

Appendix 1: The formation of the Swetox Consortium

The creation of Swetox has its background in a serendipity of needs meeting a number of possibilities. Calls for more interdisciplinary research related to chemicals, health and environment were fulfilled with the availability of highly competent professionals in pharmaceutical toxicology, as well as of well-equipped laboratory facilities originally used for pharmaceutical toxicology research. This window of opportunity was explored by foresighted actors and strategic thinking among Swedish universities. As a final step, financial support was obtained to promote the creation of something new.

The Swetox Consortium was established as a Swedish academic centre in January 2014. The establishment was preceded by work involving several partners and was initiated in early 2012 by Professor Peter Moldeus (former head of Global Safety Assessment at AstraZeneca) and colleagues after the closure of AstraZeneca's Safety Assessment Laboratory in Södertälje. The early phase involved several stakeholders and was coordinated by the Technical Research Institute of Sweden (SP). Their report focused on the formation of a toxicology institute based on commissioned work. This initiative did not generate sufficient launch funding.

In August 2012, the Swedish Society of Toxicology coordinated the publication of a debate article entitled *Rädda AstraZenecas kunskap och starta toxikologiskt institut*. In November 2012, Governor Chris Heister initiated the formation of a project, which was led by Stockholm County Administrative Board and studied several different organisational and financial alternatives. Professor Harriet Wallberg, former Vice-Chancellor of Karolinska Institutet, led the work of a Reference Group that included official representatives from a number of Swedish universities. This Reference Group gained support from the universities for the Swetox proposal. During the spring of 2013, Vinnova co-financed the planning necessary for the acquisition of the AstraZeneca property in Gärtuna. Acturum Development, co-owned by FAM (Wallenberg Foundation's management company) and Peab, acquired the properties in August, 2013. During the autumn of 2013, Harriet Wallberg and the Reference Group with significant support from Karolinska Institutet presented plans to establish an academic research centre, with an experimental facility in Södertälje. In February 2013, Swetox was formally formed based on a consortium of 11 Swedish universities under the financial and legal administration of Karolinska Institutet. Initial financial support was obtained from the Knut and Alice Wallenberg Foundation, Stockholm County Council, the Research Council Formas and Karolinska Institutet. The Swetox hub moved into the facilities in Gärtuna in March, 2014.

In the following, societal needs related to research and development in *toxicology sciences* are presented in more detail. Development of society places increasing pressure on improved and scientifically based decision-making within the area of chemicals, health and environment. This is true for development of novel chemicals related to life science or industrial use, or for existing and emerging environmental contamination. Hence the situation imposes a challenge on our scientific understanding of chemical hazards and risks posed to humans, wildlife and the environment. This challenge transcends national and economic boundaries and represents one of the most crucial and urgent areas for research, understanding and regulation on the global scale.

Swedish authorities and other governmental institutions have stimulated and implemented scientific research to effect legal and practical change, both nationally and internationally.

One such example comes from the work embodied in the government report (Reducing the risks of hazardous chemicals! Sweden's strategy for a non-toxic environment)¹⁴ which states that Sweden

¹⁴ SOU 2012:38

should take an active lead in issues addressing a non-toxic environment within EU and be a strong driving force for joint European work. The official report motivates the creation of an academic centre to pursue improved risk assessment of chemicals based on their inherent chemical and physicochemical properties together with their toxicological properties. The centre should be able to gather interdisciplinary competence for these assessments. In a further official report (SOU 2012:38) Consideration statement from the Swedish Chemicals Agency¹⁵, the considerable need for new knowledge and an appropriate risk assessment body related to manmade chemicals to be assessed under REACH is clearly indicated.

One area of current societal concern that illustrates the urgency embodied in these national reports, is the area of endocrine-disrupting chemicals (EDCs), where both the EU and UNEP/WHO have recently published reports calling for more team science, i.e. interdisciplinary cooperation in *toxicology sciences*. Since September 2012, EDCs have been declared an Emerging Policy Issue under SAICM (UN), with a call for global management which will require improved test methods, new testing strategies and novel exposure analyses. A decision made by the European Parliament in March 2013 clearly stresses the need for EDC regulation, based on both existing and emerging scientific data.

Another area of concern is the safety of nanomaterials, which are used increasingly in various consumer products. Humans and wildlife exposure rates are rising, which causes concern since our knowledge of the effects of these materials on health and environment is limited. Nanomaterials pose a number of challenges in terms of risk assessment and the EU has directed major investments into the area of nanosafety research. In Sweden, a recent government report entitled *National action plan for the safe use and management of nanomaterials*¹⁶ pointed to several weaknesses in national efforts within the field, and suggested several steps which must be taken in order to improve coordination of Swedish research in the area.

Pharmaceutical safety assessment has strong roots in *toxicology sciences* in Sweden via pharmaceutical companies such as AstraZeneca and Pharmacia. This has benefited education in toxicology as well as academic drug development. The closure of AstraZeneca's safety assessment facility in Södertälje has caused a decrease of activity within regulatory toxicology of pharmaceuticals. It is vital to retain this competence in Sweden for the benefit of academic drug development and the development of the private life science sector.

The field of risk assessment may be considered as a translational research area. Technological, computational and regulatory developments create the opportunity for greater mechanistic understanding of toxicological effects and implementation of mechanism-based data in regulatory risk assessment of chemicals. Closely linked to new approaches in risk assessment is a strong international drive for development of alternative methods to animal research. There is a gap between research innovations and implementation into guidelines for safety assessments, and also a gap between updated guidelines and practical use of validated alternative methods.

¹⁵ 12-10-01, Dnr 340-H12-01249

¹⁶ SOU 2013:70

Appendix 2: Definitions and abbreviations

Definitions

Anthropogenic chemicals include all man-made chemicals, refined natural products and novel chemicals under development for medical, pesticidal or industrial uses. The word may also refer to transformation products and metabolites.

