PFAS Considerations for Pesticide Inert and Active Ingredients

Presentation to OPP Division Directors

May 26, 2022

RD--Beth/Debra

Outline:

- Meeting purpose and Team Recommendations
- PFAS Background
- Inert Ingredients
- Active Ingredients
- Risk Management and Management Considerations
- Communications Discussion

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Meeting Purpose:

- Provide an overview of PFAS Agency strategy, definitions, and potential regulatory considerations associated with pesticide registrations

- Inert ingredients:
  - List of inerts compiled and submitted by PEER
  - status of listed/registered inert ingredients identified as PFAS

Ex. 5 Deliberative Process (DP)

Ex. 5 Deliberative Process (DP)

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Team Recommendations:

Ex. 5 Deliberative Process (DP)

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PFAS Background

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Broad PFAS Concerns:

- PFAS are a large class of chemicals with varying degrees of human toxicity linked with cancer, reproductive, developmental, liver, kidney, thyroid, and immunological effects (i.e., chronic effects).
- PFAS compounds are generally persistent and accumulate in the environment.
- The nature of effects across different taxa is variable; for aquatic taxa effects are observed at low concentrations.
- EPA developed a roadmap to research, restrict, and remediate PFAS contamination.

[1]https://www.epa.gov/system/files/documents/2021-10/pfas-roadmap_final-508.pdf

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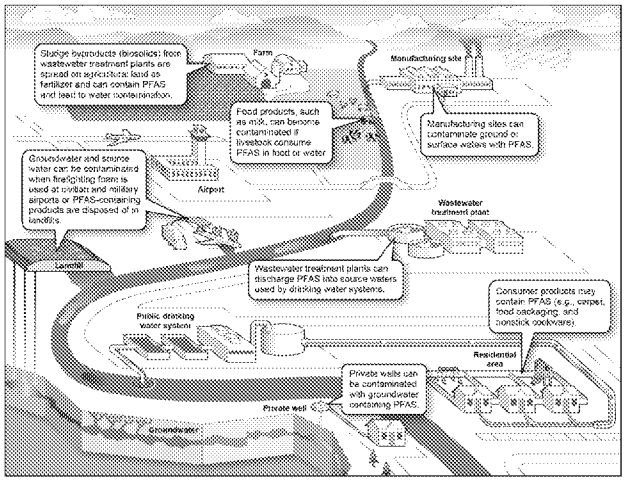
Roadmap - PFAS Lifecycle and Principles:



PFAS Strategic Roadmap: EPA's Commitments to Action 2021–2024

EPA's approach is centered around the following principles:

- Consider the Lifecycle of PFAS.
- Get Upstream of the Problem.
- Hold Polluters Accountable.
- Ensure Science-Based Decision-Making.
- Prioritize Protection of Disadvantaged Communities.

Source: GAO | GAO-21-37

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Goals in the Strategic Roadmap

RESEARCH

Invest in research, development, and innovation to increase understanding of

- PFAS exposures and toxicities;
- Human health and ecological effects; and
- Effective interventions that incorporate the best-available science.

RESTRICT

Pursue a comprehensive approach to proactively prevent PFAS from entering air, land, and water at levels that can adversely impact human health and the environment.

REMEDIATE

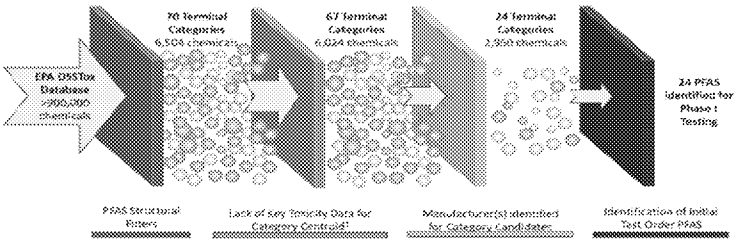
Broaden and accelerate the cleanup of PFAS contamination to protect human health and ecological systems.

