

Availability of Health and Environmental Data for High Tonnage Chemicals under REACH

Introduction to the Project

Andrea Springer, Henning Herrmann,
Dana Sittner

Topics of Presentation

- Project objectives
- Introduction to the concept
- Overall results
- Summary/conclusion
- Announcement of detailed results

Project Objectives

- Overview on the completeness of selected data
- In REACH registration dossiers of high tonnage chemicals
- Examination of available data
- Estimation of data gaps
- Reviewing compliance with REACH requirements
- Obtain traceable and reproducible information

Project Concept

A **screening method** was developed for

- A standardised check
- Using **decision trees**
- Based on REACH Regulation Annexes VII – X
- Considering *phase-in* chemicals (≥ 1000 t/a)
- Dossiers of lead registrants & *opt-out* registrants

- 1932 dossiers (as of 7 March 2014)
- <60 min/dossier

1814 dossiers with (eco-) toxicological data,
118 dossiers without data
(mainly UVCB)

Project Considered Endpoints

Human health

- Toxicity to reproduction/developmental toxicity
- Genetic toxicity
- Repeated dose toxicity

Environment

- Ecotoxicity: Aquatic toxicity
- Bioaccumulation
- Biotic degradation
- Abiotic degradation
- Environmental exposure

Project Concept

Decisions on the endpoints

'compliant'

compliant to REACH Annexes VII-X

'non-compliant'

non-compliant to REACH Annexes VII-X

'complex'

not (yet) decided due to waiving or adaptation acc. to REACH Annexes VII-X, Column 2 or Annex XI or other (endpoint specific) reasons not assessable due to time limitations

'testing proposal'

no further endpoint screening

Project Concept

Decisions on the **dossiers** based on endpoint decisions

'compliant '
dossier

if all endpoints compliant

'non-compliant '
dossier

if at least one endpoint non-compliant,
others complex, compliant or testing proposal

'complex' dossier

at least one endpoint complex, others
compliant or testing proposal

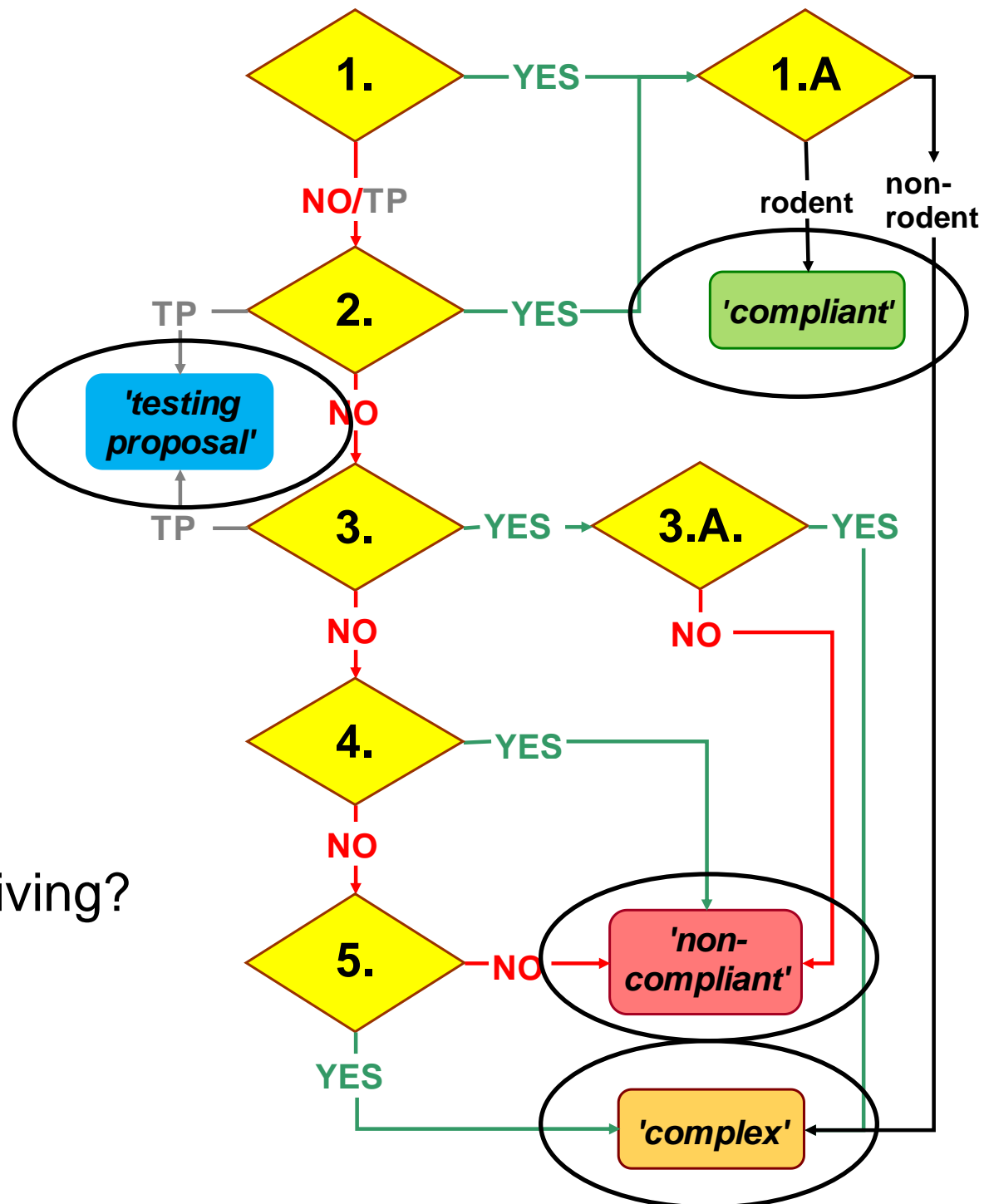
Project: Example on REACH Standard Information Requirements

