Health of Mother – Baby Cohorts

Human monitoring

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Content

- Introduction
- Human monitoring
- NewGeneris
- Validation of protocols
- NewGeneris samples (high-throughput analyses)

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Human exposure

Dioxins poisoning/exposure

Viktor Y. before

Viktor Y. after

At background levels, dioxins exposure has been associated with adverse health effects, e.g.

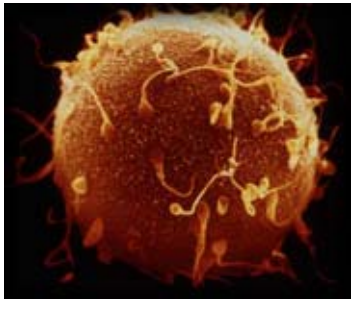
- reduced birth weight
- adverse effects on endocrine function
- cognitive development
- carcinogenisis
- diabetes type 2
- reproduction problems

Endocrine disruption

Teeny weenies

Drastic Deformities

Infertile Felines



Humans at Risk?
(e.g. breast cancer; developmental problems

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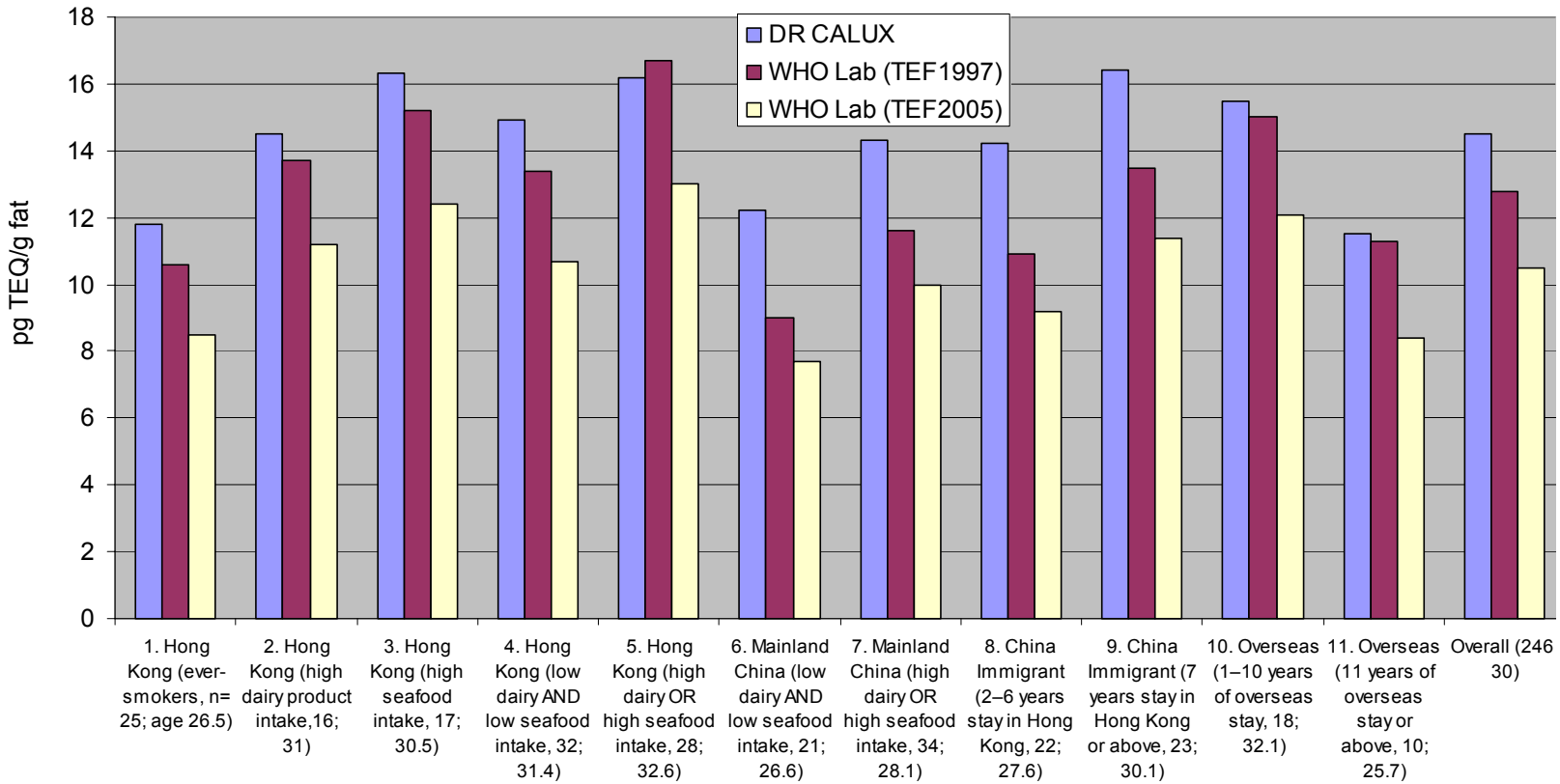
Human monitoring

