Test Requirements of REACH on the Long Term vs Basis of New Methodology:

Need for a Fresh Start!

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November 25/26, 2006, Brussels, B

“History of REACH” – a ‚developing‘ story line for alternative methods

- EU Chemical Policy White Paper Feb. 2002
- In parallel: 6th Framework Programme for RTD
- *ecopa*-”alert”: sign-in
  Commissioner Busquin’s reaction
- *ecopa* Annual Oct. 2002 – DG ENV testing figures

Quotes from the text book

Version 1 to …

„Promotion of non-animal-testing“ 2.2
„development of alternative methods“ 3.2

Source: Chemical Policy, White Paper (2001)

…version 2 to …

Footnote: „as far as possible, animal experiments and testing should be replaced by in vitro or alternative methods. Animal suffering must be avoided or kept to a minimum…“

Source: Framework Programme, p. 18 (2001)

..version 3 to …

„ECVAM is currently preparing a collection of alternative methods that will be ready in spring 2002“

Source:G. Vogelsang, DG XI Oct. 27, 2001

…version 4 …

„Commission takes development of alternative methods seriously“

Source: M- Blainey/DG ENV., Feb. 1, 2006

…more to come?!

Alternative quotes

„A flexible, tiered approach to
risk assessment is required that is scientifically valid rather than a prescribed battery of tests…"

Source: J. Bridges, Feb. 1, 2006

„How we like to spell REACH after introduction of ITS:
Reasonable, Economical, Assessment of Chemicals, with Humane methods"

Source: T. Hartung, Feb. 1, 2006

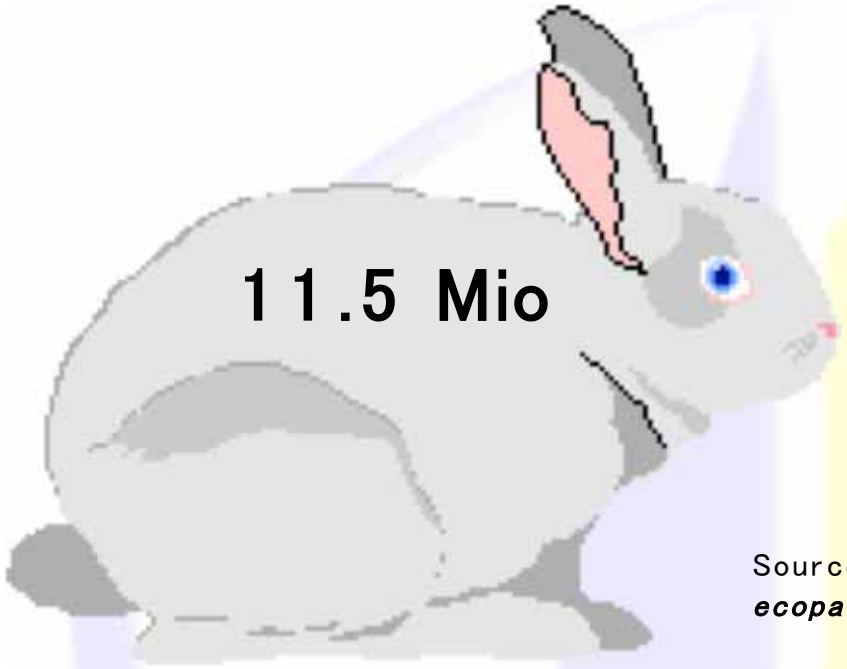
„Not everyone will laud this agreement, but we have a functioning minumum of REACH for all stakeholders."