Repeated dose toxicity for chemicals ≥ 1000 tpa

Annex VII	Annex VIII	Annex IX	Annex X
none	28 d-study, adaptations	28 d-study	
		90 d-study, adaptations	
			<i>if required: chronic or other study</i>

Project: Example Decision Tree - Repeated Dose Toxicity

- 1. Chronic study?
- 2. 90 d-study?
- 1.A Test with rodent?
- 3. 28 d-study
- 3.A Adaptation?
- 4. Exposure-based waiving?
- 5. Adaptation?



Project: KnowSEC-Software for Screening and Decision Making

Implemented decision tree

The screenshot displays the KnowSEC web interface for 'manganese oxide'. The main content area shows a decision tree with the following questions:

- 1. Liegen Studienergebnisse zur chronischen Toxizität (>12 Monate) vor?
- 2. Liegen Studienergebnisse zur subchronischen Toxizität (90 Tage) vor?
 - 1.A Wurde an Nagern oder an Nicht-Nagern getestet?
- 3. Liegen Studienergebnisse zur subakuten Toxizität (28 Tage) an Nagern oder Nicht-Nagern vor?
 - 3.A Liegt ein waiving für eine 90d Studie vor? Für Ja: Kategorie wählen. Bei Bedarf sind auch zwei waiving Kategorien wählbar, obwohl nach Anklicken der ersten bereits das Endergebnis feststeht.
- 4. Liegt ein waiving für eine 28d Studie gemäß Anhang XI, Nr. 3 (exposure considerations) vor?
- 5. Liegt ein waiving vor (gültig für 28d und 90d Studie) ?

