In 2005, the Joint FAO/WHO expert committee on food additives (JECFA) carried out a risk assessment of acrylamide in food following a FAO/WHO expert consultation on this topic in 2002. The EFSA’s Scientific Panel on Contaminants in the Food Chain (CONTAM) concurred with the principle conclusions and recommendations made by the JECFA and did not see the need for an additional evaluation by EFSA at that time. Additional information has become available since 2005, including epidemiological studies of cancer risk associated with dietary exposure to acrylamide.

In relation to previous risk assessments carried out by international bodies and new scientific information published since, the objectives of the Colloquium are:

- To discuss in an open scientific debate the state of the art, current issues and future challenges for the risk assessment of acrylamide in food in relation to its carcinogenicity and dietary exposure.

- To discuss the epidemiological evidence relating acrylamide exposure to cancer risk in humans including discussions on uncertainties.

- To discuss the applications of biomarkers for acrylamide and physiologically-based pharmacokinetic models in relation to exposure, metabolism and elimination (toxicokinetics) and the mode of action (toxicodynamics) of acrylamide in experimental animals and humans.

- To discuss the state of the art on genotoxic and non-genotoxic mechanisms for the carcinogenicity of acrylamide including new in vitro/in vivo evidence in experimental animals and humans.

- To discuss the current knowledge on dietary exposure to acrylamide across Europe and to explore if there are possibly new potential food sources contributing to the dietary intake.
- To explore whether the new evidence in epidemiology, carcinogenicity and exposure would call for a revision of the previous risk assessment of acrylamide in food.

These briefing notes have been prepared to stimulate an open interactive exchange of views and expertise on the scientific aspects of acrylamide carcinogenicity and the new evidence in relation to dietary exposure. Focus should be on the risk assessment methodology and, in particular, on quantitative and qualitative risk assessment.

**GENERAL BACKGROUND DOCUMENTS**


EFSA(2005)- Statement of the scientific panel on contaminants in the food chain to a summary report on acrylamide in food of the 64th meeting of the Joint FAO/WHO Committee on Food Additives (JECFA). Available at URL: [http://www.efsa.europa.eu/EFSA/Statement/contam_acrylamide_statement1,0.pdf](http://www.efsa.europa.eu/EFSA/Statement/contam_acrylamide_statement1,0.pdf)


EC (European Commission), 2002. Opinion of the Scientific Committee on Food (SCF) on new findings regarding the presence of acrylamide in food. Available at URL: [http://europa.eu.int/comm/food/fs/sc/scf/out131_en.pdf](http://europa.eu.int/comm/food/fs/sc/scf/out131_en.pdf)

DISCUSSION GROUP 1 - Epidemiological studies – evaluating evidence and addressing uncertainties

INTRODUCTION
Over the last few years, a number of research groups from around the world have published data from epidemiological studies in relation to dietary exposure from acrylamide and human cancer risk in different target organs (kidney, bladder, endometrium, ovaries, breast). Key aspects in establishing such relationships are; the power of the studies to detect effects, how the exposure assessment was carried out, how well can food frequency questionnaires (and other diet assessment methods) capture dietary acrylamide intake (several studies comparing FFQ-assessed acrylamide intake with biomarkers of acrylamide exposure are now available); what kind of statistical tools have been applied and what are the confounding variables. It is important to review the evidence and to identify whether the methodologies applied in various epidemiological studies are comparable and consistent, and if uncertainties have been taken into account.

DISCUSSION POINTS
1. Review the epidemiological evidence relating acrylamide dietary exposure and cancer risk.
2. Review the methodology used for the exposure assessment and if there is comparability between studies.
3. Establish whether the statistical approaches are consistent between studies and review the sources of uncertainty (exposure, food consumption, confounding variables).
5. Discuss the power of the studies to detect effects.
6. Discuss whether from the body of evidence conclusions can be drawn on the direct relationship between acrylamide dietary exposure and increased cancer risk in humans.