Source: G. Sacconi, Nov. 28, 2005

„Thus, any waiving of repeated dose studies in animals bears the probability of unforeseen effects…"

Source: H. Greim plus 8 Eur. Toxicologists
Arch.Toxicol. 2006, Jan. 13, 2006

Numbers in hind sight:



The Numbers' Game…

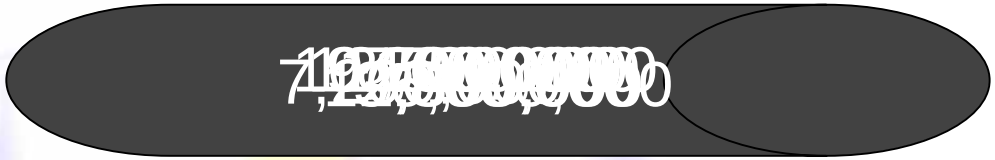
Source: J. Vogelgesang, DG XI
ecopa Workshop 2001

ecopa statement in regard to EU Chemical Policy:

„…DGs involved immediately initiate a thorough analysis on potential animal experiments induced by the regulations, and on the realistic availability of alternative tests, under neutral guidance and chairmanship by an organisation such as *ecopa* ."

Source: ***ecopa*** website 2003

Numbers in hind sight: a number‘s game



- Though almost everybody agreed that there were not enough alternative methods at the time of setting up REACH legislation, nor will be at the start of REACH regulations, European citizens were made believe there will be no major animal testing on top.

- Numbers initially varied, depending upon the assumptions (and sometimes personal agenda)

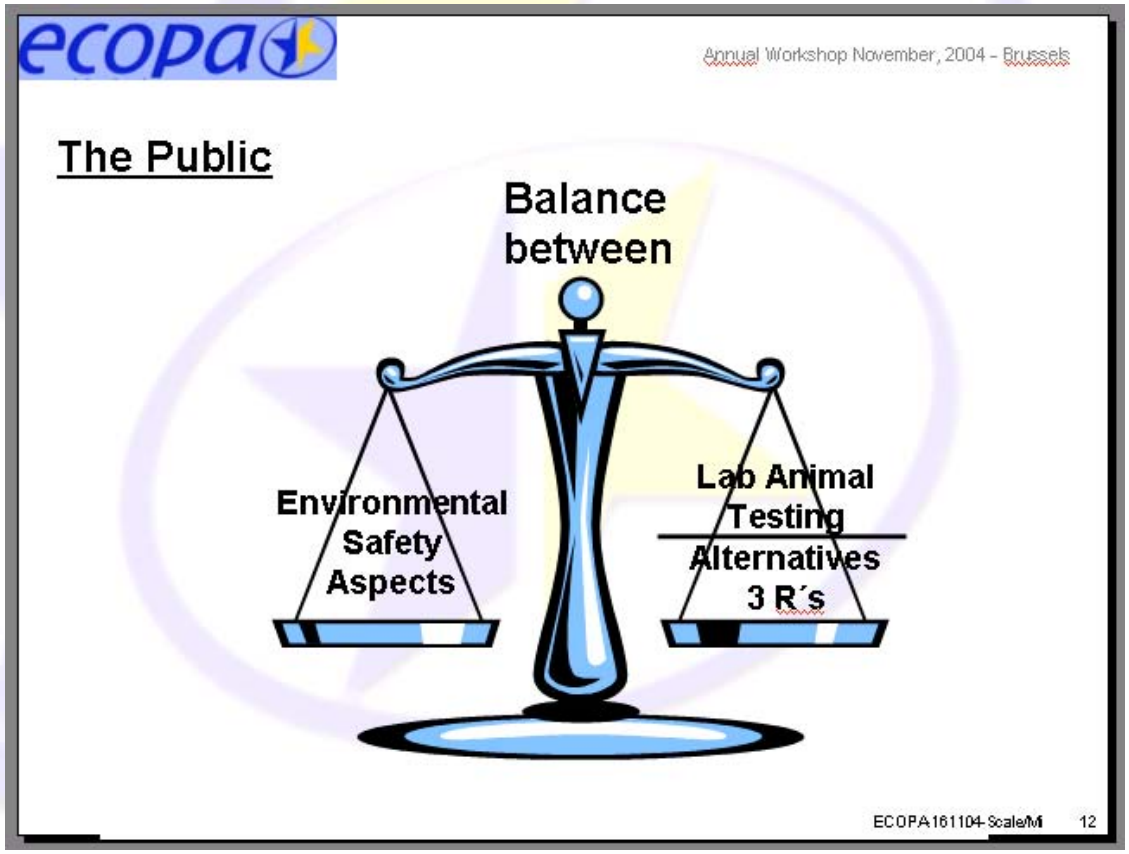
- *ecopa* within the CONAM EU project promised to check