PFAS Strategic Roadmap: EPA's Commitments to Action 2021–2024

Jeff

Analysis Supporting Testing Efforts:

- National Testing Strategy
  - Identified 70 distinct categories
  - Applied a series of structural filters to create categories
  - Described in https://www.frontiersin.org/articles/10.3389/fenvs.2022.859019/full



Ring structures of broflanilide and PQZ excluded these chemicals from the testing strategy.

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PFAS Definition Issue:

- OCSPP is using OPPT PFAS definition
  - OPPT PFAS definition: R-CF_2R-CF(R')(R") where R, R', R" do not equal H and the C-C bond is saturated
  - OECD PFAS definition: fluorinated substances that contain at least one fully fluorinated methyl or methylene carbon atom (without any H/Cl/Br/I atom attached to it)
- OW is using supplemental definition that is essentially the OPPT definition.
- Use of OECD PFAS definition would increase the number of designated active ingredients from 2 to ~100.

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Considerations Related to Agency Efforts:

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Resources for Agency Efforts on PFAS:

- General Info https://www.epa.gov/pfas
- PFAS Council https://www.epa.gov/sites/default/files/2021-04/documents/per-and_polyfluoroalkyl_substances.memo_.signed.pdf
- PFAS Roadmap https://www.epa.gov/pfas/pfas-strategic-roadmap-epas-commitments-action-2021-2024#council
- PFAS National Testing Strategy https://www.epa.gov/assessing-and-managing-chemicals-under-tsca/national-pfas-testing-strategy

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Inert Ingredients

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PFAS and Inert Ingredients-Background:

- In Feb of 2021 PEER[1] provided OPP with a list of 24 inert ingredients found in OPP's InertFinder[2] database believed to be PFAS.
- The PEER list was based on an ORD database with literature references of PFAS, and not a specific PFAS definition
- Listing on InertFinder does not automatically mean a substance is used as an inert ingredient in currently registered pesticide products.

[1] PEER = Public Employees for Environmental Responsibility

[2] https://ordspub.epa.gov/ords/pesticides/f?p=INERTFINDER:1:0::NO:1::

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PFAS and Inert Ingredients-Background:

- Are any of the chemicals listed on the PEER document PFAS chemicals based on current definitions (per OPPT and OECD) and if so, are they currently used in pesticide products?

- In conjunction with ORD's Center for Computational Toxicology and Exposure, a search was conducted to determine whether any inert ingredients from the PEER list met either the OPPT or OECD definitions.

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PFAS and Inert Ingredients – Analysis:

- Five chemicals from the list met either the OPPT or OECD definition of a PFAS chemical:
  1. Poly(difluoromethylene), alpha-chloro-omega-(1-chloro-1-fluoroethyl) (*PFAS per OPPT and OECD*)
  2. Poly(difluoromethylene), alpha-(2,2-dichloro-2-fluoroethyl)-, omega-hydro- (*PFAS per OPPT and OECD*)
  3. Ethane, 1,1-difluoro-, homopolymer (*PFAS per OECD*)
  4. alpha-(Cyclohexylmethyl)-omega-hydropoly(difluoromethylene) (*PFAS per OPPT and OECD*)
  5. Poly(difluoromethylene), .alpha.-chloro-.omega.-(2,2-dichloro-1,1,2-trifluoroethyl)- (*PFAS per OECD*)
- All 5 inert ingredients identified as PFAS chemicals are for non-food use only
- OPP databases were searched using CAS numbers and PC codes to identify any products that may contain one or more of the 5 PFAS chemicals

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PFAS and Inert Ingredients – Results:

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PFAS and Inert Ingredients – Next Steps:

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Active Ingredients

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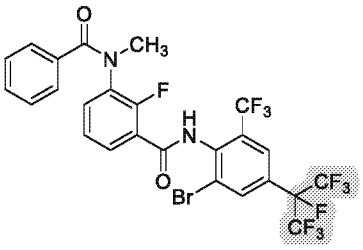
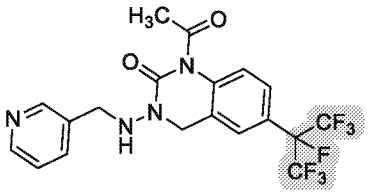
PFAS Pesticide Active Ingredients:

- Two pesticides classified as PFAS chemicals under the OPPT definition.