Chemicals, health and environment refers to all aspects of chemicals of societal impact or concern, including their transformation products, that impact on human health and environment.

Interdisciplinary research is defined as cooperation between two or more academic disciplines, within and/or across faculties, in a holistic perspective on chemicals, health and environment.

Research pillar is a particular area of expertise and instrumentation within the Swetox Consortium.

Swetox is a national resource and an academic centre for research, education and societal interaction related to chemicals, health and environment. Swetox is a consortium of eleven Swedish universities, i.e. University of Gothenburg, Karlstad University, Karolinska Institutet, Royal Institute of Technology, Linköping University, Lund University, Swedish University of Agricultural Sciences, Stockholm University, Umeå University, Uppsala University and Örebro University.

Swetox Södertälje or the Swetox hub is a research facility located in Södertälje that administratively belongs to Karolinska Institutet. It coordinates activities within Swetox.

Toxicology is defined as the scientific discipline involving the study of the actual or potential danger presented by the harmful effects of substances on living organisms and ecosystems, of the relationship of such harmful effects to exposure, and of the mechanisms of action, diagnosis, prevention and treatment of intoxications. (IUPAC, National Library of Medicine, US).

Toxicology sciences is defined as all scientific disciplines addressing and contributing research and higher academic educational inputs related to chemicals, health and environment. *Toxicology sciences* thus spans many research areas from analytical chemistry, material science, molecular biology, basic biology and ecology, ecotoxicology, epidemiology and human toxicology, environmental law and economics and political science.

Abbreviations

3C - Communication, Contacts and Collaborations

3M - Mechanisms, Models and Markers

3R - Replacement, Reduction and Refinement in animal research

AED - adsorption energy distribution

AOP - adverse outcome pathway

BBMRI - Biobanking and Molecular Resource Infrastructure of Sweden

CT - Computed Tomography

EDC – Endocrine disrupting chemicals

EGO - Ecotoxicology – from Gene to Ocean

ESS - European Spallation Source

ELISA - enzyme-linked immunosorbent assay

ELN - Electronic Notebook

EPA - Environmental Protection Agency

EU - European Union

EURL-ECVAM - European Union Reference Laboratory for Alternatives to Animal Testing

FAM - Wallenbergstiftelsernas förvaltningsbolag

FELASA - the Federation of Laboratory Animal Science Associations

FOI - Swedish Defence Research Agency

FORMAS – The Swedish Research Council Formas (Forskningsrådet för miljö, areella näringar och samhällsbyggande)

FTE - full time employee

GLP - good laboratory practise

GMO - gene-modified organisms

GU - University of Gothenburg

HCS - high content screening

IMI SAFE-T - Innovative Medicines Initiative; Safer and Faster Evidence-based Translation

IMM – Institute of Environmental Medicine

IMS - imaging mass spectrometry

IPSC - International Program on Chemical Safety

KaU - Karlstad University

KE - key event

KI - Karolinska Institutet

KTH - Royal Institute of Technology

LC-MS/MS - liquid chromatography-tandem mass spectrometry

LiU - Linköping University

LU - Lund University

MIE - molecular Initiating Event

MOA - mode of action

MSSM - Milan and Mount Sinai School of Medicine

NGO - non-governmental organisation

NMR - nuclear magnetic resonance

OECD - Organisation for Economic Co-operation and Development

PET - positron emission tomography

PFOA - perfluorooctanoic acid

PFOS - perfluorooctanesulfonic acid

PhD – doctor of philosophy

PI - principal investigator

POP - persistent organic pollutant

QTOF - quadrupole-time-of-flight

REACH - Registration, Evaluation, Authorisation and Restriction of Chemicals

RT-qPCR - reverse transcription quantitative polymerase chain reaction

SAB - Science Advisory Board

SAICM - Strategic Approach to International Chemicals Management

SciLifeLab - Science for Life Laboratory

SLU - Swedish University of Agricultural Sciences

SOP - standard operation procedures

SP - Technical Research Institute of Sweden

SPECT - Single-photon emission computed tomography

SU - Stockholm University

Swedac - Swedish Board for Accreditation and Conformity Assessment

Swetox - Swedish toxicology sciences research center

UNEP - United Nations Environment Program

UmU - Umeå University

UU - Uppsala University

WHO - World Health Organisation

ÖrU - Örebro University

Appendix 3: International scientific advisory board

Ensuring the delivery of high-impact and cutting-edge science will be a vital component of the overarching impact of the Swetox Consortium. It is therefore essential that Swetox develops an external advisory body as a guarantor for necessary developments.

A Science Advisory Board (SAB) containing 4-5 internationally-recognized experts will be appointed whose function will be characterized as follows:

- The SAB will advise on overarching aspects such as Swetox organization, internal scientific work and external scientific developments.
- The SAB is also expected to interact with any advisory bodies operating within specific projects.
- Formal appraisal of Swetox for official reviews will not be within the mandate of the SAB.
- The activities of the SAB will be governed by the board of Swetox, via an annual meeting of all partners.
- The SAB is expected to interact on a frequent, ad hoc basis with Swetox operative leadership.

Names of several national and international experts are currently under collection. An agreed remuneration will be provided for SAB members as well as all expenses for travel and accommodation during meetings.

Pending acceptance by the individuals in question, an initial meeting is planned for end October 2015.

Appendix 4: National Reference Group

The propagation of knowledge outside academia is of great importance when working towards a chemically safe world. Similarly, mutual communication between science and policy is a prerequisite for set up of projects and for societal decision making of relevance and high quality. The Swetox Consortium requires a forum for discussion of important societal aspects of chemicals, health and environment. National stakeholders external to academia include industrial and other commercial companies, state, regional and local authorities and non-governmental organisations (NGOs). It is in-line with contemporary practice that academic research projects in the area of chemicals, health and the environment align themselves with a defined reference group consisting of a small group of qualified individuals working to optimize communication primarily between national authorities and the research underway.