Balance of

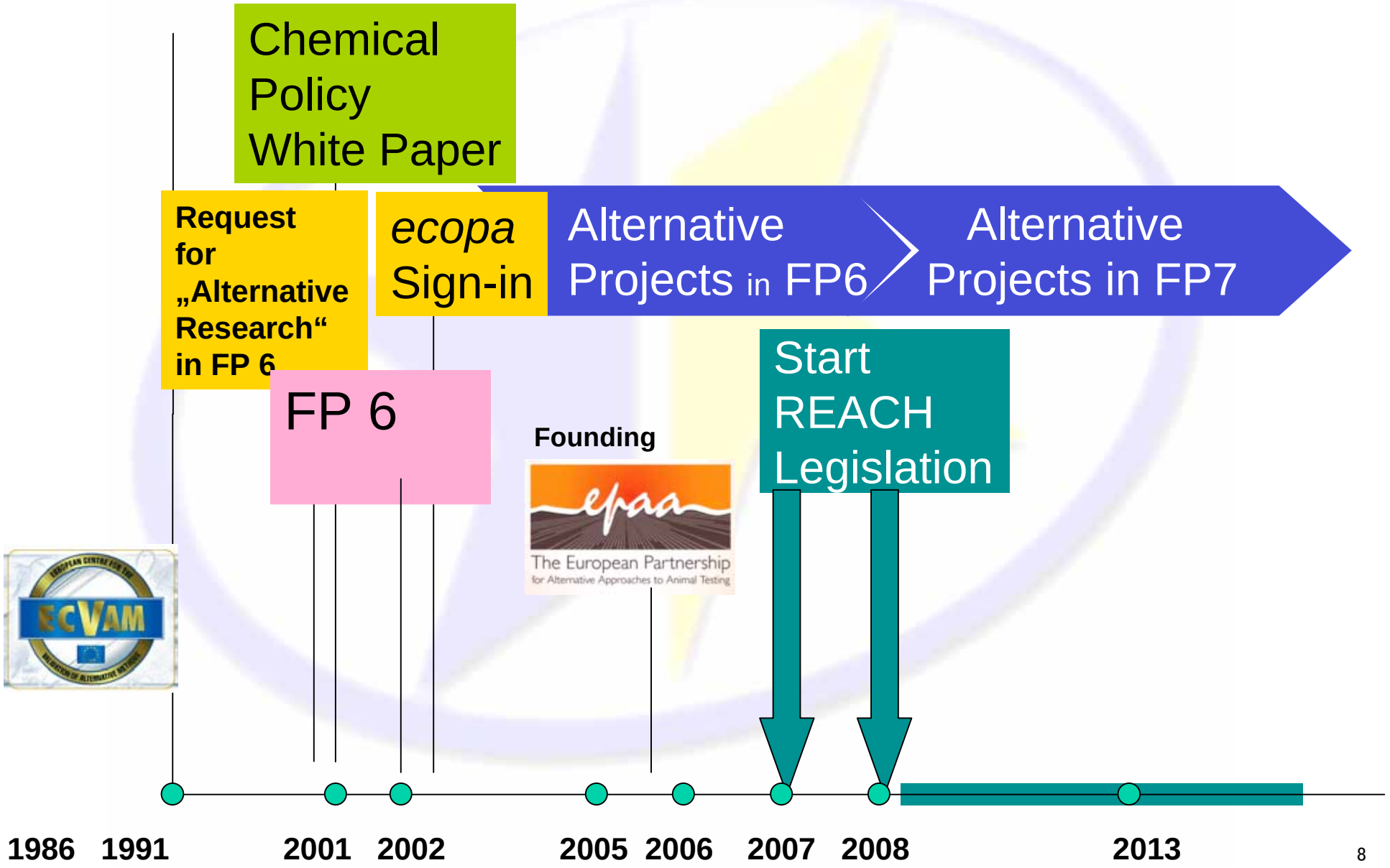
request for testing (in animals)
for safety, risk assessment reasons

vs.