Annotations on the screenshot highlight key features:

- endpoint decision:** Derived decisions for module 'Compliance Repeated Dose' include 'UC Repeated Dose: Komplexer Fall' and 'UCRD: UCRD-CX3: Komplex, weil Waiving je für 28d Studie und 90d Studie vorliegt.' The decision is labeled as *'complex' because...*
- dossier decision:** Derived decisions for module 'UFOPLAN_Compliance' include 'Dossier ist ein komplexer Fall', labeled as *'complex'*.
- questions:** A box highlights the list of screening questions.
- additional info: descriptors in memo field:** A box highlights the '5.-Yes-A Bitte die waiving Kategorie auswählen!' instruction and the list of categories: WoE | Read-across/Grouping | QSAR | Scientifically | Technically | Exposure | Other | unknown.
- additional info: implemented questions:** A box highlights the instruction: '5.-Yes-A Bitte die waiving Kategorie auswählen! Bei Bedarf sind auch zwei waiving Kategorien wählbar, obwohl nach Anklicken der ersten bereits das Endergebnis feststeht.'

Project: Example on IUCLID Dossier Screening

Repeated Dose Toxicity

The screenshot displays the IUCLID software interface for a REACH registration dossier. The main window is titled "Administrative Data" and contains a tree view on the left and several data entry panels on the right. The tree view shows a hierarchy of sections: 7.5 Repeated dose, Repeated dose, 7.5.1 Repeated, rel 1-key, r, rel 2-key, r, rel 1, rat, 2, rel 4, rat, d, 7.5., 7.5., and 7.5. The "Materials and methods" panel is open, showing "Test type" set to "subchronic", "Limit test" set to "no", and "Test guideline" set to "OECD Guideline 408 (Repeated Dose 90-Day Oral)". The "Test materials" panel is also open, showing "Identity of test material same as for substance defined in section 1 (if not read-across)" and "CAS number" set to "Add...". The "Administrative Data" panel is open, showing "Purpose flag" set to "EU: REACH", "Data waiving" set to "other justification", and "Justification for data waiving" set to "There is no long term study available using the inhalation exposure. However a study using inhalation route needs not to be performed. ...". The "Test animals" panel is open, showing "Species" set to "rat".

Administrative Data

EU: REACH

Materials and methods

Test type: subchronic

Limit test: no

Test guideline: according to

Qualifier	Guideline
according to	OECD Guideline 408 (Repeated Dose 90-Day Oral

Test materials

Identity of test material same as for substance defined in section 1 (if not read-across)

Test material identity

CAS number

Add...

Administrative Data

EU: REACH

Purpose flag

Data waiving: other justification

Justification for data waiving: There is no long term study available using the inhalation exposure. However a study using inhalation route needs not to be performed. ...

Study result type

Reliability

Rationale for reliability incl. deficiencies

Test animals

Species: rat

Overall Results

Project Overall Results

Dossier decisions

Possible endpoint decisions

Endpoints

'complex'

'compliant'

'non-compliant'

'testing proposal'

'non-compliant' dossiers

58%

42%

'complex' dossiers

All endpoints

'compliant'

← 0.06%

1 'compliant' dossier

Endpoints

'complex'

'compliant'