Broflanilide



PQZ



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Broflanilide Registration Status:

- First registered in 2021.
- Agricultural application methods include in-furrow (corn and subgroup 1C) and seed treatment (small grains)
- Also registered for control of insects inside and around industrial, commercial (including food handling establishments), and residential areas.

Broflanilide Pending Uses:

Ex. 5 Deliberative Process (DP)

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Applied using handheld sprayers, applicator tubes (gel formulations), aerosol cans, injection systems, and Centrobulb® equip

PQZ Registration Status:

- First registered in 2013 for indoor ornamental uses
- Currently registered for use on multiple commodities.
- Approved application methods include aerial, ground (chemigation, air blast).

Pending use[1]:

Ex. 5 Deliberative Process (DP)

[1]Pending first residential uses are awaiting ESA completion.

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Environmental Fate Summary:

Broflanilide

- Broflanilide and known major (>10%) PFAS-containing metabolites are persistent in the environment
  - No fate for terminal PFAS degradate
- Parent and degradates likely to accumulate in aquatic and terrestrial environments

PQZ

- PQZ and known major (>10%) PFAS-containing metabolites are *not* persistent in the environment
  - Fate studies do not track to terminal PFAS degradate(s)
  - There may be currently unknown PFAS degradates that could persist in aquatic and terrestrial environments not captured in prior exposure assessments (drinking water and ecological)

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Human Hazard Summary

Broflanilide

- Absorption and excretion is rapid, no evidence of bioaccumulation.
- Target organs are the adrenal glands and ovaries.
- Broflanilide is classified as "likely to be carcinogenic to humans"

PQZ

- No evidence of bioaccumulation of PQZ at relevant doses
- Target organs are the testes, nasal passage, liver, thyroid, hematopoietic system and the kidneys.
  - Most sensitive effects include decreased anogenital distance, and decreased body weights
- PQZ is classified as "Not likely to be carcinogenic to humans"

Both pesticides have:

- Comprehensive and complete AI-specific datasets in support of proposed pesticidal uses (i.e., not considering PFAS as residue of concern). Any human health effects of parent and its observed metabolites would be expected to be captured in the studies.

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Ecological Effects Summary:

Broflanilide

- No chronic data for PFAS degradates
- No studies for terminal PFAS degradates
- Chronic risks to birds and mammals on-field from consumption of treated seeds.
- Acute and chronic risks identified for terrestrial and aquatic invertebrates
  - Risk after a single application
  - Risk increases with subsequent applications
- Identified risks consistent with PFAS type chronic exposure and cumulative risk
  - Parent based assessment, parent is persistent

PQZ

- No chronic data for PFAS degradates
- No studies for terminal PFAS degradate
- Chronic risks identified for mammals
- Acute and chronic to terrestrial and aquatic invertebrates
  - Risk after a single application
  - Parent does not accumulate in the environment so risk was not expected to increase over time
- Risk assessment findings may not be protective of potential PFAS risks
  - Parent based assessment, parent is short lived

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Risk Management

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Broflanilide - Risk Mitigation for Registered Uses:

Environmental

- To reduce drift concerns for pollinators, agriculture uses were limited to in-furrow and soil applications.
- A requirement to use and maintain a vegetative buffer strip within at least 15 feet of waterbodies is required.
- Treated seed must be incorporated into the soil.
- Language instructing applicators to cover or collect spilled seeds.

Human Health

- To reduce the cancer risk estimate:
  - Indoor broadcast application removed.
    - Spot, banded, removable bait placement, and crack & crevice remain
  - Outdoor granular broadcast treatment removed.

