Should nanoparticles be used in sunscreens? – a unique study

(First use of stable isotopes in nanotechnology)

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Sunscreen Summit Brisbane 19-20.3.18

Outline

- Metal oxides in sunscreens/Issues/ Previous testing
- Stable Isotope Tracing ZnO
- Human Trials ZnO
- Results blood ZnO
- Summary ZnO
- Should we be concerned?

- (TiO_2)
- (Products with active ingredients in Australia & US)

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Sunscreens – some actives

To minimise UV exposure, 2 types of active ingredients are used in sunscreens – "chemical" ("organic") and "physical" ("inorganic")

Disadvantages of "chemical" sunscreens

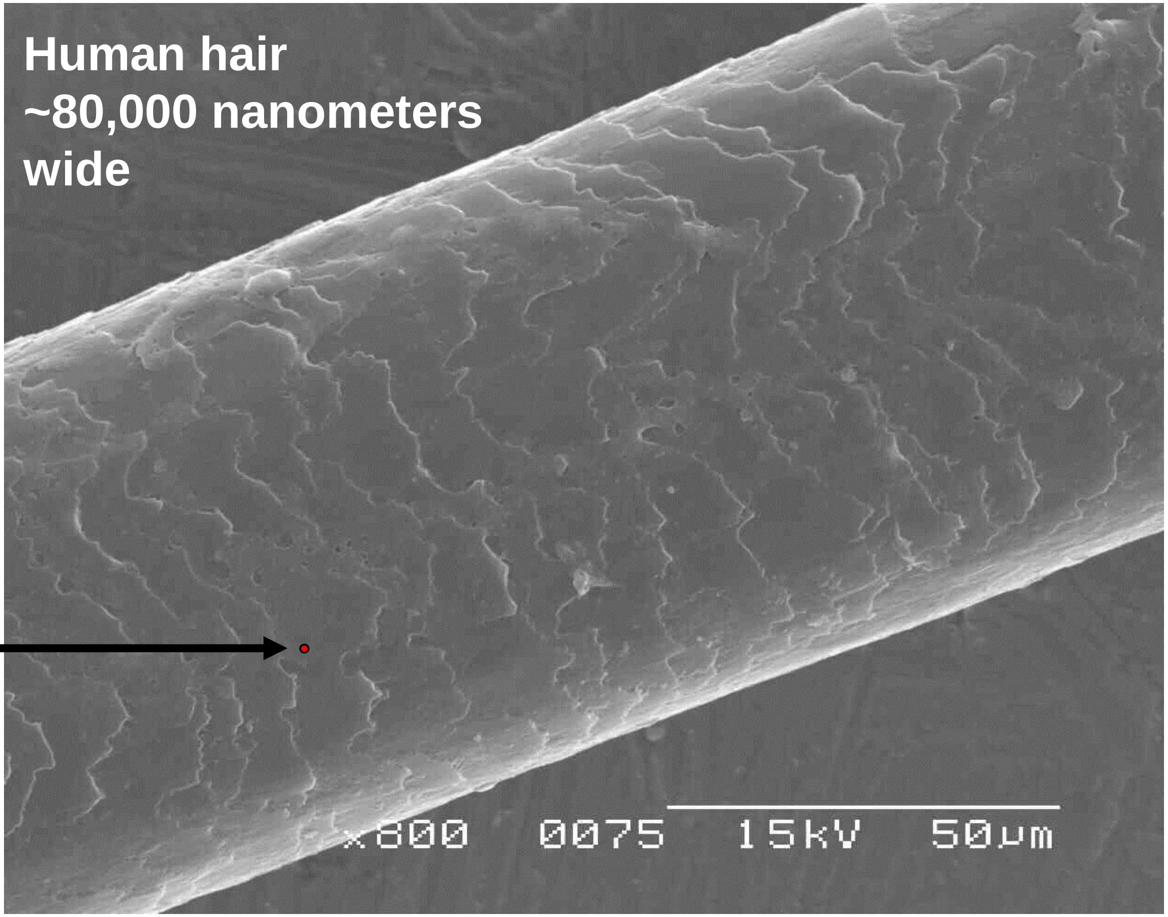
- absorption through the skin – found in breast milk/urine
- certain chemicals may cause damage to sensitive organs or hormone receptors (endocrine disruptors)
- may cause skin irritation a mixture of UV-absorbers is needed to provide full (broad) spectrum protection
- can interact & break down in sunlight (e.g. avobenzone needs octocrylene)

Advantages of "physical" sunscreens containing metal oxide nanoparticles

- Zinc oxide (ZnO) and titanium dioxide (TiO_2) are largely stable
- nanoparticles of ZnO and TiO_2 appear clear on the skin
- ZnO and TiO_2 provide broad spectrum protection against UVA and UVB

Nanoparticles are tiny!

