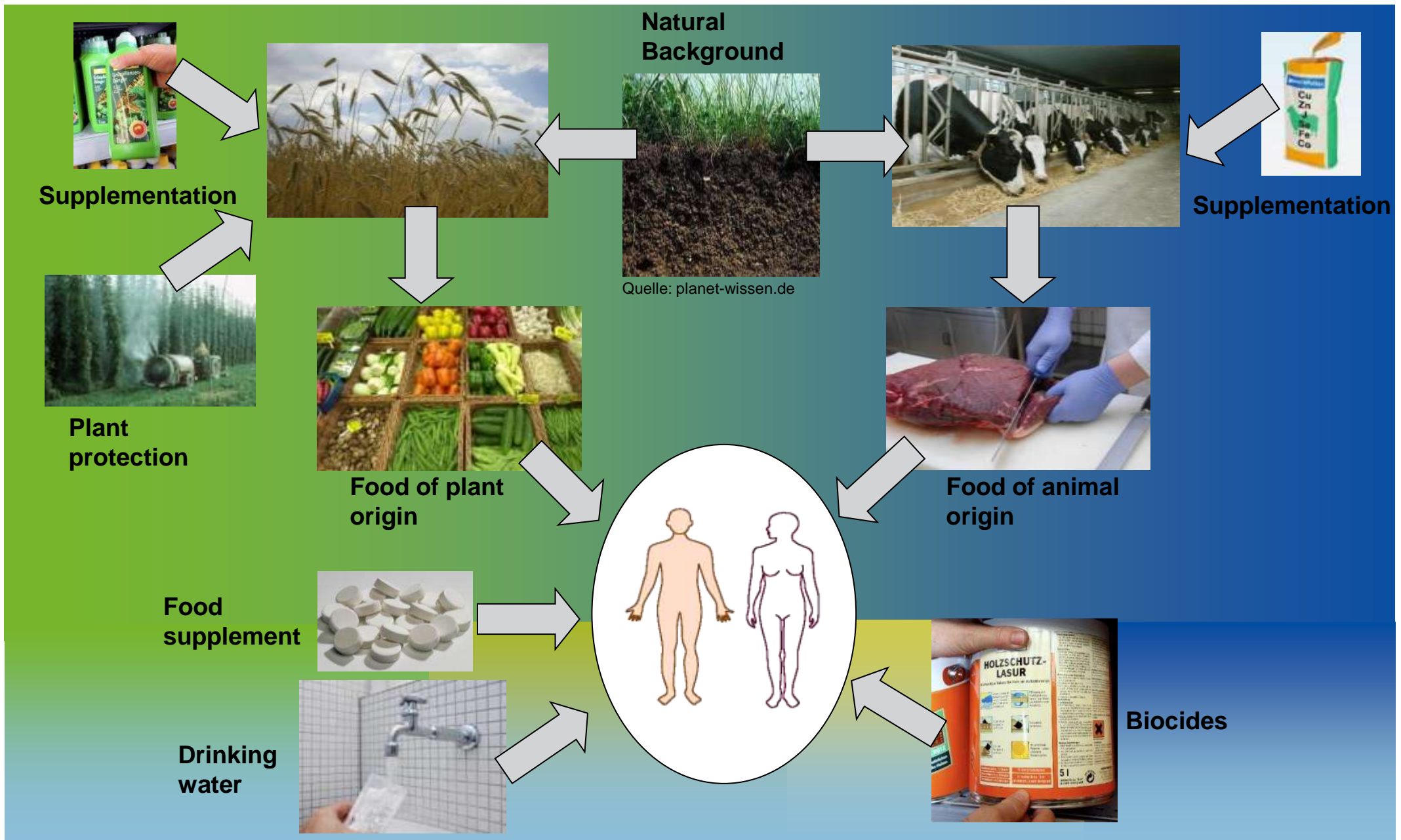
Question: Does copper play a role in the development of antibiotic resistance in bacteria and does this impact human or animal health?

