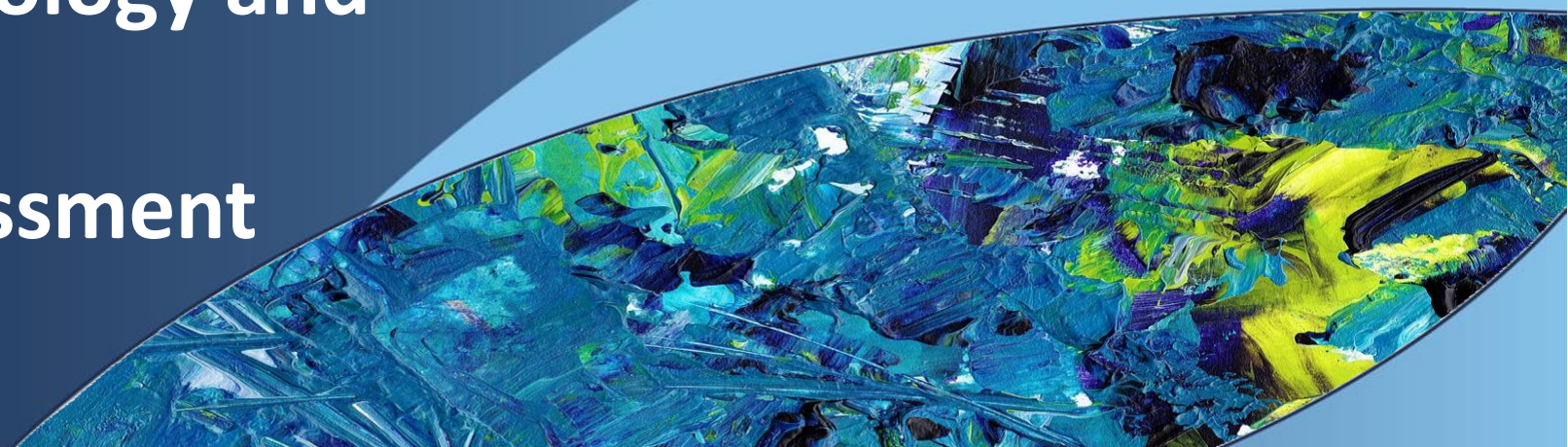
CEHTRA

Science Beyond Regulatory Compliance

Consultancy for Environmental and Human Toxicology and Risk Assessment



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SERVICES REACH

Contact : Paul.Thomas@cehtra.com

Nos services pour l'enregistrement

Compilation des dossiers

- Dossiers Lead Registrant (LR) ou co-registrants
- Stratégies alternatives non-testing pour diminuer les coûts

Administration des dossiers

- Gestion via **consortium** ou LR seul
- Communication au sein des SIEF
- Gestion administrative et financière des LoAs

Mise à jour des dossiers

- Modifications des outils (IUCLID, REACH-IT)
- Retours de l'ECHA
- Augmentation des tonnages
- Nouvelles données

CEHTRA partenaire privilégié des entreprises Européennes

REACH 2018: 330 dossiers LR

Les Natural Complex Substances (NCS): adaptation des critères d'identification avec l'ECHA, QSAR sur les constitutants…

Nos services REACH

Conseil / Analyse

- Analyse des obligations en fonction du statut dans la chaîne d'approvisionnement.

Substances préoccupantes

- Revue du portefeuille substance: analyse substances candidates. Dossiers d'autorisation

Hygiène industrielle

- Audit pour mise en conformité : scenarios d'exposition, conditions strictement contrôlées, CSR

Stratégie

- Design des programmes d'essai combinant les approches réglementaires, scientifiques, financières, voire programme de développement de l'entreprise à l'International (Offre Worldwide)