Swetox requirements

The Swetox Consortium requires close contact with societal organisations outside academia in order to effectively detect and react to developments in the life sciences as well as to identify the needs of Swedish decision-makers dealing with risk assessment of chemicals in relation to health and environment. Conversely, stakeholders should also strive to remain informed of the research and educational activities within Swetox for incorporation into various national, regional and local authority activities, industrial and commercial practices and the activities of NGOs. Swetox is therefore best served by establishment of one or more contact interfaces with society.

Proposal

Swetox aims to form an open, broad reference group for information exchange once a year through an invitation to authorities at national, regional and local levels, the private sector and NGOs. The members of the reference group are charged with the communication of their constructive comments and advice on the output generated by Swetox. Exchange of information between the reference group and the Swetox Consortium will occur on an annual basis on a mutually selected day (perhaps linked to the annual Swetox conference in December).

Since Swetox has five prioritised areas of research (EDCs, emerging chemicals, nanosafety, pharmatox and environment, and risk assessment) a focus of these areas is of particular interest. Consequently it is particularly important to create close contacts between stakeholders working/active in these areas. It may therefore be of interest to look into the possibilities of creating Stakeholder Expert Reference Subgroups. Such groups are charged with delivering and raising new issues and challenges related to their own opinions and needs. Exchange of information between the reference group and the Swetox Consortium will occur on an annual basis on a mutually selected day (perhaps linked to the annual Swetox conference in December).

Appendix 5: Budget 2015-2017

The budget for the Swetox Consortium 2015 to 2017 is summarised in the table below. In the initial phase activities and costs are concentrated to Swetox Södertälje.

SEK thousand	2015	2016	2017
REVENUES			
Appropriations	0	0	0
Fees and other remunerations	0	0	0
Grants	31 281	30 977	15 155
Internal funding (KI)	11 179	10 381	10 000
TOTAL REVENUE	42 460	41 358	25 155
COSTS			
<i>Direct costs</i>			
Personnel costs	16 636	17 252	17 274
Operating costs	7 177	7 101	7 278
Depreciation	1 209	1 509	1 500
Premises costs	5 692	5 700	5 843
<i>Indirect costs</i>	8 335	8 524	8 593
TOTAL COSTS	39 050	40 086	40 487
TRANSFERRED AMOUNTS	3 410	4 759	4 878
NET CHANGE IN CAPITAL	0	-3 487	-20 211

Appendix 6: Policy for commissioned research at Swetox Södertälje

Swetox Södertälje may conduct commissioned research and is engaged in external collaborations to deliver societal benefits of its research in *toxicology sciences*.

The overarching aims for commissioned research and external collaboration are:

- To be identified by stakeholders (private and official partners) as a competent academic resource for joint scientific projects relating to chemicals, health, and environment.
- To improve knowledge and science-based decisions on problems of importance for society, nationally, in EU as well as globally.
- To collaborate with companies, institutes or other partners outside academia to develop novel technology and methods on the frontline of *toxicology sciences*.
- To make strategic use of existing resources within the Swetox hub to maintain and develop necessary experimental infrastructure and skills.

Financial basis

All commissioned research at Swetox Södertälje requires full cost coverage. In addition to direct expenses, remuneration must be claimed for maintenance and development of instrumentation and skills.

Swetox Södertälje may contribute resources in kind to research collaborations when the counterpart provides similar resources/knowledge. This to be regulated by agreement and be consistent with Swetox activities and strategic areas.

Pricing of commissioned research should take into account the prevailing market price. It is important to ensure that governmental grants and subsidies do not cause price dumping and competitive advantage.

IP - Intellectual Property

The results from research collaboration/commissions should become publicly available and should maintain such a level of scientific quality as to allow publication in peer-reviewed scientific journals. In cases where research generates knowledge that justifies an academic or commercial competitive advantage, publication may be delayed but no longer than 2 years, so that patents can become effective or a commercial window be exploited. Swetox Södertälje should always retain the rights to utilise IP in their own operations including partners under confidentiality agreements. If the IP generated is in accordance with the exemption for teachers (Swedish law) Swetox should promote commercialization.

Appendix 7: Current research projects

A record of all incoming (research applications and research commissions) and ongoing projects is kept on file at Swetox Södertälje. In the table below, ongoing research projects as of February 2015 are presented and in the following abstracts of major projects have been included.

Title	Area	Description and current activities	Funding	Type of research project	Principal Investigator (Contribution)	Start	End
EDC-2020	EDC	Research program on endocrine disruptors in the areas of mechanisms and models, bioanalysis, toxicokinetics, respiratory exposure and science to policy. Three research fellows have been recruited (Joëlle Rügge, Paulina Damdimopoulou and Annette Kraus) and projects have been initiated. Recruitment ongoing for toxicokinetics, respiratory exposure and science to policy.	Formas	Internal	Åke Bergman	Dec 2013	Nov 2018 With prolongation, mid 2019
Toxicology Sciences	3M	Research funds for two projects within toxicology sciences. Two research fellows have been recruited - Vesna Munic Kos (Oct 2014) and Ernesto Alfaro-Moreno (Jan 2015) and projects have been initiated.	KI	Internal	Åke Bergman	Oct 2014	Dec 2018
Helleday	Pharma	Scientific collaboration with Helleday Lab at SciLifeLab supporting ongoing drug development with toxicology strategy and preclinical studies on candidate drugs. Continuous support on toxicology-related issues and study design. In silico studies performed, immunotoxicology studies started, in vivo studies performed at St Görans ögonsjukhus.	SCC	Collaboration	Björn Platzack	Mar 2014	open ended
Alternative plasticizers	EDC	Review of safety data on alternative plasticizers that are used in medical devices. Gap-analysis and suggestion of further research on alternative plasticizers.	SCC	Commission	Heike Hellmold	Jan 2014	Aug 2015
EDC-MixRisk	EDC	Research program for improved decision making regarding human exposure risks to mixtures of anthropogenic chemicals over the entire life span. The project will determine and assess the risk for multiple adverse health outcomes based on molecular mechanisms involved, after early life exposure to complex mixtures of endocrine-disrupting chemicals.	EU	Collaboration	Åke Bergman	May 2015	Apr 2019
Peptonic	Pharma	Toxicology support to pharmaceutical company prior to marketing approval. The aim is to use in silico, in vitro and human ex vivo studies to produce convincing data and scientific rationale for risk assessment of carcinogenic potential.	Peptonic	Commission	Ian Cotgreave & Johan Lindberg	Dec 2014	Dec 2017