- Blood / serum
- Breast milk
- Urine / feaces
- Tissue

Mother milk in Hong Kong and China

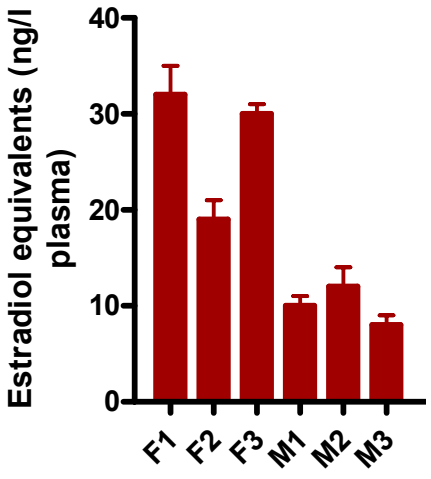
DR CALUX-Total-TEQ (BDS) vs HRGC/HRMS WHO-Total-TEQ (WHO Reference lab)

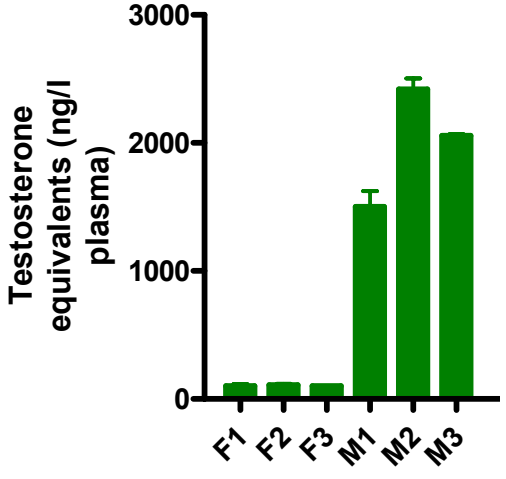
- pooled breast milk

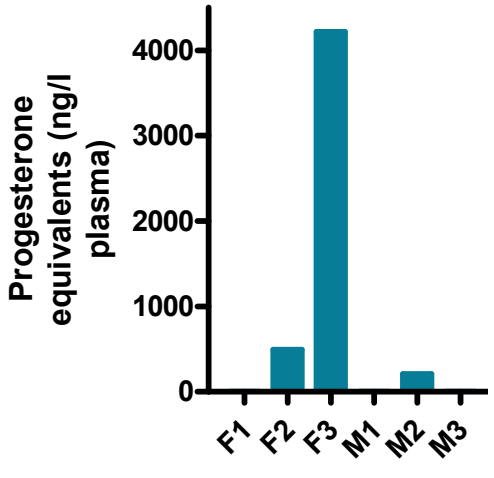


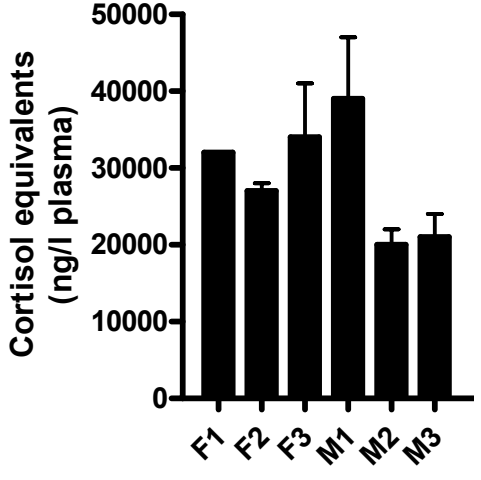
Hui et al. Chemosphere 69, 1287 (2007)

WADA: plasma steroid profiles









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NewGeneris

Newborns and Genotoxic exposure risks: development and application of biomarkers of dietary exposure to genotoxic and immunotoxic chemicals and of biomarkers of early effect, using mother-child birth cohorts and biobanks

Workpackage 6: Biomarkers of exposure – application of currently available techniques

Participant: BioDetection Systems BV (BDS)
Kruislaan 406
1098 SM Amsterdam
The Netherlands

Project summary

Hypothesis to be tested:

maternal exposure to dietary compounds with carcinogenic and immunotoxic properties results in *in utero* exposure and molecular events in unborn child leading to increased risk of cancer and immune disorders in later childhood.

Existing mother-child cohorts will be used while new biobanks will be set-up

Overall goal: Development and application of two categories of biomarkers in relation to dietary exposure and childhood disease.