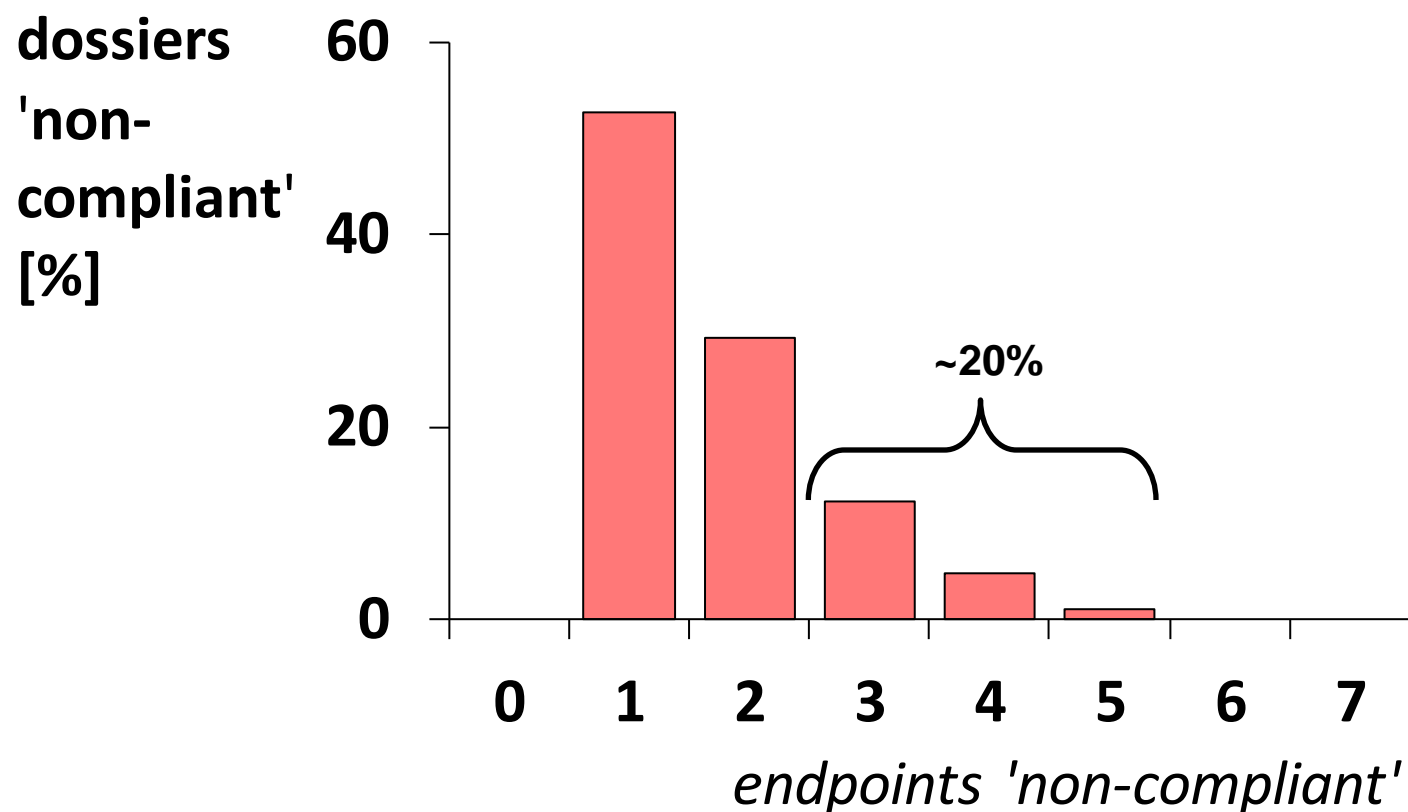
'testing proposal'