existing
alternative
methods



REACH: Unlimited Time Line for Alternatives?



from agencies

Long term testing…

Quote

„A concept to prioritize the need for testing and risk assessment of specific compounds will be developed by the „Agency“!“

Issues such as:

- Carcinogenicity
- Mutagenicity
- Repeated dosing/sub-/chronic tests
- Endocrine disrupters

from tox experts

„To continue with the existing methods until such time as properly validated methods are available.“

An Industry Expert:

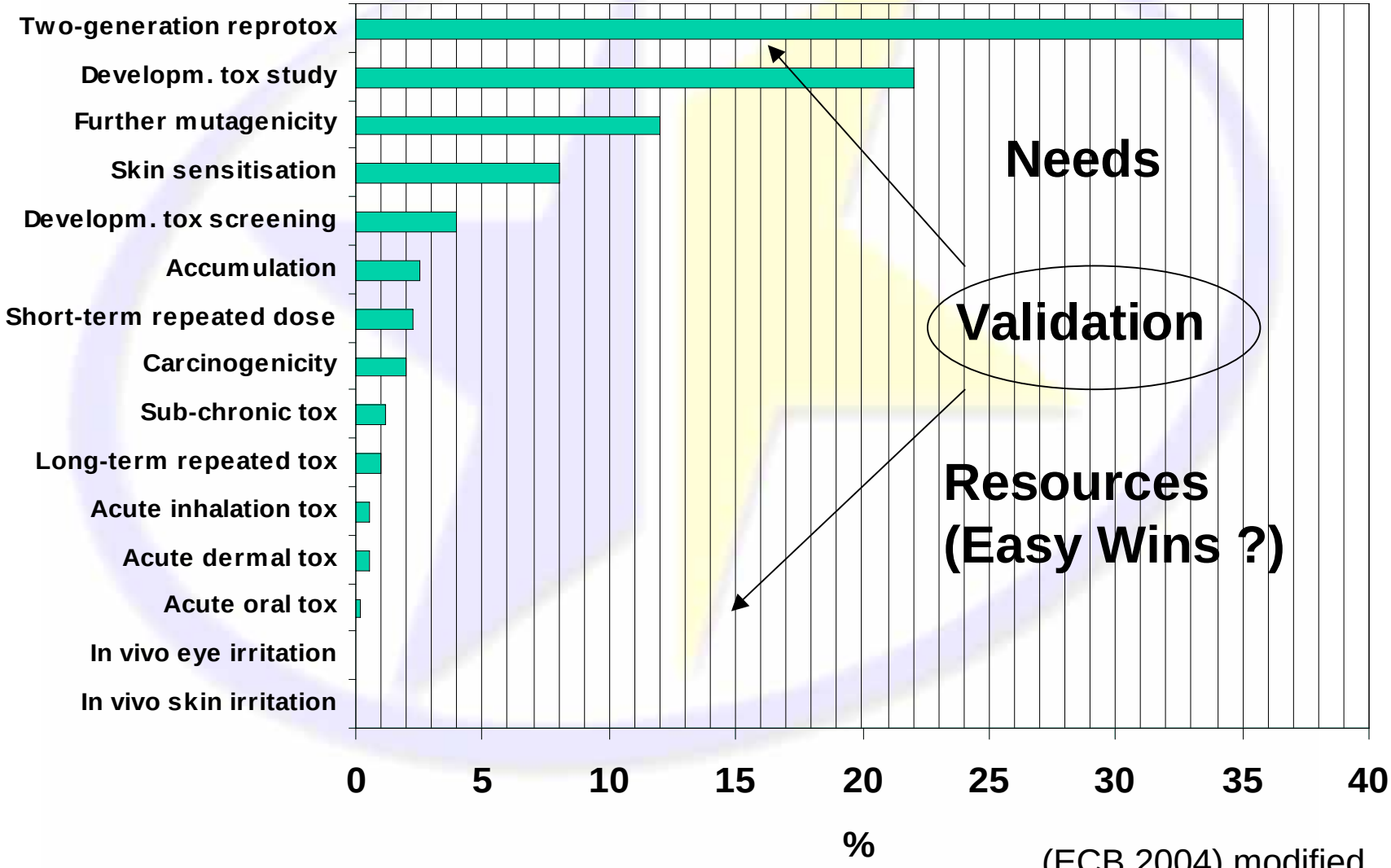
„Areas where Alternatives are Needed

Area	Replacement by 20..?
Acute toxicity	not foreseeable
Toxicity, repeated dosing	not foreseeable
Reprotoxicity	not foreseeable
Genotoxicity	partly implemented
Carcinogenicity	not foreseeable
Local tolerance	possible, if validation successful
ADME	not foreseeable

CPMP 1997
(CSTEE 2004)

…“

REACH: Test animal need for different endpoints
(% of total test animals needed)



(ECB 2004) modified

New methodology: helpful?

Or just helpful for a fresh start?

examples	evaluation
• (Q)SAR	doubtful, „new“?
• Genomics/Proteomics	promising, but…
• Transporter systems	„
• System Biology approach	„

- Problem with any new technology, already developed or developing, we are not prepared
  - nanotech for regulatory
  - biotech testing

- And its application for alternative methods not ouvert, example STED-microscopy (Nature 440, 2006, p 935)

Have we got everything?

Timing of REACH

- All the alternative tests needed,
  requested by REACH,
  the authorities in general,
  the future Chemical Agency,
  others
- Experiences from other „sectors“:
  ICH (International Conference on Harmonization)
  in pharmaceuticals
- Why is still a new initiative needed in this area?
  IMI
- Are we prepared for nanotech e.g.?

No, we have not!

Timing of REACH