1 - biomarkers of exposure to chemicals with carcinogenic and immunotoxic properties

2 - biomarkers of precarcinogenic and immunotoxic effects

Workpackage 6:
Biomarkers of exposure – application of currently available techniques

Main objective:

To **apply** currently available assays for DNA- and protein adducts as biomarker of exposure to genotoxins with concomitant features, as well as **CALUX reporter gene assay** for analysis of other immunotoxicants such as dioxins/furans and dioxin-like PCBs, thereby **using existing biobanks from mother/child cohorts**

- **To develop and validate bio-based CALUX® methods for human monitoring.**
- **To analyse total dioxins content and/or endocrine potency for several different activity classes (ER, AR, DR).**
- **To apply CALUX® bioassays for e.g. screening low volume human blood samples.**

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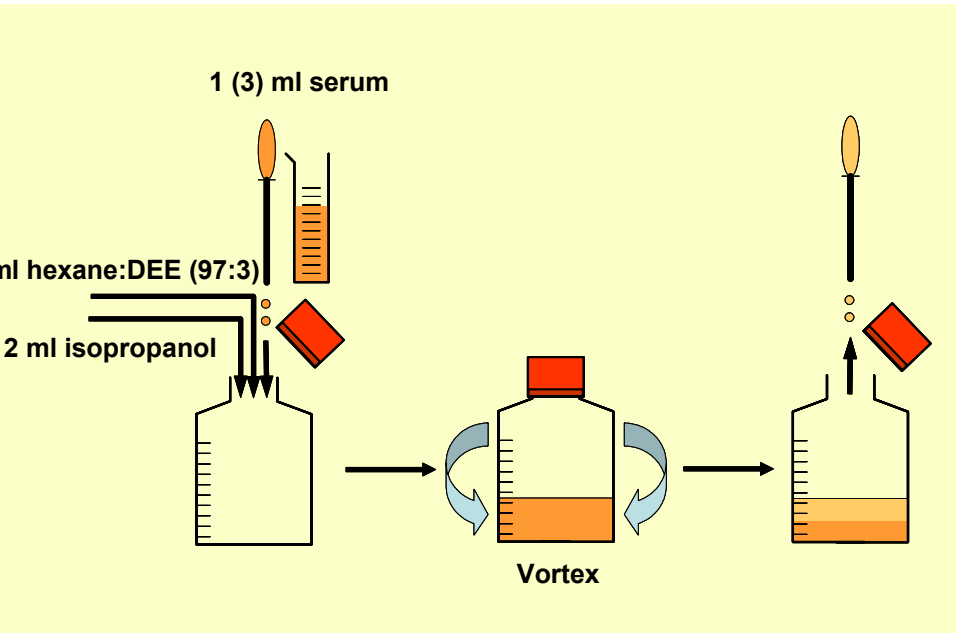
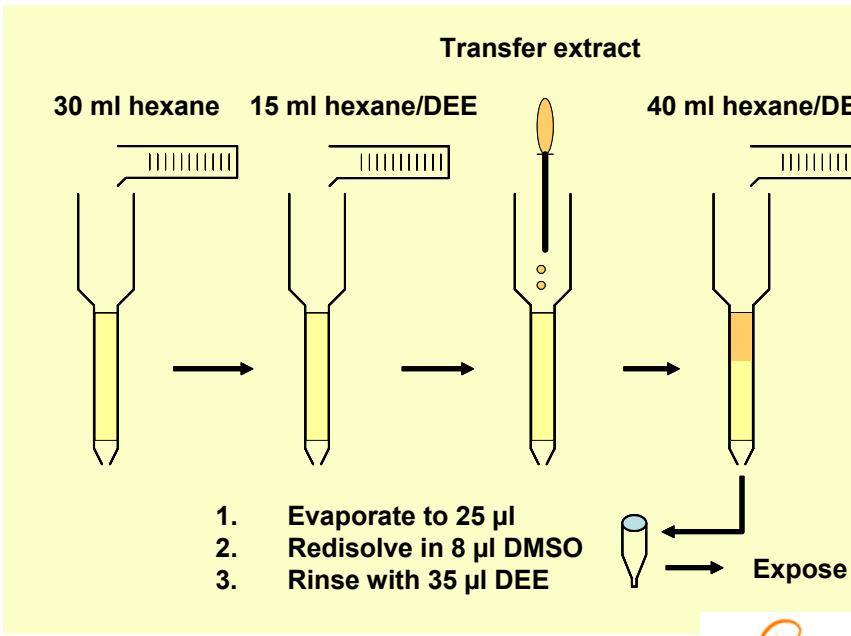
DR CALUX® - extraction and clean up

