Reach for the Stars:
An introduction to
NPS REFORM and CHLOFFIN
Eurostars projects

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CHIRON AS: 1983

*Your **quality** is our **business***

PRODUCT SECTORS

Food Safety

Toxicology

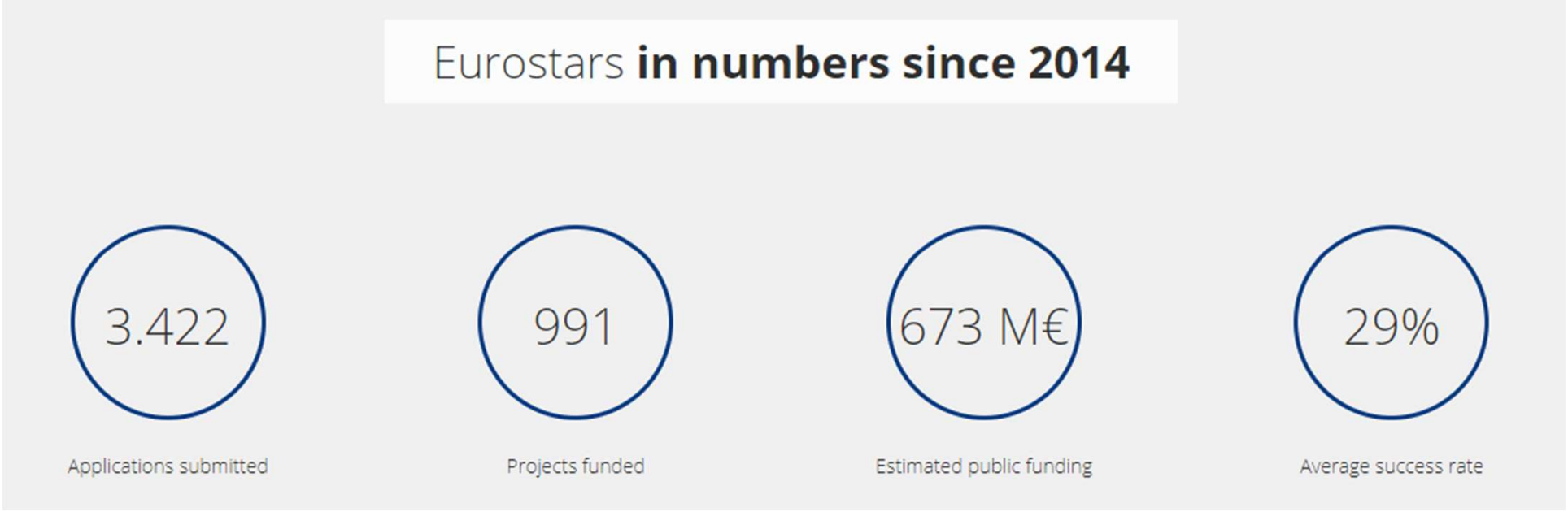
Environment

Petroleum

EUROSTARS

EUROSTARS

- Supporting innovative product development
- Driven by R&D performing SMEs
- Fast track to market
- International Cooperation



Eurostars is backed by €861 million of national funding from its countries. It is further supported by €287 million of EU funds, for a total of €1.14 billion.

Toxicology Related Eurostars Projects

Quantum SPICE (2013-2016)

- Chiron - Nal Von Minden

PSYCHOMICS (2016-2019)

- Chiron - Linköping University (LiU)

NPS-REFORM (2019-2022)

- Chiron - Linköping University (LiU)

NPS-REFORM (2019-2022)

New **P**sychoactive **S**ubstances – **RE**ference Materials for the **FOR**ensic **M**arket

Development of the scale-up and proactive platform for forensic toxicology in the NPS market