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PQZ - Risk Mitigation for Registered Uses:

Environmental and Ecological Exposure

- Requirement for vegetative filter (buffer) strip - All food crops – All application methods
  - Ex: Vegetative Filter (Buffer) Strip All crops: 15-foot vegetative filter (buffer) strip
- Requirement for buffer zones for aquatic habitats - All food crops
  - Ex: Buffer zone for aerial application: Do not apply within 150 feet of aquatic habitats.
  - Ex: Buffer zone for ground application: Do not apply within 15 feet of aquatic habitats.
- Application timing – certain crops/uses to limit exposure to sensitive non-target taxa – including the pending use for outdoor ornamentals (including residential areas).
  - Ex: Do not apply this product while bees are foraging.
  - Ex: Do not apply this product until flowering is complete and all petals have fallen.

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Management Considerations

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Broflanilide - Management Considerations:

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PQZ - Management Considerations:

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Team Recommendations for Current and Future Actions:

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Communications Discussion:

Ex. 5 Deliberative Process (DP)

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Back Pocket Slides

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PFAS Strategic Roadmap: EPA's Commitments to Action 2021-2024:

- EPA's integrated approach to PFAS is focused on three central directives:
  - Research. Invest in research, development, and innovation to increase understanding of PFAS exposures and toxicities, human health and ecological effect, and effective interventions that incorporate the best available science.
  - Restrict. Pursue a comprehensive approach to proactively prevent PFAS from entering air, land, and water at levels that can adversely impact human health and the environment.
  - Remediate. Broaden and accelerate the cleanup of PFAS contamination to protect human health and ecological systems.
  - https://www.epa.gov/system/files/documents/2021-10/pfas-roadmap_final-508.pdf
- EPA has developed a national testing strategy to assist with requesting toxicity data and information on categories of PFAS chemicals to help inform future regulatory efforts.
  - https://www.epa.gov/assessing-and-managing-chemicals-under-tsca/national-pfas-testing-strategy

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Broflanilide

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Broflanilide Summary:

- Parent is PFAS and persistent
- Known major transformation products (≥10%) are PFAS and persistent
- Individual environmental fate data available for broflanilide. Only soil adsorption coefficient data available for few degradates.
- Individual ecological effects data available for broflanilide and some major transformation products
- Residues (parent and transformation products) likely accumulating in sediments within aquatic and terrestrial systems

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Broflanilide - Human Health Risk Picture:

- The Broflanilide database is completed. No data gaps were identified.
- The target organs are the adrenal glands (rats, mice, and dogs) and ovaries (rats and mice).
- There is no evidence of increased qualitative or quantitative susceptibility in the developmental studies or the 2-gen rat reproductive study. There was no evidence of neurotoxicity or immunotoxicity. The Food Quality Protection Act (FQPA) Safety Factor (SF) has been reduced to 1x.
- Broflanilide is classified as "Likely to be Carcinogenic to Humans" with a quantification of risk using a linear approach (Q_1*).
- Dietary (chronic), occupational (inhalation), and residential (inhalation and oral) endpoints are based upon increased adrenal weight with corroborative histopathological findings. Based on the toxicological database, assessment of acute dietary and dermal exposure is unnecessary.
- **No residential, occupational, or aggregate risks of concern were identified.**
- The HHRA adequately accounts for exposure to broflanilide and the identified metabolites.

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Broflanilide - Fate Picture:

Fate Summary:

Persistent and relatively stable with half-life degradation on the scale of several years.

- Major degradates are also classified as PFAS chemicals
- Broflanilide has a potential to bioaccumulate in the environment
- No data gaps

Abiotic degradation half-lives: slow degradation to stable

- Hydrolysis: Stable at pH 4, 5, 7, and 9 at 50°C
- Photolysis: DT_{50} = 70 days (aqueous @ pH 7) and Stable (soil)

Biotic degradation half-lives: Persistent in soil and water

- Aerobic soil metabolism: DT_{50} = 829 to 2220 days
- Anaerobic soil metabolism: DT_{50} = 157-2354 days
- Aerobic aqueous metabolism: DT_{50} = 945 to 1430 days in the total system
- Anaerobic aqueous metabolism: DT_{50} = 871 to 1411 days in total system

Degradates: Five major degradates and five minor degradates observed in laboratory fate studies