Minimal amount of serum required:
Maternal: 1 ml
Fetal: 3 ml

Extraction



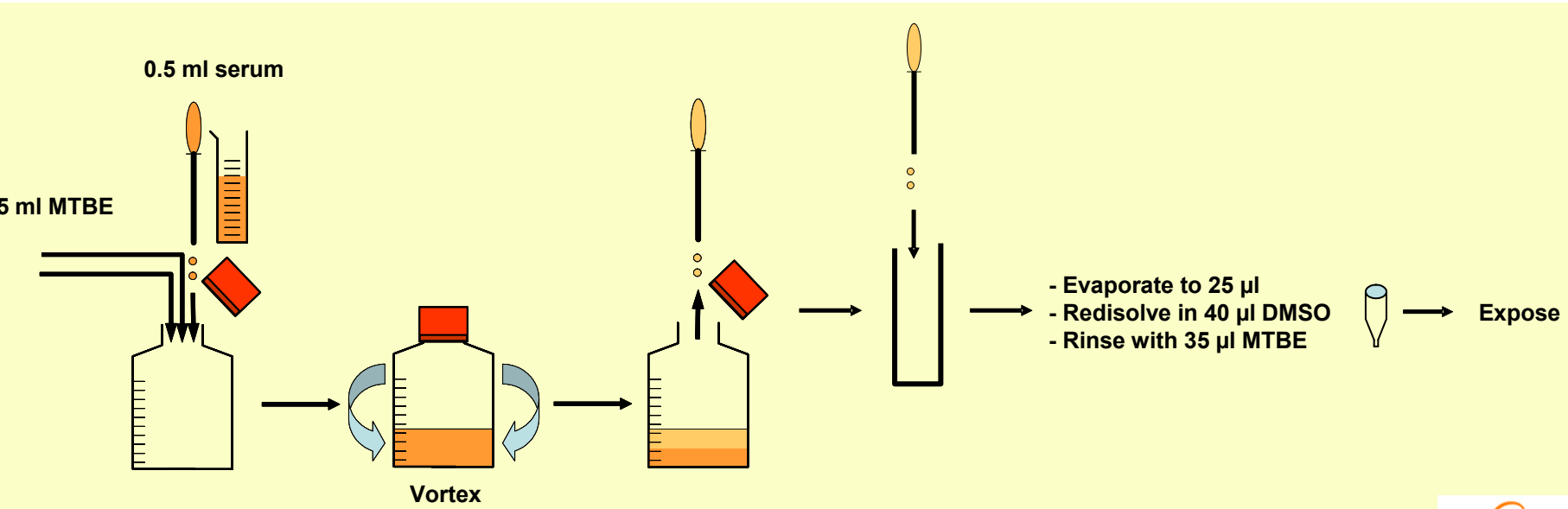
Clean-up



Sample size, extraction/clean-up, luminescence

ER and AR CALUX® - extraction and clean up

- Extraction; no clean-up required
- Minimal amount of serum required: 0.5 ml per sample



Performance characteristic

	DR CALUX®	ER CALUX®	AR CALUX®
Limit of Detection (LOD) (pM/well)	0.3	0.7	7.2
Limit of Quantitation (LOQ) (pM/well)	0.5	2.4	17
Correctness	7.4%	4.4%	6.9%
Intralaboratory repeatability	21%	18%	24%
Intralaboratory reproducibility	22%	25%	24%
Measure uncertainty	23%	25%	25%
Selectivity	7.7%	12.4%	1.0%
Robustness	$VC_r \sim VC_R$	$VC_r \sim VC_R$	$VC_r \sim VC_R$

ER CALUX® LOD: 0.02 ng estradiol equivalents/ml plasma
AR CALUX® LOD: 0.09 ng DHT equivalents/ml plasma
AR CALUX® LOD: 20 pg 2,3,7,8-TCDD TEQ/g fat

Official (Dutch) guidelines for validation were followed: NEN:7777, NEN:7778.

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- **NewGeneris samples (high-throughput analyses)**

Number of samples to be analysed

Number of maternal samples received: 847
Number of cord blood samples received: 726
Number of pairs: 563

Perfusion study: 175

Samples received from:

