CP Industry Testing (past, present, future):

Overview of REACH Dossiers and How to Access Data

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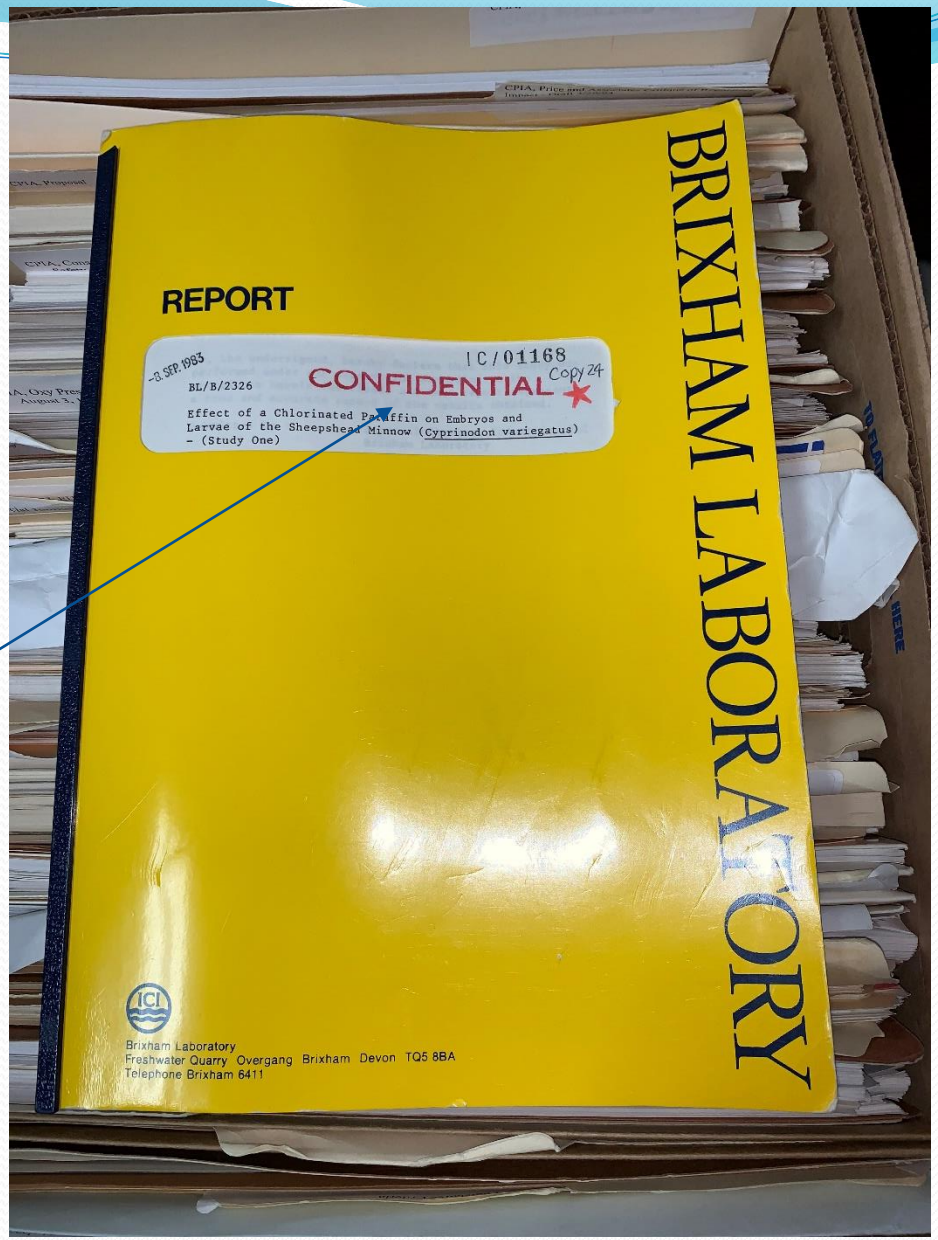
Disclaimer

- This presentation is focused on testing initiated by the CP industry
- There has been extensive research/testing done by agencies and academia, much of it considered in the REACH dossiers and other assessments
- The purpose of this presentation is just to provide an overview/history of the work done by the CP industry and how to access this information

Regulatory driven testing is often not published, but just submitted to the reviewing agency

