POLITECNICO DI MILANO

School of Industrial and Information Engineering

Course 096125 (095857)

Introduction to Green and Sustainable Chemistry





REACh Legislation 1907/2006.

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What is REACh?

- **Is a chemical legislation in EU affecting the sale and manufacture of all chemicals, unless specifically exempted, on their own, in preparations or articles (if intended to be released)**

- **REACh : Registration, Evaluation, Authorization and Restriction of Chemicals**
  - *Is underpinned by the Precautionary Principle (Art. 1)*
  - *No (pre)-registration – no Market*
  - *Responsibility is put on enterprises*

- REACh replaces EU 40 existent Norms and Directives on Chemical Substances

Chemical Products:

*http://www.reachteam.eu/italian/legislation/docs/launchers/launch-2006-1907-EC.html

ECHA website (https://echa.europa.eu/it/home).

Scope and Aims.

- Chemicals of most concern for the environment or human health due to environmental exposure
- Focus activities on achieving environmental improvement (local and national)
- Select the right tool for the job
  - Monitoring and evaluation

Opportunity.

Industry

- Chemicals are produced which meet the needs of society
- Health, safety and environment issues are addressed
- Public access to relevant information

Regulators

- Risk assessments are proportionate and focus on end points of concern
- Develop systems to further encourage innovation and reduced environmental exposure
- Shared learning.

Structure of “REACH” Legislation (CE) n.1907/2006.

TITLE I: GENERAL ISSUES

TITLE II: REGISTRATION OF SUBSTANCES

TITLE III: DATA SHARING AND AVOIDANCE OF UNNECESSARY TESTING

TITLE IV: INFORMATION IN THE SUPPLY CHAIN

TITLE V: DOWNSTREAM USERS

TITLE VI: EVALUATION

TITLE VII: AUTHORISATION

TITLE VIII: RESTRICTIONS ON THE MANUFACTURING, PLACING ON THE MARKET AND USE OF CERTAIN DANGEROUS SUBSTANCES AND PREPARATIONS

TITLE IX: FEES AND CHARGES

TITLE X: AGENCY

TITLE XI: CLASSIFICATION AND LABELLING INVENTORY

TITLE XII: INFORMATION

TITLE XIII: COMPETENT AUTHORITIES

TITLE XIV: ENFORCEMENT

TITLE XV: TRANSITIONAL AND FINAL PROVISIONS

Annexes to “REACH” Legislation (CE) n.1907/2006.

- Annex I GENERAL PROVISIONS FOR ASSESSING SUBSTANCES AND PREPARING CHEMICAL SAFETY REPORTS
- Annex II GUIDE TO THE COMPILATION OF SAFETY DATA SHEETS
- Annex III CRITERIA FOR SUBSTANCES REGISTERED IN QUANTITIES BETWEEN 1 AND 10 TONNES
- Annex IV EXEMPTIONS FROM THE OBLIGATION TO REGISTER IN ACCORDANCE WITH ARTICLE 2(7)(a)
- Annex V EXEMPTIONS FROM THE OBLIGATION TO REGISTER IN ACCORDANCE WITH ARTICLE 2(7)(b)
- Annex VI INFORMATION REQUIREMENTS REFERRED TO IN ARTICLE 10
- Annex VII STANDARD INFORMATION REQUIREMENTS FOR SUBSTANCES MANUFACTURED OR IMPORTED IN QUANTITIES OF ONE TONNE OR MORE
- Annex VIII STANDARD INFORMATION REQUIREMENTS FOR SUBSTANCES MANUFACTURED OR IMPORTED IN QUANTITIES OF 10 TONNES OR MORE,
- Annex IX STANDARD INFORMATION REQUIREMENTS FOR SUBSTANCES MANUFACTURED OR IMPORTED IN QUANTITIES OF 100 TONNES OR MORE

Annexes to “REACH” Legislation (CE) n.1907/2006.

Annex X STANDARD INFORMATION REQUIREMENTS FOR SUBSTANCES MANUFACTURED OR IMPORTED IN QUANTITIES OF 1 000 TONNES OR MORE

Annex XI GENERAL RULES FOR ADAPTATION OF THE STANDARD TESTING REGIME SET OUT IN ANNEXES VII TO X

Annex XII GENERAL PROVISIONS FOR DOWNSTREAM USERS TO ASSESS SUBSTANCES AND PREPARE CHEMICAL SAFETY REPORTS

Annex XIII CRITERIA FOR THE IDENTIFICATION OF PERSISTENT, BIOACCUMULATIVE AND TOXIC SUBSTANCES, AND VERY PERSISTENT AND VERY BIOACCUMULATIVE SUBSTANCES

Annex XIV LIST OF SUBSTANCES SUBJECT TO AUTHORISATION

Annex XV DOSSIERS

Annex XVI SOCIO-ECONOMIC ANALYSIS

Annex XVII RESTRICTIONS ON THE MANUFACTURE, PLACING ON THE MARKET AND USE OF CERTAIN DANGEROUS SUBSTANCES, PREPARATIONS AND ARTICLES

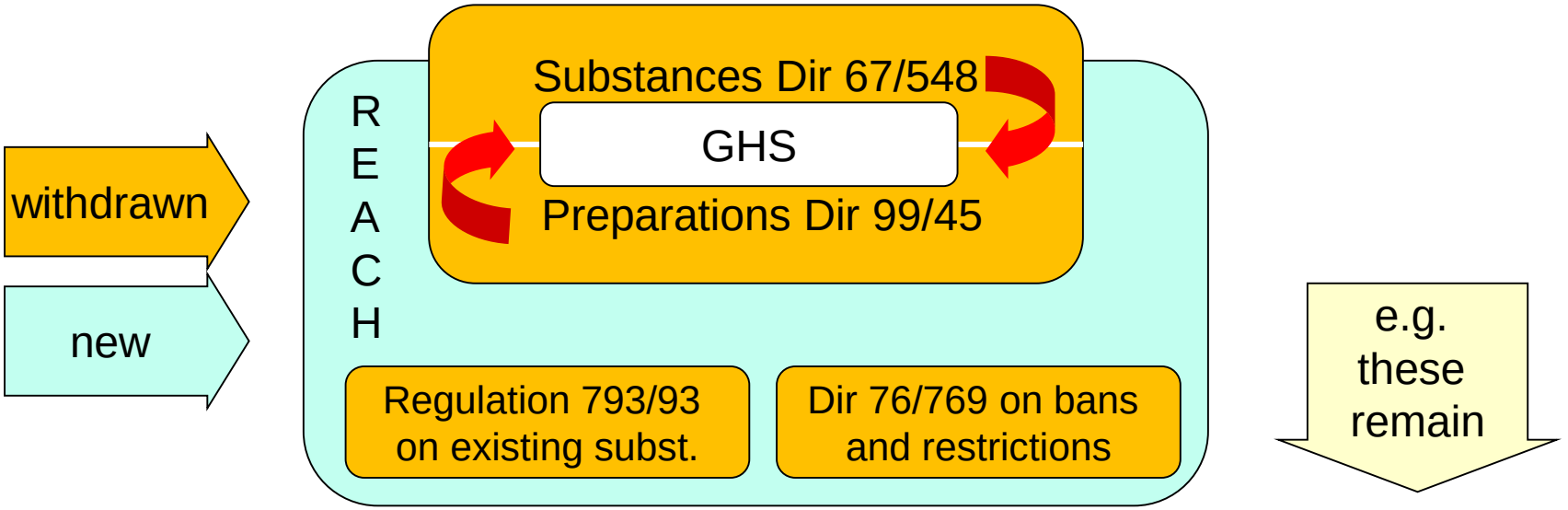
General Aim of REACH Legislation.

Purpose: high level of protection of human health and the environment, including the promotion of alternative methods for assessment of hazards of substances, as well as the free circulation of substances on the internal market while enhancing competitiveness and innovation:

- **Registration:** coherent system designed to provide basic hazard and risk information on new and existing chemical substances manufactured in or imported into the EU
- **Evaluation:** in hands of the authorities to check the completeness of the registration dossiers and to ensure that risks raised by chemicals are safely controlled
- **Authorisation**: procedure for the most hazardous substances with the aim to gradually squeeze them out of the market and consequently **substitute** them by safer substances, providing they are economically and technologically equivalent; **Restriction** process in parallel of **Chemicals.**

- Burden of proof up to industry moving it away from Member States‘ authorities to producing and importing companies, who will be responsible for demonstrating that substances can be used safely

REACH Replaces only Part of Chemical Legislation.



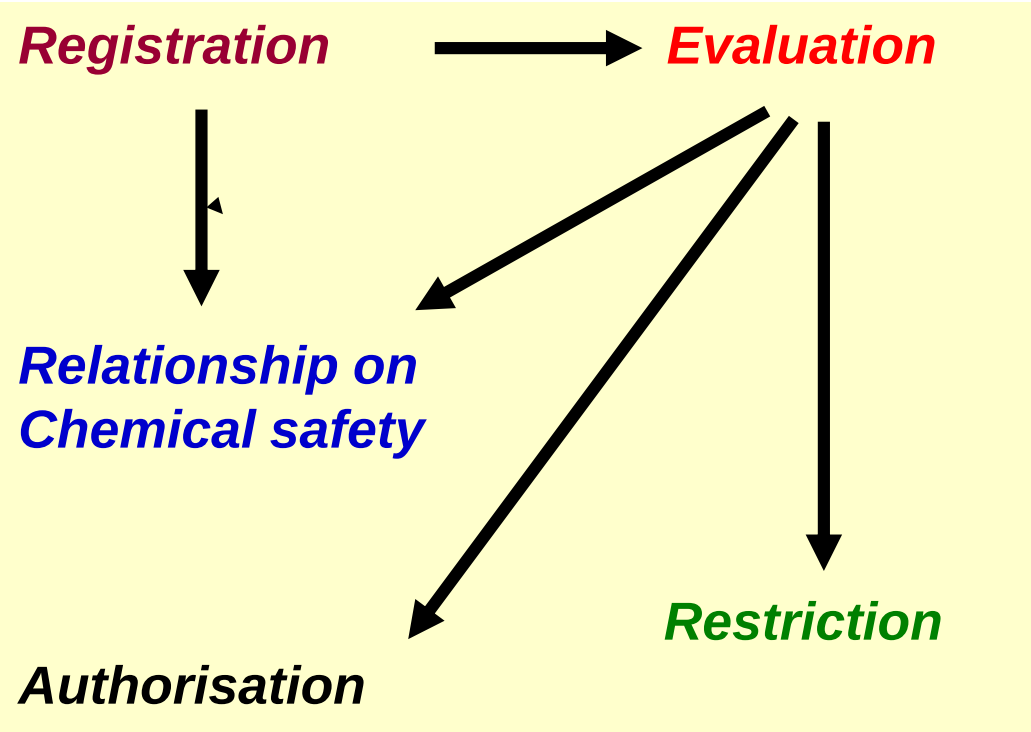
medicines	food, feed, food additives	biocides	Plant Protection Products
fertilizers	cosmetics	detergents	product safety
transport of dangerous goods	Seveso	worker protection	liability
international conventions	waste	environment protection	

