



AXLR8

Alternative Testing Strategies: Progress Report 2011

& AXLR8-2 Workshop Report on a
'Roadmap to Innovative Toxicity Testing'

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Madrid 2011
Workshop ecopa



AXLR8

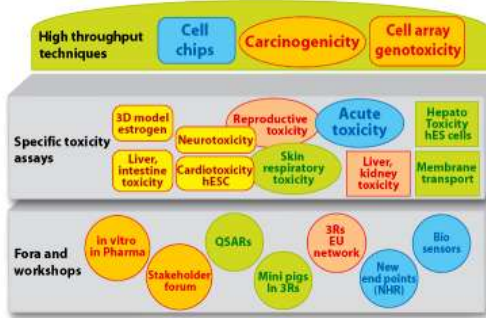
Overview

- ✧ **What:** EU 7th Framework Programme (FP7; Health) coordination project
- ✧ **Purpose:** to fulfill the growing need for coordination among 'predictive safety assessment' projects funded by the European Commission Directorate General for Research & Innovation and relevant projects at EU member state and international levels
- ✧ **Aim:** to provide the tools and opportunities for increased networking, information exchange, problem solving, strategic planning and collaboration among scientific disciplines with the goal of accelerating the transition towards predictive, non-animal approaches in toxicology and risk assessment
- ✧ **Duration:** 40 months (1 January 2010 – 30 April 2013)



Linking Predictive Safety Assessment Projects

EU Alternative Testing Strategies Research (FP6)



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The AXLR8 Consortium



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Monika Schäfer-Korting
Freie Universität Berlin



Troy Seidle, Emily McIvor &
Andrew Rowan
Humane Society International/UK



Greet Schoeters
Centre for Advanced R&D on Alternative
Methods at the Flemish Institute for
Technological Research

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Objectives

- ✦ **To establish a Scientific Panel** to independently monitor the progress of DG R&I-funded health projects and related international efforts as a basis for planning annual scientific workshops
- ✦ **To produce annual progress reports on the state of the science**, including recommendations on priority research and funding targets, to ensure a prominent role for European science in this rapidly developing global research area
- ✦ **To organise a series of annual workshops** to map research progress, gaps and needs in EU and international research programmes
- ✦ **To engage authorities and other end-users of test methods** to ensure they are kept informed of R&D-level activities and that their needs are communicated to and understood by method developers



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AXLR8 Scientific Panel

European Experts

Name	Institution	Sector	Country
Nathalie Alépée	L'Oréal	Cosmetics	FR
Patric Amcoff	OECD	Intergovernmental	SE
Jürgen Borlak	Fraunhofer Institute	Research institute	DE
Steffen Ernst		Pharmaceuticals	SE
Julia Fentem	Unilever	Consumer products	UK
Ellen Fritsche	University of Duesseldorf	Academic	DE
Joanna Jaworska	Procter & Gamble	Consumer products	BE
Robert Landsiedel	BASF	Chemicals	DE
Maurice Whelan	European Commission	Governmental	IT

AXLR8 Scientific Panel cont'd

International Experts

Name	Institution	Sector	Country
Harvey Clewell	The Hamner Institutes for Health Sciences	Research institute	US
Robert Kavlock	Environmental Protection Agency	Governmental	US
Hajime Kojima	National Institute of Health Sciences	Governmental	JP

Representatives of EU-Funded Projects

Name	Institution	Project	Country
Manuel Carrondo	Instituto de Biologia Experimental e Tecnologica	VITROCELLOMICS	PT
Barry Hardy	Douglas Connect	OpenTox, ToxBank	CH
Jürgen Hescheler	Universität Köln	ESNATS, DETECTIVE	DE
Jos Kleinjans	Maastricht University	carcinoGENOMICS, DETECTIVE	NL
Carl-Fredrik Mandenius	Linköping University	INVITROHEART, VITROCELLOMICS	SE
Michael Schwarz	Universität Tübingen	ReProTect, COACH	DE
Flavia Zucco	Consiglio Nazionale delle Ricerche	LIINTOP	IT

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Alternative Testing Strategies Progress Reports 2008-2010



Online at AXLR8.eu/publications

Progress Report 2011

- ✧ Introduction to the AXLR8 project
- ✧ Annual progress (& in some cases, final) reports of 'predictive safety assessment' projects funded under FP6-7 health & environment themes
- ✧ AXLR8-2 workshop report, including presentation manuscripts & reports from breakout groups
- ✧ AXLR8 Scientific Panel recommendations for future EU research & innovation funding
- ✧ Directory of projects & co-ordinators