Title	Area	Description and current activities	Funding	Type of research project	Principal (Contribution)	Start	End
SAFE-T	3M	Contribution to the SAFE-T consortium that aims at qualifying translational safety biomarkers for drug-induced kidney, liver and vascular injury to enable potential new medicines to be evaluated more quickly and safely in patients. Analysis of bile acids in human samples. Analyses have started.	SAFE-T	Commission	Johan Lindberg	Dec 2014	May 2015
Gene array data analysis	3R, 3M	Multivariate data analysis of gene array data from C17.2 neural progenitor cell differentiation	Internal	Collaboration with SU	Anna Forsby	Dec 2014	Feb 2015
MIAA	3M	Collaboration with Sven-Erik Dahlén and Johan Kolmert in the MIAA (Methyl Imidazole Acetic Acid) project. Analysis of histamine metabolites. Analysis started and partly performed by Johan Kolmert	Joint	Collaboration	Johan Lindberg	Oct 2014	Mar 2015
Refinement in toxicity studies	3R	Evaluation of animal welfare using different types of animal housing in connection with start-up of animal facilities at Swetox Södertälje. Collaboration with SLU.	KI	Collaboration	Elin Törnqvist	Nov 2014	Jun 2015

EDC-2020

This research focus is on endocrine-disrupter chemicals (EDC-2020) based on 3R (Replace, Reduce, Refine; referring to animal use in research) and 3M (Mechanisms, Markers, Models; a mode-of-action approach to toxicology and risk assessment). Research aims to include all relevant scientific areas defined under *toxicology-related sciences*, organized under five spokes.

EDC 2020 is focused on: i) creating an enabling environment for strong research on EDCs and for scientific advances and innovations which will benefit the field of toxicologically-related sciences as a whole; ii) establishing an overarching national program for research on EDCs, optimizing cooperation between national universities and the Swetox Research Centre, and improving interdisciplinary research; iii) establishing an international EDC collaboration platform including leading world experts, and iv) establishing a national research school on toxicology-related sciences.

EDC-MixRisk

The long-reaching goal of EDC-MixRisk is to move forward and meet societal needs for improved decision-making regarding human exposure risks to mixtures of anthropogenic chemicals over the entire life span. Hence the project will determine and assess the risk of multiple adverse health outcomes based on the molecular mechanisms involved, after early life exposure to complex mixtures of endocrine-disrupting chemicals (EDCs). To enable us to address such a complex research task, the project relies on interaction between advanced expertise in epidemiology, toxicology and risk assessment i.e. toxicology sciences. The value of these combined research efforts include:

- Identification of mixtures of EDCs that are associated with multiple adverse health outcomes in three health domains (growth and metabolism, neurodevelopment and sexual development)

in two epidemiological pregnancy cohort studies by use of novel and advanced bio-statistical methods.

- Identification of molecular mechanisms and pathways underlying the associations between exposure to EDC mixtures and adverse health outcomes by the use of experimental animal and cell models.
- Development of a transparent, consistent and systematic (TCS) framework in risk assessment – sometimes referred to as a weight of evidence approach 2 - for integrating epidemiological and experimental research to facilitate risk assessment for EDCs and mixtures.

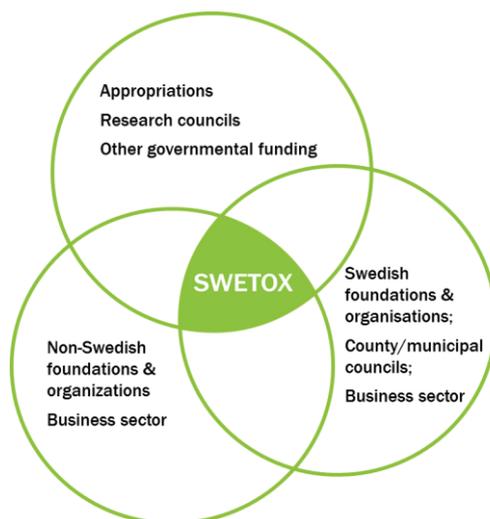
Participating organisations are Swetox*/Karolinska Institutet (KI), Swetox*/Karlstad University, Swetox*/Gothenburg University, Swetox*/Lund University, Swetox*/Stockholm, Swetox*/Uppsala University, Muséum National d'Histoire Naturelle, Paris, Clinic for Children and Adolescents, University Hospital Leipzig, School of Health Sciences, University of Athens, National Institute for Health and Welfare, Helsinki, the European Institute of Oncology, Milan and Mount Sinai School of Medicine (MSSM), New York.

Peptonic

Peptonic Medical (publ) is a company developing pharmaceuticals based on oxytocin. Peptonic and Swetox Södertälje have entered into a collaboration with the objective of studying and describing the mechanisms whereby oxytocin exerts its growth stimulating effects on vaginal mucosal cells through topical administration. The project is a collaboration between the parties where Swetox contributes its expertise in toxicology and Peptonic contributes its profound knowledge of oxytocin. Coordinator at Swetox is Ian Cotgreave and at Peptonic Medical Kerstin Uvnäs Moberg. The results of this collaboration will provide valuable insights into how oxytocin promotes positive effects in the treatment of e.g. vaginal atrophy, that have been seen in clinical studies with Peptonic Medical's product candidate Vagitocin®.

