



# REVIEW OF NEW INFORMATION ON THE SAFE UPPER LEVEL FOR ZINC

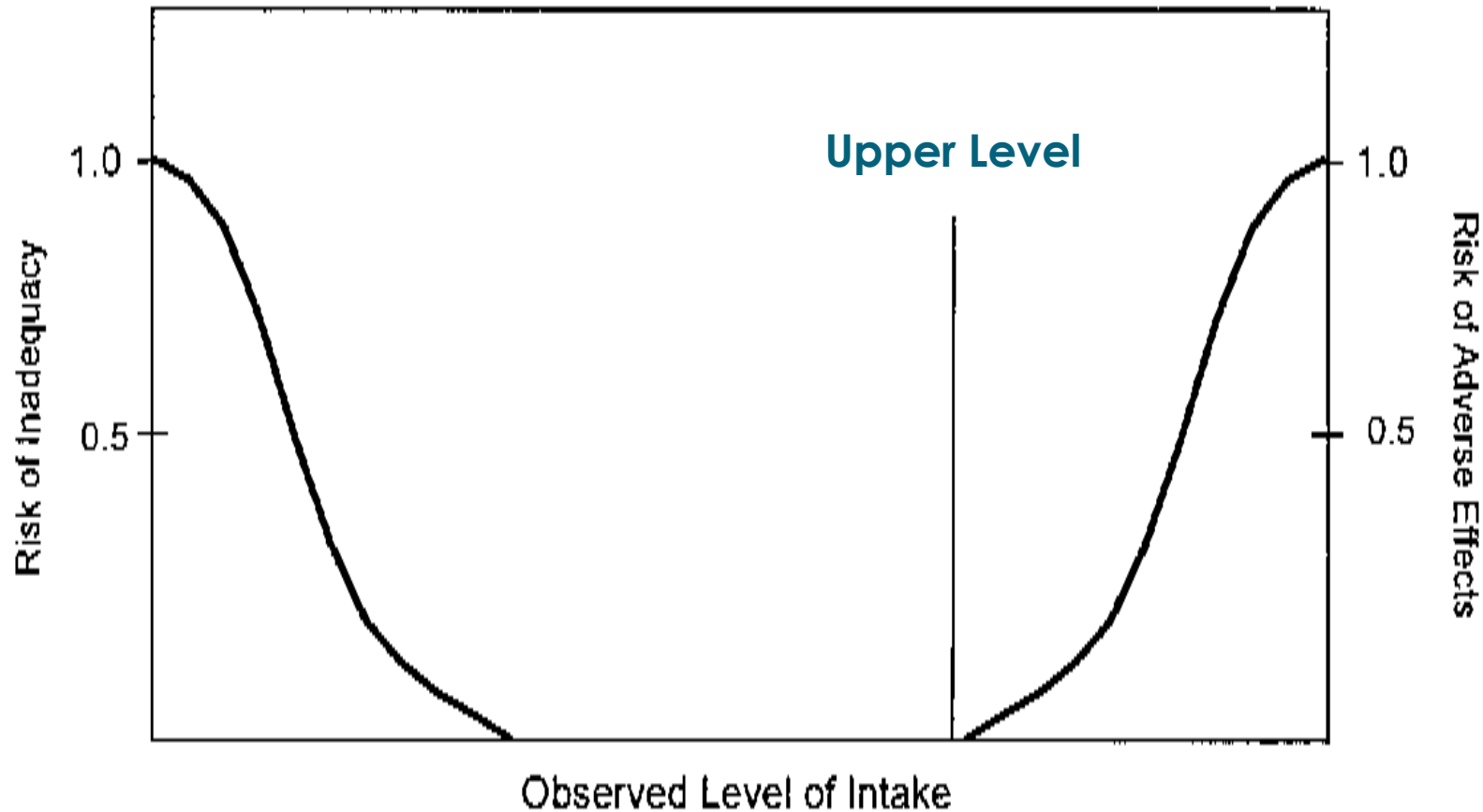
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# AIM OF REVIEW & ROLE OF IZINGG

- ◉ To review published information contributing to knowledge on dietary reference intakes for zinc
  - Review and present recommendations for updating dietary zinc requirements and upper limits
- ◉ Information will be useful to those engaged in:
  - evaluating population zinc intakes
  - developing recommendations for food fortification and supplementation programs that include zinc