- Therefore, initiatives such as IMI needed (Innovative Medicine Initiative)
- Therefore, *ecopa* had initiated eSi (ecopa Science Initiative)
- Therefore, follow-up to eSi has to come

↳ just to take advantage of all the science and methodologies to prepare for new product technologies

We do need the scientific network
for alternative method development

- The *ecopa* CONAM-project in the 6th Framework Programme to start with
- The *ecopa*-participation in the 6th FP Projects an absolute need

↳ next step: fresh start with the follow-up PROJECT in the 7th FP!

What does it mean – starting fresh?

- Initiate cross-country industries‘ information
- Organize update meetings with stakeholders
- Cover all of the 3Rs (including **R**efinement until alternative for REACH developed)
- Identify centers of excellence for alternatives
- Involve the European Research Council!

What's next?

- Retrospective analysis
  „mapping": alright,
  but partly lip service
- Forward looking: tackle the
  real problems,
  e.g. carcinogenesis testing solutions

What is critically important, in that regard?

- Get the Commission even more involved (only 2 DGs!) :

a start only

- Get the registration authorities involved (the EMEAs, EFSAs, CA, Nationals!)
  example: blue print

- Build a focal point:
  the *ecopa*-based

START now

Start
Technology
Alternative
Research
Timely

And, therefore,

ACTION

- 1. form START network
- 2. get science parties addressed
- 3. finally, implement „dialogue“ science + authorities

Thank you for your attention!

Let me wish you

- a Merry Xmas and
- a Happy New Year!

New methodology: … just helpful for a fresh start?

Characterization of primary rat proximal tubular cells by gene expression analysis

Weiland, C., Ahr, H.J., Vohr, H.W., Ellinger-Ziegelbauer, H.,, Toxicology in Vitro (2006), doi: 10.1016/j.tiv.2006.10.008

