TDS Exposure and LIFE-Persuaded - Emerging issues in the assessment of exposures to chemicals in food products

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Endocrine disrupter website (http://www.iss.it/inte)
The risk assessment of intended and undesirable chemicals in food products is an evolving field, whose developments bear significant impacts on health and dietary habits of consumers as well as on regulations and on food production chains.

Exposure assessment is an essential step of risk characterization. But

What does it mean “exposure”?

- **dietary**: how much chemicals we take through foods? through what foods? In what population groups?
- **internal**: how much chemicals from diet (e.g. food contact materials) and living environment (e.g. consumer products) in our bodies? Are internal exposure levels associated with biomarkers of effect?
Definition of the Total Diet Study (TDS) concept

A TDS consists of selecting, collecting and analysing commonly consumed food purchased at retail level, processing the food as for consumption, pooling the prepared food items into representative food groups, homogenising the pooled samples and analysing them for harmful and/or beneficial chemical substances.

Essentials principles of a TDS:

1. Representative of the whole diet
2. Pooling of foods
3. Food analysed as consumed

TDSs are designed to cover the whole diet and to measure the amount of each chemical substance of interest ingested by the population living in a country over their lifetime, using average and high-level consumption data. The chronic dietary exposure calculations assist in determining whether specific food chemical substances pose a risk to human health.
Guidance to a harmonised Total Diet Study approach

Reference:
European Food Safety Authority (EFSA), Food and Agriculture Organization (FAO), World Health Organization (WHO). Towards a harmonised total diet study approach: a guidance document.
EFSA J 2011;9(11):2450-515
TDS-Exposure project

An on-going four-year FP7-funded Collaborative Research Project with 26 partners from 19 countries: harmonizing population exposure assessment via total diet studies (TDS)

http://www.tds-exposure.eu/
Harmonizing population exposure assessment via TDS

Even though the key aspects of a TDS are well defined, there are many methodological differences in the way this type of study is performed at the national level that limit the possibility to compare exposure of different populations across Europe and worldwide.

- **TDS-Exposure** launched in February 2012 with the aim of creating an EU-wide network of TDS-Centres using common tools like databases and modelling software. Goal: harmonizing the TDS methodology and ensuring data collected in the future can be compared across countries.

- AIM: establishing a legacy of harmonised methods and science-based recommendations for public health worldwide.

- TDS-Exposure provides training for those countries without total diet studies, enabling best practice in the creation and execution of TDS programmes in those regions lacking such population studies, and ensuring the data collected are coherent with others studies globally.
Output example #1: Assessment of the relevance of the TDS approach for all major groups of chemical substances

TDS exposure project: relevance of the total diet study approach for different groups of substances.


Eight main groups of relevance for food safety (natural components, environmental contaminants, substances intentionally added to foods, residues, naturally occurring contaminants, process contaminants, contaminants from packaging and food contact materials, other substances)

Four relevance criteria: (i) the substance has to be present in a significant part of the diet or predominantly present in specific food groups, (ii) a robust analytical method has to be available to determine it in potential contributors to the dietary exposure of the population, (iii) the dilution impact of pooling and (iv) the impact of everyday food preparation methods on the concentration of the substance.
Output example #2: Criteria for the prioritization of substances to be analyzed in a TDS


TDS exposure project: application of the analytic hierarchy process for the prioritization of substances to be analyzed in a total diet study.

Papadopoulos A, Sioen I, Cubadda F, Ozer H, Basegmez Hl, Turrini A, Lopez Esteban MT, Fernandez San Juan PM, Sokolić-Mihalak D, Jurkovic M, De Henauw S, Aureli F, Vin K, Sirot V.

A general method based on the analytic hierarchy process (AHP) methodology to rank the substances to be studied in a TDS.

The AHP methodology is based on a score system.

10 substances of highest interest in the framework of a TDS: trace elements (methylmercury, cadmium, inorganic arsenic, lead, aluminum, inorganic mercury), dioxins, furans and polychlorinated biphenyls (PCBs), some additives (sulfites and nitrates).

Priority list: national situation (geographical variations, consumer concern, etc.) and availability of data (reachable analytical performances).