Time to completion: 36 months

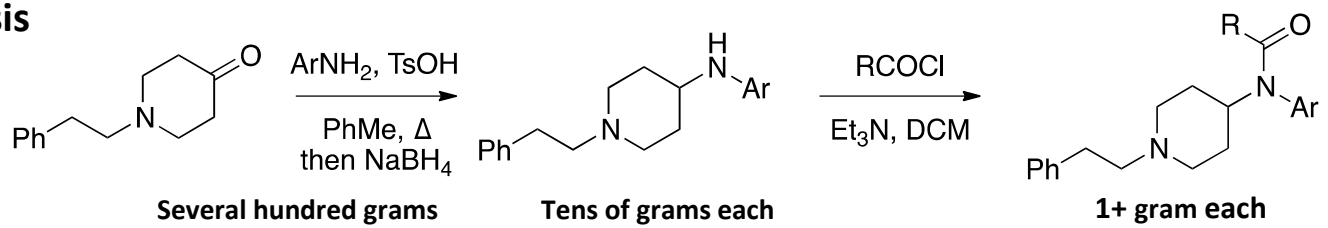
Total funding: 1,346,624 €

Predictive **P**arallel **P**roduction **P**latform

Intermediates

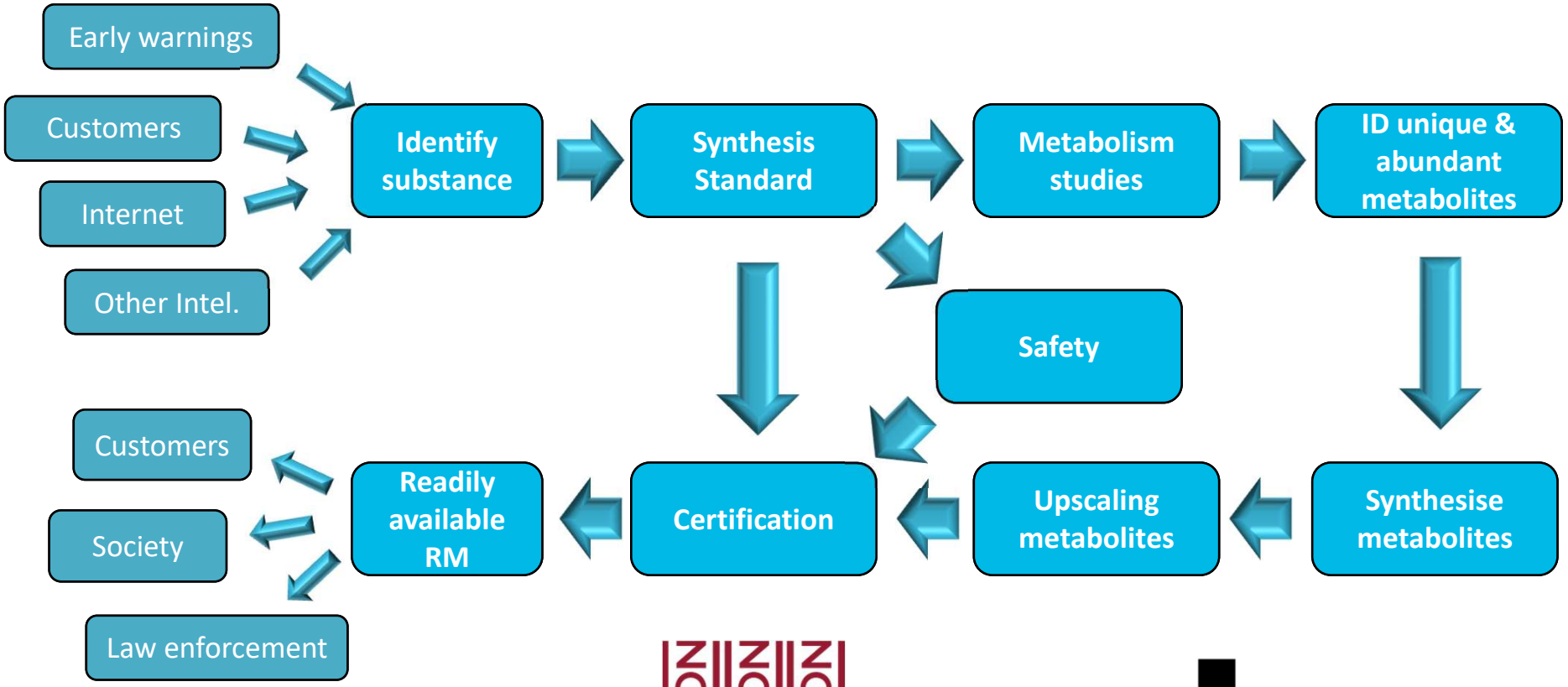
Synthesis
Synthesis
Synthesis
Synthesis
Synthesis
Synthesis
Synthesis
Synthesis