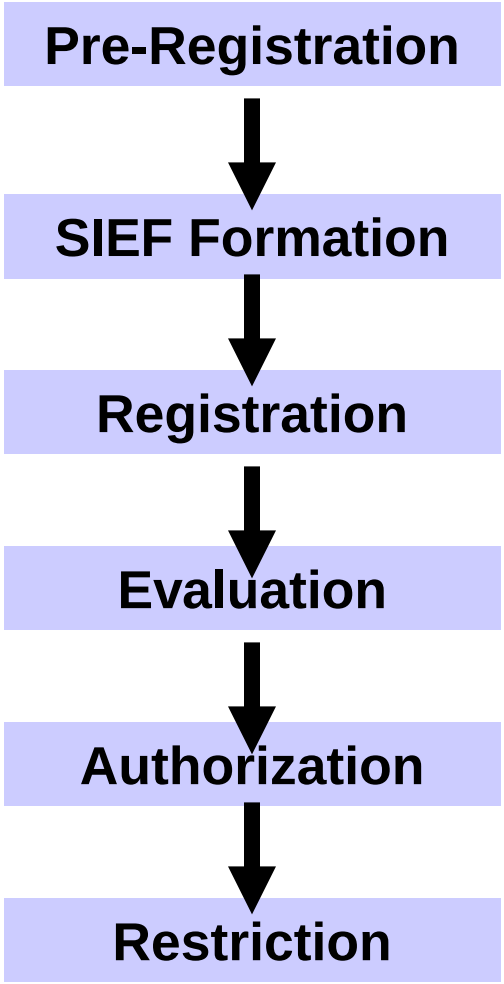
Exemptions (Title 2)

- Regulation not Applied to:
  - radioactive substances
  - substances in customs supervision under specified conditions
  - non-isolated intermediates
  - waste – not considered to be a substance, preparation or article
  - transport of dangerous goods
  - MS discretion: substances used for defence purposes
- New notified substances considered to be registered
- Furthermore a lot of other exemptions: e.g. on Registration, Evaluation, Authorisation and Downstream user obligations.
- Public Access to information, Unification of legislations

No data = No market

Essential Elements and REACH System Phases.





SIEF = Substance **I**nformation **E**xchange F**o**rum

Registration (Titles 5-24).

- General obligation to gather information on substances made or imported in quantity ≥ 1 ton/year The information is directly communicated to European Agency.
- Substances to register: substances produced or imported as such, substances present in preparations, substances in articles and intended to be released in normal condition of use, monomers present in polymers > 2%
- Shall be deemed to have "registered" the active substances of plant protection products and biocides and substances “notified” as “new substances” in accordance with 67/548/CEE Directive;
- Exemption from registration: substances used for research/development activity, drugs for human or veterinary use, food additives, substances listed in Annexes IV and V, polymers, recovered substances.

Needed Information for Registration on Substance Amount (Articles 10-13, Annex III).

- The registration dossier must contain relevant information on physico-chemical, toxicological and ecotoxicological properties from registrant. Depending on the amount of trade substance or to put on the market the following information must be provided:
- Between 1 to 10 ton/year: Annex VII (chemical-physical data, in vitro tests + oral acute toxicity + acute test on fish and daphnia, biodegradation); there is an exemption for substances that do not raise concerns (mandatory, however, the physical-chemical data)
- Between 10 to 100 ton/year: Annex VII and VIII
- Between 100 to 1000 ton/year: Annex VII , VIII and test proposal of Annex IX
- More than 1000 ton/year: Annex VII, VIII and test proposal of Annex IX and X;
- It is provided for a mechanism for updating the data, the overcoming of the quantitative thresholds.

Registration Dossier (Titles 10-13, Annex III).

Chemical Safety Assessment (CSA) of a chemical substance aims to establish the safe conditions of manufacture and use of a substance for all life-cycle stages. Manufacturers, importers and downstream users on their own or in preparations have to ensure that these are manufactured and can be used in such a way that human health and environment are not adversely affected.

Annex VII (≥ 1 tonne per year)

Physico-chemical properties

Human health: in vitro irritation, sensitization, mutagenicity, acute toxicity (route)

Environmental: acute aquatic toxicity (daphnia, algae), biodegradation

Annex VIII (≥ 10 tonnes per year)

Human health: including in vivo irritation, and 28-day repeat dose studies

Environmental: acute toxicity fish, fate studies (hydrolysis, adsorption/desorption)

Annex IX (≥ 100 tonnes per year)

Long term, repeat dose, chronic toxicity, fate etc.

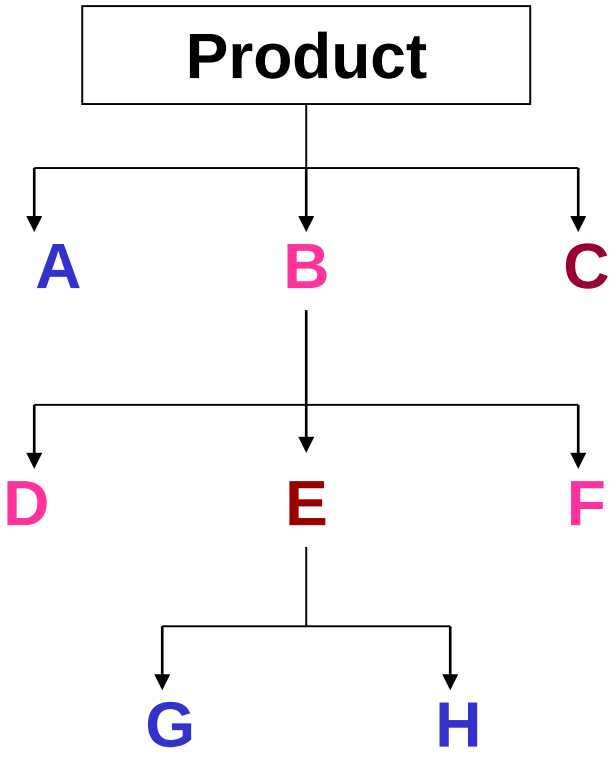
Annex X (≥ 1000 tonnes per year)

Further long term, repeat dose, chronic toxicity, fate etc.

SIEF (Substance Information Exchange Forum).

- Title 29 of REACH settle that all which have made pre-registration, but also all producing or importing substances whose information are hold by ECHA based on title 15 participate to a SIEF.
- For example, manufactures/importers of biocide substances does not participate to SIEF because potential registrants, but because “Data Holders”. Therefore cannot apply for data to other participants of SIEF, but must provide their data if required by potential registrants.
- The aim is basically to avoid duplication of studies, mainly those on vertebrate animals.
  - Confidentiality
  - Emphasis on competition law compliance
  - Structured communication and information flow
  - Pro-active behaviour of Non-Lead Members
  - Cost sharing / compensation
  - Several options
  - Payment terms
  - Limitation of liability
  - Facilitating nomination of a Lead Registrant

REACh is a Substance-specific Regulation.



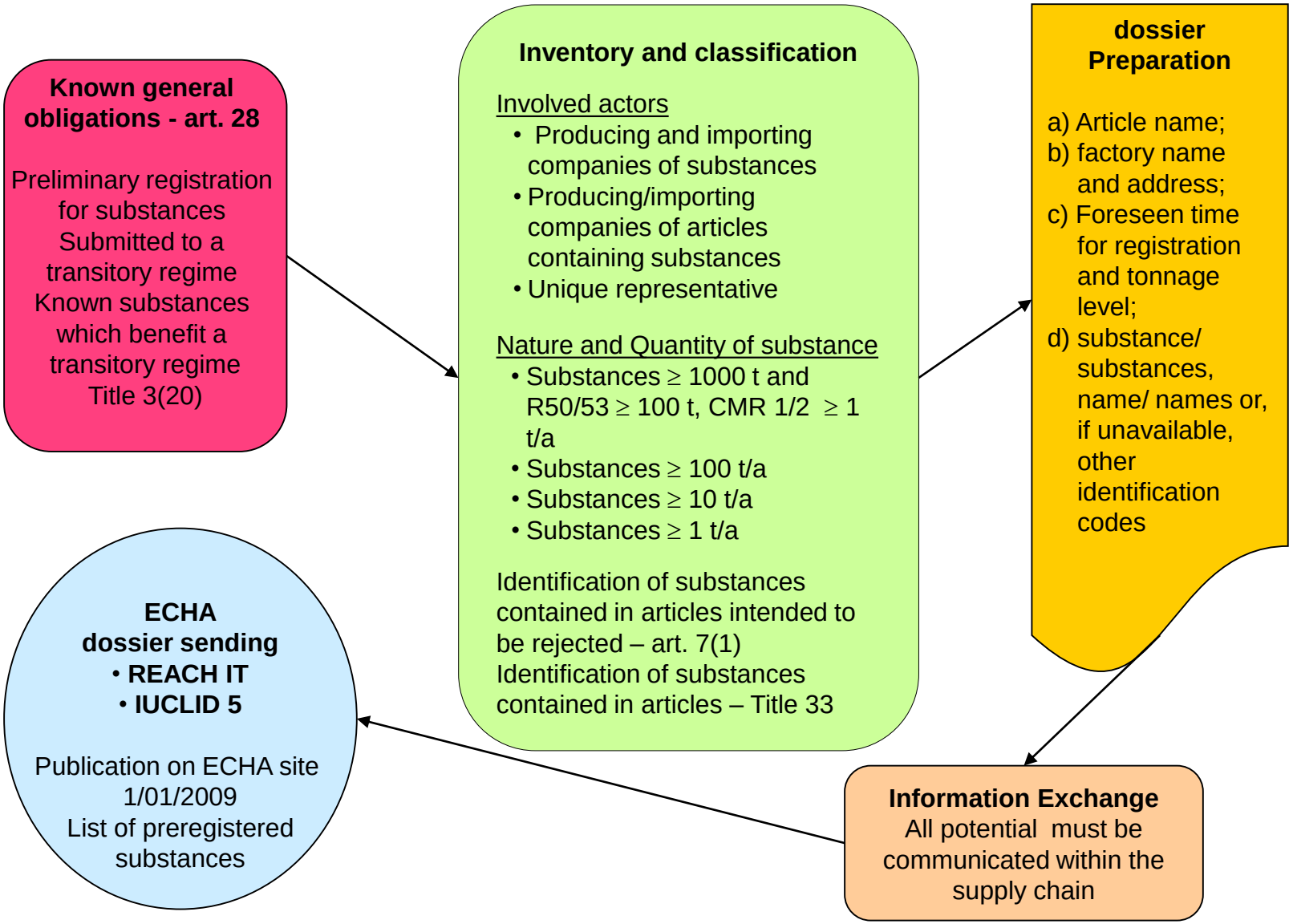
This product contains **8** substances

If (> 0.1% w/w)