Appendix 8: Project prioritization and balancing

Swetox Södertälje, the hub of Swetox, is an academic centre which is supported financially through governmental, non-governmental and international (e.g. EU) funding of projects as visualised in the figure below. The funding is divided into free academic research, commissioned research and higher academic education projects. A first and fundamental prerequisite for any project is that it meets our vision of *A chemical safe world*. Prioritised projects also need to meet the overarching objectives of Swetox (cf. Swetox Strategic Plan, Swetox Södertälje Operational Plan and the text below).



The project portfolio must be balanced between the three major areas: academic research, commissioned research and higher academic education projects.

The aim of this document is to outline a tool for prioritisation and balancing of new potential projects for Swetox Södertälje. The design of the tool for project prioritisation includes:

- 1) A set of criteria for prioritisation (further elaborated on below).
- 2) Estimated resources for preparation and implementation.
- 3) Estimated probability of success of funding.
- 4) Area of research.

Project prioritisation

Relevant overarching Swetox objectives must be fulfilled by a new project in order to enter the prioritisation process. The relevant objectives are presented under *Prioritisation criteria* below.

Prioritisation criteria

Degree of alignment with Swetox objectives (Weight: 25%, Fit parameter: 0-5):

This criterion defines how well the proposal is related to the overarching Swetox objectives. It includes an assessment on how well the project proposal meets these objectives (Table 1).

Table 1. Degree of alignment with Swetox objectives

Objective	Description	Questions	Alignment YES/NO
To strengthen research on chemicals, health and environment	Swetox will be established as a national resource for academic interdisciplinary cooperation within toxicology sciences. Swetox will seek both novel interpretations of existing scientific data and generation of new scientific data, which find application in both human and environmental risk assessments.	1. Is the research within chemicals, health and environment?	
To improve knowledge on anthropogenic chemicals of concern	Swetox will focus efforts on endocrine disrupting chemicals/effects, nanosafety and on the toxicology of pharmaceuticals and their environmental effects. In addition, Swetox will be prepared to engage in the area of emerging chemicals and their effects in response to scientific and societal concern.	2. Is the research on safety of EDC, nanomaterial or pharmaceuticals?	
		3. Is the research on an emerging chemical of societal or scientific concern?	
To improve contacts between disciplines and scientists (networking)	Swetox will aim at catalysing interactions between all relevant disciplines to "meet the needs of society", via the establishment of networks of existing academic groups in Sweden, in or outside Swetox, and abroad.	4. Is the research interdisciplinary between two or more academic disciplines, within and/or across faculties, in or outside Swetox or abroad, on chemicals, health and environment.	
To contribute to increased use of alternative methods according to the 3Rs in toxicology sciences for use in research and regulatory safety assessments	Swetox will be a national force when it comes to 3R awareness, 3R research and 3R education, and aims at building 3R networks and collaborations that include academia, industry, authorities and NGOs.	5. Does the project concern 3R research or education?	
		6. Does the project increase 3R awareness or networking across academia, industry, authorities or NGOs?	
To develop and optimize academic education in toxicology sciences	Swetox will, through collaboration and coordination, stimulate the development of Swedish education in <i>toxicology sciences</i> , based on state-of-the-art science as well as on educational and societal needs.	7. Does the project develop or optimize education within chemicals, health and environment?	
To better contribute to the societal decision-making processes	Swetox will contribute via directed research efforts in various strategic areas, and by fostering a more direct dialogue between academic groups and authorities, thereby catalysing the implementation of both existing and emerging scientific data in societal decision making at various levels. Swetox will also contribute with science-based data and assessments to intergovernmental organisations and international authorities, nongovernmental organisations and the private sector and thereby contribute to bridging the gap between science and policy.	8. Will the projects contribute with science based data and assessments to intergovernmental organisations, international authorities, nongovernmental organisations or the private sector?	
		9. Does the project increase the dialogue and knowledge transfer between research and policy?	
To use available financial and human resources in an optimized manner	Swetox will facilitate the current injection of national investment in infrastructure and projects and seek better coordination and synergy in the utilization of existing skills, infrastructure and experience within the eleven universities linked in the organisation. Swetox also aims to contribute to the development of fora (centres) related to its current prioritised activities in nanosafety and the 3Rs, but also for computational risk assessment and pharmaceuticals and the environment.	10. Does the project lead to increased utilisation of existing skills or instrumentation within the Swetox consortium?	
To become highly competitive for large grants	Swetox will provide greater opportunities for Swedish academic groups to join together in applying for national and international program grants, particularly through EU funding.	11. Does the project increase the probability of funding from EU or other international large funds?	

Number of YES

0

1-2

3-4

5-6

7-8

9-10

Rating

0

1

2

3

4

5

Degree of estimated impact on society (Weight: 20%, Fit parameter: 0-5):

In order to meet the vision *A chemical safe world*, all Swetox/Swetox Södertälje projects must exert societal impact. Issues such as stakeholder involvement, national impact, international impact and scientific strength are to be raised in order to assess the degree of estimated impact on society, as requested in Table 2.

Table 2. Degree of estimated impact on society

Questions	YES/NO	Sum of YES	Rating
Is the project linked to a stakeholder?		0	0
Private business?		1-2	1
Authority?		3-4	2
NGO?		5-6	3
Other?		7-10	4
Is the project initiated by a stakeholder?		11-14	5
Private business?			
Authority?			
NGO?			
Other?			
Does the project include a stakeholder reference group?			
Does the project involve Swedish stakeholders?			
Does the project involve EU stakeholders?			
Does the project involve intergovernmental stakeholders?			
Is the project related to potential regulatory measures?			
Is the project related to life science activities?			