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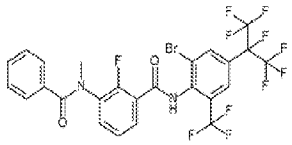
Broflanilide and the Major Degradates:

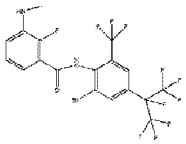
DC-8007
- forms in anaerobic soil (71%) and aerobic and anaerobic aquatic environments (19%).
- considered in drinking water assessment

AB-Oxa, and S(Br-OH)-8007, MFBA and benzoic acid
- identified in acidic and alkaline conditions of the aqueous photolysis study. (14-44%)
- may not be relevant under a neutral aquatic environment.

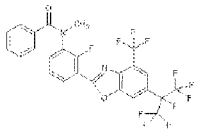
Broflanilide
CAS#:1207727-04-5



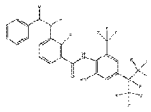
DC-8007



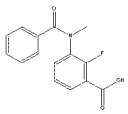
AB-oxa



S(Br-OH)-8007



MFBA



Benzoic acid
CAS#: 65-85-0

Degradates with PFAS side chain

Degradates without PFAS side chain

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Broflanilide - Drinking Water:

No drinking water concerns for human health dietary assessment

- The DWA was performed for broflanilide for the Residue of Concern (ROC), combining broflanilide and its major degradate of concern (DC-8007).
- Recommended EDWCs for corn use: 1.6 ppb for acute, 0.9 ppb for non-cancer and 0.7 ppb for cancer chronic for surface water.
  - There are no drinking water risk concerns based on broflanilide specific data

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Broflanilide - Ecological Risk Picture:

Environmental Effects Data Gaps:

- A few chronic studies did not define a No Effects concentration, and thus technically are data gaps
- Invertebrate risks were determined when comparing the lowest tested concentration (LOAEC) against the EECs for all registered uses
  - Available data are extensive so there is sufficient coverage of the potential toxicity

Major Degradates

- Toxicity data provided for all major degradates
  - All are significantly less toxic than parent for all taxa
  - Residue of Concerns- Parent only

Potential risks for:

- Birds and mammals (chronic)
  - Treated seed consumption only
  - No bioaccumulation related concerns
- Terrestrial and aquatic invertebrates (acute and chronic)
  - Primarily sediment dwelling/interacting
  - Persistence and accumulation in soils and benthic sediments increases the risk over time

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Broflanilide - Management Considerations:

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Pyrifluquinazon

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PQZ Summary:

- Parent and known major transformation products (≥10%) are PFAS and non-persistent
- However, it seems likely there would be a terminal relatively low molecular weight PQZ degradate(s) that are PFAS and persistent
- Individual environmental fate and ecological effects data for PQZ and major transformation products is not complete for known residues
- Unknown low molecular weight PFAS residues (as well as parent and intermediate transformation products) may accumulate in sediments in aquatic systems

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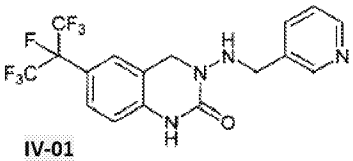
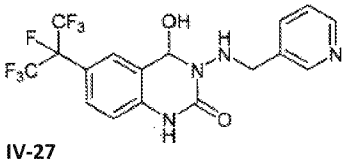
PQZ Major Degradates:

- Major (>10% AR) identified PQZ degradates are pictured on this slide
- All included as drinking water ROCs (total residues) – no concerns
- Only IV-01, IV-02, and IV-28 are Eco ROCs – risks to …
- Eco and human health assessments did not consider unknown PFAS degradate(s)


IV-01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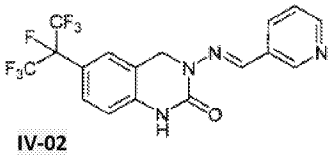
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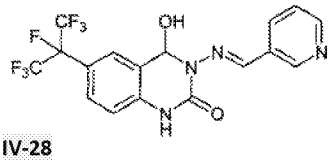
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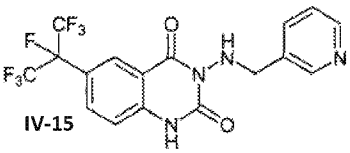
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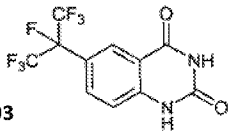
IV-203