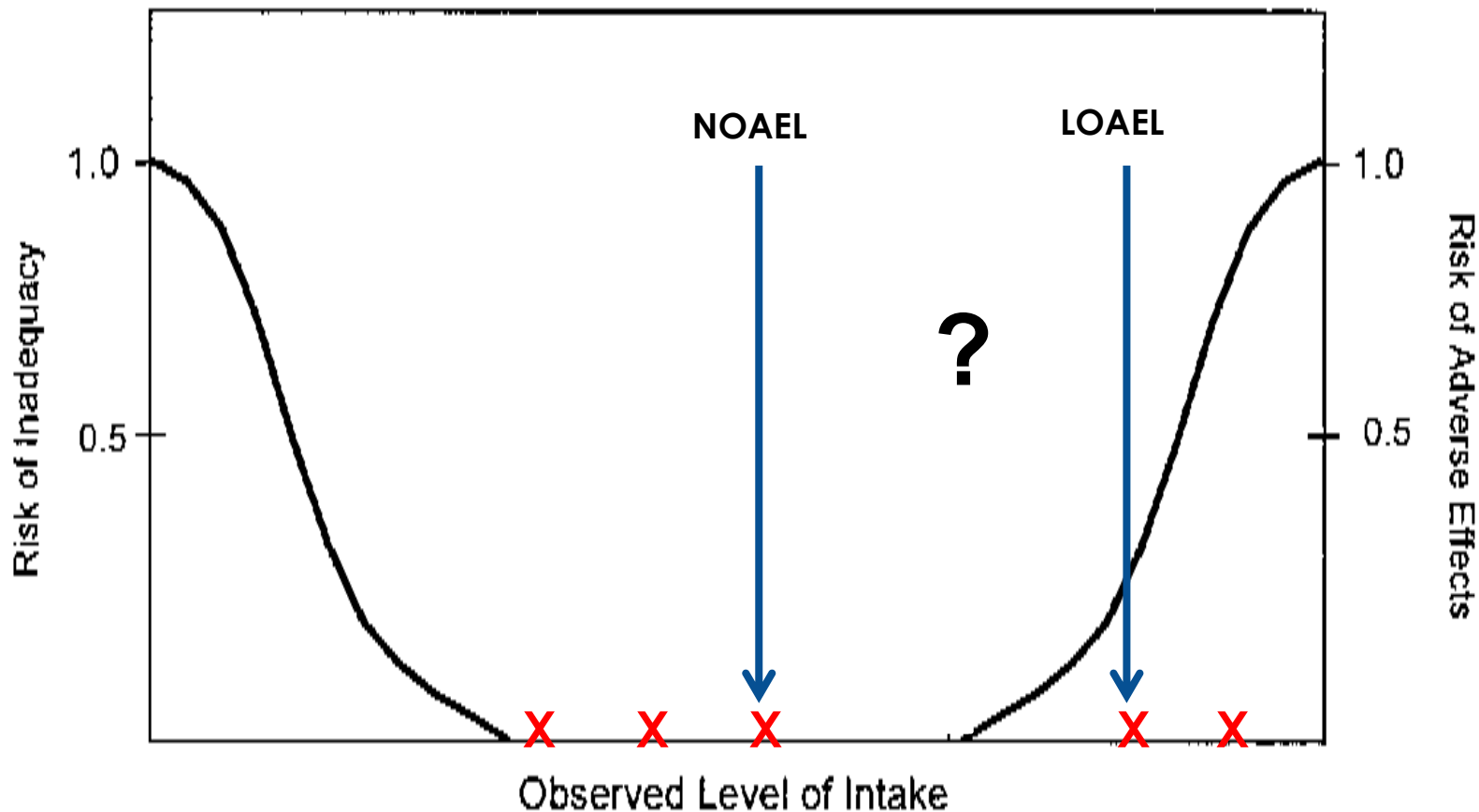
# THEORETICAL POPULATION RISK CURVE



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**LOAEL:** 'Lowest level of intake at which adverse effects are observed'