Prioritized research areas (Weight: 25%, Fit parameter: 5 if Swetox focus areas, 0 if not):

Swetox focus areas of research are endocrine-disrupting chemicals (EDCs), nanosafety (Nano), pharmaceutical toxicology and environment (Pharma), emerging chemicals (Emerging) and risk assessment. If the project proposal addresses any of these areas, the fit parameter is 5, if it covers any other area the fit parameter is 0. Assessed as described in Table 3.

Table 3. Prioritized research areas

	Rating
If prioritised research area	5
If outside prioritised research area	0

Annual funding amount (Weight: 5%, Fit parameter: 1-5):

The expected annual project funding is assessed. The fit parameters are dependent on funding amount as presented in Table 4.

Table 4. Annual funding amount.

Funding	Rating
MSEK<1.0	1
MSEK 1-2	2
MSEK 2-3	3
MSEK 3-4	4
MSEK >4	5

Funding duration (Weight: 5%, Fit parameter: 1-5):

The funding duration stretches from 1 year or less to 5 years or more with the fit parameters 1-5, respectively (Table 5).

Table 5. Funding duration.

Years of funding	Rating
1	1
2	2
3	3
4	4
5	5

Degree of interdisciplinary collaboration (Weight:10%, Fit parameter: 0-5):

Swetox Södertälje promotes interdisciplinary cooperation, particularly among Swetox consortia universities. If it is a single discipline project it is rated 0 while if it includes one or two other disciplines: 2. If it includes three or more disciplines within natural sciences: 3. If two or three faculty areas are included in the project the fit parameter is 4 or 5, respectively (Table 6)

Table 6. Degree of interdisciplinary collaboration.

Collaborative effort	Rating
Single discipline involved	0
Including two disciplines	1
Including three disciplines	2
Including four or more disciplines	3
Including disciplines from two faculties	4
Including disciplines from three faculties or more	5

Network promotion (Weight: 10%, Fit parameter: 0-5):

This criterion refers to number of researcher/researcher groups involved in the project proposal. If a single applicant, the fit parameter is 0 and accordingly with 1, 2, 3, 4 and 5 or more the fit parameter is 1 – 5, respectively (Table 7).

Table 7. Network promotion

Number of researchers/ research groups	Rating
1	0
2	1
3	2
4	3
5	4
6 or more	5

Cost and risk assessment

Cost; Estimated employee hours of Swetox resources for applications, project planning and implementation:

Different grant application or project plans require quite different resources in relation to employee hours, travel costs and other planning cost. The best way to assess these costs is to build on experience with different types of applications/project plans and to identify who is involved in the project. The cost is measured first-hand only in relation to employee hours multiplied by a general employee hour cost at Swetox (1000 SEK/h).

In a second column, the costs are stated for implementing the project at Swetox if grant is approved. It is quite common that a project will benefit from the organization and require co-founding. The total amount of co-founding is given in thousand SEK.

Risk; Estimated probability of success:

The success rate of research project proposals may be given in two ways, a more conservative manner relying on statistics from the granting agencies/organisations, i.e. that a percentage of all applications will be granted; 5%, 10% etc. of applications received. The other way to estimate the probability of success is to grade the application ourselves. The latter way may overestimate the chances of winning the grant, however.

Swetox competence areas project time consumption

Swetox Södertälje is organized into competence areas, the pillars, including educational coordination and administration. Expected time consumption for each competence area spent/to be spent on ongoing projects/planned projects is to be inserted in Table 8. This will enable the assessment of specialist opportunities for taking part in new projects. The information in the table may be visualised in a set of diagrams.

Table 8. Resource estimate (hours/week) related to Competence areas (Pillars or corresponding; employee hours)

Project	Status	Admini- stration	Bioanalysis	In silico	In vitro	In vivo	Risk assessment	Education coordination	Strategic planning
EDC-2020	Funded								
EDC-MixRisk	Funded								
PEPTONIC	Funded								
FLUOROMAN	Under evaluatio								
SafeT	Funded								
SLL Helleday Lab	Funded								
SLL Alternative plasticers	Funded								
KI Toxicology Sciences	Funded								
XX	Rejected								
Sum weekly hours									

Assessment matrix and diagram presentation of assessment

The assessment matrix base on the prioritisation criteria above, cost and risk assessment of the project proposal is shown in Table 9 below.

The parameters introduced in the assessment matrix are presented graphically in a diagram (see below) as the sum of Prioritisation Criteria (Prio Criteria) in relation to estimated probability of success. The sum of the Prioritisation Criteria may be translated to the value of the project for Swetox.

Table 9. Project assessment matrix for Swetox hub project proposals.

	Value								Cost		Risk	Balancing criterias	
	Degree of alignment with objectives/unifying concepts (0-5)	Degree of estimated impact for society (0-5)	Prioritized research areas (EDC, Emerging, Nano, Pharma) 5 if prio, 0 if not	Annual funding amount for Swetox (1-5 according to table)	Funding duration (years, 1-5)	Degree of interdisciplinarity (0-5)	Network promotion (0-5)	SUM	Estimated cost for Swetox resources for application (kSEK). Swetox 1000 kr/tim	During project: estimated Swetox cost not funded by project (kSEK)	Estimated probability of success (%)	Area of research (EDC, Emerging, Nano, Pharma, Other)	Type of project (Academic, Educational, Commissioned)
Weight factor (%)	25	20	25	5	5	10	10						
EDC-2020	5	4	5	5	5	3	4	330	120	0	90	EDC	Academic Res
EDC-MixRisk	5	5	5	5	4	3	5	345	600	200	5	EDC	Academic Res
Peptonic	2	1	5	1	1	1	1	115	200	0	95	Pharma	Commissioned res
FLUOROMAN	2	2	5	1	3	4	4	190	40	250	5	Emerging	Educational proj
SafeT	1	0	5	1	1	1	0	70	40	100	80	Pharma	Commissioned res