List variable with time and new data (e.g. social context, vulnerable population groups, emerging substances, new toxicological data).
Main substances investigated

- Toxic trace elements and element species (e.g. inorganic arsenic)
- Mycotoxins
- PCDDs, PCDFs, PCBs
- Essential elements

Methodology

- The 2012-2014 TDS entails the collection of > 3000 food items, bought at retail in 4 cities selected to represent the four main geographical areas of Italy
- The food items were pooled according to the TDS food list, based on individual food consumption data, into 51 core foods
- Three sampling campaigns undertaken and seasonal aspects accounted for by sampling fruits and vegetables in two different seasons
- Dietary exposure assessed for the general population and for children, teenagers, adults, and elderly of the two sexes, both at the national level and for each of the four main geographical areas of Italy

Phthalates and bisphenol A biomonitoring in Italian mother-child pairs: link between exposure and juvenile diseases

http://www.iss.it/lifp
Phthalates (diethylhexyl phthalate [DEHP] in particular) and Bisphenol A (BPA), extensively used as plasticizers, are non-persistent environmental contaminants whose well documented presence in humans raises concern since they act as endocrine disruptors (EDs), thus potentially affecting human health. EDs exposure during childhood deserves special attention since this represents a crucial susceptible phase of development. Recent studies have associated the exposure to DEHP and BPA to endocrine related multi-factorial diseases in children, in particular precocious puberty and obesity.

*BPA*: weak agonist of estrogen receptor alpha, interferes with thyroid homeostasis and with the PPARgamma

*DEHP*: antiandrogen inhibiting steroid biosynthesis, interferes with PPARα.
PERSUADED stems from the Italian project on ED biomonitoring PREVIENI (http://www.iss.it/prvn)

Results revealed unexpectedly widespread and high levels of BPA and DEHP in the Italian adults, especially in infertile women from large metropolitan area (Roma)

Main objectives

- To estimate internal levels of DEHP and its metabolites and BPA in children and adolescents of Italian population
- To investigate whether internal levels of DEHP and its metabolites and/or BPA are related with endocrine related diseases in children
- To evaluate effects due to BPA/DEHP exposure by an innovative experimental approach, the rodent juvenile toxicity study

http://www.iss.it/lifp
Main actions

**Human biomonitoring study:**
Three Italian macro-areas (North, Centre, South); urban and rural sampling areas in each macro area

Involvement and training of pediatricians from the National Health System

- Enrollment of mother-child/adolescent pairs by age and gender;
  administration of informed consensus, questionnaires on lifestyle/food habits; filling in the food diary two days before urine sampling;
  collection of urine samples
- Analysis of the levels of BPA and DEHP/DEHP metabolites in urine samples

http://www.iss.it/lifp
The Human biomonitoring study will be integrated with Case-control study (Case-control studies (Rome):
  i) idiopathic premature thelarche: enrollment of 30 girls aged 2-7 years
  ii) idiopathic central precocious puberty: enrollment of 30 girls aged 2-7 years
  iii) idiopathic childhood obesity: enrollment of 30 boys and 30 girls aged 6-10 years.
Control groups consisting of an equal number of girls and boys of corresponding age will be enrolled for each study.
Urine sampling for analysis of the BPA and DEHP/DEHP metabolites levels. Blood sampling for analysis of relevant toxicological biomarkers (hormones, lipid and glucose metabolism, liver and thyroid function).

And a juvenile toxicology study on rats to explore the biological plausibility of association
Preliminary deliverables and milestones

Identification of urban and rural sampling areas within Northern (Veneto, Lombardia, Friuli regions), Central (Marche region) and Southern (Puglia, Basilicata) macro-areas

**Structured questionnaire** on lifestyle, food habits and socio-demographic conditions potentially related to DEHP/MEHP/BPA exposure of enrolled child-mother pairs (it can be filled out online)

**Food diary** for two days before the urine sampling (it can be filled out online)

**Involvement and training** of about 90 family Pediatricians of National Health System on a voluntary basis in each sampling areas
- Training of regional representative pediatricians at ISS
- Training of regional pediatricians by each regional representative

Starting of the recruitment of child-mother pairs (Veneto, Lombardia, Marche)
Outcomes and models developed within TDS Exposure and Life PERSUAED are expected to contribute to the selection of national priorities for food monitoring and prevention of chemical exposures by the Italian Ministry of Health as well as by the health services of the Italian Regions

Risk assessment by EFSA as well as by the European Chemical Agency (ECHA), that both request actual and well-targeted data on food contamination and human exposure

Risk management measures by both public authorities and food and chemical industries, such as the risk-driven control of food chains and the substitution of chemicals of concern in consumer products, such as food contact materials, etc.: this latter issue is specifically addressed by another ISS-led project, Life EDESIA (http://www.iss.it/life)
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