Re-Evaluation of the FQPA Safety Factor for Pyrethroids

Bottom Line

The FQPA safety factor has been reduced from 10X to 1X for pyrethroids based on a wealth of evidence, including available studies in the open literature, studies submitted to EPA for registration, over a decade of research specifically trying to address the FQPA safety factor, and recommendations from multiple science advisory panels (SAP).

Background-2011 Decision

- In 2011, the FQPA safety factor was reduced from 10X to 3X, based on available information at the time
- Additional information on rats and humans was needed to conclude that there were no differences between children and adults (i.e. to reduce all the way to 1X)

Available Information for the 2019 Reevaluation

- Published studies (>ten thousand citations reviewed)
- Studies submitted to EPA as part of registration/registration review
- Research conducted by CAPHRA (consortium of pyrethroid registrants)
  - CAPHRA was formed in 2011 with the aim of obtaining additional information to further refine the FQPA SF
  - Research mostly uses cells (instead of whole animals) and mathematical models known as PBPK models

CAPHRA = Council for the Advancement of Pyrethroid Human Risk Assessment

CAPHRA Members

- ADAMA
- Amvac Chemical Corp
- BASF Corp
- Bayer HealthCare LLC Animal Health Division
- Bayer Crop Science, LP
- FMC Corp
- LG Chem
- McLaughlin Gormley King
- Meghmani
- S.C. Johnson & Sons, Inc.
- Sumitomo Chemical Company
- Syngenta Crop Protection, LLC
- Valent USA Corp
- Wellmark International

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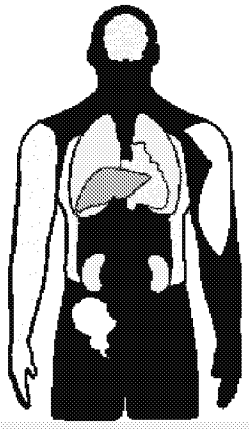
How EPA Evaluated Available Information

- Comprehensive review of publicly available literature and studies submitted for pesticide registration
  - Incorporated information into individual pesticide assessments, when appropriate
- Extensive involvement on the pyrethroids by the public and scientific experts from outside the Agency
  - Multiple Science Advisory Panel (SAP) meetings (2007, 2009, 2010, and 2015)
  - Expert peer-review panel (2018)

CAPHRA PBPK Model

- CAPHRA constructed mathematical models (known as physiologically based pharmacokinetic [PBPK] models) using rat and human tissues.
- Models were recommended by federal advisory groups and the National Academy of Sciences as a scientifically sound way to assess differences between children and adults
- Models specifically provide information for humans, which was not available at the time of the 2011 evaluation

PBPK models predict chemical concentrations inside the body over time



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Conclusions on FQPA SF

- PBPK models in 2019 support the conclusion that there are no differences between children and adults in humans following pyrethroid exposure
- The 10X FQPA SF can be reduced to 1X for all populations

Conclusions on FQPA SF

- White paper with 2019 conclusions on FQPA SF published August 2nd, 2019.

https://www.epa.gov/ingredients-used-pesticide-products/2019-evaluation-fqpa-safety-factor-pyrethroids

- Paper is available for public comment with the pyrethroid preliminary interim decisions (PIDs) (released 11/12/19)

CAPHRA models- Other uses

- CAPHRA models were specifically designed to address concerns regarding FQPA (i.e. potential differences between human juveniles and adults)
- Models are not ready to be used to address other uncertainty factors (additional data are needed)
- A second white paper is being drafted on this topic and will be released in the future

Public Reception/Perception of the FQPA SF Decrease

- Some members of the public may distrust the data used to decrease the FQPA SF because part of these data were created by registrants
- Some NGOs such as the Center for Biological Diversity and the Environmental Working Group erroneously believe that any decrease in the FQPA SF means EPA is not protecting children

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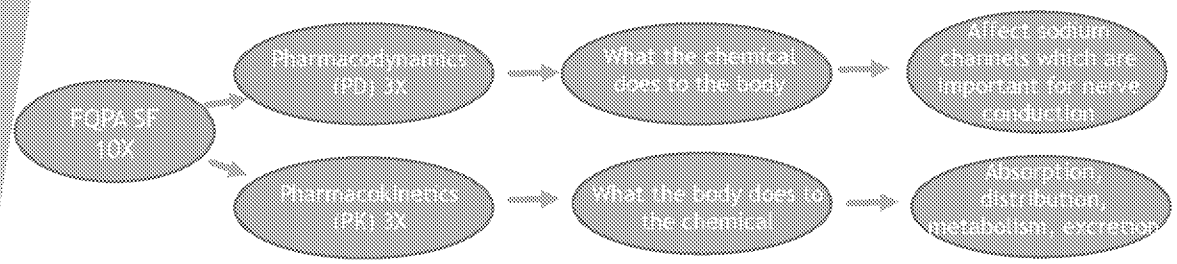
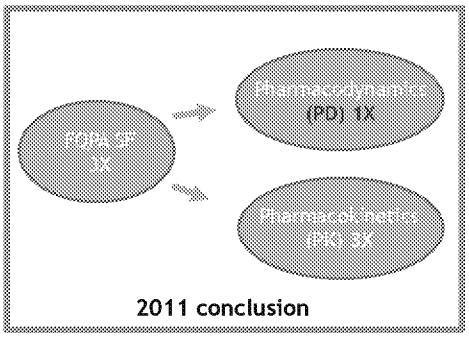
Additional slides- if needed

FQPA Safety Factor

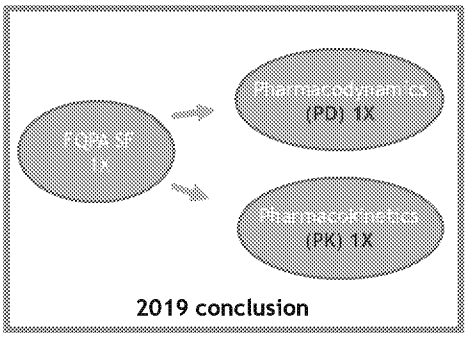
- FQPA default assumption → children/pregnant women up to 10X more sensitive than non-pregnant adults
- The 10X FQPA SF is retained unless there are reliable data to remove it



Conclusions on FQPA SF



2011 conclusion



2019 conclusion

- Based on the 2019 analysis, the Agency concludes that the FQPA SF (PDxPK) can be reduced to 1X for all populations for the pyrethroid pesticides