Confidential treatment was common

OECD SIDS, HPV, REACH, etc. have helped get this information out to the public



A (very) Brief History of CP Consortia Testing

1970-2010's

1970's

- 1970 - ICI and Shell form cooperative effort, initially on CP chemical analysis – thin layer chromatography (TLC) – in environment
  - Campbell (1980) paper provides history and results of early environmental monitoring
- November 1975 – EPA releases report "Investigation of Selected Potential Environmental Contaminants: Chlorinated Paraffins".
- 1976-1977 – industry begins to organize around initial ICI effort.
- September 1977 – first global CP conference; lead to the formation of the first consortium/testing program.
- October 1977 – First report of the Interagency Testing Committee (ITC) send to EPA on October 4, 1977 includes chlorinated paraffins on the list of substances recommended for testing.
- Late 1970's – early 1980's – international CP group goes by both the Chlorinated Paraffins Consortium and the Chlorinated Paraffins Producer's Testing Consortium.
  - CPIA (USA) and CAPG (Europe) came out of this original consortium
- 1978-1980 - negotiations between American members of Consortium and EPA regarding testing program. EPA ultimately issues FR notice January 8, 1982 announcing voluntary testing agreement (47 FR 1017).
  - **This EPA testing program created the SCCP, MCCP and LCCP ranges/names**

Creation of SCCP, MCCP, LCCP

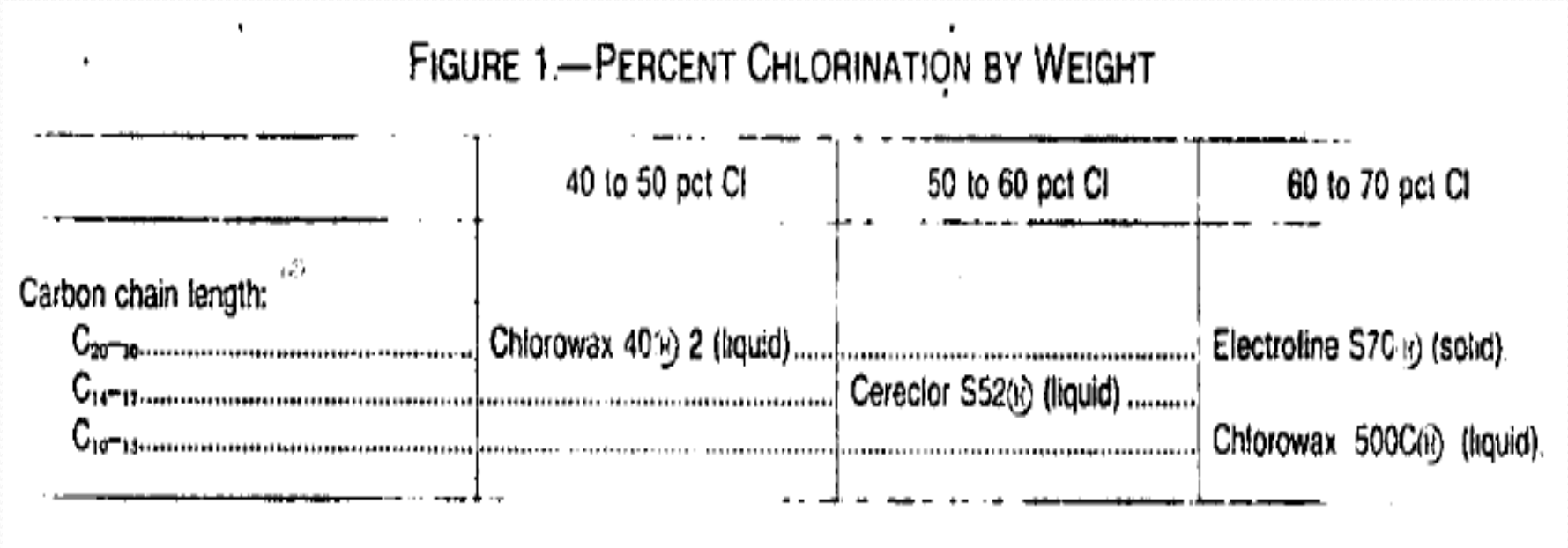


FIGURE 1.—PERCENT CHLORINATION BY WEIGHT

Carbon chain length:	40 to 50 pct Cl	50 to 60 pct Cl	60 to 70 pct Cl
C_{20-30}	Chlorowax 40(R) 2 (liquid)		Electroline S70(R) (solid).
C_{14-17}		Cereclor S52(R) (liquid)	
C_{10-13}			Chlorowax 500C(R) (liquid).