1000
nanometres



Nanoparticles in sunscreens are typically ~10-30nm

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Source: Maxine McCall CSIRO

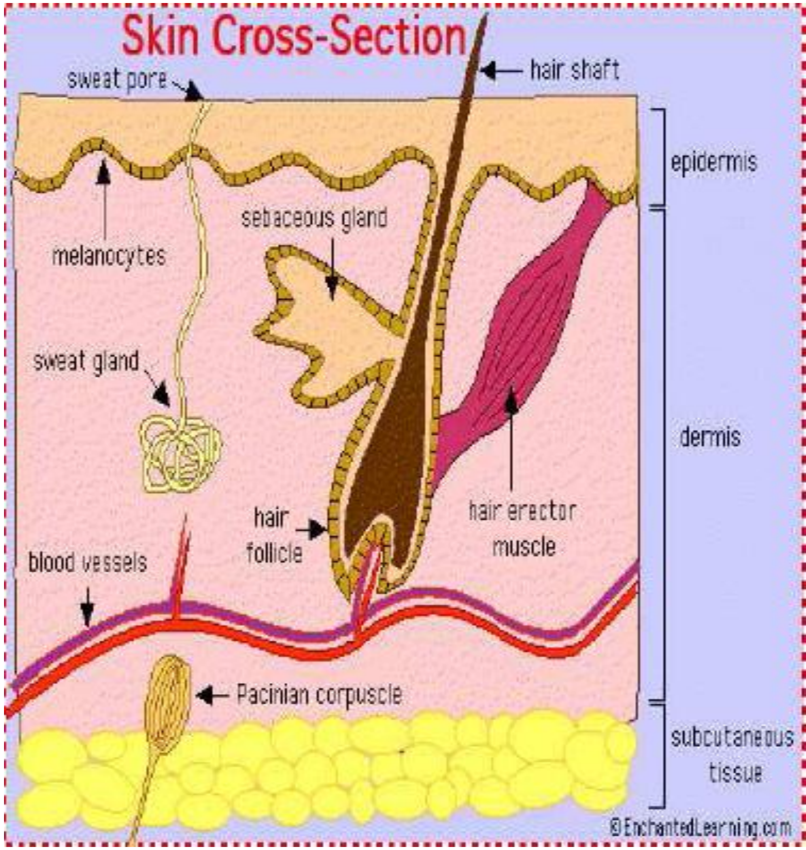
Skin absorption of nano zinc (and TiO_2) oxide - The Issues

- Use of nanoparticles in cosmetics is highly controversial: CC 2016 survey 13% respondents wouldn't use sunscreen because of nanoparticles
- Friends of the Earth

- have called for a moratorium on their use,

- convinced the Victorian Teachers Union to ban the use of sunscreens containing NP at child-care centres

- didn't believe the manufacturers so carried out their own testing with NMI



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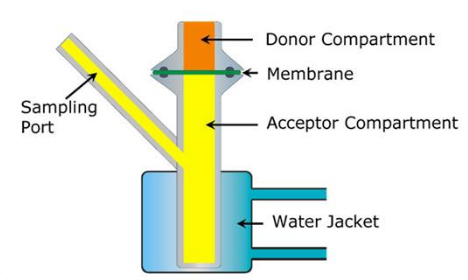
Previous testing