Therefore, this product will require **8** registrations

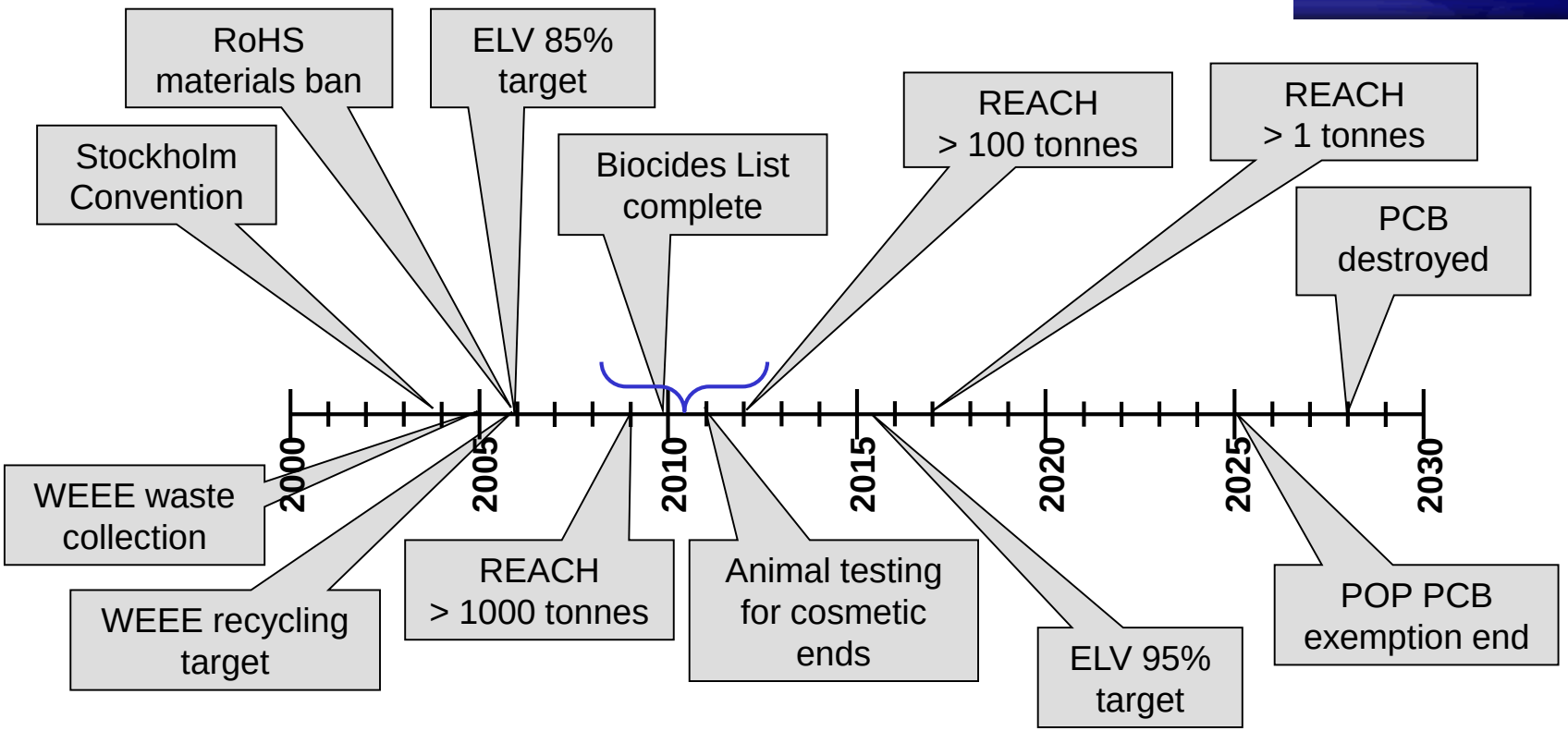
"article: means an object which during production is given a special shape, surface or design which determines its function to a greater degree than does its chemical composition."

The 5 PHASES of Pre-registration Procedure of “Phase In” Substances.



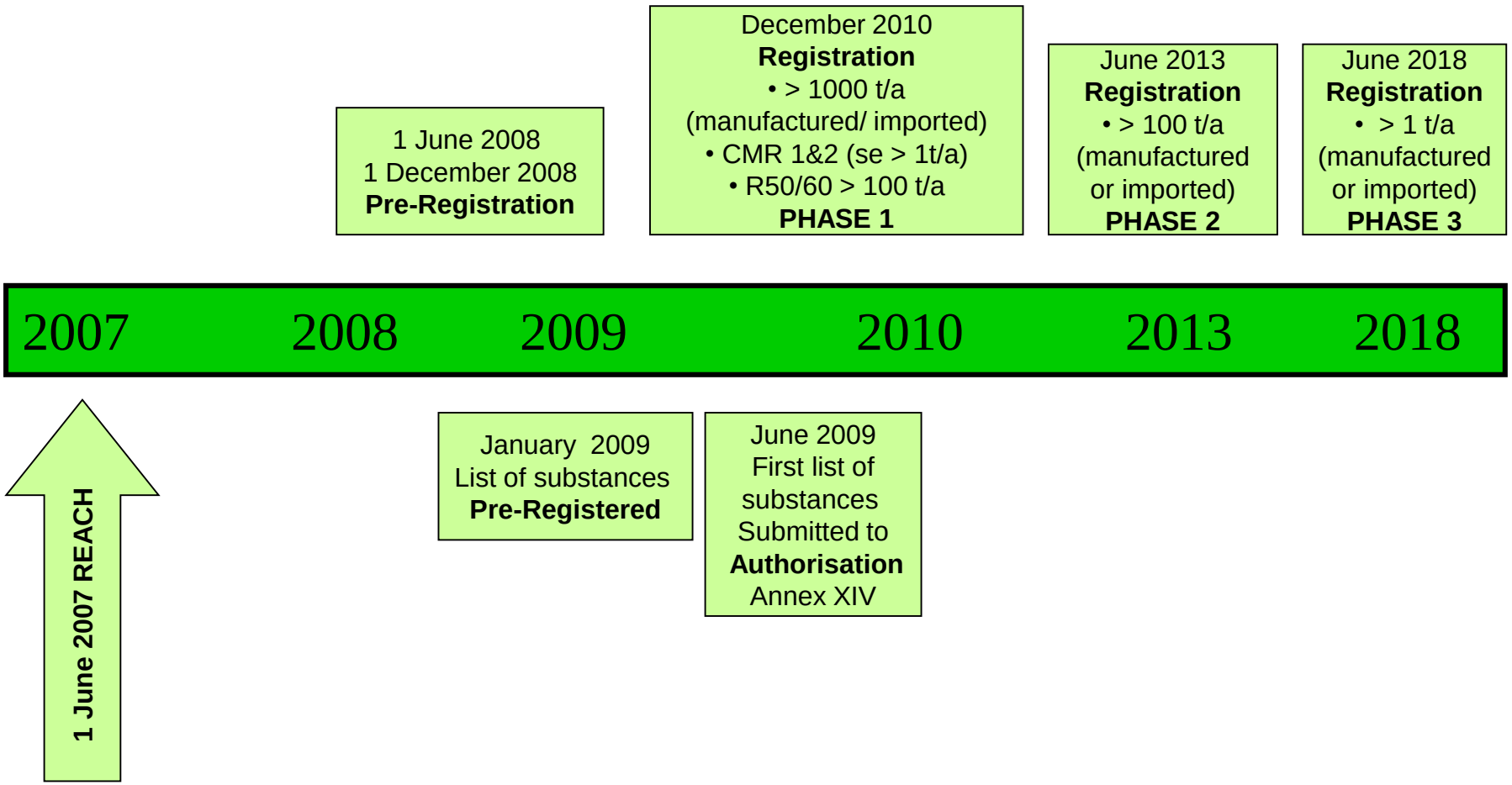
REACH Legislation Timeline (EU).