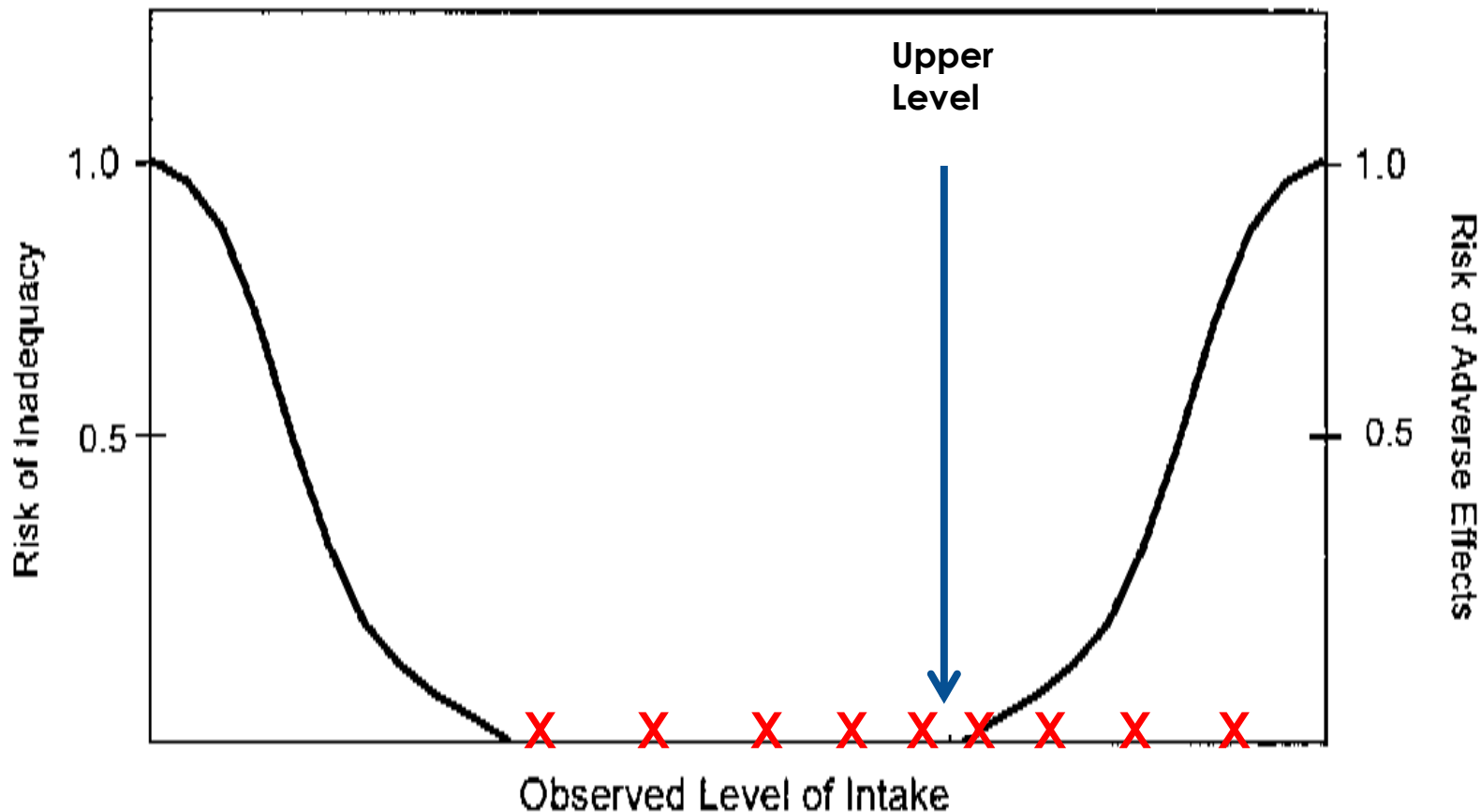


**X** - studies of adverse effects

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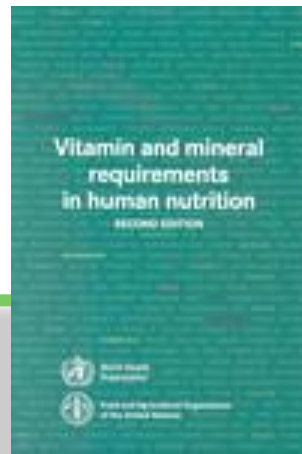
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# MAJOR SOURCES OF ZINC ULS