Diffusion cells with skin

- Human excised
- Pig



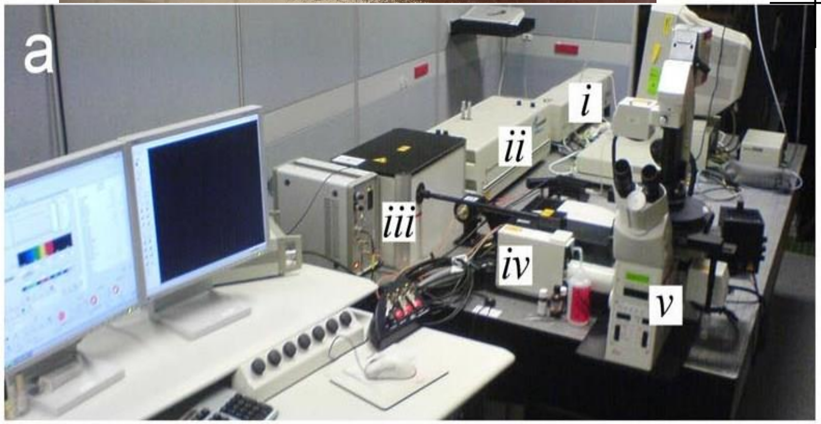
Frenz diffusion cell

http://www.scf-online.com/english/37_e/images37_e/Skinpenetration37_11_large.jpg

In Vivo rodents/pigs/rabbit

(Sadrieh et al TiO_2 minipigs/mice CSIRO)

Tape stripping



Multiphoton Microscopy in vivo

Source: Andrei Zvyagin MU/ Tarl Prow/Michael Roberts

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STABLE ISOTOPE TRACING

- a new approach for detection of absorbed zinc from sunscreens

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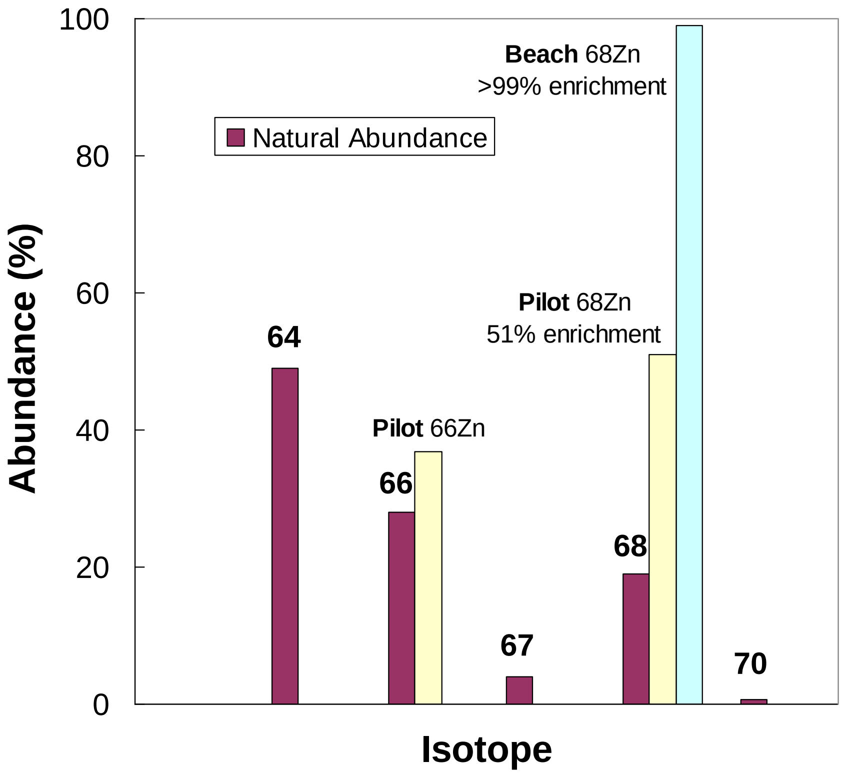
Testing skin absorption -Stable Zn Isotopes



- To distinguish between Zn from sunscreen and that occurring naturally in the body (e.g. from diet), the ZnO used in sunscreens in our studies was enriched with the stable Zn isotope, ^{68}Zn (~18-20% w/w in oil/water "commercial" formulation)- i.e. not radioactive
- An increase in the amount of ^{68}Zn in blood and urine samples compared with control samples indicates Zn from sunscreen has entered the body

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Human trials – Trial 1 & 2
Nanoparticle ZnO in sunscreen

Trial 1 – 2 males **51% enriched ^{68}ZnO**
1 day

Trial 2 – **51% enriched ^{68}ZnO 5 days**
Winter (July 2008)