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NOTIFICATIONS GLOBALES

Contact: aurelie.sevestre@cehtra.com

Nos services

AUSTRALIA
CANADA
CHINA
EU REACH
JAPAN
KOREAN-REACH
NEW-ZEALAND
PHILIPPINES
SWITZERLAND
TAIWAN
TAILAND
TAIWAN
TURKEY
USA

Stratégie de conformité globale

Interprétation des schémas d'enregistrements

Revue en amont de la stratégie à adopter

Respect de la règlementation et des délais

Programme de tests adapté

Prise en compte des spécificités locales

Monitoring des tests en laboratoire

Expertise scientifique

Alternatives aux tests *in vivo*

In vitro/In chemico, analogies, SAR/QSAR…

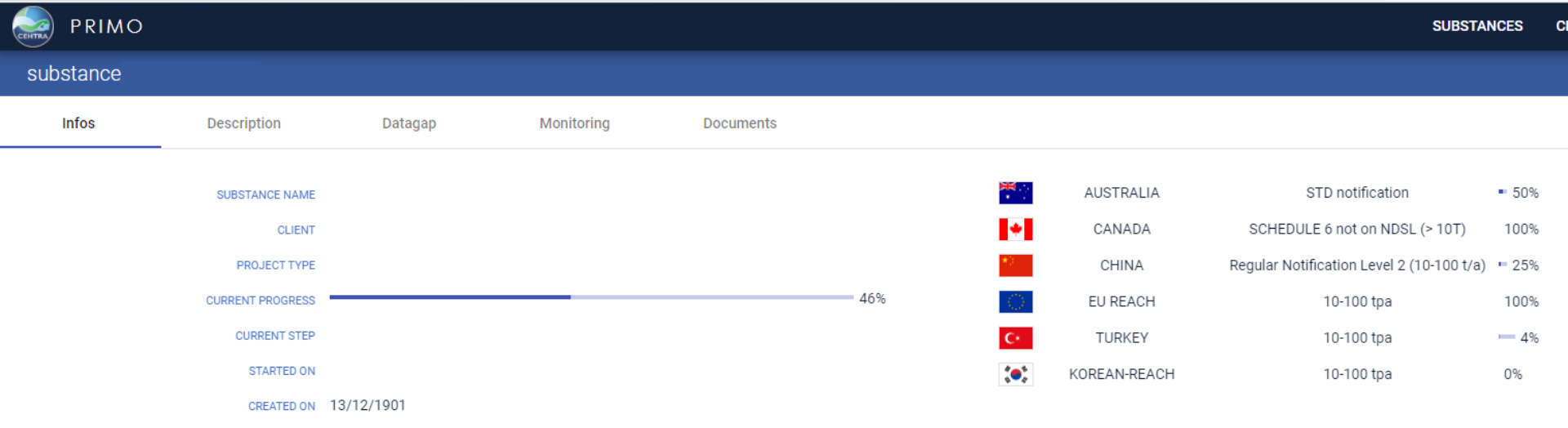
Soumissions

Respect des exigences par pays cible

Communication avec les autorités

PRIMO – Principal Raw Ingredient Management Organiser

- Outils règlementaire innovant
  - ✓ Gestion et suivi de projets plus performants
  - ✓ Accès aux informations du projet en instantané
  - ✓ Interactif – Convivial – Personnalisable



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SERVICES BIOCIDES

Contact : Cyril.Durou@cehtra.com

Biocides
Conseils & Services

- Analyse des données en vue de leur intégration pour les dossiers
  - Recherches bibliographiques, évaluation de la fiabilité et de leur pertinence, (Q)SAR
- Nouveau concept sur les familles de produits: similarité de compositions et des utilisations, niveaux d'efficacité et des risques similaires
  - Accompagnement sur mesure (analyse de vulnérabilités dossiers soumis, affinement des familles à soumettre, formations
- Appels à formations de consortium pour constituer des dossiers d'AMM
  - Gain de temps, optimisation des ressources, partage de la charge et des coûts, limiter la répétition des dossiers

Biocides
Conseils & Services

- Evaluations de risques pour la santé humaine et pour l'environnement
- Evaluations de propriétés perturbation endocriniennes Guidance ECHA/EFSA
  - Ré-évaluation des données (éco)toxicologiques, weight of evidence, intégration de l'ensemble es données disponibles
- Analyse comparative de candidats à la substitution
- Evaluations des co-formulants et criblage des substances préoccupantes
  - Dangers (éco)toxicologiques, évaluation PE

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PLANT PROTECTION PRODUCTS (PPP) SERVICES

Contact : Philippe.Adrian@cehtra.com

Regulation 1107/2009 - Services

- Offre complète de la stratégie de test à la soumission, en passant par le monitoring d'études
  - Design strategies and testing proposals (development of molecules, uses, markets)
  - Technical dossiers (zonal/national) according to regulation (EC) No. 1107/2009 and dRR format
  - Monitoring of studies
  - Modelling of human and environmental exposures
  - Communication with the Authorities
  - Rational for exemption submissions (study waivers)
  - Review of scientific documents
  - Task Force Management
  - Electronic submissions (CADDY)