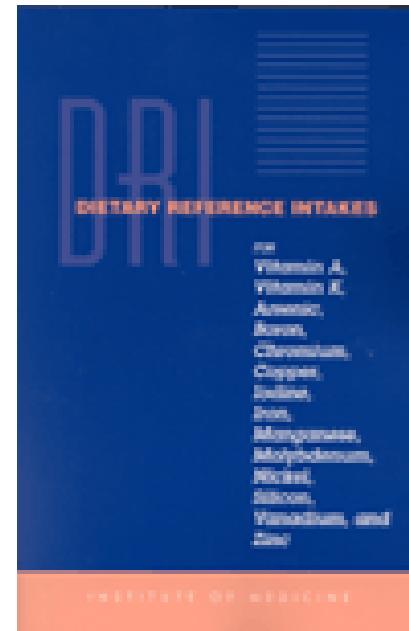
- WHO/FAO/IAEA , Trace Elements in Human Nutrition & Health, 1996



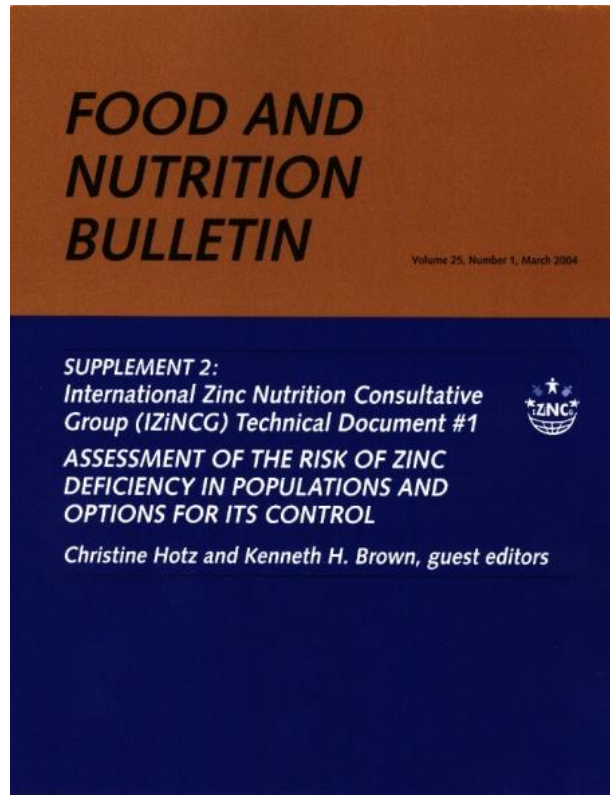
- WHO/FAO, Vitamin & mineral requirements in human nutrition, 2<sup>nd</sup> Ed., 2005



- Food and Nutrition Board & Institute of Medicine (USA), Dietary Reference Intakes for Vitamin A....and Zinc, 2001



# SOURCES OF ZINC ULs



- IZiNCG, 2004
  - Reviewed ULs
- Adults:
  - Accepted UL from FNBIOM
- Children:
  - Insufficient information to derive UL for children
  - Added 1 study to increase the NOAELs for children

# ZINC UPPER LEVELS (MG/DAY)

WHO, 2005		FNB/IOM, 2001		IZiNCG, 2004	
<u>Age/sex</u>	<u>UL</u>	<u>Age/sex</u>	<u>UL</u>	<u>NOAEL</u>	<u>UL</u>
7-12 m		7-12 m	5	6	-
1-3 y		1-3 y	7	8	-
3-6 y	23-28	4-8 y	12	14	-
6-10 y		9-13 y	23	26	-
10-18 y		14-18 y	34	39 / 44	-
≥18, F	45	≥19 y, F	40		40
≥18, M	45	≥19 y, M	40		40

Children's ULs derived from adult UL by adjusting for basal metabolic rate

Children's ULs derived from study of zn-fortified infant formula

Children's NOAEL derived from study of zn-supplements among 1-3 y old children



# ZINC UPPER LEVELS AND EARS (MG/D)

FNB/IOM, 2001			IZiNCG, 2004	
<u>Age/sex</u>	<u>EAR</u>	<u>UL</u>	<u>EAR *</u>	<u>NOAEL</u>
6-11 m	2.5	5	4	6
1-3 y	2.5	7	2	8
4-8 y	4	12	3 / 4	14
9-13 y	7	23	5 / 7	26
14-18 y, M	8.5	34	8 / 11	44
14-18 y, F	7.3	34	7 / 9	39
≥19 y, M	9.4	40	10 / 15	40
≥19 y, F	6.8	40	7 / 8	40