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Human trials – Trial 2

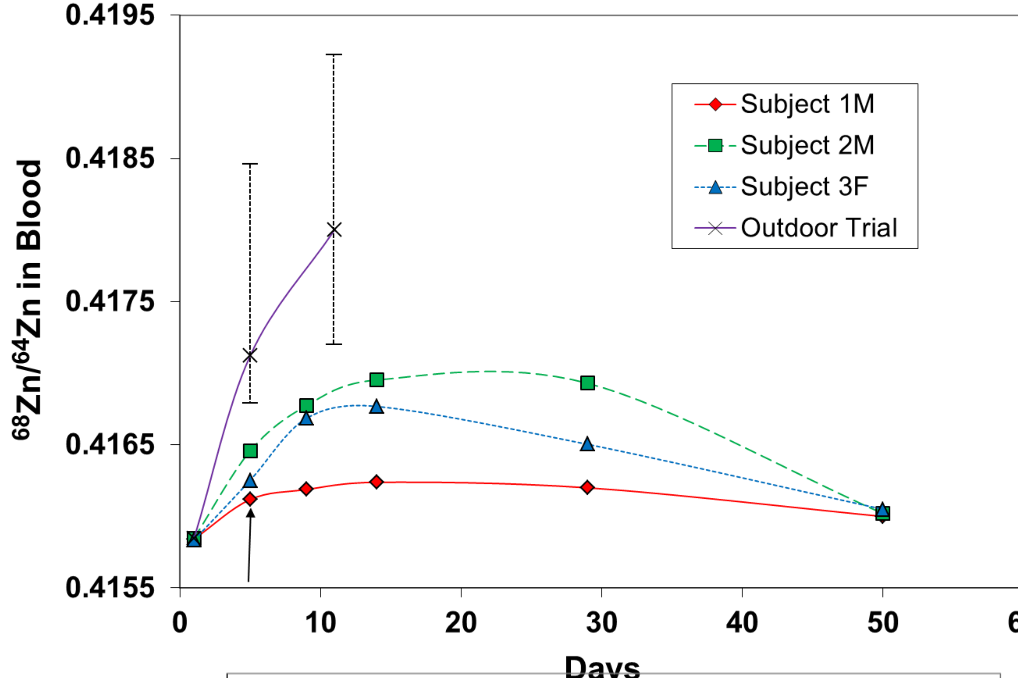
^{68}Zn is tracer, ^{64}Zn is natural abundance

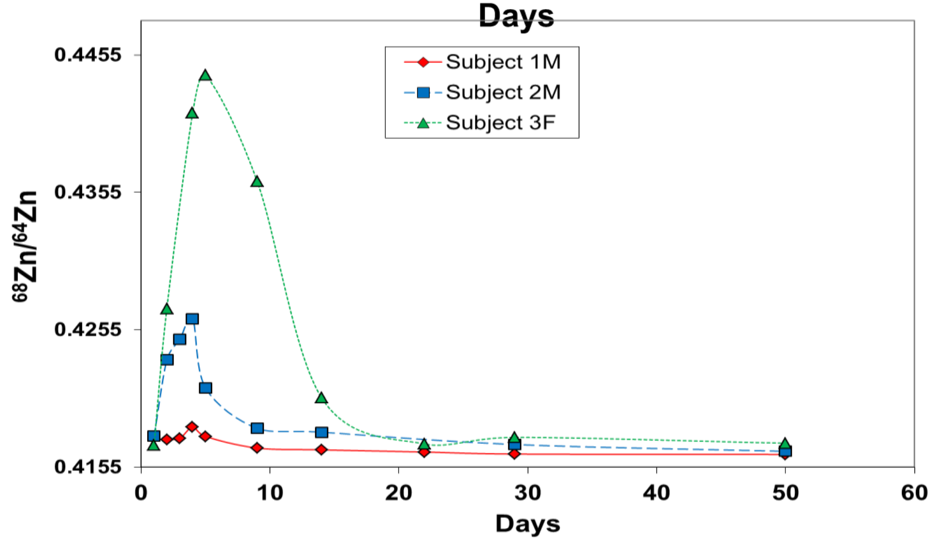
Blood

- Max uptake day 14
- Cleared by day 50

Urine

- Max 5 days
- Cleared by day 22





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Beach Trial 3-subjects & sampling