+ Analyse du potentiel de Perturbation endocrinienne

Regulation 1107/2009 - Experience

- 20+ "**active substance**" dossiers completed (including **plant extracts** and **microorganisms**…)
- 600+ projects on pesticide formulations in Europe
- 25 studies of **field operator exposure** (OPEX)
  - Optimised conditions (Long experience + thorough understanding of the issues + problem solving and use of the study data)
  - Diverse experience (Field, Greenhouses, Seed treatment, Storage stations, Pharmaceutical Plants- Studies of liquid, solid and gases)
- Involvement in EU projects such as OPEX
- Participation in 6 different task forces for EU dossiers, 4 of which as the technical manager

Extensive and renowned experience in Plant Protection Products

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PARFUMS & COSMETIQUES

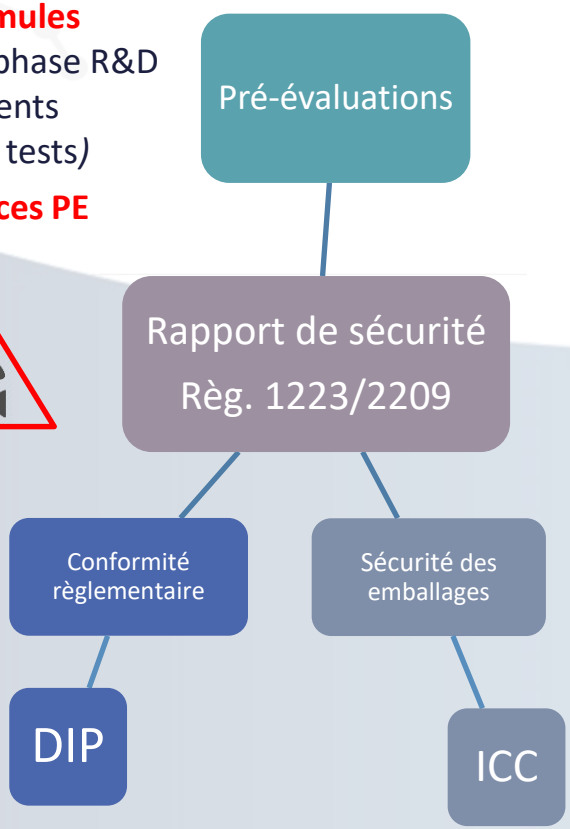
Contact : Clarisse.Bavoux@cehtra.com

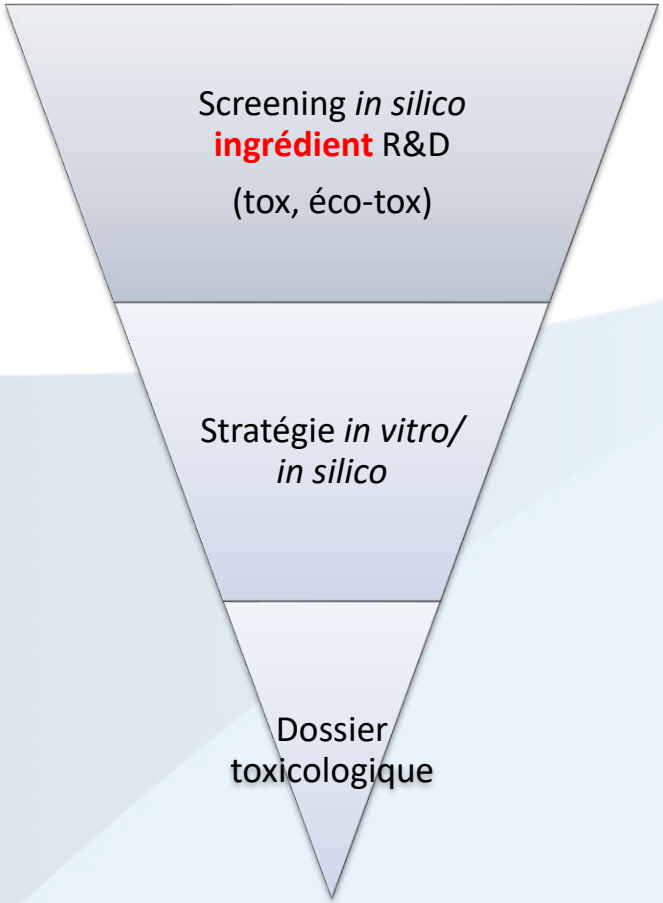
Produits et ingrédients cosmétiques

Pré-évaluations de **formules** cosmétiques lors de la phase R&D (calcul de MOS, ingrédients préoccupants, conseils tests*)*