From EPA Federal Register (1982)

1980's

- Testing program for U.S. EPA
  - Comprehensive toxicology, aquatic toxicology, phys-chem, fate
  - Toxicology studies conducted at International Research and Development Corp (IRDC) in USA (now part of Charles River) and ICI Central Toxicology Lab (CTL) in UK
  - Aquatic/fate studies conducted at ICI Brixham Lab (now part of Univ of Plymouth)
  - Studies from this program used extensively in risk assessments since 1980's (EPA RM1/2, EU RAR, REACH, EFSA)
- U.S. National Toxicology Program (NTP) conducts series of repeat-dose (14-day, 90 day) chronic/cancer studies (2-yr) in rats and mice and genetic toxicity studies
  - SCCP (60% Cl)- TR308 [Note: title suggest this was a study of C12 but it was a commercial SCCP product (C10-12).]
  - LCCP (43% Cl) – TR305 [Note: title suggest this was a study of C23 but it was a commercial LCCP product (C22-26).]

EPA (Original) Testing Program

TABLE 1

	Chlorowax 500C®	Chlorowax 40®	Cereclor S52®	Electrofine S70®
MAMMALIAN HEALTH				
Phase 1:				
Tissue level and decay studies after single dose (rat)	X[a]	X	X	X
90-day oral subchronic toxicity[b] and metabolism studies	X	X	X	X
Cell transformation (styles) test[c]	X			X
Dominant lethal mutation test (rat)[d]	X			
In vivo cytogenetic test (rat)	X	X	X	X
Teratology (rat, rabbit)	X	X	X	X
Phase 2 (1 compound, most toxic in phase 1): 2 generation reproduction study (rat).				
ENVIRONMENTAL				
Phase 1:30-60 day lethal and sublethal (mussel, rainbow trout)	X	X	X	X
Phase 2 (Chlorowax 500C®R, already known to be most toxic from phase 1 aquatic studies):				
Growth (rainbow trout, mussel)				
Bioconcentration (rainbow trout, mussel)				
Life cycle (*Daphnia*, mysid shrimp)				
Embryo-juvenile (sheepshead minnow)				
14-day bioassay (freshwater alga, marine alga)				
Chronic (partial life-cycle) (midge)				
Solubility				
Biodegradation (aerobic, anaerobic)				
Avian Study (test substance to be selected)				
Reproductive study (duck)[e]				

[a] X = Study being performed by Consortium.
[b] The Agency considers that 90-day subchronic toxicity tests are acceptable in most cases as predictive of chronic effects.
[c] Because NTP is doing full scale 2-year bioassays on Chlorowax 500C® and Chlorowax 40® the EPA did not feel it was necessary to do cell transformation tests for these substances. The cell transformation tests for Chlorowax 500C® and Electrofine S70® are being done for the Consortium's purpose.
[d] Information is already available on dominant lethal mutation tests for Chlorowa 40® and Chlorowax 70® (an analogue of Electrofine S70).
[e] This study is not part of the proposal by the international Chlorinated Paraffins Manufacturers Consortium, and will be performed by the American members.

EPA Testing Program Summary

- Between 1980-1984 CPIA conducted over 60 studies on SCCP at 58% Cl (29), MCCP at 52% Cl (12), LCCP at 43% Cl (9) and LCCP at 70%Cl (11)
- Toxicology on all 4 test materials
  - 14-day repeat dose (rat)
  - 13-week repeat-dose (rat)
  - in vivo cytogenetic – bone marrow (rat)
  - Teratology (rat and rabbit)
- Aquatic Toxicity
  - Chronic 60-day fish and mussels (MCCP and LCCP)
  - Additional organisms for SCCP

1990's

- Based on original testing program U.S. EPA conducts Risk Management (RM) 1 and 2.
  - SCCP added to Toxics Release Inventory
  - Downstream users adopt waste management practices, such as handling of spent metalworking fluids
- EU SCCP and MCCP risk assessments lead to a second round of aquatic, soil and sediment testing at Brixham (UK) lab
  - Acute and chronic aquatic (daphnia, algae, gammarus)
  - Soil and sediment invertebrates and plants