- Two groups of various: ages, skin types, countries, BMI
- Two sunscreens tested to compare effect of particle size:
  -“**Nano**” group (n=11) containing 19nm ^{68}ZnO particles
  -**“Bulk”** group (n=9) >100nm particles
- ZnO uncoated
- Venous **blood** samples collected:
  - at the start of the trial,
  - twice daily during the trial, and
  - at 6 days post-trial.
- Sunscreen applied to **backs** of volunteers twice daily for 5 days/non ZnO formulation to exposed areas
- Subjects experienced a minimum of 1 hr UV exposure in two episodes following sunscreen application
- **Urine** sampled minimum 3 times daily

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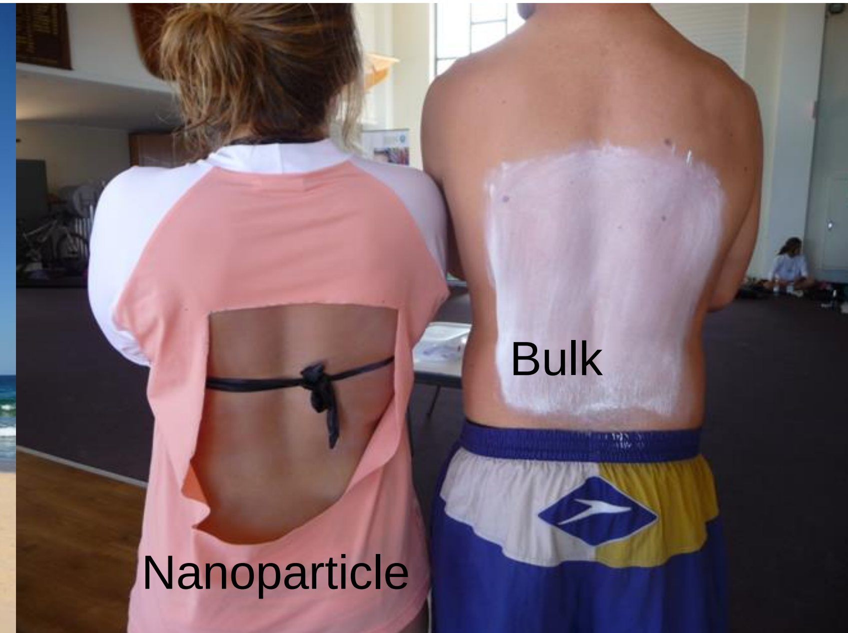
The volunteers



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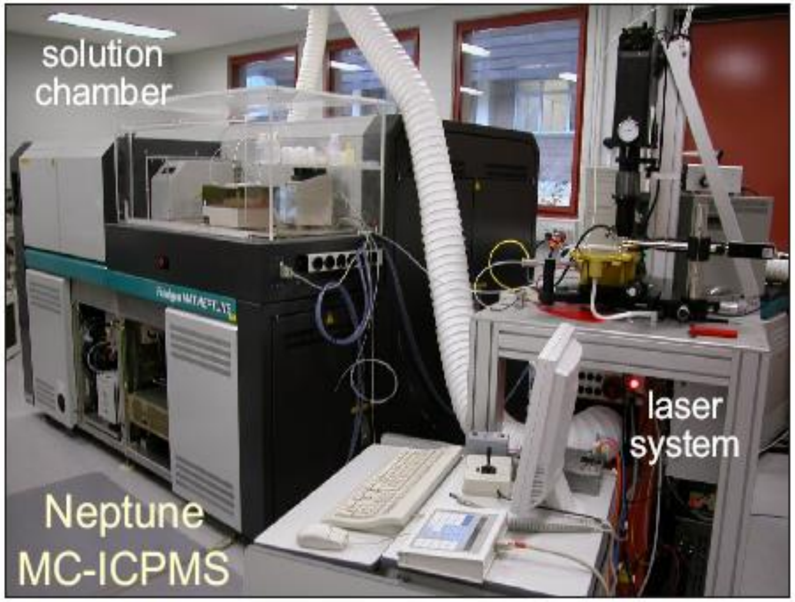
Analytical methods

Multicollector inductively coupled plasma mass spectrometer (RSES ANU)