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Talking point about unknown metabolites

PQZ - Human Health Risk Picture:

- Chemical-specific data were used for the PQZ HHRA. No data gaps were identified in the CFR-required studies and any potential health effects of PQZ would be expected to be captured in these data.
- The target organs of PQZ are the testes, nasal passage, liver, thyroid, hematopoietic system and the kidneys. PQZ is classified as "Not likely to be carcinogenic to humans at levels that do not alter rodent hormone homeostasis."
  - The leydig cell tumors (testicular tumors) in mice were considered treatment-related; using the 2005 Cancer Guidelines, the CARC accepted the registrant's mode of action proposal and determined that the chronic dietary endpoint is protective of the key events leading to testicular carcinogenicity.
  - In both rodent species and dogs there is no evidence of immunotoxicity.
  - There is no evidence of bioaccumulation in the PQZ hazard database at doses relevant for risk assessment.

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PQZ - Human Health Risk Picture (Continued):

- Dietary, occupational, and residential assessment endpoints for PQZ are based upon neurotoxicity (acute dietary for the general population), developmental effects (acute dietary ages 13-49), systemic effects noted on the previous slide (chronic dietary for the general population), co-critical developmental and offspring effects (dermal), and portal of entry effects (inhalation).

- This proposed new use does not appreciably add to the existing dietary (food + drinking water) exposures, all of which are below the level of concern.

- **No residential, occupational, or aggregate risks of concern were identified in the HHRA for this proposed use.**

- The available suite of PQZ-specific data used in the human health risk assessment adequately accounts for potential exposure to PQZ and its major metabolites (including those with the PFAS moieties) and potential effects at relevant exposure durations.

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PQZ Environmental Fate Picture:

- PQZ degrades into several known (retained radiolabel) environmental degradates that would also be classified as PFASs
  - It is likely that there are additional unknown (not radiolabeled) small molecular weight PFAS degradate(s)
  - Known degradates were considered in ecological and drinking water assessments using a total residues approach

- PQZ degradation of total known residues of concern (ROCs) in the environment
  - Aerobic soil metabolism half-life = 105 days
  - Aerobic water metabolism half-life = 233 days

- Known PQZ ROCs not anticipated to accumulate in the environment

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PQZ: Drinking Water Assessment:

- No drinking water concerns for human health dietary assessment (known ROCs)
- EDWCs used in dietary assessment – 10.3 µg/L acute; 9.0 µg/L (chronic)
- Does not capture small molecular weight PFAS degradate(s)

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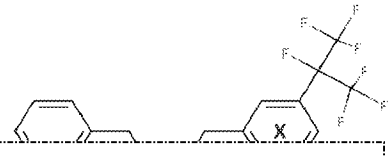
PQZ Ecological Risk Picture:

- Essentially Complete Dataset for Parent PQZ
  - May need higher tiered pollinator studies for some uses (not this proposed use)
  - Refined assessment (and data) may be needed in the future
  - Only have acute degradate data for Daphnids (equally or less acutely toxic than parent) and mammals (less acutely toxic than parent). Have no chronic data for degradates which may be more informative regarding PFAS effects.
- Known PQZ ROCs not anticipated to accumulate in animals
- Potential risks for:
  - Mammals (chronic) – based on reduced body weight
  - Honey bees (acute and chronic for adults) – based on reduced survival
  - Aquatic invertebrates (acute and chronic) – based on reduced survival or reproduction/growth
- While ecological endpoints are based on apical measures (survival, growth, reproduction) as surrogates for potential population effects, chronic studies are intended to capture effects observed by PFASs

INTERNAL DRAFT DELIBERATIVE

Management Considerations:



Ex. 5 Deliberative Process (DP)

INTERNAL DRAFT DELIBERATIVE