Chemical Products: Registration Evaluation Authorization



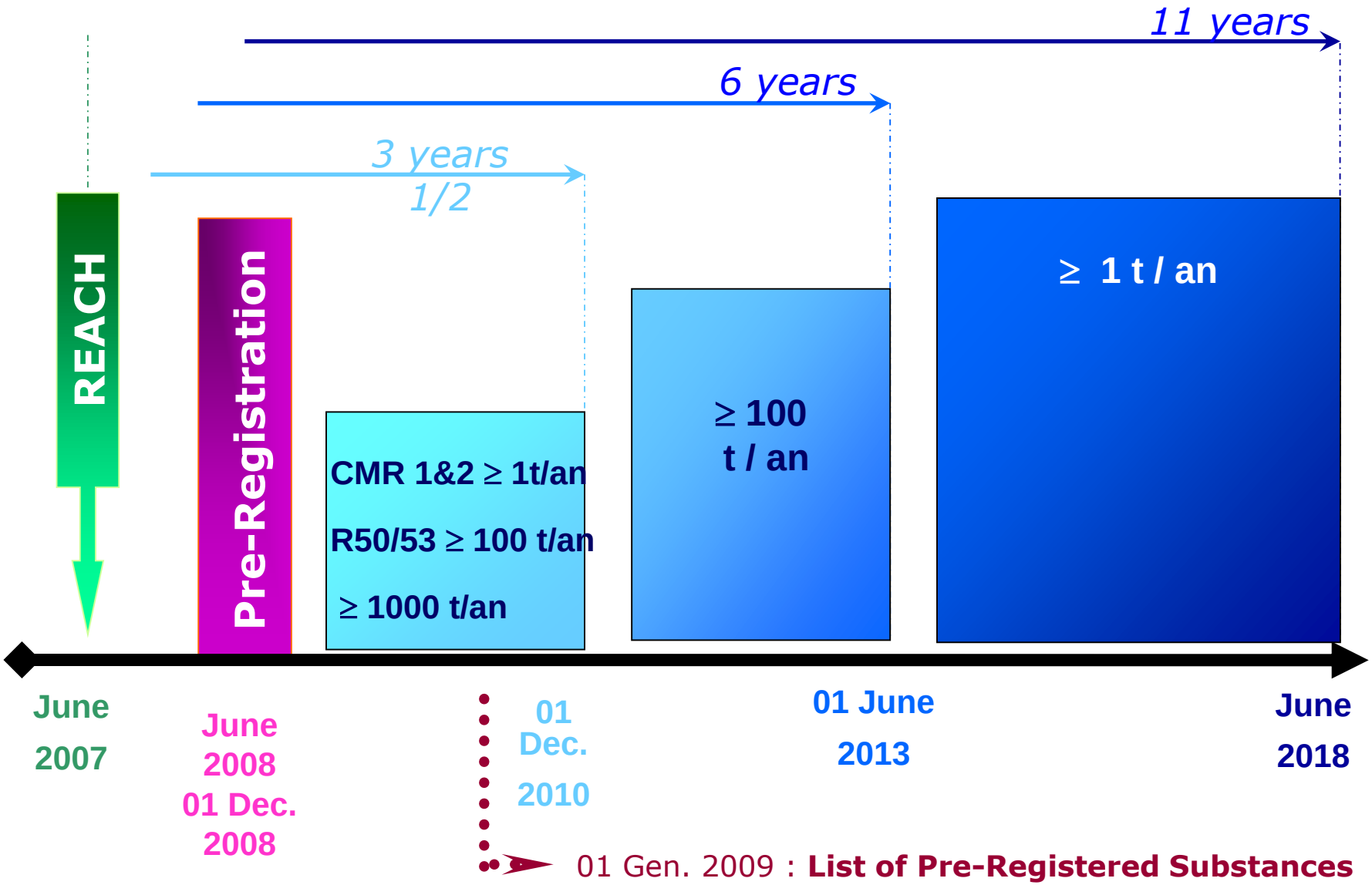
http://www.ec.europa.eu/environment/chemicals/reach/reach_intro.htm; EC 1907/2006

REACH Timesheet : Deadline of “Phase In” Substances Registration.



• CMR Carcinogenic, Mutagenic or toxic to Reproduction (CMR) category 1 or 2, according to the criteria of Directive 67/548/EEC
• R50/53: Substances classified as highly toxic for aquatic organisms and can induce negative long term effects for aquatic environment.

REACH Timesheet: Registration of "Phase In" Substances.



Chemical Safety Report (CSR) (Title 14 and Annex I).

For all substances subjected to Registration and manufactured/imported at > 10 tonnes/year.

The CSA is documented in the CSR (Chemical Safety Report) in accordance with the format reported in Annex I.

- 1st Phase – hazard identification and assessment:
  - a) Human health hazard assessment
  - b) Physicochemical hazard assessment
  - c) Environmental hazard assessment
  - d) Persistent, bioaccumulative and toxic (PBT) and very persistent very bioaccumulative (vPvB) assessment;

- If the substance is classified as dangerous (in accordance to 67/548/EEC) or meets PBT or vPvB criteria, then:
  - Exposure assessment, including Generation of the Exposure Scenarios (ES) and Exposure estimation
  - Risk characterisation (human health, environment)

… For production of the substance and its life cycle in any identified use

Hazard Identification.

- Data retrieval or generation:
  - The information requirements to provide depend on the tonnage level at which the substance is to be registered
  - All the existing information has to be submitted, independently from the tonnage band
  - If data generation is needed, a study proposal (including timeline for the submission) shall be presented for the information requirements specific to high tonnages (> 100 tonnes/year)
  - One of the main objectives of the Regulation is to promote the development of alternative method for the hazard identification. Key political issue but the “validated” and “widely accepted” alternative methods may come late in the process. Ex. long term Tox, CMR, etc.
  - Sharing of existing data on vertebrates will be obligatory and no repetition of already existing studies will be allowed (confidentiality issues, cost-sharing issues) – via SIEF and Consortia
  - Study waiving is accepted, provided the presentation of a detailed justification explaining why data generation is not necessary
  - Testing on vertebrates (in vivo) has to be undertaken as the last resort.

Hazard Identification - Data Adequacy.

Data must be evaluated on the base of their reliability and relevance

Data reliability can be evaluated by means of the Klimisch code of reliability (Klimisch et al. 1997)

1. : reliable without restriction
   - According to valid and internationally accepted guidelines (preferably GLP)
2. : reliable with restrictions
   - Not entirely according to accepted guidelines (other not GLP) but well documented
3. Non reliable
   - Methods not accepted, irrelevant exposure, species, etc.
4. Non assignable
   - Do not give sufficient experimental details.

All Substances > 1 ton/year - (Annex VII).

Chemical-Physical Data

- State of the substance at 20°C and 101.3 kPa
- Melting/freezing points
- Boiling points
- Relative density
- Vapour pressure
- Surface tension
- Water solubility
- Partition coefficient n-octanol /water (flash shake method)
- Flash point
- Flammability, liquids
- Explosive properties
- Self-ignition temperature for liquids and gases
- Oxidizing properties
- Granulometry (particle size distribution)

Toxicological/Ecotoxicological Data

- Short term toxicity testing on Daphnia
- Growth inhibition study on algae
- Ready biodegradability – Modified Sturm test
- Ready biodegradability – closed bottle test.

- Skin irritation (in vitro)
- Eye Irritation (in vitro)
- Skin sensitisation
- in vitro gene mutation study in bacteria
- Acute toxicity, oral route (OECD 420, 423 or 425)

Fonte: http://www.api.org/ehs/health/upload/API_REACH_Guide.pdf

Substances at 10 - 100 ton/year - (Annex VIII).

- Short-term toxicity test on fish
- Activated sludge respiration inhibition testing
- Hydrolysis as a function of pH and identification of degradation products
- Adsorption/desorption screening study (HPLC method)

- in vitro cytogenicity in mammalian cells
- in vitro gene mutation study in mammalian cells
- Other in vitro mutagenicity test : micronucleus test (OECD 474) or UDS assay (OECD 486)
- Acute toxicity, inhalation
- Acute toxicity, dermal route
- Short-term repeated dose toxicity in rats (28 days), oral/dermal/inhalation
- Screening for reproduction / development toxicity in rats
- Assessment of toxicokinetic behaviour (based on required studies)

Substances at 100 - 1000 tons/year (Annex IX).

Fish early-life stage (FELS) toxicity test

Fish short term toxicity test on embryo and sac-fry stages

Fish, juvenile growth test

Test of simulation on end degradation in fresh waters

Simulation testing on ultimate degradation in surface water

Soil simulation testing (for substances adsorbing to soil)

Identification of degradation products

Bioconcentration in (one) aquatic species, preferably fish.

Further studies on adsorption/desorption

Short term toxicity to invertebrates

Effects on soil micro-organisms

Short term toxicity to plants

Long-term toxicity on Daphnia, (21 days)

Sub-chronic toxicity study (90 day) in rats, oral/dermal/inhalation

Development toxicity study, rats

Development toxicity study, rabbits (depends on 1st result)

One-generation reproduction study (enhanced)

Two-generation reproduction toxicity study.

Substances > 1000 tons/year - (Annex 10).

Stability in organic solvents and identity of relevant degradation products

Dissociation constants

Viscosity

Further environmental fate and behavioural studies

Long-term toxicity testing on invertebrates (unless in Annex IX)

Long-term toxicity testing on higher plants (unless in Annex IX)

Long-term toxicity to sediment organisms

Long-term or reproductive toxicity to birds

Chronic toxicity (12 months or longer), rats (exposure/use driven)

Carcinogenicity study/combined chronic toxicity, rats (exposure driven)

Other studies (to be listed below)

Confirmatory testing on biodegradation rates (aerobic and/or anaerobic)

Long-term toxicity testing on soil invertebrates other than earthworms
Emissions in water
Emissions in land
Emissions in air
Occupational exposure in manufacture
Occupational Exposure in use
Consumer exposure
End of life

Analytical methods (may be requested or lack of availability justified)

Data Requirements under REACH Annex VII for ≥ 1 ton.

Physicochemical properties:

- **Skin irritation or skin corrosion**
  - 8.2 Eye irritation
  - 8.3 Skin sensitisation
  - 8.4.1 Mutagenicity (gene mutation in bacteria)
  - 8.5.1 Acute toxicity (oral route)

- **Eco toxicological information**
  - 9.1.1 Short-term toxicity invertebrates (*Daphnia*)
  - 9.1.2 Growth-inhibition plants (algae)
  - 9.2.1.1 Ready biodegradability

Data Requirements under REACH Annex VIII for ≥ 10 ton.

- **Toxicological information**
  - 8.1.1 Skin irritation (*in vivo*)
  - 8.2.1 Eye irritation (*in vivo*)
  - 8.4.2 Cytogenicity in mammalian cells (*in vitro*)
  - 8.4.3 Gene mutation in mammalian cells (*in vitro*)
  - 8.5.2 Acute toxicity (inhalation)
  - 8.5.3 Acute toxicity (dermal)
  - 8.6.1 Repeated dose toxicity (28-days)
  - 8.7.1 Reproductive/developmental toxicity screening test; (OECD 421 or 422)
  - 8.8.1 Toxicokinetics

- **Ecotoxicological information**
  - 9.1.3. Short-term toxicity fish
  - 9.1.4. Activated sludge respiration inhibition test
  - 9.2.2.1 Hydrolysis as a function of pH
  - 9.3.1 Adsorption/desorption screening test

Data Requirements under REACH Annex IX for ≥ 100 ton.

- **Toxicological information**
  - 8.6.1 Repeated dose toxicity (28 days)
  - 8.6.2 Sub-chronic toxicity (90 days)
  - 8.7.2 Developmental toxicity; OECD 414
  - 8.7.3 Two-generation reproductive toxicity study
- **Ecotoxicological information**
  - 9.1.5 Long-term toxicity invertebrates (*Daphnia)*
  - 9.1.6. Long-term toxicity to fish
  - 9.1.6.1 Fish early-life stage test
  - 9.1.6.2 Fish short term toxicity embryo and sac fry
  - 9.1.6.3 Fish juvenile growth test
  - 9.2.1.2 Ultimate degradation in surface water
  - 9.2.1.3 Soil simulation testing
  - 9.2.1.4 Sediment simulation testing
  - 9.2.3 Identification of degradation products
  - 9.3.2 Bioaccumulation in aquatic species (fish)
  - 9.3.3 Further information on adsorption/desorption
  - 9.4.1 Short-term terrestrial toxicity (invertebrates)
  - 9.4.2 Effects on soil micro-organisms
  - 9.4.3 Short-term toxicity to terrestrial plants

Data Requirements under REACH Annex X for ≥ 1000 ton.