PII: S0887-2333(06)00233-5

DOI: 10.1016/j.tiv.2006.10.008

Reference: TIV 1566

To appear in: Toxicology in Vitro

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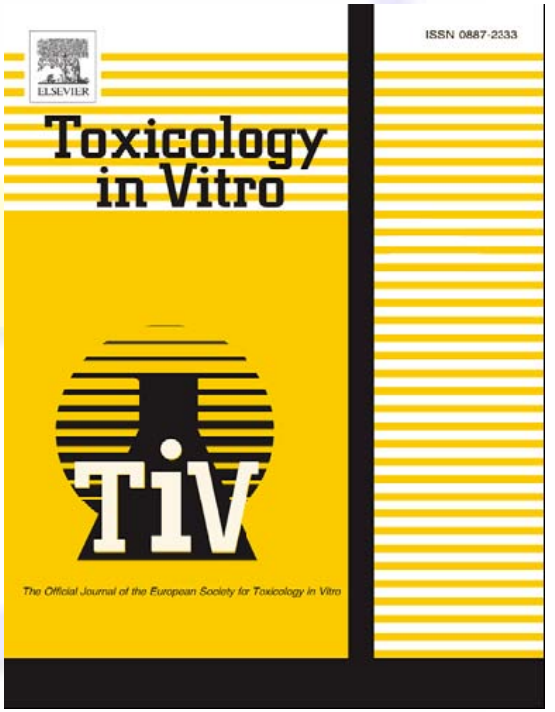

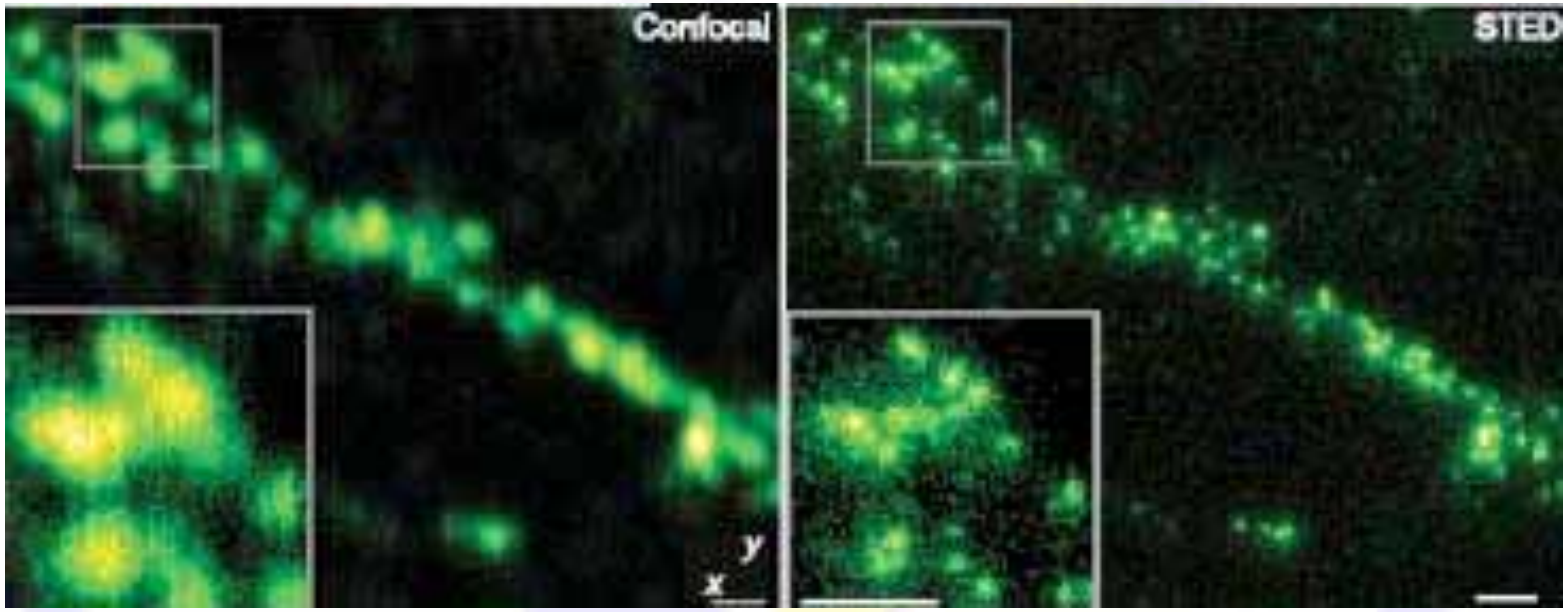

STED

Chance for intra-vitam-observation of cells!

Neuronal vesicles – usual light microscope (left) and with STED-microscope (right).
Source: Nature