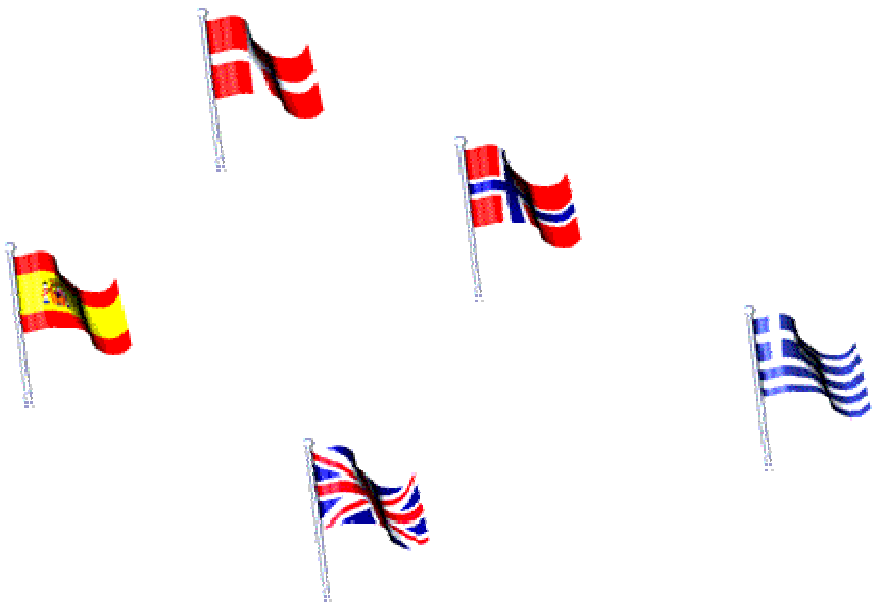
DK BioBank (Denmark)

BraMat (Norway)

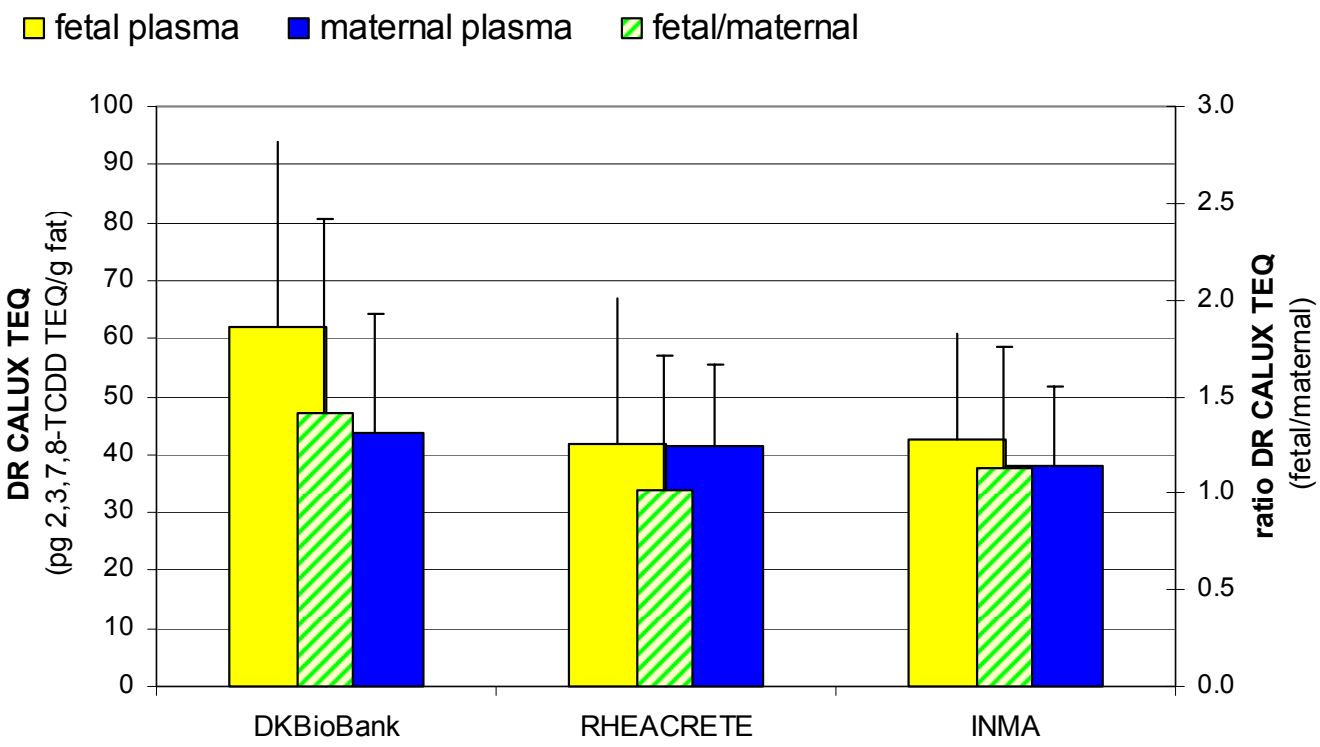
INMA (Spain)

RHEACRETE (Greece)