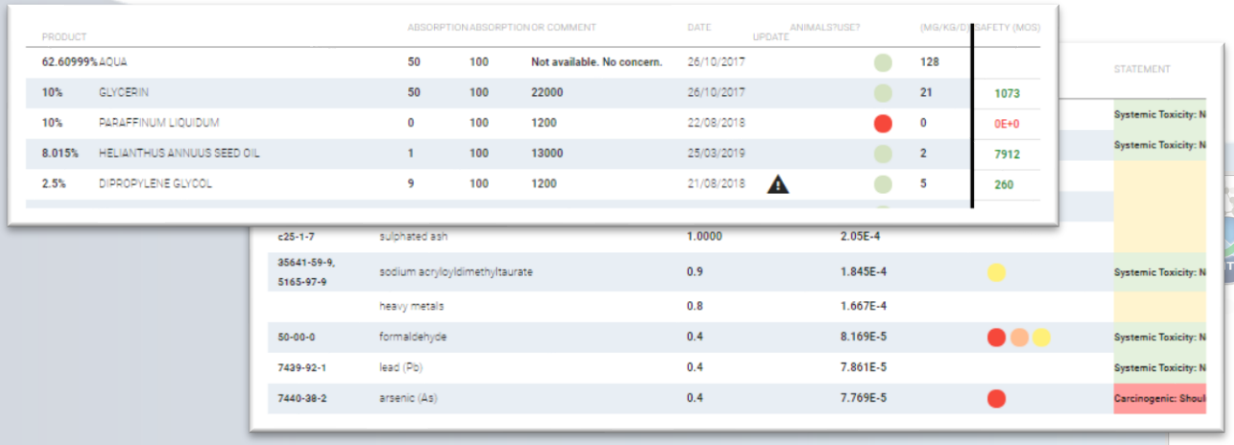
Préoccupation **substances PE**

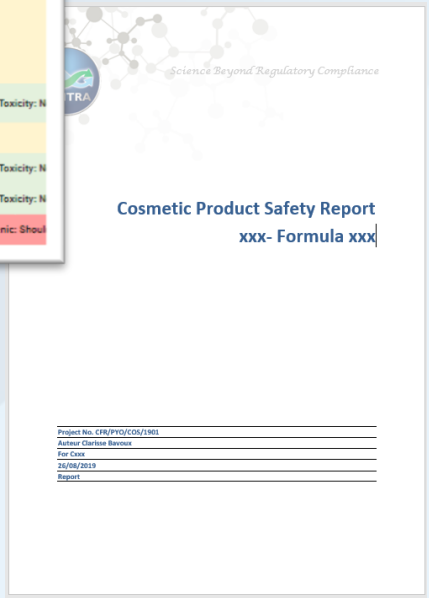
Analyse de l'**impact** des changements toxicologiques et règlementaires





Produits cosmétiques





- Outils de gestion en ligne
  - ✓ Calculs ingrédients, impuretés…
  - ✓ Bases de données multiples, sources exhaustives
  - ✓ Traçabilité des données des rapports de sécurité
  - ✓ Impact immédiat des changements

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FOOD & PACKAGING SERVICES

Contact : francois.renon@cehtra.com

Risk assessment of cosmetic packaging

Regulatory Requirement

– Interactions with Primary packaging

⇒ Our knowledge of food contact materials has permitted to develop a pragmatic approach to the management of ICC:

- **Questions to suppliers of the packaging** (in a precise and detailed form)
- **Analysis and use of calculated data**: worst-case migration scenarios, modelling of migration, use of specific or overall migration test results
- **Database management** using in-house tool to capture the flow of collected information and to generate the risk assessment reports for each packaging and product combination

➥ Our approach is globally in line with the Cosmetics Europe Advisory document "INFORMATION EXCHANGE ON COSMETIC PACKAGING MATERIALS ALONG THE VALUE CHAIN IN THE CONTEXT OF THE EU COSMETICS REGULATION EC 1223/2009" (2019)

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DOSSIERS PHARMACEUTIQUES

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Exposition journalière admissible (PDE)