2000's

- High Production Volume (HPV) Programs – OECD and U.S. reviews - culminates in SIDS dossier, SIAP/SIAR for MCCP and LCCP.
  - LCCP SIDS dossier, SIAR and SIAP available on OECD's website https://hpvchemicals.oecd.org/ui/Default.aspx
- EU Risk Assessment Reports on SCCP and MCCP; UK developed both
- REACH transitional dossier for MCCP (UK also)
- REACH consortia for MCCP and LCCP formed in 2009

2010's

- Closed Bottle Testing (OECD 301D) biodegradation on range of MCCP (and one SCCP) products
  - MCCP: 25 separate experiments with 11 distinct test materials
  - Several later studies included congener analysis of test vessels to analyze decay patterns
- REACH MCCP testing (all using congener analysis)
  - OECD 305 – fish dietary bioaccumulation
  - OECD 308 – sediment biodegradation
  - Kow and water solubility
- U.S. EPA MCCP testing
  - OECD 225 – sediment toxicity

2020's

- More testing is underway
- New e-tox/fate research using tritiated (^{3}H) radiolabelled test materials
  - Tritium is randomly dispersed on carbon-chain
  - Synthesis process does not degrade the CP test material
  - High radioactivity (can test at very low concentrations)
  - Excellent recovery in complex/organic media (e.g. sediment)
  - Can track radiolabelled metabolites using RAD-TLC or RAD-HPLC

Phys-Chem

- Very low water solubility
  - Solubility appears to decrease with increase in chain-length and chlorination level
  - In 2019 study, the bulk of the solubility of a C14 (50% Cl) came from the lower chlorinated congeners – overall solubility was ~6 µg/L
- High Kow, though no trends were observed with increasing Cl groups (in a 2019 study that analyzed the Kow of individual congener groups)

E-Fate

- Biodegradation rate slows with increasing chlorination level
  - CBT studies run at incremental chlorination levels allow for comparison
- Some evidence that bioaccumulation may decrease with increasing chlorination level, though pattern is not as clear
  - Bioaccumulation testing is impacted by low absorption efficiency
  - Several expert reviews have also placed a lot of emphasis on field/TMF data for assessment of bioaccumulation

Toxicology

- CPs have limited absorption through the skin and in the digestive track.
- Dermal absorption appears to decrease with increasing chain-length and chlorination level
  - MCCP (52% Cl): 0.7% absorbed through the skin in human (in vitro) skin testing
  - C18 (50-53% Cl) 0.70% (male) and 0.61% (female) over 96 hr rats (in vivo)
  - C28 (47% Cl) <0.1% over 96 hr rats
- High-levels of MCCP in the gut (likely due to limited absorption) in oral gavage testing are understood to inhibit vitamin K uptake
  - In reproductive testing this led to pup deaths due to hemophilia from a severe lack of vitamin K (MCCP is classified based on this phenomenon)
- Aquatic toxicity primarily in daphnia
- Sediment toxicity observed in lumbriculus (worms)

CP REACH Dossier (and how to access data)

REACH

- CP substances registered under REACH
  - SCCP (CAS 85535-84-8; EC 287-476-5) – NOT ACTIVE
  - MCCP (CAS 85535-85-9; EC 287-477-0)
  - LCCP (CAS 63449-39-8; EC 264-150-0)
  - di-, tri- and tetrachlorotetradecane (EC 950-299-5) "range of chlorinated isomers of C14 alkane"
- All REACH dossiers, including inactive chemicals, can be accessed at: https://echa.europa.eu/information-on-chemicals/registered-substances

Registered substances

The data comes from registration dossiers submitted to ECHA by the date indicated as last update. The Total Tonnage Band is compiled from all the dossiers with two exceptions; any tonnages claimed confidential and any quantity used as an intermediate to produce a different chemical. The Total Tonnage band published does not necessarily reflect the registered tonnage band(s).

Please note that some of the information on registered substances may belong to third parties. The use of such information may therefore require the prior permission of the third party owners. Please consult the *Legal Notice* for further information.

Please note that information on chemical properties of registered substances is directly accessible via *eChemPortal*.

Chemical Property Data Search

The result of the search 'Substance has nanoform' returns all factsheets containing data related to nanomaterials. However, this does not mean that a registration covering nanoforms of the substance has been submitted in line with the revised annexes of REACH by all the registrants concerned. Note that since 1 January 2020, before manufacturing or importing a nanoform of a substance, the operators concerned must submit the required nano-specific information to ECHA using IUCLID version 6.4 (released on 30 October 2019).