General synthesis cascade of fentanyl derivatives



Several hundred grams **Tens of grams each** **1+ gram each**

NPS REFORM



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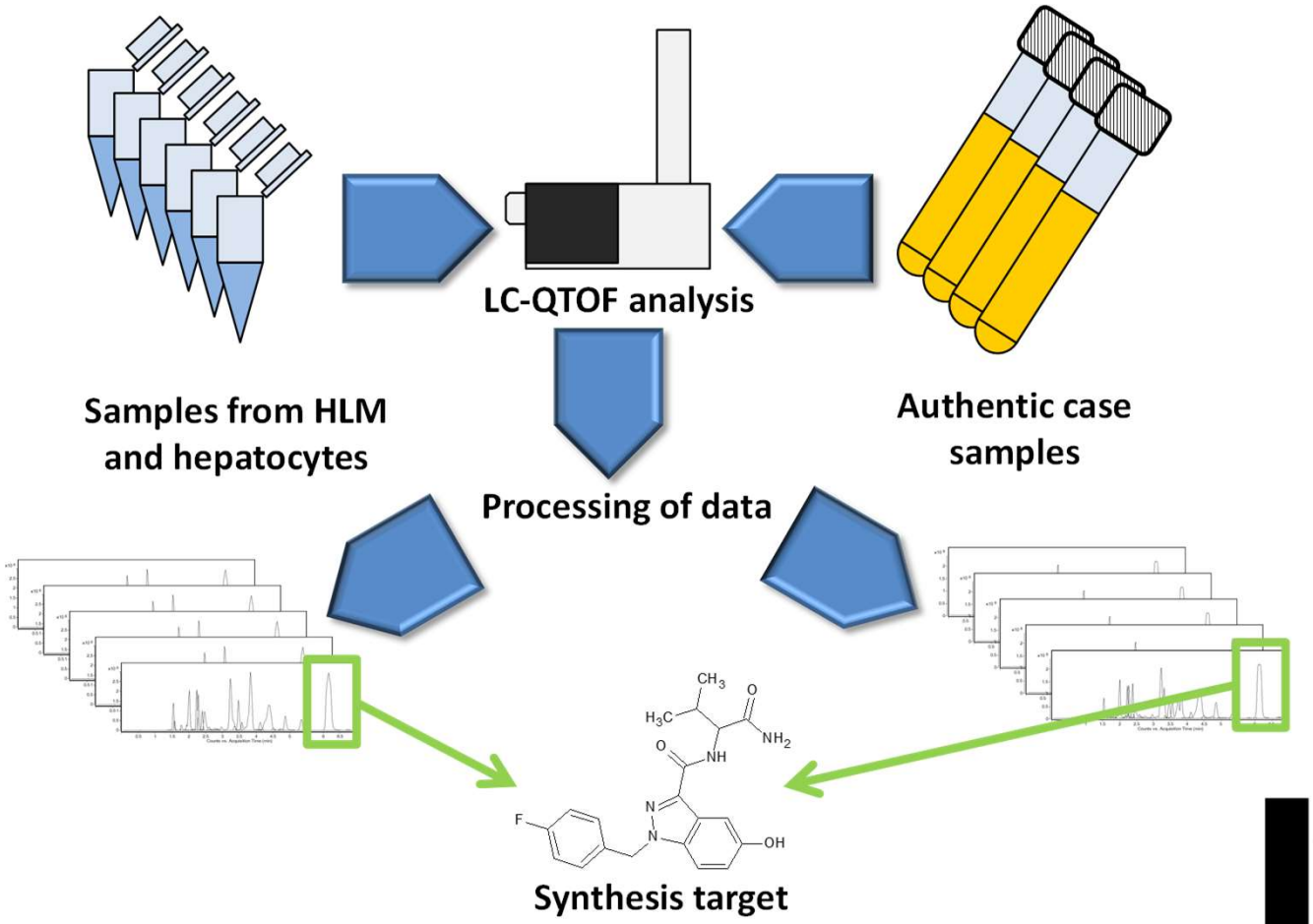
NPS REFORM