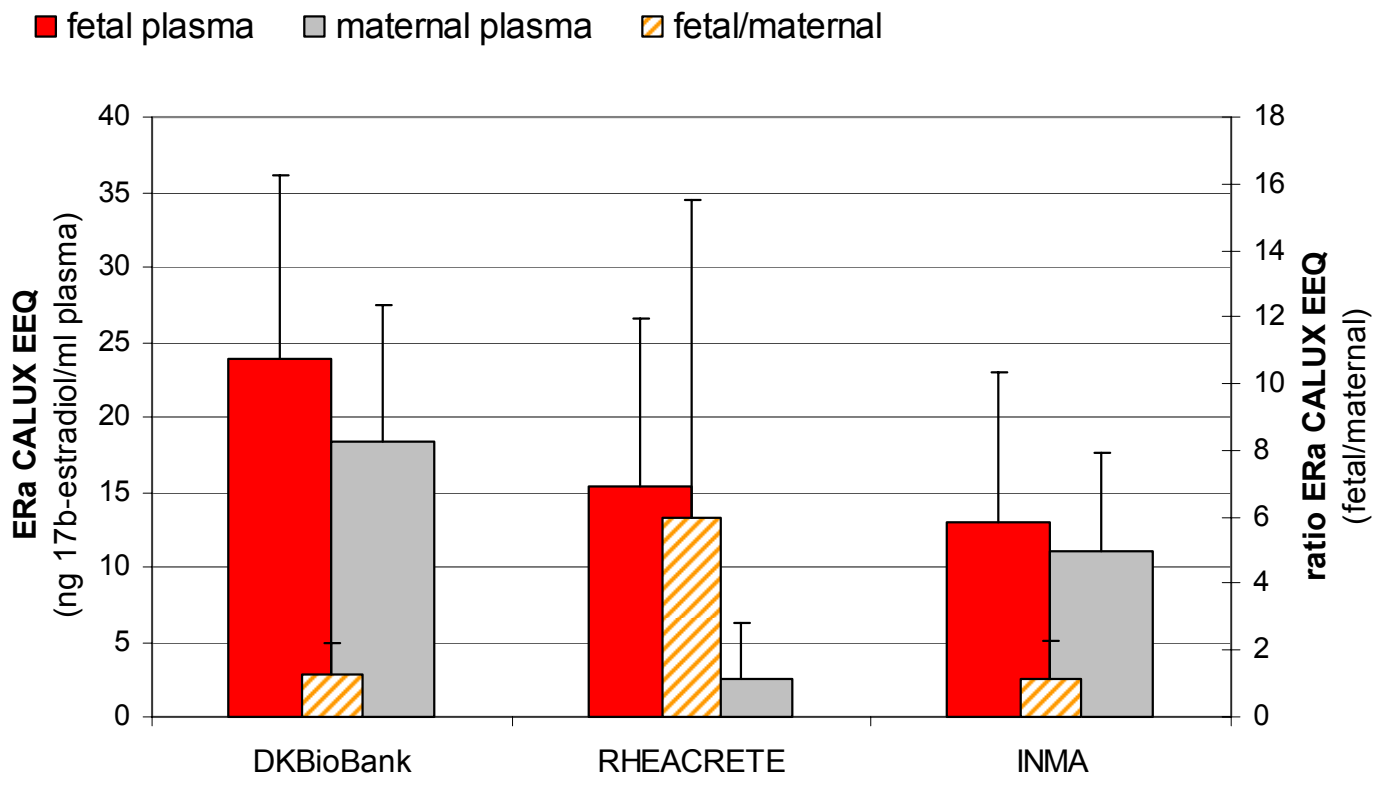
BiB (UK)