Total dossiers: 1814

Project Overall Results

58% (1043) 'non-compliant' dossiers

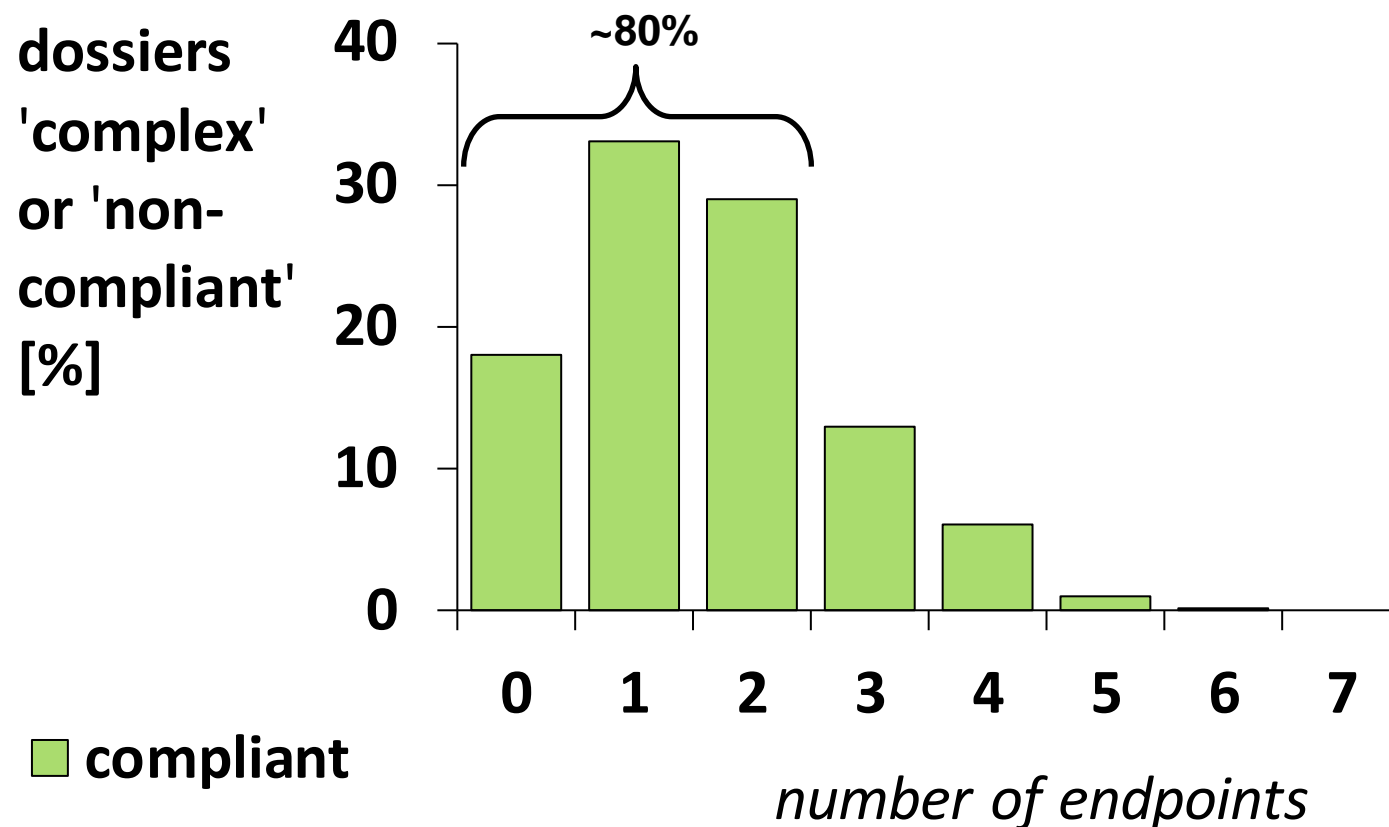
How many 'non-compliant' endpoints?