\* EARs for moderate / low bioavailability diets

# SOURCES OF DATA

- ULs derived largely from studies of zinc supplementation/fortified infant formula
  - Aim to determine positive effects of zinc
  - Some included measures of adverse effects
  - Many do not account for dietary zinc intakes

Those with indicators of copper status are considered for the ULs

# SOURCES OF DATA - CHILDREN

15 studies identified



Eliminated 7 studies:

- 3 - weekly/biweekly doses
- 2 - Cu response by Zn dose unclear
- 1 - insufficient information
- 1 - no control



8 valid studies considered

# SOURCES OF DATA

Reference age range	# studies	Zn intake, mg/d	Data source Author, year - country
0-5 m	2	3.2 – 4.5	Walravens, 1976 - USA Matsuda, 1984 - Japan
6-11 m, 1-3 y	1	10	Sazawal, 2004 – India
1-3 y	2	3-10	Lind, 2003 – Indonesia Wuehler, 2007 – Ecuador
1-3 y, 4-8 y	2	10 – 17.1	Walravens, 1983 - USA Ruz, 1997 – Chile
4-8 y	1	16.7	Gibson, 1989 - Canada

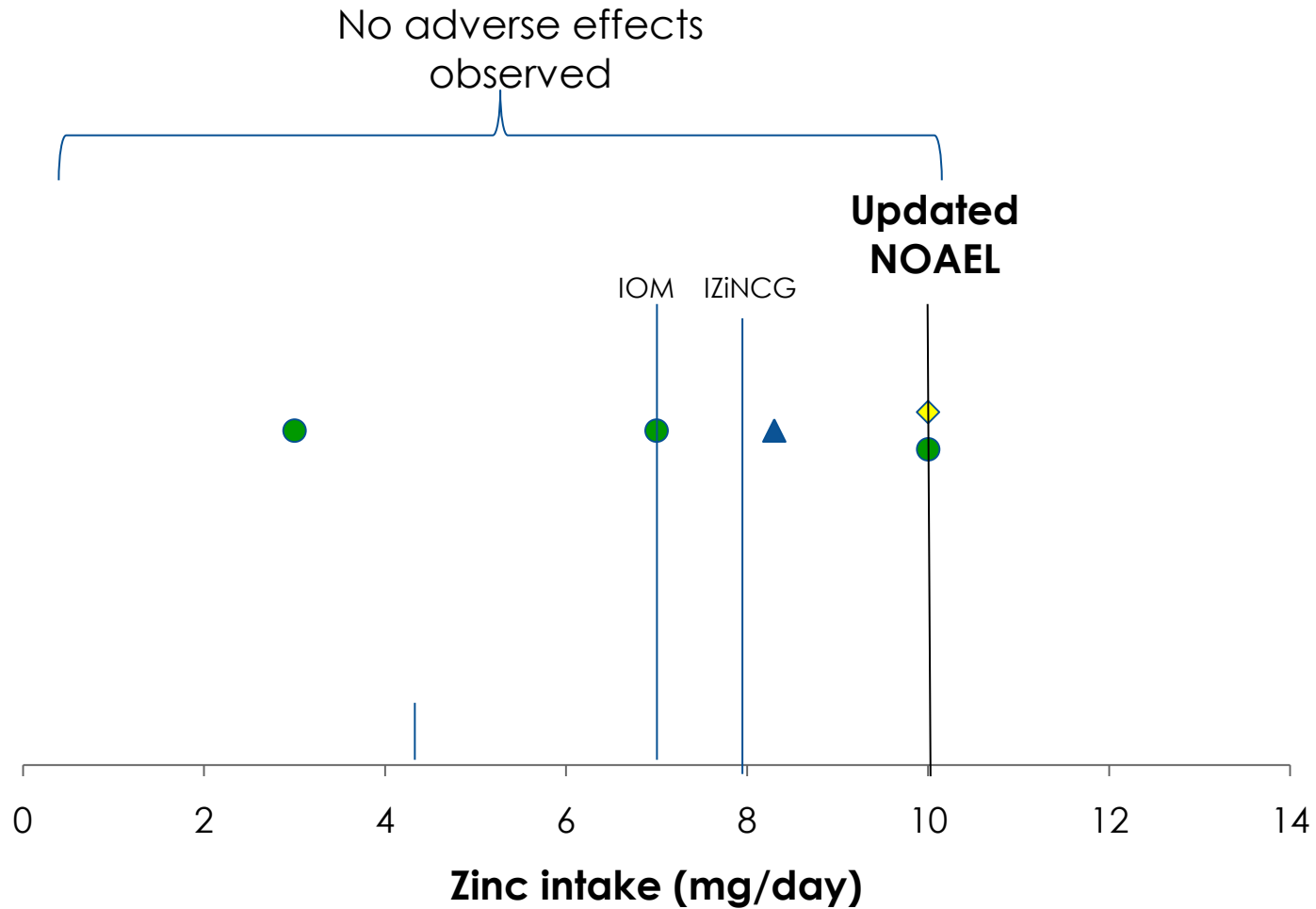
# STUDIES USED TO DERIVE REVISED NOAEL FOR CHILDREN 1-3 YEARS

	Wuehler et al., 2007 Ecuador	Sazawal et al., 2004 India
n	102	38/43
Age, at end	1-2 y	0.8 – 1 y
Age group	1-3 y	6-11 m, 1-3 y
Supplementary Zn, mg/d	10	10
Zn diet, mg/d	-	-
<b>Total zinc, mg/d</b>	<b>10</b>	<b>10</b>
Duration, months	6	4
Indicators	Serum Cu ESOD Serum ceruloplasmin	Plasma Cu ESOD
Response	No change	No change

# STUDIES USED TO SUPPORT A REVISED UL FOR CHILDREN

	Ruz et al., 1997 Chile	Gibson et al., 1989 Canada
n	69	38/43
Age, at end	3-5 y	5-8 y
Age group	1-3 y; 4-8 y	4-8 y
Supplementary Zn, mg/d	10	10
Zn diet, mg/d	7.1	6.7
<b>Total zinc, mg/d</b>	<b>17.1</b>	<b>16.7</b>
Duration, months	14	12
Indicators	Plasma Cu	Plasma Cu; ESOD
Response	No change	No change

