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 preparation for registration review and due to the need for additional refinements for the pyrethroid risk assessments, EPA initiated the analysis of data that could inform the FQPA safety factor
- In 2011, the FQPA safety factor was reduced from 10X to 3X, based on available information at the time
- Additional information was needed to evaluate the potential differences between children and adults (i.e. to reduce all the way to 1X)
- Due to the complexity of data and the large amount of information, a significant amount of time and resources has been invested in the FQPA analysis.

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 the Council for the Advancement of Pyrethroid Human Risk Assessment (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 for humans

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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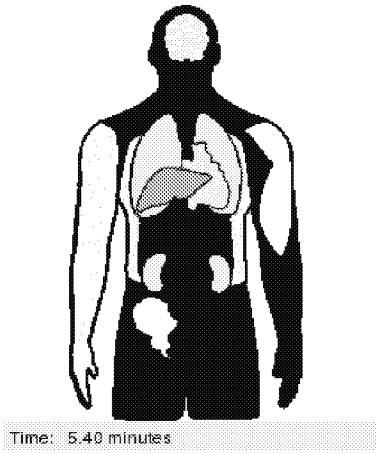
How EPA Evaluated Available Information

- Comprehensive review of publicly available literature and studies submitted for pesticide registration
  - Incorporated study information (i.e. toxicity effects) 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 human data
- PBPK models were recommended by federal advisory groups and the National Academy of Sciences as a scientifically sound tool to assess differences between children and adults
- This human model was not available at the time of the 2011 evaluation

PBPK models predict chemical concentrations inside the body over time



Conclusions on FQPA SF

- PBPK models in 2019 support the conclusion that there are no differences between children and adults 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 investigate potential differences between children and adults (i.e., FQPA SF)
- Models are not ready to be used to address other uncertainty factors (additional data are needed)
- A 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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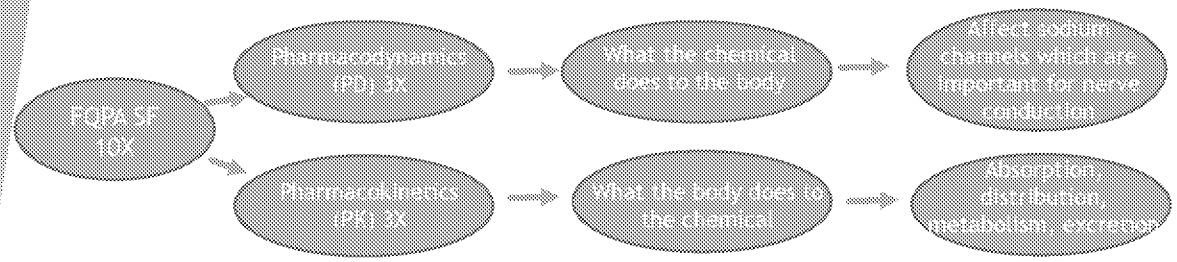
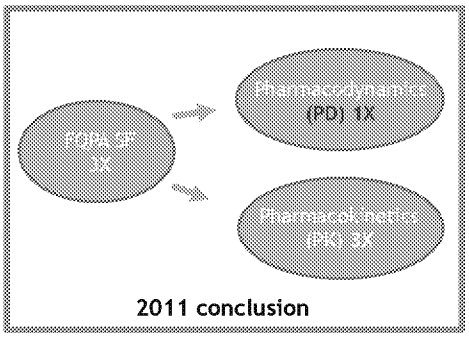
Additional slides- if needed

FQPA Safety Factor

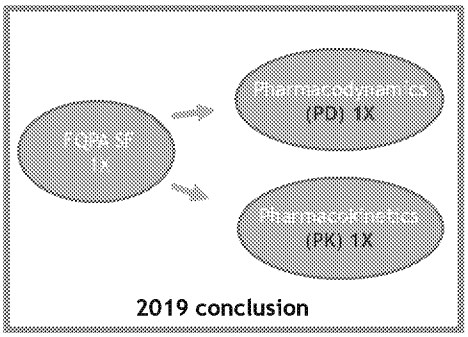
- FQPA default assumption → children/pregnant women up to 10X more sensitive than non-pregnant adults
- The 10X FQPA SF is retained unless there are reliable data to remove it



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