Measures changes in amount of ^{68}Zn in samples using isotope ratios

Ultraclean chemistry

- Digest samples in clean HNO_3
- Anion exchange resin to separate Zn

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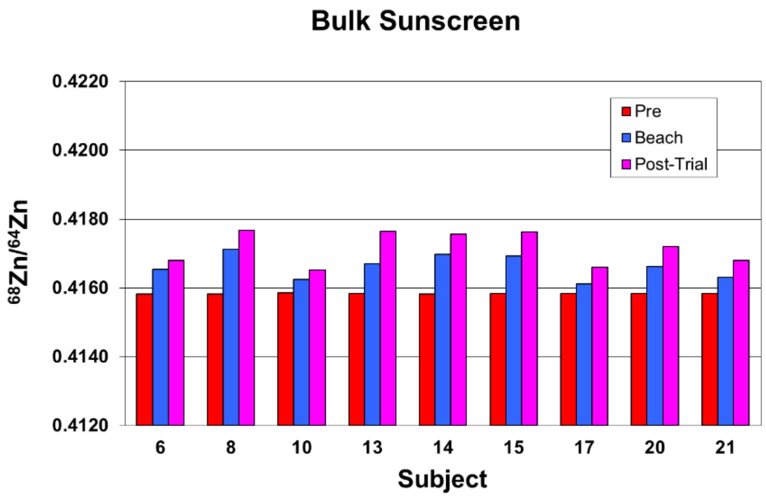
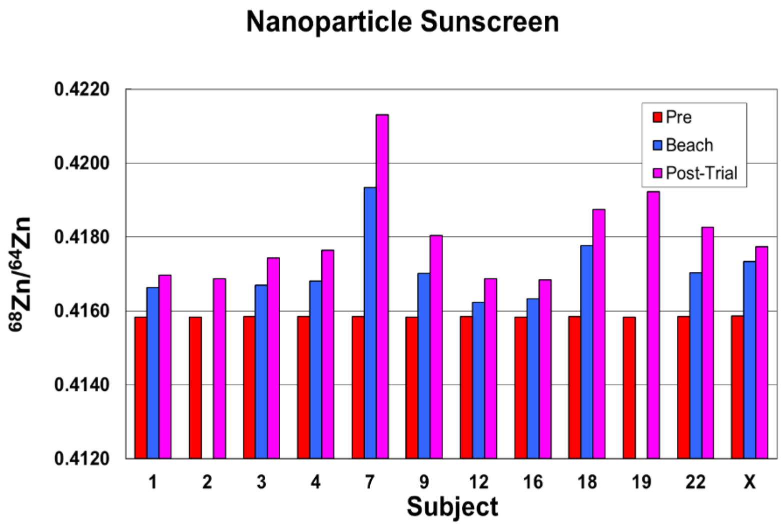
Changes in amount of zinc in blood coming from sunscreen





Bar graphs showing the ratio $^{68}Zn/^{64}Zn$ in blood from subjects receiving bulk or nano sunscreens

- Each subject acts as their own control
- The pre-exposure data (red) illustrate the uniformity in $^{68}Zn/^{64}Zn$ ratios prior to sunscreen application, reflecting the isotopic composition of naturally-occuring Zn
- Statistically significant increases in the ratio in all subjects at end of the beach exposure phase (blue) and 6 days post-exposure (purple) are due to skin absorption of ^{68}Zn from the sunscreens