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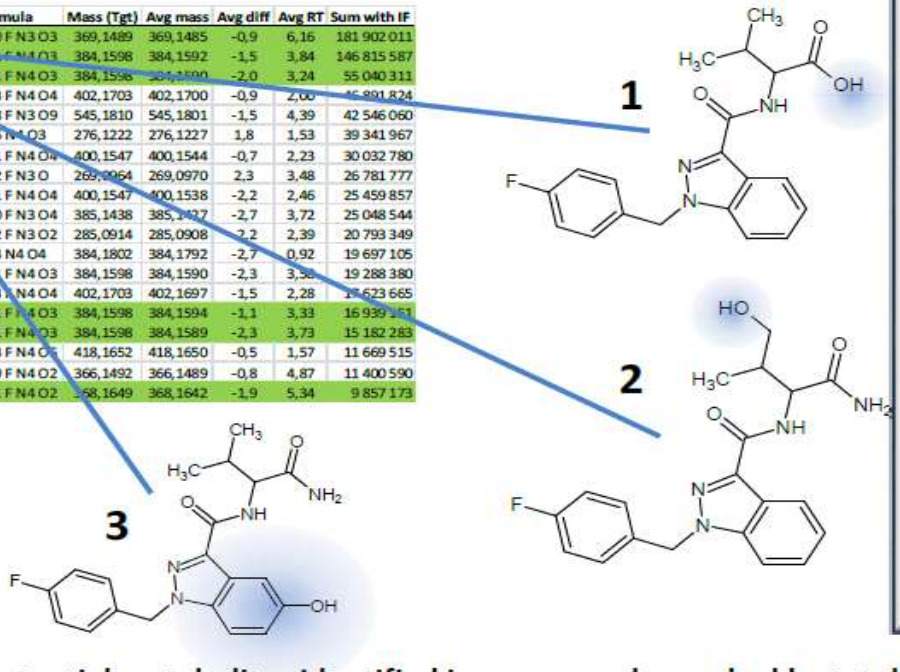
The power of this approach is well illustrated by the example of NPS drug AB-FUBINACA

List of potential metabolites in case samples ranked based on total area

Name	Formula	Mass (Tgt)	Avg mass	Avg diff	Avg RT	Sum with IF
AB-FUB N>O	C20 H20 F N3 O3	369,1489	369,1485	-0,9	6,16	181 902 011
AB-FUB 1 OH	C20 H21 F N4 O3	384,1598	384,1592	-1,5	3,84	146 815 587
AB-FUB 1 OH	C20 H21 F N4 O3	384,1598	384,1590	-2,0	3,24	55 040 311
AB-FUB diol	C20 H23 F N4 O4	402,1703	402,1700	-0,9	2,60	45 891 824
AB-FUB N>O +Glu	C26 H28 F N3 O9	545,1810	545,1801	-1,5	4,39	42 546 060
AB-FUB N-dealk +1 OH	C13 H16 N4 O3	276,1222	276,1227	1,8	1,53	39 341 967
AB-FUB 2 OH	C20 H21 F N4 O4	400,1547	400,1544	-0,7	2,23	30 032 780
AB-FUB N-dealk(#2)	C15 H12 F N3 O	269,0964	269,0970	2,3	3,48	26 781 777
AB-FUB 2 OH	C20 H21 F N4 O4	400,1547	400,1538	-2,2	2,46	25 459 857
AB-FUB N>O +OH	C20 H20 F N3 O4	385,1438	385,1427	-2,7	3,72	25 048 544
AB-FUB N-dealk(#2) +1 OH	C15 H12 F N3 O2	285,0914	285,0908	-2,2	2,39	20 793 349
AB-FUB diol - F	C20 H24 N4 O4	384,1802	384,1792	-2,7	0,92	19 697 105
AB-FUB 1 OH	C20 H21 F N4 O3	384,1598	384,1590	-2,3	3,58	19 288 380
AB-FUB diol	C20 H23 F N4 O4	402,1703	402,1697	-1,5	2,28	17 623 665
AB-FUB 1 OH	C20 H21 F N4 O3	384,1598	384,1594	-1,1	3,33	16 939 251
AB-FUB 1 OH	C20 H21 F N4 O3	384,1598	384,1589	-2,3	3,73	15 182 283
AB-FUB diol + 1 OH	C20 H23 F N4 O5	418,1652	418,1650	-0,5	1,57	11 669 515
AB-FUB 1 DB	C20 H19 F N4 O2	366,1492	366,1489	-0,8	4,87	11 400 590
AB-FUB	C20 H21 F N4 O2	368,1649	368,1642	-1,9	5,34	9 857 173