Project Overall Results

All dossiers except the 'compliant' dossier: $1814 - 1 = 1813$

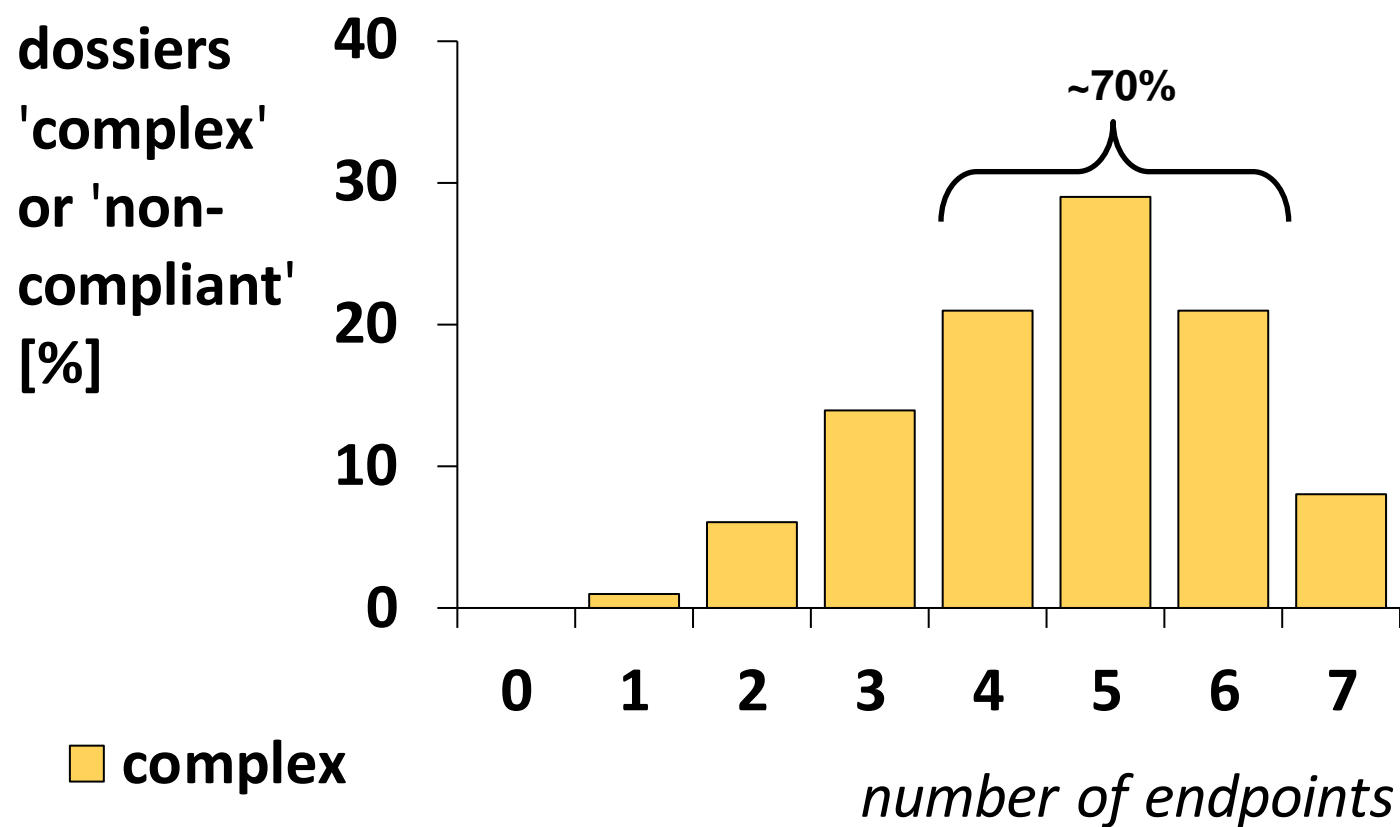
How many 'compliant' endpoints?