- **Toxicological information**

  8.6.3 Long-term repeated toxicity (≥12 months)

  8.7.2 Developmental toxicity; OECD 414

  8.7.3 Two-generation reproductive toxicity

  8.9.1 Carcinogenicity study

- **Ecotoxicological information**

  9.3.4 Further fate and behaviour in the environment of the substance and/or degradation products

  9.4.4 Long-term toxicity on invertebrates

  9.4.6 Long-term toxicity on plants

  9.5.1 Long-term toxicity to sediment organisms

  9.6.1 long-term toxicity to birds

Data Sharing on Substances (Titles 25-30).

Substances not phase-in:

The potential registrant must in advance ask the Agency if the substance is already registered; in this case ask the first registrant for the letter to access data, after compensation of costs incurred (The Agency will define guidelines for the calculation of appropriate cost). For data obtained on vertebrate animals sharing is mandatory in all cases, whereas for other data the owner is required to provide the required data, but the potential registrant can supply their own.

Phase-in substances:

A step is provided of pre-registration, in which each firm register data in its possession.

A forum has been established to exchange information on substances (SIEF). Rules for data sharing are the same of non-phase-in substances.

Data Protection: 12 years from registration date.

Information Provided Along the Supply Chain (Titles 31-36, Annex II).

The main tool for transferring information is the safety data sheet (SDS), i.e. Annex II.

- The structure of SDS (with 16 points) does not change compared to the previous structure.
- In REACH are transferred all provisions on SDS of substances and preparations
- A SDS is also envisaged for PBT and vPvB substances
- In SDS must be included a synthesis of relevant exposition scenario for the expected use of the substance.

Downstream User (37-39 Titles).

- DU must inform the manufacturer or importer about identified uses, provides sufficient information to prepare an exposure scenario;

- Can provide information to substance supplier if it consider that exposition scenery of intended use are not adequately described in SDS transmitted by the supplier; the supplier in this case must modify the chemical safety relation (CSR) based on received data from DU.

- If DU uses the substance outside the scenery described by its supplier and prefers that these uses remain unknown to supplier, it must provide own to draw up a CSR (in this case the quantitative threshold is 1 ton/year e and not 10 ton/year) ⇨ Annex XII.

Evaluation (Titles 40-54).

Besides chemical safety evaluation made by **supplier** (> 10 ton/year ⇨ annex I) or by **downstream user** (> 1 ton/year ⇨ annex XII)

two other types of evaluation are scheduled:

- **Evaluation of dossier**, carried out by the **Agency**, including:
  - ***Evaluation of test proposal***
  - ***Evaluation of conformity*** (completeness of information, adequacy of waiving required, adequacy of CSR, etc.) of provided information in the registration framework. This evaluation is not systematic: a large number of evaluation is expected.

- **Evaluation of substances**, made from **Member States:**

  on the basis of a rolling plan of substances. Each member State indicates the substances that it intends to annually assess.

Authorization (Titles 55-66).

Authorization obligations is not limited to 1 ton/year. Manufacturer, importer or downstream user has to apply for authorization of uses of a SVHC.

Inside authorization procedure is present Environmental Assessment for:

a) C/M/R substances: categories 1 and 2 (Carcinogenic/Mutagenic/toxic for Reproduction);
b) PBT substances (**P**ersistent, **B**ioaccumulative & **T**oxic) and vPvB (**v**ery **P**ersistent & **v**ery **B**ioaccumulative);
c) Endocrinal disruptors and substances which, even if are not part of criteria b), can present risks analogue for human and environment

Substances subject to authorization obligations are listed (temporarily) in the list of annex XIV.

Authorization (Titles 55-66).

- If a firm ask for authorization of a substance included in Annex XIV, for one or more specific uses, it must document to be able to ensure a “adequate control” of risks of this substance.

- If this control is not possible, it can equally present a socio-economic analysis to demonstrate that benefits from the use of the substance outweigh the risks; this analysis must contain consideration of the availability of alternative substances or technologies.

- The assessment is carried out by the Agency and the authorization is issued by Commission based on opinions of Agency Committees and with a Committee procedure (Member States' voting by qualified majority).

- Authorization is always issued for a specified period (determined on a case-by-case). If there are available alternative substances or technologies, a substitution plan must be provided. Research and development aimed at identifying substitutes are taken into account for the authorization.

Restrictions (Titles 67-73, Annex XVII).

- The provisions of Directive 76/769/CE have been transposed into REACH regulation
- Leaving aside the quantitative limit of 1 ton/year
- A restriction can be established with fast procedure, by a Member State proposal or by initiative of the Commission itself.
- A restriction can be adopted in response to the findings of the evaluation
- there is a specific annex (Annex XVII) which lists all the restrictions adopted, included the substances for which no undertaking has required specific authorization (in this case all uses of the substance are prohibited)

European Agency (Titles 75-111).

- The “European Agency for chemical substances” is established
- Agency headquarter: Helsinki
- Incomes: Commission contribute, rate system, voluntary contributions from S.M.
- Inside the Agency are created:
  a) a Member States committee
  b) a Forum to exchange information between S.M. on regulation application (inspection activity and control);
  c) a Committee for risk evaluation with S.M. experts involvement
  d) a Committee for socio-economic analysis, with S.M. experts involvement
  e) An appeal Committee
- The information on the identity, hazards, uses and risks of substances compiled in previous phases must be documented in a standardised IT format in registration dossiers. For this purpose, ECHA provides a free software called IUCLID 6. In the simplest cases, it is also possible to create the dossier directly in ECHA’s submission tool REACH-IT.

Public Access to Information (Titles 118-119).

The Information must be provided to public by Agency via internet:

- IUPAC Name and/or EINECS name
- Classification
- Physico-chemical data
- Results of toxicological and ecotoxicological studies
- The “derived no effect level” (DNEL) and the PNEC (Predicted no-effect concentration)
- Instructions on safety use
- Analytical methods to detect the substance in environmental sectors or to determine direct human exposure.

Tasks of National Authority (Titles 121-127).

- Establishing a system of inspections and checks
- Establishes penalties for breach of the rules
- Shall submit reports on the results of the checks
- Takes initiatives to inform the public about the risks of using chemicals
- Establishing a national help desk for companies
- Expresses opinion on applications for R & D
- Receives information on the substances produced or imported into its territory
- Participates in the definition of “Rolling Plan”, undertake the evaluation of the substances assigned and require additional information to complete the assessment
- Arrange, if appropriate, a dossier following Annex XV for substances eligible for the authorization procedure or for the restriction procedure or for a proposal for harmonized classification
- Participate with representatives and experts in the committees of the Agency
- Presents every five years a report on the implementation of Regulation

Revisions.

- Annex I (general prescriptions for substances evaluation and for CSR filing), and Annex IV and V (substances exempted from registration obligation);
- Annex XIII (criteria to identify PBT and vPvB substances) ;
- Check of possible need for modifications of application field if overlapping to other communitarian legislations are evidenced
- Check of possibility to substitute actual reproductive toxicity tests with other alternative tests.

REACH Implementation Projects (RIP).

RIP 1: Description of the process

To provide stakeholders with a better understanding of the REACH procedures and other RIPs projects .

RIP 2: Information systems development (REACH-IT)

Harmonize the work between Agency, Competent Authorities, Industry, Commission e other interested stakeholders with an appropriate information system. (IUCLID 5 and ad hoc web sites)

RIP 3-4: Guidance documents for industry and authorities, respectively

Develop before the entry into force of the REACH guidance documents and tools to facilitate the implementation of the legislation

RIP 5-6: Preparation for the start of the Agency

Define, within 18 months after REACH entry into force, the European Chemical Agency structure, assuring that it can perform the work in an efficient and transparent.

RIP 7: Preparation of Commission for REACH

REACH Implementation Projects (RIP).

RIP 3: Guidance documents for industry
consists of 10 sub-projects :