- According to scientific literature a correlation between resistance to copper and resistance to antibiotics can not be excluded
- General conclusions to a possible antibiotic co-selection from the use of copper according to the good agricultural practice are currently not possible
- With regard to the question in view of BfR, no reliable risk assessment for human or animal health is currently possible – based on the current scientific and technical knowledge

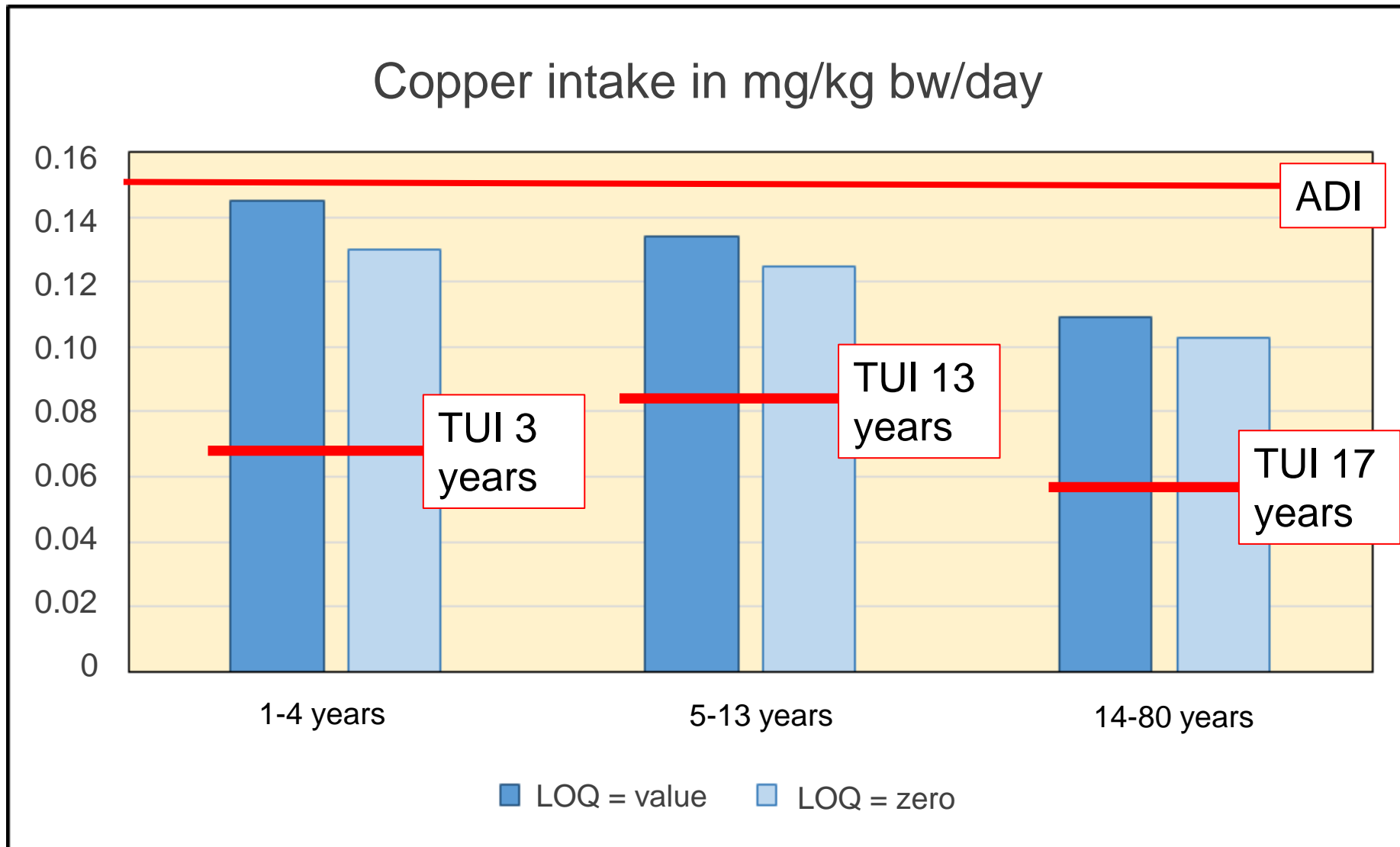
Risk communication



Conclusion



Conclusion



Conclusion

- Consideration of all exposure routes – e.g. via drinking water
- Due to various exposure routes, risk assessment should use monitoring data
- Alignment of the different regulatory areas necessary
- Copper intake should be further monitored!



Thank you for your attention

Dr. Jens Schubert

German Federal Institute for Risk Assessment

Max-Dohrn-Str. 8-10 • 10589 Berlin, GERMANY

Phone +49 30 - 184 12 - 33 25 • Fax +49 30 - 184 12 - 47 41

Jens.Schubert@bfr.bund.de • www.bfr.bund.de/en