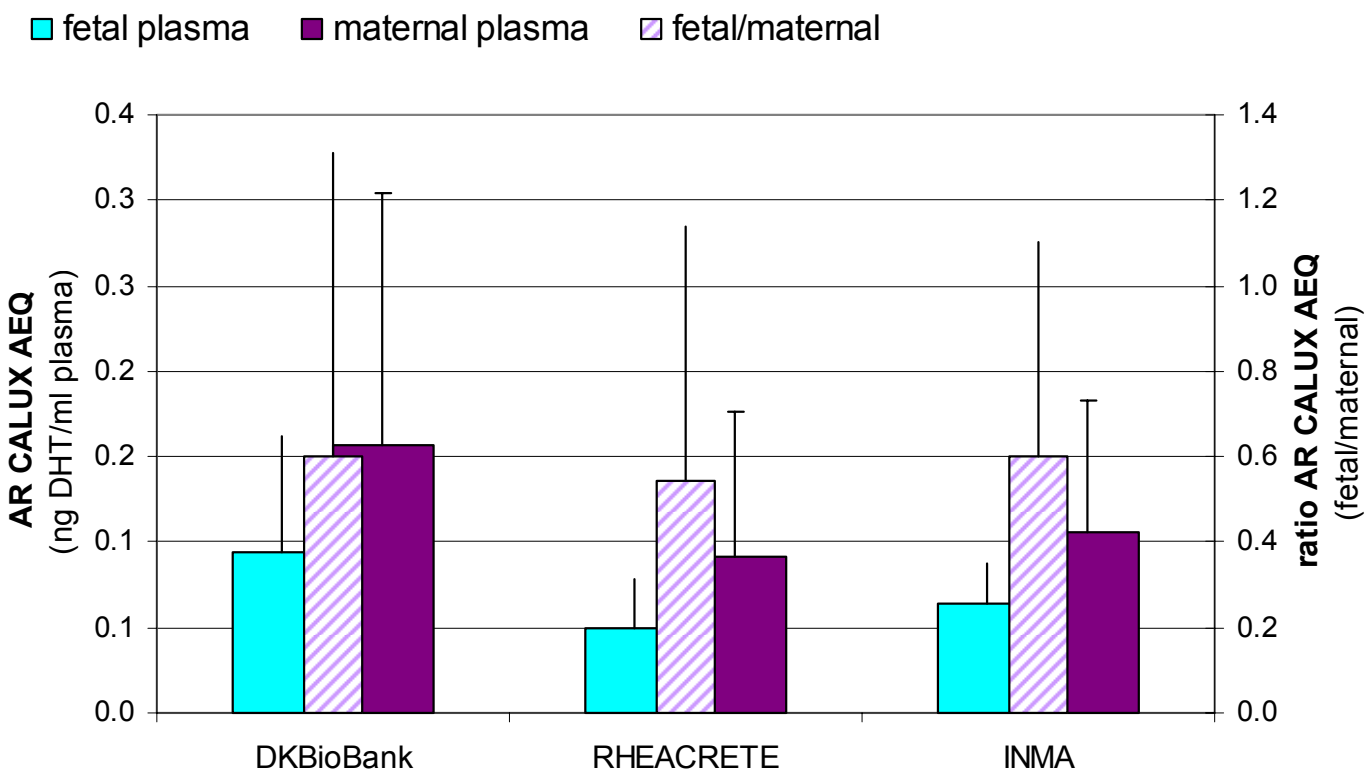
DR CALUX analysis results



ER CALUX analysis results

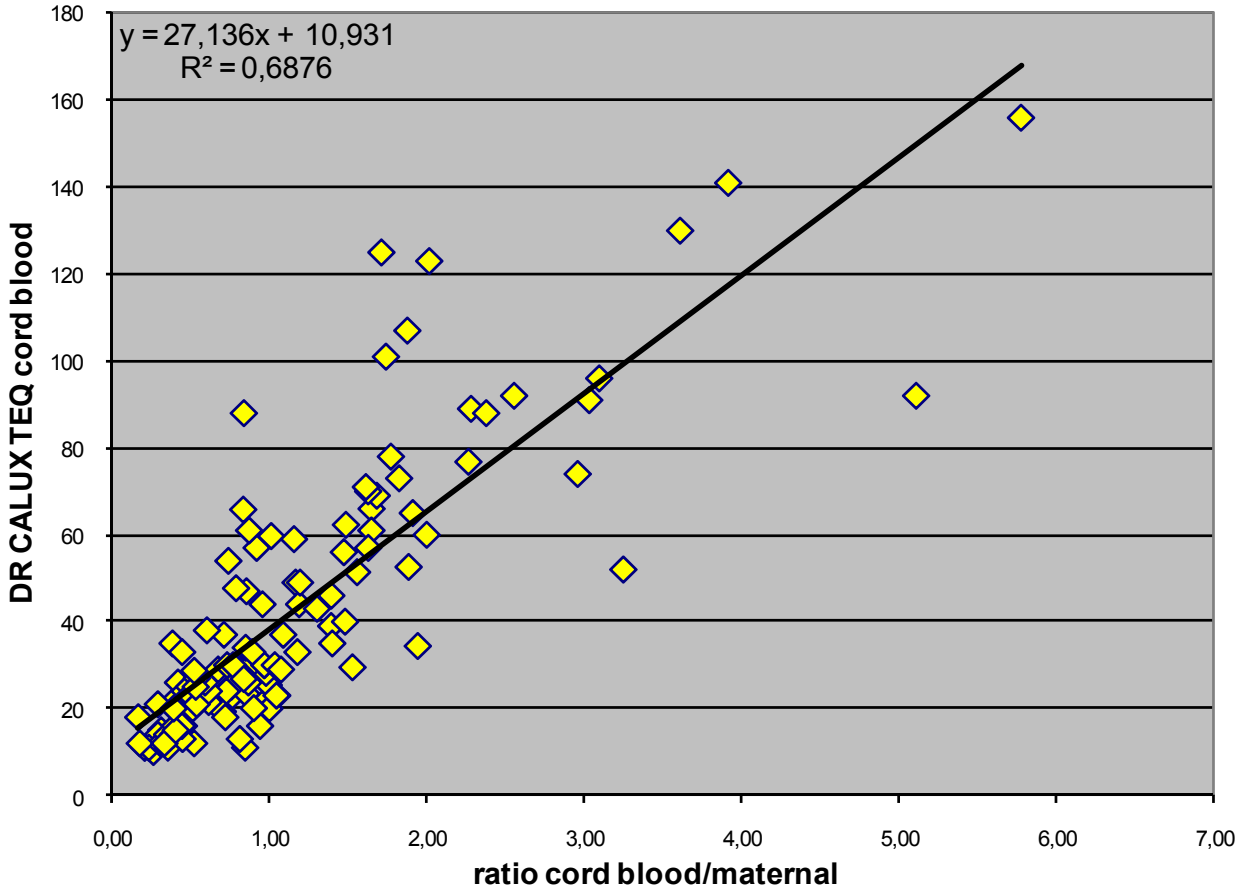


AR CALUX analysis results

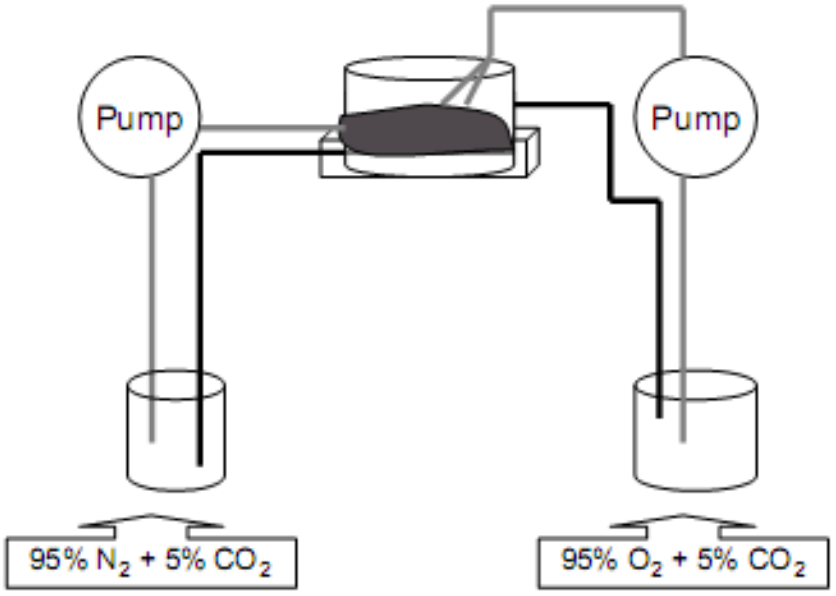


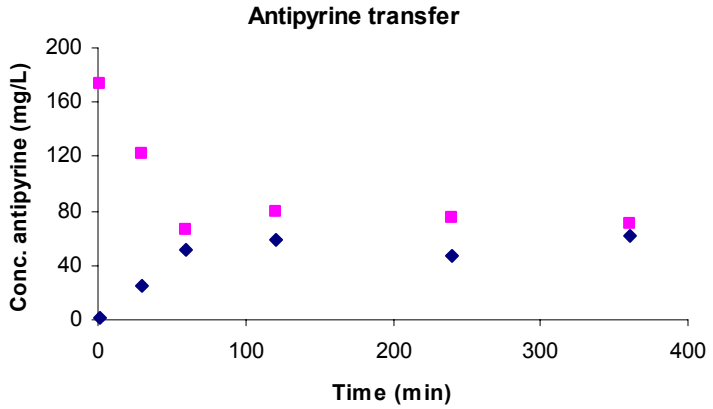
Mother – baby correlation

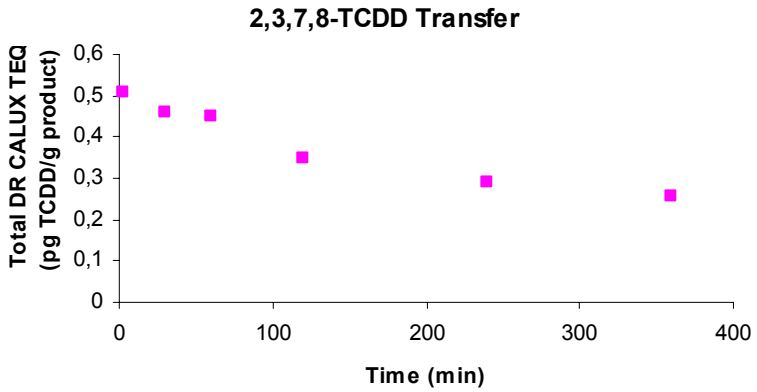
Ratio cord blood plasma/maternal plasma vs cord blood plasma



Perfusion study







- Epidemiology (existing and new biobanks)
- Diagnostics / clinical studies
- Screening

Thank you
for your attention