FURTHER INFORMATION

- Registered substances information
- How to determine what will be published (Data Submission Manual 15)
- Understanding REACH Regulation
- Q&A on registered substances
- What is an Infocard? [PDF]
- What is a Registered substance Factsheet? [PDF]
- eChemPortal
- REACH study results download

See a problem or have feedback?

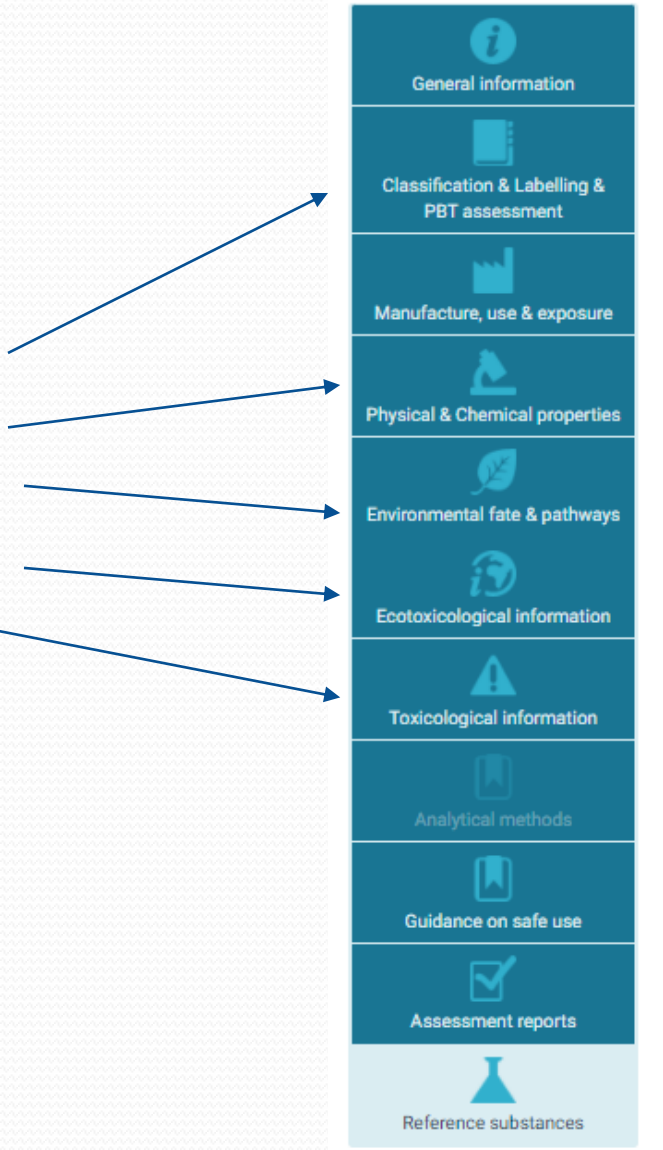
Last updated 21 August 2020. Database contains 22950 unique substances and contains information from 100340 dossiers.