Metbolites 1 and 2 are good synthesis targets as they are the most abundant metabolites in the case samples, they have been confirmed to be formed from the parent drug by HLM and their structures are clearly defined by their MS/MS spectra. For metabolite 3, four different analogs are possible, making it less suitable as a synthesis target.

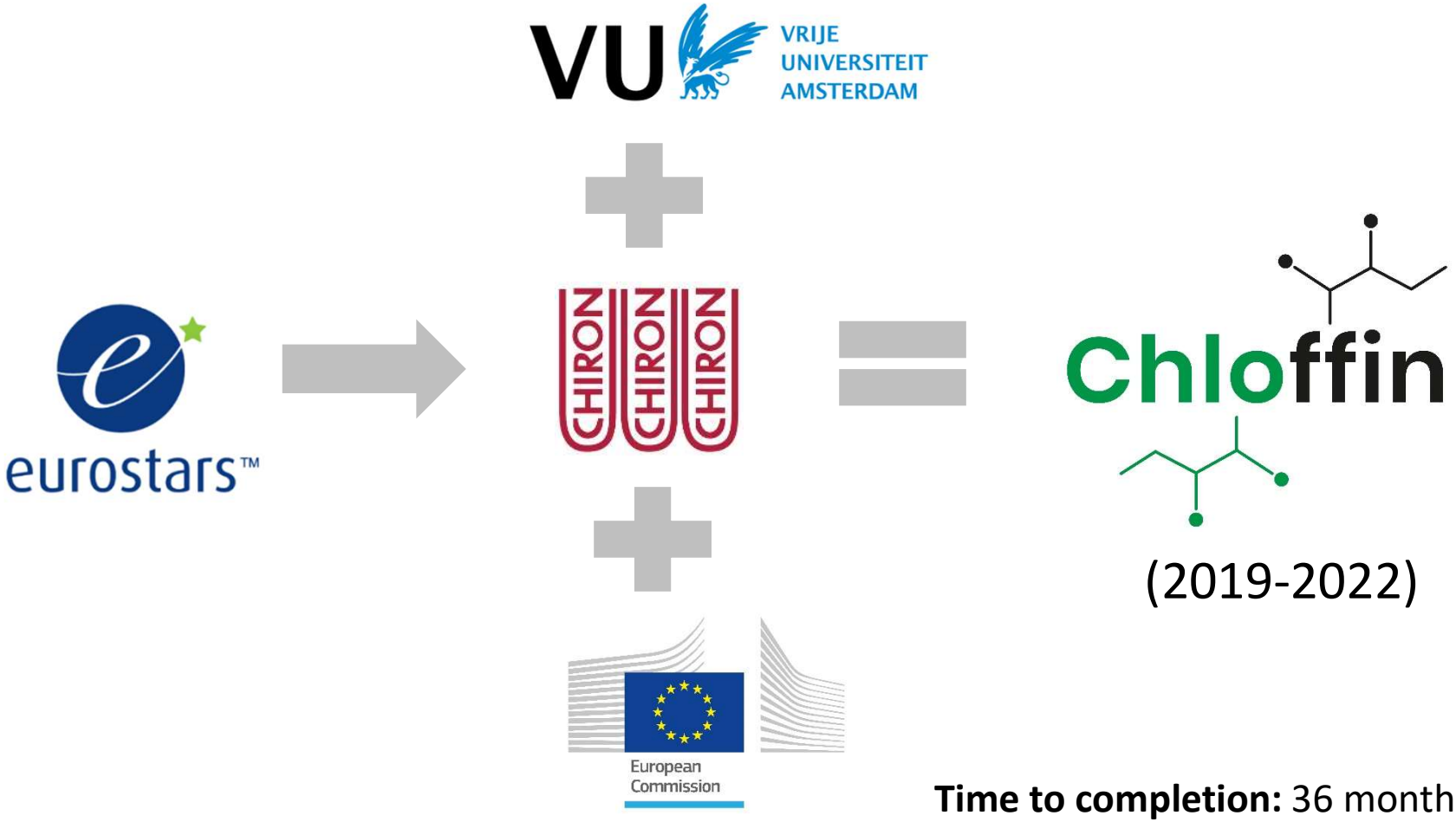
Figure 10: List of potential metabolites identified in case samples ranked by total area.
Green lines are also identified by HLM. Shaded area of structure indicate site of metabolism.