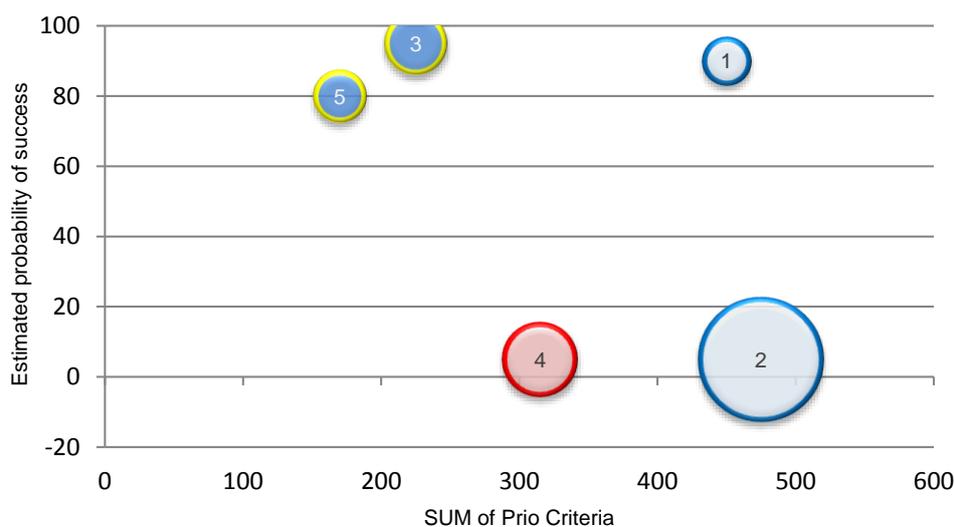


Diagram 1. The shading within the circles shows the type of project i.e. light blue is EDC, pink is Emerging Contaminants, light green is Nanosafety, light blue is Pharmatox & Environment and dark blue is other project areas. The diameter of the circle gives the estimated internal costs for Swetox to perform the project if granted (i.e. including both application/project planning and implementation costs). The colour of the circle border presents the type of project: blue = academic research, red = education and yellow = commissioned research.

Project balancing

One Swetox goal is to balance a number of activities. Projects may be divided into the following categories.

Type of project:

The projects may be divided into three groups, i.e. 1) *Academic research projects* from funding through research councils, organisations or foundations; 2) Funding of *Higher academic educational projects* via research councils, organisations or foundations; and 3) *Commissioned research projects*, i.e. projects financially supported by a certain stakeholder with an interest in a specific research task.

Area of research:

Swetox has prioritized five areas of research. These are, in alphabetical order: Endocrine-disrupting chemicals/effects (EDCs), Emerging chemicals (Emerging), Nanosafety (Nano), and Pharmaceutical toxicology and environment (Pharma).

Diagram 1 is a tool aimed at tracing the balance between major areas of projects, academic research and commissioned research, and educational project proposals. The diagram also describes the balance between prioritized areas of research and educational projects (EDCs, Emerging, Nano and Pharma).

The model can be adjusted to present diagrams in a number of different ways as requested by the assessors.

Appendix 9: Management of projects at Swetox Södertälje

Swetox Södertälje runs academic and commissioned research projects as well as educational projects. It is essential that all projects are managed in a manner that allows progress and reporting according to the approved project plans. The management of these projects must be documented.

The following points are to be addressed in the management of projects, independent of type (academic, commissioned or educational project):

- Project plan as presented in project proposal (academic projects) or approved for commissioned research projects, is a prerequisite. Depending on the outline of the project plan it may be necessary to make further specifications in order to structure the project and enable its implementation, i.e. prepare a detailed project plan. The principal (PI) is responsible for this being carried out if and when necessary. The detailed project plan must be agreed on by the project staff and communicated to others that may have an influence on the project. Project deliverables must be specified.
- Each project has a researcher responsible, a Principal (PI), to organize the execution and management of the project. The PI is responsible for staffing the project and organizing the administrative matters that the project requires, with the approval of the head of Swetox Södertälje. Since the project proposal has required the signature of the head of Swetox Södertälje to certify any need of additional resources, instrumentation and space, no further needs to be done at this stage unless there are changes to the original plan.
- The PI has to decide how the project plan and results are to be communicated, i.e. press releases, other PR activities, website, scientific reporting, data sharing etc.
- The PI has to ensure that the project enjoys the necessary Swetox support for budgeting and financial follow up.
- The PI has the responsibility of maintaining the financial limits of the project.
- The project team must establish a meeting structure for communication within the project to make everyone aware of status and progress. This is the forum for identification of problems and advances in the project, as well as for measures within and outside the project. The project team must continuously review the project and check that it is following its schedule. Project team meetings must be documented.
- All scientific publications will be prepared for publication in open access literature. Results should, if applicable, be translated and communicated to society outside academia.
- The PI is responsible for concluding the project and presenting the final financial and scientific reports.

Appendix 10: Brief activity report for Swetox Södertälje, 2014

The first year at Swetox Södertälje has been characterized by start-up, which includes building of networks, defining scientific opportunities, start-up of laboratory facilities and recruitment of competent personnel. Details are presented in the 2014 Operational Report for Swetox Södertälje and only a summary of activities and achievements are presented below.

General

During the autumn site visits from Swetox Södertälje have been arranged at all but one of the Swetox Consortium universities. At these workshops researchers, students and educational personnel from the universities participated with 2-6 employees of Swetox Södertälje. The Swetox Consortium, selected relevant research competences at Swetox Södertälje and research at the universities were presented. The university meetings were all linked to meetings with the university managements (vice chancellors, deputy/vice presidents and faculty deans).