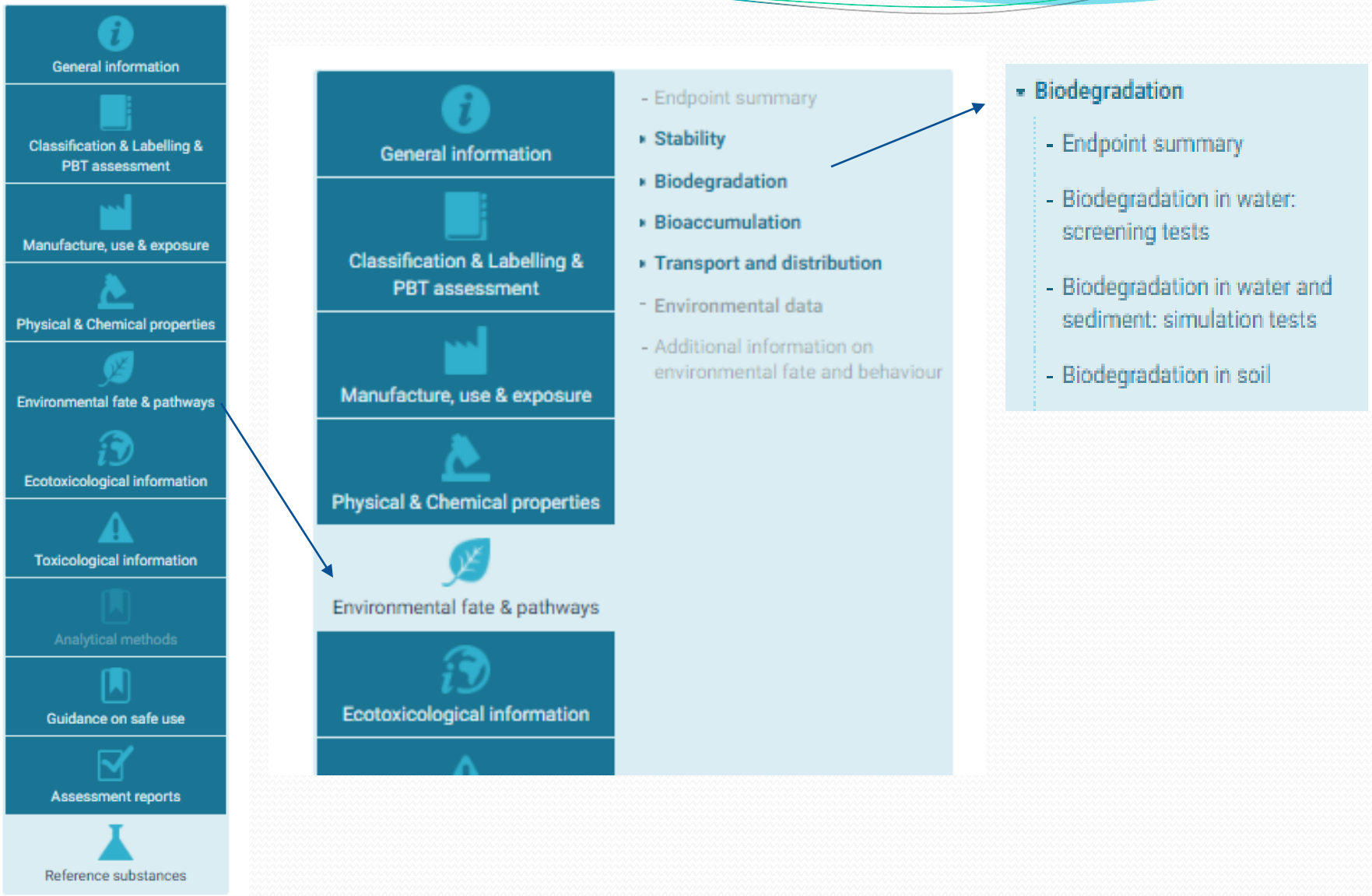
Substance identity

Substance name: CAS number:

EC / List number: Other Numerical Identifiers: Type

Most of the REACH dossier is readily available to public, including classification and labelling, phys-chem,
e-fate, e-tox and tox




General information
Classification & Labelling & PBT assessment
Manufacture, use & exposure
Physical & Chemical properties
Environmental fate & pathways
Ecotoxicological information
Toxicological information
Analytical methods
Guidance on safe use
Assessment reports
Reference substances
General information
Classification & Labelling & PBT assessment
Manufacture, use & exposure
Physical & Chemical properties
Environmental fate & pathways
Ecotoxicological information
- Endpoint summary
Stability
Biodegradation
Bioaccumulation
Transport and distribution
- Environmental data
- Additional information on environmental fate and behaviour
Biodegradation
- Endpoint summary
- Biodegradation in water: screening tests
- Biodegradation in water and sediment: simulation tests
- Biodegradation in soil

Supporting Data/Study Reports

- All of the CPIA and CP consortia study reports have been transferred to electronic format
- Full study reports can be accessed upon request for qualified organizations/purposes
  - Reports are routinely shared with government/research agencies. For example, CPIA provided dozens of reports to EFSA for its recent review
  - Data remains compensable, so CPIA must ensure data are being used for appropriate, non-commercial purposes
- Please contact Andrew Jaques (see last slide) with requests

Summary

- CP industry has conducted 100's of studies over the past 50 years
  - These studies have been reviewed by numerous agencies in North America and Europe
  - Mammalian toxicity is felt to be well characterized and not a priority for additional testing
  - For the past 20+ years the focus has been primarily on environmental effects and fate
  - These data are summarized in the REACH dossiers (along with other data)
- Additional environmental studies underway

Thanks!

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