# DATA USED TO DERIVE A UL FOR CHILDREN 1-3 YEARS OF AGE



# RECOMMENDED REVISIONS TO ZINC UPPER LEVELS (MG/D)

	FNB/IOM, 2001	IZiNCG, 2004		Updated
<u>Age/sex</u>	<u>UL</u>	<u>EAR</u>	<u>NOAEL</u>	<u>NOAEL</u>
6-11 m	5	4	6	7
1-3 y	7	2	8	<b>10</b>
4-8 y	12	3 / 4	14	<b>17</b>
9-13 y	23	5 / 7	26	31
14-18 y, M	34	8 / 11	44	53
14-18 y, F	34	7 / 9	39	46

Adjust by body weight to other age groups



# LIMITATIONS

- Caution in interpreting adverse effects from studies of zinc supplementation in children prone to infection
  - Zinc supplementation reduces morbidity
  - Serum copper increases during infection and may decrease.
  - Zn supplemented groups may have lower serum copper (relative to control) secondary to decreased infection rates
- **LOAELs should thus be interpreted with caution**

# LIMITATIONS

- Most zinc supplementation trials do not include information on dietary zinc intakes
  - Assumed daily zinc intake is limited to the zinc supplement dose
  - Daily intake used for UL may be underestimated

# LIMITATIONS

- ◉ Controlled, zinc dose-response studies in healthy populations with zinc intakes including both the NOAEL and LOAEL are absent
- ◉ If ULs were derived from studies of staple food fortification levels, they may be different:
  - Absorption of zinc from fortified staple foods may be lower than from supplements, and UL could be higher

# CONCLUSIONS

- Newly reviewed information from zinc supplementation trials indicate that the zinc UL can be increased from the FNB/IOM levels.
  - For children 1-3, the UL can increase from 7 to 10 mg/d
  - By extension, ULs for children in other age groups will increase as well
- Food fortification programs including zinc could monitor copper status
  - Controlled studies of fortified foods should not exclude zinc levels providing amounts >NOAEL