CHLOFFIN – CHLORINATED PARAFFINS (CP)

3rd out of 325 Eurostars proposals
(1st in Norway)

CHLOFFIN – CHLORINATED PARAFFINS (CP)

Development of reference standards for the analysis of chlorinated paraffins (CPs)



(2019-2022)

Time to completion: 36 months
Total cost for all parts: €1,557,462

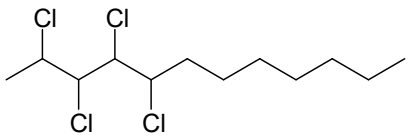
What are they?

Complex mixtures of polychlorinated n-alkanes (PCA)

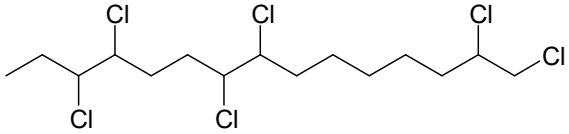
CPs are subdivided according to their carbon chain length:

- Short chain CPs (SCCPs, C10–13)
- Medium chain CPs (MCCPs, C14–17)
- Long chain CPs (LCCPs, C>17)
- Very long chain CPs (vLCCPs, >C21)

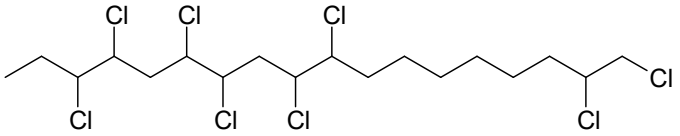
Degree of chlorination CPs can vary between 30 and 70 wt%



SCCP
12425.10
2,3,4,5-Tetrachlorododecane



MCCP
141331.15
3,4,7,8,14,15-Hexachloropentadecane



LCCPs
1470.18
3,4,6,7,9,10,15,17,18-Octachlorooctadecane

Applications

- Extreme pressure additives in metal working fluids (~70%)
- Flame retardants in rubbers (~10%)
- Plasticisers/flame retardants in paints and coatings (~9%)
- Sealants/adhesives (~5%)
- Fat liquoring agents in leather processing (~3%)
- Flame retardants in textiles (~1.5%)

Why are they important?

- Emerging environmental concern
- High volume of production
  (>2 million tonnes per yr)
- Long-range transport
- Persistence in the environment
- Bio-accumulation
- Toxicity (Carcinogenic)

SCCPs were classified as POPs under the UN Stockholm Convention in 2017.

Placed on several monitoring lists, such as the 2000/60/EC Water Framework Directive.

Toxicity and transformation studies on MCCP and LCCP is scarce.

Current challenges

No suitable and generally accepted reference standards are commercially available yet.

Currently available standards differ significantly in chain length and Cl distribution from those seen in technical mixes and the environment.

CP mixtures used today for quantification are not well characterised nor purity assessed.

Only semi-quantitative (sum of SCCP, MCCP and LCCP)

Lack of matrix reference materials.

CHLOFFIN aim

To develop standards with defined composition and response factors, which are similar to industrial mixtures.

These standards will enable accurate quantification of CPs as well as helping in distinguishing the various congener groups according to carbon chain length and chlorine content.

- 40 individual CP standards
- 8 ^{13}C-labelled individual CPs
- 10 congener mixtures
- 1 matrix CRM

So far we have produced 4 standards, which are representative of what is seen in the environment and have defined carbon length and %Cl content.


Watch this Space

Your **quality** is our **business**