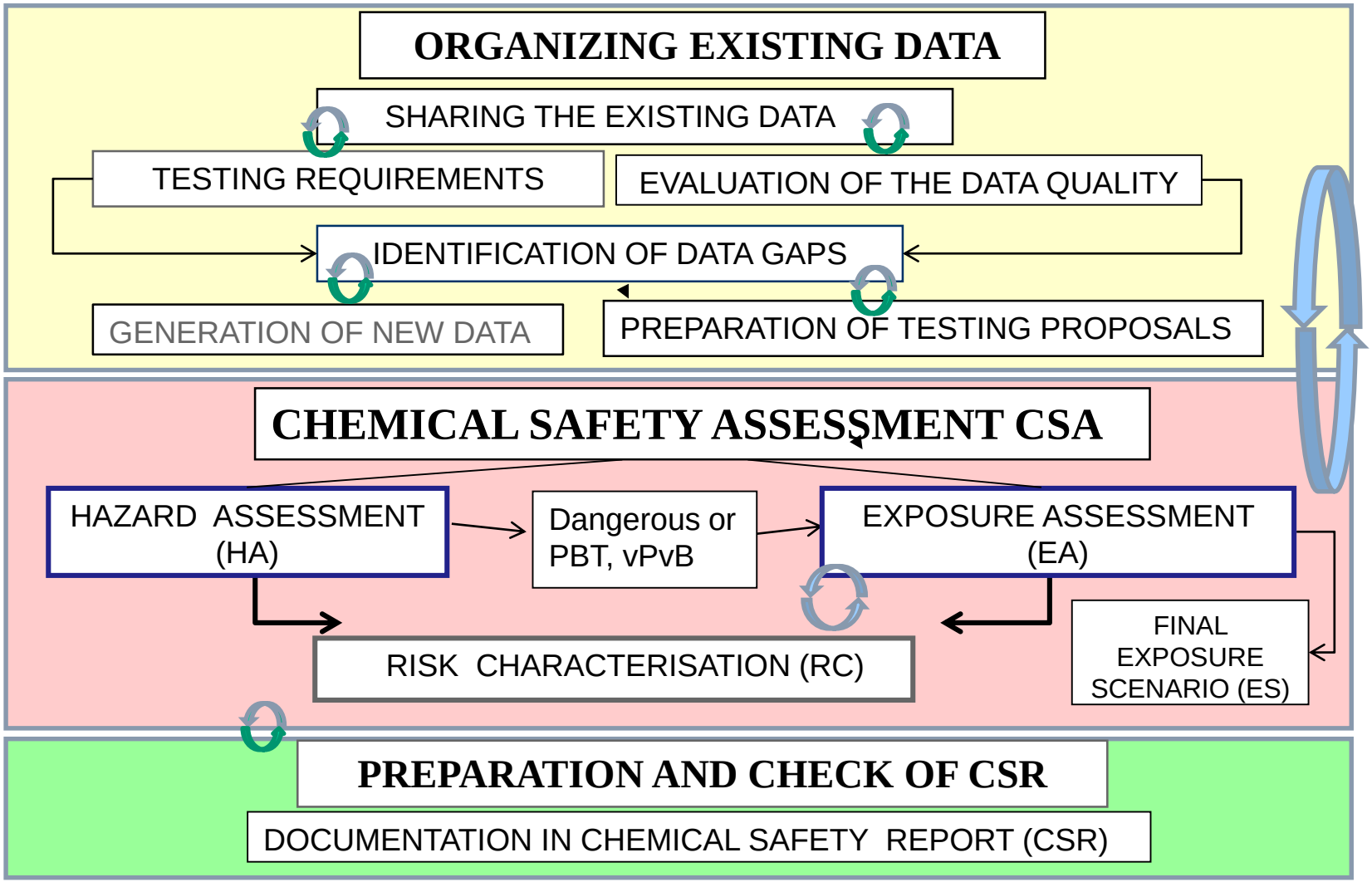
- RIP 3.1: Develop guidelines for manufacturers and importers to prepare the dossier recording engineer;
- RIP 3.2: Develop guidelines for manufacturers, importers and downstream users to perform the chemical safety assessment for workers, consumers and the environment, how to bring in the evaluation report, including a list of possible exposure scenarios and risk management measures, and how to communicate information with the safety data sheet in accordance with REACH (is divided into 5 subgroups: exposure scenarios, hazard and PBT assessment, IT tools, general guidelines, and consolidation in the REACH;
- RIP 3.3: Develop guidelines on how the industry has to comply with all requests for information under the REACH regarding the intrinsic properties of substances (important to know how to use alternatives to in vivo data (Q)SARs, “chemical category approach”, in-vitro data, information on exposure);
- RIP 3.4: guidelines for industry on data sharing (pre-registration).
- RIP 3.5: guidelines for downstream users;
- RIP 3.6: guidelines for GHS classification;
- RIP 3.7: guidelines for the preparation of a dossier for Authorization;
- RIP 3.8: Substances in articles – guidelines for producers and importers about their obligations in accordance with the REACH requirements;
- RIP 3.9: Socio-Economic analysis;
- RIP 3.10: Identification and nomenclature of substances according to REACH.

REACH Implementation Projects (RIP).

RIP 4: Guide documents for Agency and le Competent Authorities consists of 5 sub-projects :

- RIP 4.1, RIP 4.2: Together in a single working group, the aim is to develop guidelines on the assessment of the dossier to the Agency (compliance check, testing proposals) and substances by the Member States;
- RIP 4.3, RIP 4.5: This, too, brought together in a single group with the aim of developing guidelines for the inclusion of substances in Annex XIV (list of substances subject to authorization), allowing the identification of "Substances of Very High Concern“ (SVHC) and related prioritization (4.3) and development of prioritization criteria between dossiers for the compliance check and for substances evaluation;
- RIP 4.4: Development of guidelines for Member States and Agency (on behalf of the EU Commission) to verify proposals in accordance with Annex XV for three types of dossiers:
  - Harmonized classification and labelling;
  - Identification of SVHC to be included in annex XIV;
  - Restrictions

Technical Work in REACh.



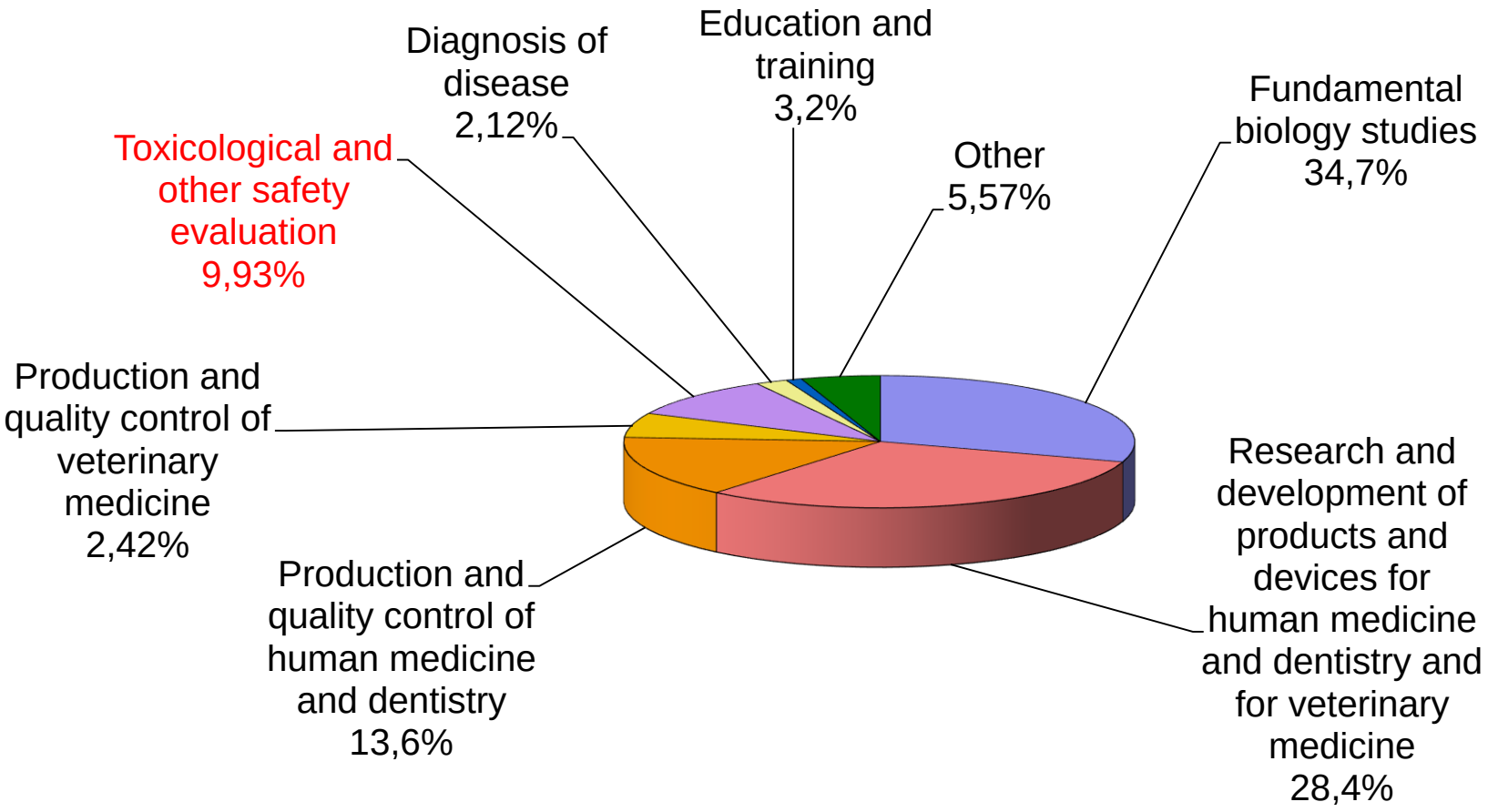
Alternative Methods.

- An important principle of REACH is to limit animal testing, in particular testing on vertebrate animals shall be undertaken only as a last resort
- Alternative *in vitro* tests, when possible, must be used.
- Information may be generated by models of qualitative and quantitative structure:activity relationship (Q)SAR's (computer based models)

In vitro alternative methods:

- Very few *in vitro* toxicological alternatives have regulatory acceptance – skin corrosion and positive irritation to eyes
- The skin corrosion model has been developed in 15 years
- The models for skin irritation and sensitization are difficult to develop - complex biological processes
- Moreover, they often are not cheaper than studies on animals

Use of Animal Experiments in the EU in 2002 COM(2005) 7 Final.



total number in 2002 = 10.7 million

Alternative (Q)SAR.

- **Aims**
  - **To relate the biological activity of a series of compounds to their physico-chemical parameters in a quantitative fashion using a mathematical formula**
- **Requirements**
  - **Quantitative measurements for biological and physicochemical properties**

- Testing may be wavered if there are results derived from valid (Q)SAR's
- (Q)SAR's may be used to support grouping of chemicals, thereby minimising testing
- The Joint Research Centre of the European Commission has been empowered to promote the Development, Validation and Implementation of (Q)SAR's
- Estimated that there could be an overall cost saving potential of 940M euro

Hansch Equation for (Q)SAR.

- A QSAR equation relating various physicochemical properties to the biological activity of a series of compounds
- Usually includes log P, electronic and steric factors
- Start with simple equations and elaborate as more structures are synthesized
- Typical equation for a wide range of log P is parabolic

$$\log\left(1/C\right) = -k_1\left(\log P\right)^2 + k_2 \log P + k_3\sigma + k_4 E_s + k_5$$

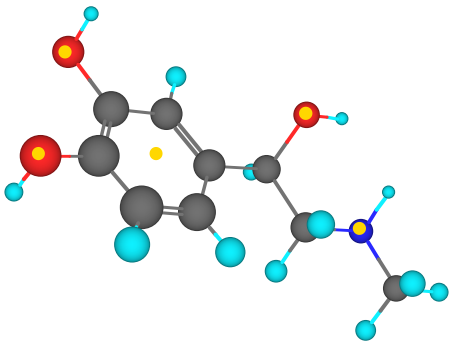
Hydrophobicity (partition coefficient)

Hammett substituent constant

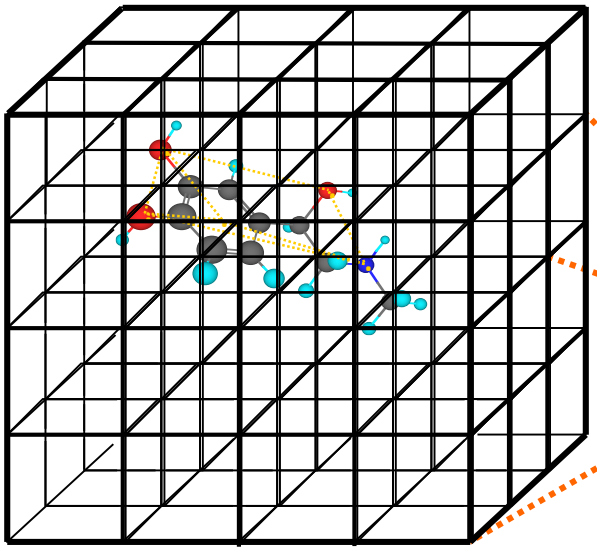
Taft's steric factor

3D-QSAR.