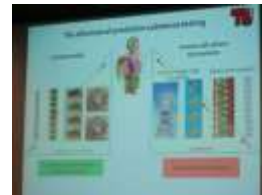


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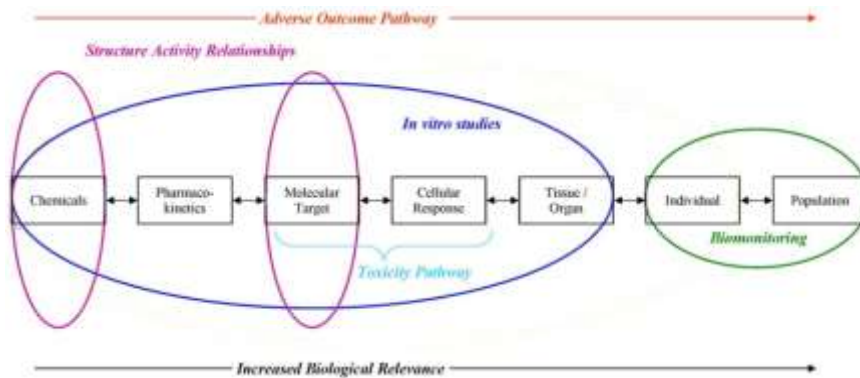
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AXLR8-2 Workshop 2011 'Roadmap to Innovative Toxicity Testing'

- ✦ 2.5 day meeting in Berlin with 50+ experts
 - ✦ EU FP6-7 project co-ordinators, Member State & international molecular toxicology/3Rs initiatives, EU Commission, AXLR8 Scientific Panel & Consortium
- ✦ Half-day satellite meeting on innovative disease models & bioinformatics tools
- ✦ Brief project updates from invited participants
- ✦ Case studies & breakout groups
 - ✦ Reproductive toxicity
 - ✦ Sensitisation
 - ✦ Pathway approaches in general



AXLR8-2 Workshop 2011 'Roadmap to Innovative Toxicity Testing'





2011 Workshop Summary & Recommendations

- ✧ Vision for large-scale, interdisciplinary effort based on a public-private partnership model to further develop the 'pathway' paradigm
- ✧ Build on SEURAT-1 model of research 'cluster' of 4-5 individual research projects
- ✧ Recommend 5 clusters to address 5 priority health concerns
 - ✦ Cancer/carcinogenicity, developmental disorders/toxicity, immune disorders/toxicity, fertility/reproductive toxicity, specific target organ toxicity
 together with an infrastructure cluster & overarching co-ordination action
- ✧ Key element = functional integration of separate research 'building blocks'
- ✧ Assuming €50M per cluster, projected 'price-tag' = €340M

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2011 Workshop Summary & Recommendations

- ✧ Recommend strong focus in all clusters on the following cross-cutting building blocks:
 - ✦ Identification & understanding of toxicological modes-of-action associated with adverse health effects, including elucidation of critical pathways
 - ✦ Development of models that capture specific MOA events at different scales, underpinned by a systems biology approach to integrate models & make quantitative predictions
 - ✦ Expansion & refinement of PBPK modelling & computational chemistry methods to predict *in vivo* bioavailability, biotransformation & bioactivity
 - ✦ Translational research & proof-of-concept activities to realise fit-for-purpose methods & tools for hazard/potency prediction & demonstration of how these are applied in a safety assessment/decision-making context

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Benefits & Opportunities

- ✧ Build on & learn from FPs & SEURAT-1 – an evolution in approach to maximise return on investment and delivery to EU policy & industry needs
 - ✦ Strategic alignment within & across projects against clear priorities & outputs
- ✧ Further embed & improve Public-Private Partnerships model
 - ✦ Consider focal 'centre of expertise' for developing EU/international networks
- ✧ Avoids the EU getting left behind in developing 21c approaches to predictive safety assessment
 - ✦ Strong US investment in 'Tox21'; significant interest from Chinese Academy of Sciences, etc.
 - ✦ Re-establish thought leadership & scientific progress aligned to EU policies
- ✧ New innovative ways to better protect human health & environment which both facilitate innovation & deliver 3Rs successes

Brussels Policy Roundtable

- ✧ High-level meeting with Commission officials, EU trade associations, Member State funding organisations to discuss AXLR8-2 workshop recommendations
- ✧ Positive & constructive dialogue



AXLR8 encourages much wider EU stakeholder buy-in to 'pathway paradigm' as basis for future 3Rs research & innovation agenda

success = focus, align, plan, resource, work hard + deliver to objectives

Next Steps

- ✧ 2011/11/30: Proposed date for adoption by European Commission of draft legislative proposal for 'Horizon 2020' – the next research & innovation framework programme
- ✧ 2011/12/01: 1st Innovation Convention
- ✧ 2011/12/06: Presentation of Horizon 2020 to the Competitiveness Council
- ✧ 2012: Political process begins
 - ✦ Stakeholder messaging opportunities in European Parliament & Member States