Project Overall Results

All dossiers except the 'compliant' dossier: $1814 - 1 = 1813$

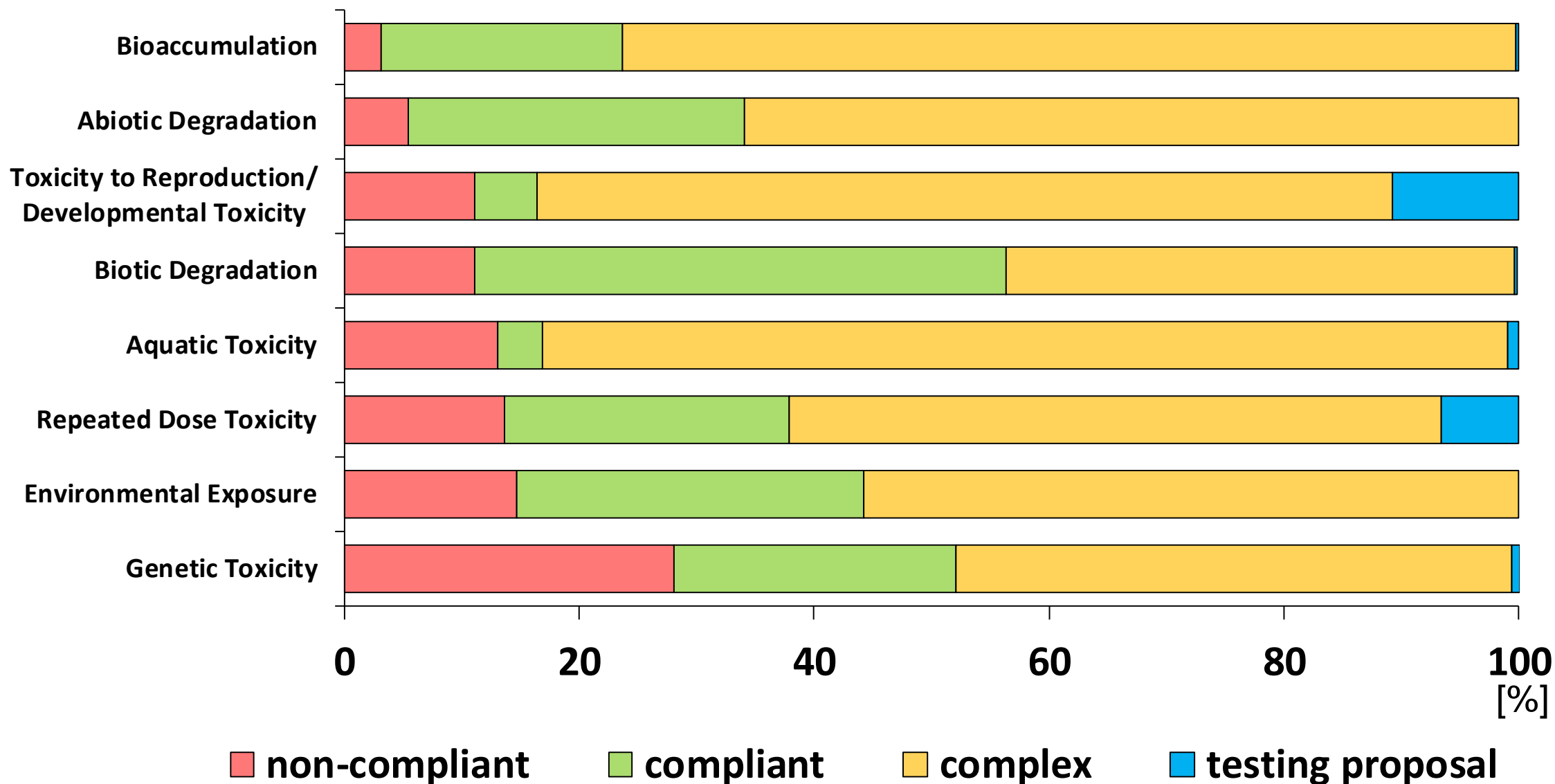
How many 'complex' endpoints?



Project Overall Results

Endpoint decisions overview [%]

Sorted by 'non-compliant', ascending



Total dossiers: 1814

Project Summary of Overall Results

- In 58% of dossiers at least one 'non-compliant' endpoint
- ~20% of 'non-compliant' dossiers were 'non-compliant' for 3-5 endpoints
- Only 1 dossier with 'compliant' data in all endpoints
- ~ 80% of dossiers were 'compliant' in only up to 2 endpoints
- ~ 70% of dossiers were 'complex' in 4-6 endpoints
- Endpoints were mostly 'complex' due to adaptations/waiving of standard requirements or other reasons not assessable. Plausibility examined in single cases.
- Differences between endpoints

Project Conclusions from Overall Results

- ✓ Overview on the availability of data in REACH registration dossiers of high tonnage chemicals was achieved
- ✓ Data gaps were detected

Follow-up actions

- Further examination of 'complex' endpoints

Project: Further Results

Next presentations on

- Results on human health endpoints
- Results on environmental endpoints

- Single case analysis of complex cases
(read-across/grouping approaches excluded)

Thank you for your attention

Andrea Springer

Federal Institute for Risk Assessment

Max-Dohrn-Str. 8-10 • 10589 Berlin, GERMANY

Tel. +49 30 - 184 12 - 0 • Fax +49 30 - 184 12 - 47 41

bfr@bfr.bund.de • www.bfr.bund.de