- Physical properties are measured for the molecule as a whole
- Properties are calculated using computer software
- No experimental constants or measurements are involved
- Properties are known as ‘Fields’
- Steric field - defines the size and shape of the molecule
- Electrostatic field - defines electron rich/poor regions of molecule
- Hydrophobic properties are relatively unimportant



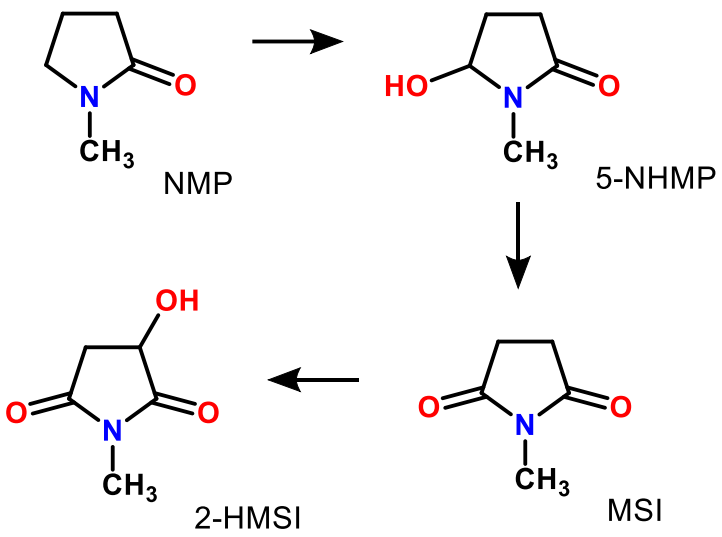
Active conformation

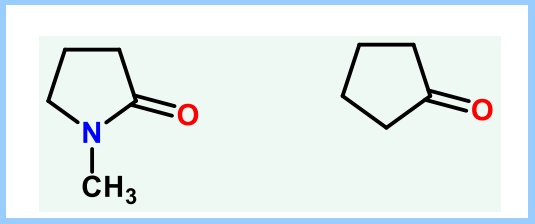


Grid points

Examples of Possible C/M/R Substitutions.

Substitution of dangerous solvents:





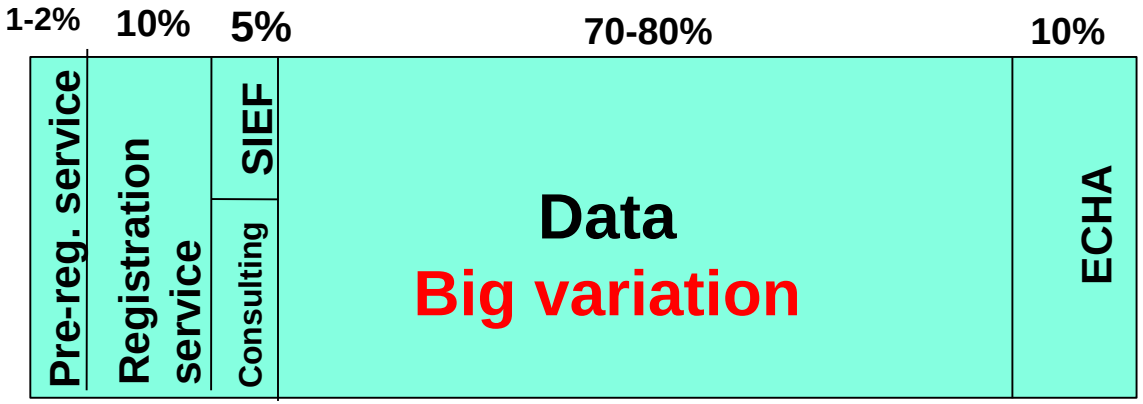
1-Methyl-2-pyrrolidone
CN1CCCC1=O
$LogK_{o/w}$ = - 0.026
TPSA = 20,309 A2
Repr.Cat.2 R61 Xi R10
R36/37/38

Cyclopentanone
O=C1CCCC1
$LogK_{o/w}$ = 1.087
TPSA = 17,071 A2
Xi R36/38

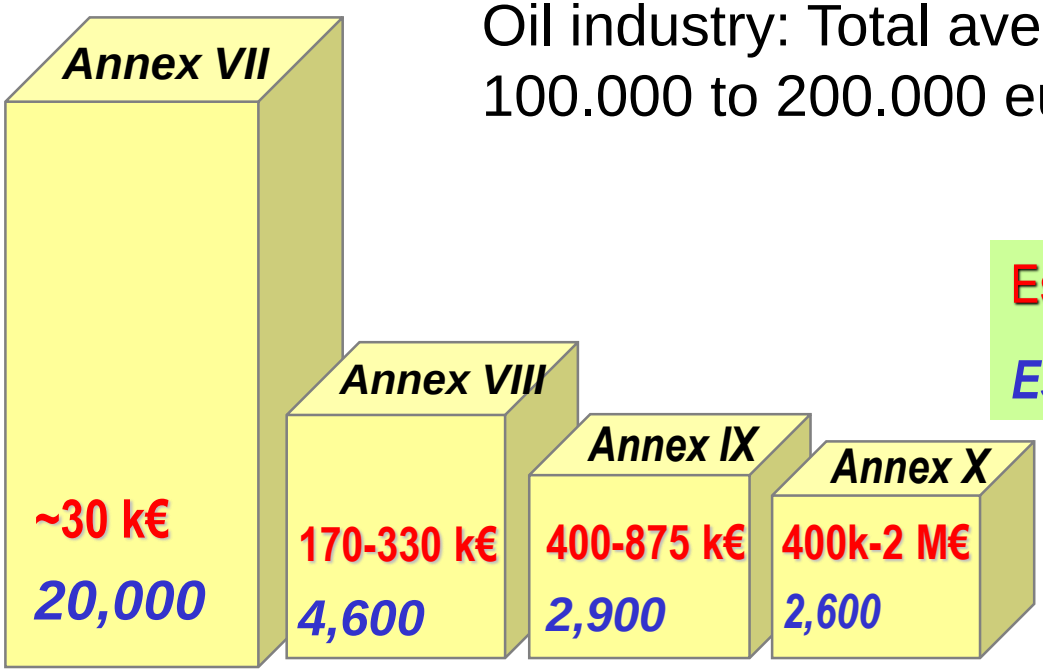
Embryo- and fetus-toxicity of NMPO in rat SD

V. Resp. Aerosol conc.	**100 – 360 mg/m³**	**GD 6-11 no effect**
V. Resp. Vapour conc.	**680 mg/m³ (6h/j)**	**GD 0-21 fetal weight -, ossification-**
V. Skin	**750 mg/kg**	**GD 6-15 resorptions +, N° living fetus -, schel. anomalies +**
V. Oral	**250 mg/kg**	**GD 6-20 fetal weight, schel. anomalies +**

REACH Data Requirements and Costs.



Oil industry: Total average cost estimate 100.000 to 200.000 euro/substance



Estimated costs per dossier

Estimated N° of substances

Substances of Very High Concern (SVHC).

- **C**arcinogenic, **M**utagenic or toxic to **R**eproduction (**CMR**) category 1 or 2, according to the criteria of Directive 67/548/EEC
- **P**ersistent, **B**ioaccumulative and **T**oxic (**PBT**) according to the criteria in Annex XIII of the REACh Regulation or
- **v**ery **P**ersistent and **v**ery **B**ioaccumulative (**vPvB**) according to the criteria in Annex XIII of the REACh Regulation and/or
- Identified, on a case-by-case basis, from scientific evidence as causing probable serious effects to humans or the environment of an equivalent level of concern as those above e.g. endocrine disrupters.

- ~ 1500 estimated substances

- Ultimate objective: **substitute** SVHC by less hazardous substances or technologies.

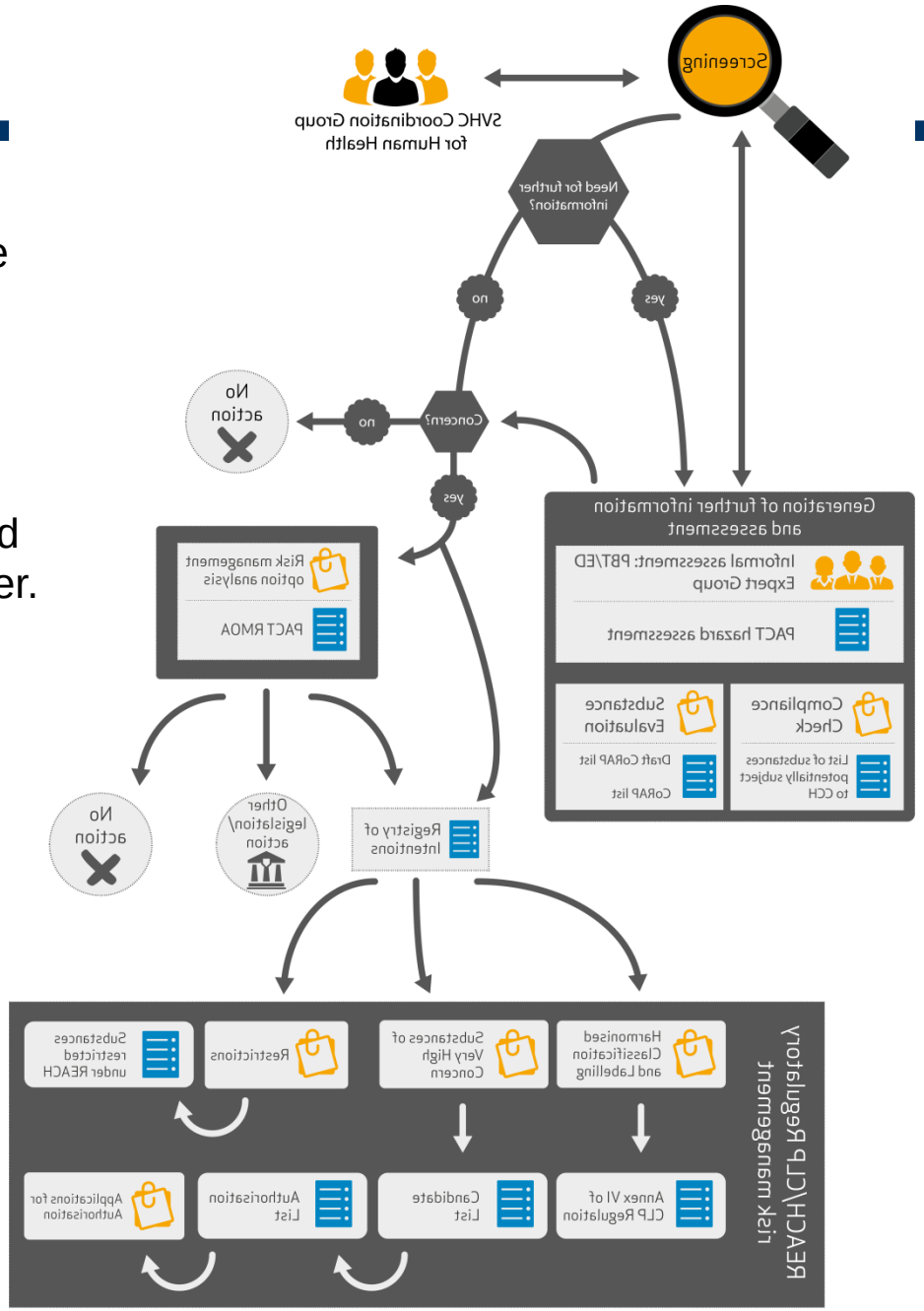
Substances of Potential Concern (SHC).