Selon la Ligne Directrice EMA/CHMP/ CVMP/ SWP/169430/2012:
"Guideline on setting health-based exposure limits for use in risk identification in the manufacture of different medicinal products in shared facilities" Application: à partir du 1er Juin 2015 jusqu'au 1er juin 2016 (vétérinaire)

- **Rédaction de monographie/ dérivation de PDE**

Support HSE & Aide stratégique et opérationnel pré-Clinique

- **Derivation d'OEL/OEB**
- **Audit sur site**
- **Mise en place de RMM adapté à chaque OEB**
- **Classification CLP**
- **Détermination des impuretés et des produits de dégradation**
- **Plan de développement**
- **Mise en place du programme d'étude**
- **Monitoring d'étude**

Environmental risk assessment

- Directive 2004/27/EC amendant la Directive 2001/83/EC :

  → ERA effective depuis décembre 2006

  Une ERA doit accompagner toute demande d'autorisation de mise sur le marché de substance pharmaceutique pour couvrir le point 1.6 du CTD (document technique commun)

Support dossier reglementaire pré-clinique

- **Developpement:** **CTA/IB-IMPD, PIP**
- **Avis scientifique**
- **Réunions pré MAA**
- **Enregistrement:** **CTD, RMP, SmPC pour MAA**

Replacing Experimentation

KREATiS services

iSafeRat® | *In Silico* consulting | Research | Trainings

KREATiS, 23 rue du Creuzat, 38080 L'sle d'abeau, France| Email: contact@kreatis.eu

Visit us at www.kreatis.eu

Company profile

- Based in France (L'Isle d'Abeau - Near Lyon)
- Created in January 2014
- Subsidiary of CEHTRA
- 7 employees

In-silico prediction models ((Q)SARs) for physicochemical, ecotoxicological and human health properties

KREATiS models meet REACH requirements, fulfills the five OECD principles, and are validated according to the Joint Research Centre

KNOWLEDGE & RESEARCH IN ENVIRONMENT AND TOXICOLOGY IN SILICO

4 pillars of our business model

Knowledge & Research in Environment And Toxicology in Silico

Validated High Accuracy QSARs to replace experimentation

iSafeRat ®

In Silico Consulting

Support with off-the-shelf tools for endpoints and chemical domains currently not covered by iSafeRat

International R&D projects, Proposal writing, Publications

Research Projects

Training support

Introduction to QSARs
OECD QSAR Toolbox
Off-the-shelf models

iSafeRat High Accuracy QSAR services

Knowledge & Research in Environment And Toxicology in Silico

Log n-octanol/water partition coefficient

Water Solubility

Vapour Pressure

iSafeRat®

ONLINE | DESKTOP | EXPERT SERVICES

Skin and Eye irritation/corrosion

Skin Sensitisation (beta)

Dermal absorption (beta)

Acute/chronic aquatic toxicity:

Fish, Daphnia, Algae

Toxicity to micro-organisms

Endocrine Disruption

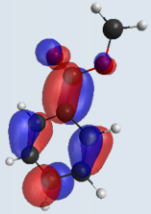
iSafeRat® HA-QSARs

iSafeRat High Accuracy QSAR services

- Aim: to predict « no direct Endocrine Disruptor potential » with high confidence
- Method proposing 3 screening steps:

- Use of traditional MechoA scheme but updated with specific rules to specifically map EDCs

- 3D Molecular Modelling of the substance structure to check if the molecule docks with an endocrine receptor



- Use of off-the-shelf tools (structural alerts e.g. for steroid binding) to strengthen our prediction using a consensus approach

VEGA
QSAR TOOLBOX

iSafeRat® HA-QSARs

Endocrine Disruption

KNOWLEDGE & RESEARCH IN ENVIRONMENT AND TOXICOLOGY IN SILICO

In Silico Consulting

Objective	To address a query that concerns endpoints and chemical domains currently outside the scope of iSafeRat®
Models	Using existing tools from other providers. e.g. OECD QSAR Toolbox, VEGA, Danish QSAR Database, Toxtree, AMBIT etc.
Approach	An endpoint is predicted using multiple models available and a consensus prediction is generated to minimise errors
Reporting	An in silico study report is provided as a supplement with each prediction; IUCLID support

QSAR TOOLBOX

VEGA

iSafeRat® HA-QSARs

Endocrine Disruption

Off-the-shelf tools

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