Research

- Formas funded EDC-2020 Project – recruitment of 3/6 scientists and initiation of research projects and advertised the other 3 positions a second time in 2014.
- KI funded project on *toxicology sciences* – recruitment of 2 scientists and initiation of research projects.
- Participated in the development of a framework for the systematic review and assessment of endocrine disruption as part of a Mistra project on Weight of Evidence, now discussed as A framework for systematic review and assessment of EDCs.
- Collaboration with Helleday Laboratory at SciLifeLab on toxicology support in drug development – funded by Stockholm County Council.
- Stockholm County Council project on replacement plasticisers in medical equipment.
- Research commissions – several incoming projects on toxicology support in pharmaceutical development (academic partners and small companies) planning underway.
- Prioritization of research areas within Swetox – endocrine disruptors, human toxicology and environmental aspects of pharmaceuticals, nanosafety.
- Development of the 2 step applications: EDC-MixRisk, Horizon 2020, including partners from six of the Swetox consortia universities, and in total six partners outside Sweden.
- Organization of national workshop on nanosafety.
- Definition of strategy for all pillars at Swetox Södertälje including 3R and 3M strategies.
- Eleven publications, see Swetox website.
- First stage inventory of research within *toxicology sciences* in Sweden.
- Several presentations on metabolomics, immunotoxicology, computational toxicology and 3R at meetings and workshops.
- Swetox annual workshops in December 2013 and in 2014.

National networking

Several new networks have begun to be established after visits to Swetox Consortium universities and other organizations. These networks will serve as the basis for active expansion.

- Scientific network in the *toxicology sciences*.
- Scientific network specifically in the 3Rs.
- Scientific network specifically in nanosafety research.
- Scientific network specifically for EDC research.
- Educational network covering graduate and post-graduate teaching.
- Network with selected Swedish authorities and governmental bodies (Swedish Chemicals Agency, Medical Products Agency, Swedish Defence Research Agency, Ministry of Education and Research, Ministry of the Environment and Energy).
- Network within university science parks and other commercial entities.
- Network within the local municipality in Södertälje.

International networking

Several international networks are under formation based on specific areas of research and development interests within Swetox Södertälje.

- Brunel University London, London, UK; Scientific cooperation and exchange, joint EU application for education at doctoral level.
- Tongji University, Shanghai, China; Scientific cooperation.
- International Centre for Research and Research Training in Endocrine Disruption of Male Reproduction and Child Health, University Department of Growth and Reproduction, Rigshospitalet, Copenhagen, Denmark; Contacts initiated for scientific and educational exchange.
- WHO, Geneva, Switzerland (expert support, EDC research, Science to policy).
- UNEP Chemicals Branch, Geneva, Switzerland; expert support.
- Partner in ITC: Immunotoxicology Technical Committee, International Life Science Institute – Health and Environmental Sciences Institute (ILSI-HESI).
- Center for Alternatives to Animal Testing in the US (3R research).
- National Centre for the Replacement, Refinement & Reduction of Animals in Research (NC3R) in the UK (3R research).
- International Life Science Institute – Health and Environmental Sciences Institute (ILSI-HESI) (guidelines and research).
- European Union Reference Laboratory for Alternatives to Animal Testing (EURL-ECVAM) at the JRC Italy (Education, 3Rmethod validation).
- Collaboration in the Innovative Medicine Initiative -Safer and Faster Evidence-based Translation (IMI-SAFE-T)

Education

- Interactions with the Swetox Consortium universities during site visits.
- Planning for a doctoral course on Safety in Drug Discovery and Development, that will be run in collaboration with KI as part of a Vinnova-funded national research school in Drug Discovery and Development.
- Planning for collaborations with the Master Program in Toxicology at KI, regarding e.g. regulatory toxicology (with a special focus on in vivo testing of chemicals), 3R and in silico toxicology.
- Preparing for collaboration involving KI and Swetox Södertälje regarding a course in risk assessment within a new Master program in chemistry (environmental forensics) at Örebro university.
- Teaching basic toxicology and risk assessment on a Master course at the Royal Institute of Technology (KTH)
- Initiating exam projects for students from different Swetox consortia universities who will come to Swetox Södertälje in 2015.

Societal interactions

- Initiative and coordination of a letter from 19 Swedish experts to the Swedish Government demanding an accident investigation on the occurrence of PFAS in drinking water.
- Follow-up communication in relation to a report on chlorinated paraffin leaking during use of hand blenders.
- Participation in the formation of Biovation Park and Södertälje Science Park.
- Inspirational science day for high school students in Södertälje.
- Lectures for organisations and the general public and debate participation.

Infrastructure and security

- Start-up of existing and new equipment laboratory equipment.
- Adjustment and refurbishment of laboratory facilities.
- Construction of IS/IT infrastructure.

Personnel

- Employment of 1 operations director, 8 specialists (7 FTE), 2 research specialists, 5 research engineers, 1 financial controller, 1 administrator, 1 communications officer, 5 senior research fellows and 2 education coordinators (1.2 FTE).
- Introduction program for new employees.

Administration and governance

- Implementation of KI administrative routines at Swetox Södertälje.
- Four Swetox board meetings.

Communication

- Numerous presentations of the Swetox Consortium in different fora.
- Construction of the Swetox Consortium website, graphic profile, logotype and brand.
- Swetox newsletter 5 editions since March 2014.
- Numerous interviews and articles about the Swetox Consortium in local, national and international media (television, radio, newspapers, magazines).

Finances

- Build-up of financial structure and routines for purchase and procurement.
- Budget.

Work environment and health

- Build-up of routines and structures for a safe work environment at Swetox Södertälje.
- Coordination of work environment with other employers operating in Södertälje facilities.