The substances that potentially have certain hazardous properties need to be identified and subsequently processed using relevant regulatory steps to make sure that the risks associated with their use are properly addressed.

The chart displays how the activities and regulatory processes relate to each other. It also shows the various lists of substances that result from the work of the authorities and are published by ECHA on its website.

The chart is a simplified representation of how the activities and processes are linked to each other

.



- Information on regulatory process and activities
- Substance list

https://echa.europa.eu/addressing-chemicals-of-concern/substances-of-potential-concern

15 SVHC Substances Published in May 2009.

Substance	Basis for SVHC
Anthracene	**PBT**
4,4'-Diamonodiphenylmethane*	**C cat 2**
Dibutyl phthalate (DBP)*	**R cat 2**
Cobalt dichloride	**C cat 2**
Diarsenic pentoxide	**C cat 1**
Diarsenic trioxide	**C cat 1**
Sodium dichromate	**CMR cat 2**
5-tert-butyl-2,4,6-trinitro-m-xylene Musk xylene*	**vPvB**
Bis (2-ethyl(hexyl)phthalate) (DEHP)*	**R cat 2**
Hexabromocyclododecane (HBCDD), α-HBCDD, β-HBCDD, γ-HBCDD*	**PBT**
Alkanes, C10-13, chloro (SCCP)*	**PBT, vPvB**
Bis(tributyltin)oxide	**PBT**
Lead hydrogen arsenate	**CR cat 1**
Benzyl butyl phthalate (BBP)	**R cat 2**
Triethyl arsenate	**C cat 1**

The Substitute Should be Chosen Very Carefully.

1. Not sufficient info available on many substances → **risk to substitute by equivalent or more hazardous substances** → years of work, costs for changes, liability

Proper Hazard assessment

2. Risk to shift problem to another area: environment ↔ workers ↔ consumers; air ↔ water ↔ waste; damage to equipment or facilities

Proper Risk & LCA (Life cycle assessment)

3. Loose the quality of product → competitiveness, trust of client

4. Raise of indirect costs → e.g. control measures, longer process

The Substitution of C/M/R as of Other Products have its Limits.

- **Does not exists an universal substitution and all proposals of substitution need always an study of validation by the customer.**

- **A solution of substitution will not be valid that for a limited time.**
- **Developing the Best Science to Achieve the Best Decisions**

References and Supports.

- Website of the European Chemicals Bureau: http://ecb.jrc.it/reach/
- Website of the European Chemicals Agency: http://ec.europa.eu/echa/home_en.html
- Websites of the European Commission http://ec.europa.eu/environment/chemicals/reach/reach_intro.htm
  http://ecb.jrc.it/DOCUMENTS/REACH/REACH_in_brief_0207.pdf
- Helpdesks of the EU member states, i.e.:
  http://www.reachright.ie **http://helpdesk-reach.it**

http://echa.europa.eu

http://www.iss.it/cnsc/

http://www.cefic.org

CLP and REACH.

67/548/EEC

1999/45/EC

UN GHS

incl. SDS

EU GHS
CLP (EC) No 1272/2008

Commission

(EC) No. 1488/94

1999/45/EC

2000/21/EC

93/105/EC

91/155/EEC

93/67/EEC

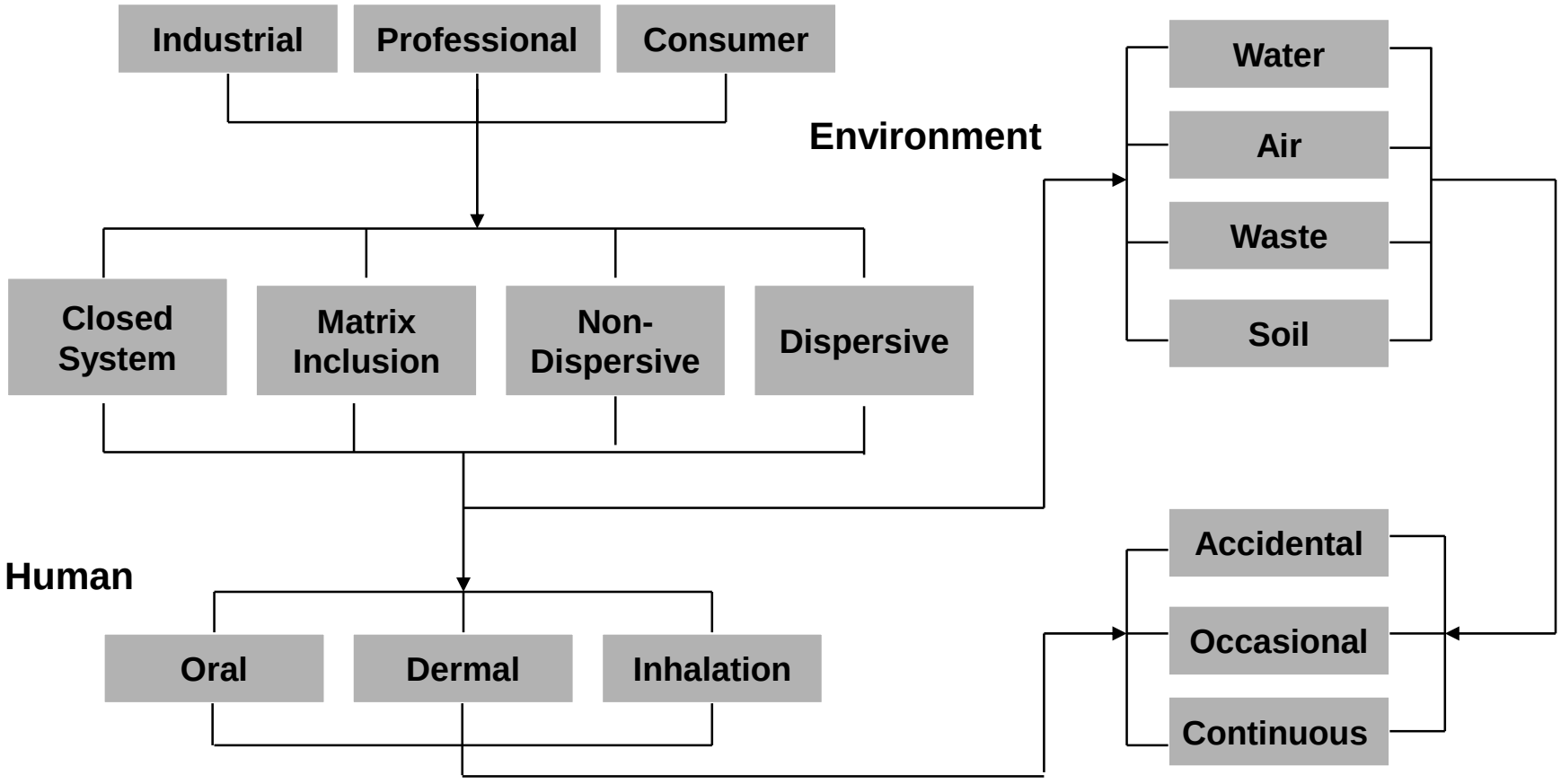
Council

(EEC) No. 793/93

76/769/EEC

REACH (EC) No. 1907/2006
European Chemicals Agency

Exposure Patterns.



REACH and Nanomaterials.

Nanomaterials:

- Tiered gathering of HSE information acc. to REACH Annexes VI – X
- Recommendation for additional physicochemical information on top of REACH requirements:
  - surface chemistry/coating, morphology, crystalline phase, shape, surface structure, specific surface area, particle size/size distribution, agglomeration/aggregation in native material or in preparation, known catalytic activity
  - in special cases: dustiness, porosity, dispersion stability in water (or in other media), zeta potential (surface charge), photocatalytic activity, radical formation potential

Law 46/82 F.I.T. - D.M. 13 march 2009.

a) sostanze che rispondono ai criteri di classificazione come sostanze cancerogene, **categoria 1** (convertita in Carc. 1 A – Allegato VII Reg. CE n. 1272/2008) o **categoria 2** (convertita in Carc. 1 B – Allegato VII regolamento CE n. 1272/2008), a norma della direttiva 67/548/CEE;

b) sostanze che rispondono ai criteri di classificazione come sostanze mutagene, **categoria 2** (convertita in Muta. 1 B – Allegato VII regolamento CE n. 1272/2008) , a norma della direttiva 67/548/CEE;

c) sostanze che rispondono ai criteri di classificazione come sostanze tossiche per la riproduzione, **categoria 1** (convertita in Repr. 1 A – Allegato VII regolamento CE n. 1272/2008) o **categoria 2** (convertito in Repr. 1 B – Allegato VII regolamento CE n. 1272/2008), a norma della direttiva 67/548/CEE;

d) sostanze che sono **PBT** (Persistenti, Bioaccumulabili e Tossiche) o **vPvB** (molto Persistenti e molto Bioaccumulabili) secondo i criteri previsti dall'Allegato XIII del Reg. (CE) n. 1907/2006.