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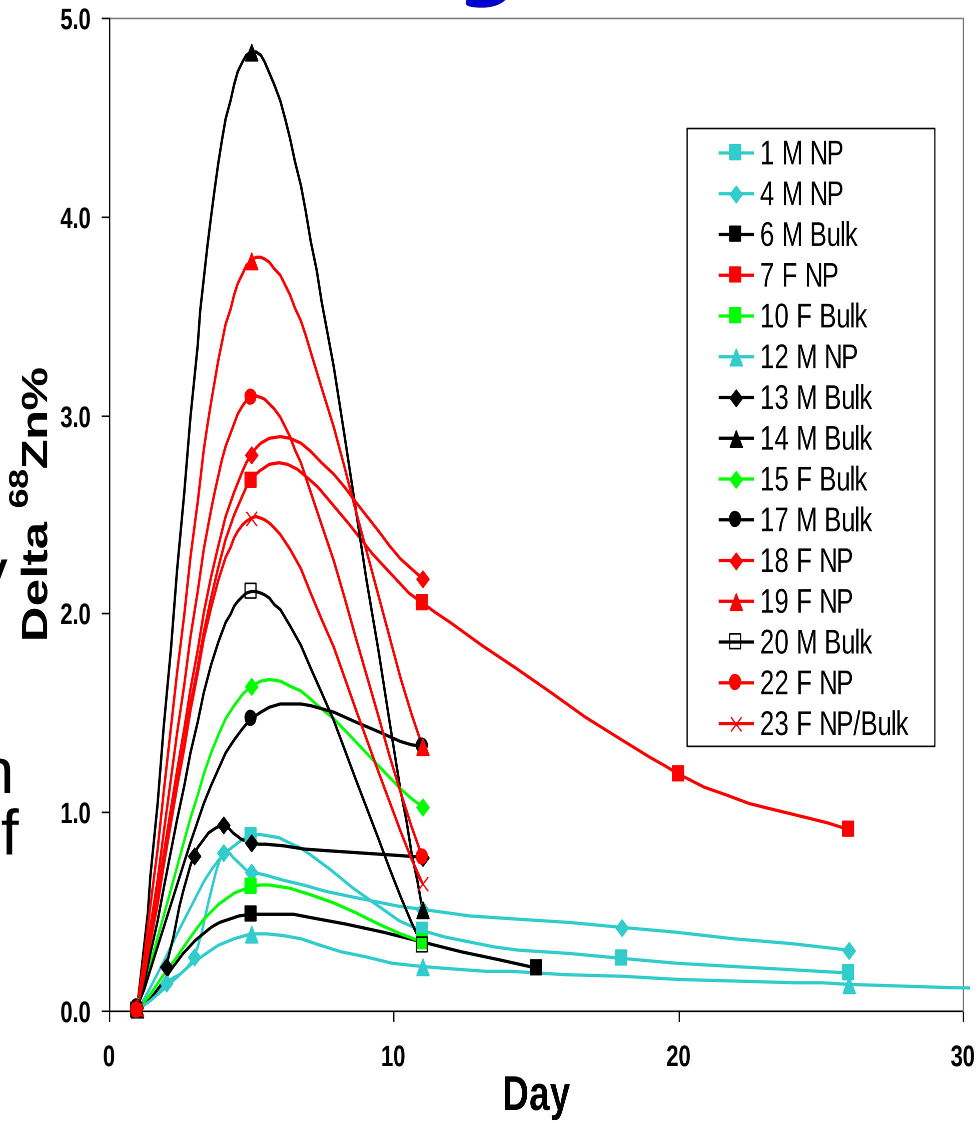
Urine results show Zn coming from sunscreen being wee'd out

- Larger increases in tracer ^{68}Zn than in blood
- Peak at Day 5 (end of days at beach)
- Still some ^{68}Zn signal at Day 40 in some subjects but most cleared by day 14
- Females (red) who had nano sunscreen had higher uptake of ^{68}Zn tracer than other groups



Summary – What did we find?

- In contrast to all previous studies, small amounts of Zn from our sunscreens found their way into the blood and urine of volunteers under real-life conditions.

- The amounts of Zn entering the body over the 5 day study (mean 15µg) were miniscule – around 1/1000th of the concentration of Zn already in the volunteers' bloodstream (~12mg), and around 1/1000th of the amount of Zn recommended in a person's daily diet.

- Even though some of the tracer Zn entered the bloodstream either as nanoparticles or soluble Zn, tracer was excreted in urine within a month.

- Thus the overwhelming majority of applied Zn was not absorbed.

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Should we be concerned?

- **No –** given the tiny amounts we have detected with a very sensitive method
- **No** - given the absolutely critical need for Zn and homeostasis (‘tight control’) for Zn in the body
- **No** - Zn used in topical applications (ointments) for ~100 years and no reported ill effects
- **No** - for an occasional user going to the beach at weekends or even a 3 week holiday
- **Perhaps** - for occupational user and young children, BUT more research to find out if the Zn we found is present as nanoparticles in the body

  although new research is encouraging
- Until we know more SLIP/SLOP/SLAP

  shade, not at high UV time, & sunglasses!!

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Thank you for your attention