BACKGROUND DOCUMENTS

Acrylamide and Cancer: recent epidemiological evidence


Discussion Group 2 – Biomarkers – new insights in exposure and mode of action

Introduction
The characterisation of acrylamide metabolism has been the basis for the development of biomarkers. Acrylamide metabolism follows two basic routes: (1) CYP2E1-mediated epoxidation to glycidamide (GA) which is then conjugated by glutathione to N-acetyl-S-(2-(hydroxyl-ethyl)-carbamoylethyl) cystein (GAMA) and N-acetyl-S-(1-(hydroxyl-ethyl)-carbamoylethyl) or further metabolized by epoxide hydrolase to glyceramide; (2) Direct conjugation of acrylamide with glutathione to form the urinary metabolites N-acetyl-S-(3-amino-3-oxypropyl) cysteine and N-acetyl-S-(2-carbamoylethyl) cysteine (AAMA). However, only free unchanged glycidamide is thought to account for the genotoxicity of acrylamide by formation of DNA adducts and since the early 1990s, haemoglobin adducts of acrylamide have been used to reflect long term exposure to acrylamide since erythrocytes have a half life of 120 days. More recently, the mercapturic acid metabolites of acrylamide and GA have been quantified in human urine to reflect biomarkers of short term exposure with half-lives ranging from hours up to a few days. Physiologically based pharmacokinetic models (PB-PK) have also been developed for acrylamide, GA and the glutathione conjugates of acrylamide and liver GA-DNA adducts and hemoglobin adducts have been included as pharmacodynamic components of the model.

Discussion Points

1. Discuss new insights into species differences in the kinetics of acrylamide
2. Review the current state of the art on the knowledge on acrylamide’s biomarkers in relation to exposure and effects and whether some biomarkers provide better estimates than others.
   - Discuss the use of haemoglobin adducts and DNA adducts as biomarkers
   - Discuss the use of urinary metabolites (acrylamide and glycidamide) as biomarker
3. Review the available physiologically based pharmacokinetic models
4. Impact of these biomarkers on the risk assessment (both for exposure and the mode of action)

Background Documents


DISCUSSION GROUP 3 – Mechanism of carcinogenicity

INTRODUCTION

Acrylamide exposure has been shown to increase incidences of thyroid, adrenal medulla, and testicular mesothelium neoplasia in male rats, and in thyroid, adrenal medulla, and mammary gland neoplasia in female rats. The rat thyroid follicular cell tumours and the mammary tumours from two studies were considered of possible relevance for human health and benchmark doses and benchmark dose lower confidence limits (BMDL) have been determined. Overall, genotoxic and non-genotoxic modes of action of acrylamide and its metabolites have been proposed: Although acrylamide is mostly negative for mutagenicity in prokaryotic cells, it increases chromosomal aberrations, sister chromatid exchanges, unscheduled DNA synthesis, DNA breaks and deletions, cell transformation, and mitotic disruption in mammalian cells. GA has been shown to be mutagenic and genotoxic in various in vitro and in vivo test systems. Conjugation of acrylamide with glutathione can result in depletion of cellular glutathione stores, thereby, changing the redox status of the cell which can increase cellular oxidative stress and potentially affect gene expression directly or through regulating various redox-dependent transcription factors. Consequently, cell transformation or proliferation and apoptosis might occur independently of acrylamide induced genotoxicity. Another non genotoxic mechanism of action of acrylamide refers to its hormonal mode of action in rat endocrine (thyroid) and mammary glands. Another recent report described the first evidence of acrylamide and GA inhibition of a mitotic/meiotic motor protein and was speculated as an alternative mechanism to DNA adduction in the production of cell division defects and potential carcinogenicity.

DISCUSSION POINTS

1. Review the recent evidence for the mutagenicity and genotoxicity of acrylamide and glycamide
2. Review the recent evidences for the non-genotoxic mechanism of acrylamide (and glycamide)
3. Weight the evidence as to whether AA acts via a non-genotoxic or genotoxic mechanism in contrast to its genotoxic metabolite.
4. Exploration of the consequences of changed conclusions about genotoxic versus non-genotoxic mechanism of carcinogenesis for human risk assessment.

BACKGROUND DOCUMENTS


DISCUSSION GROUP 4 - Dietary exposure across Europe - current situation

INTRODUCTION
Since 2003, European Union Member States have been submitting occurrence data for acrylamide in food commodities to the Joint Research Centre (JRC) of the European Commission. The submission of the data to the JRC from member states, was done through official food control laboratories directly or via their Competent Authorities, and from the food industry on a voluntary basis. The database and the reliability of the data will be discussed with special regards to the analytical techniques, their sensitivity and specificity used to report acrylamide concentrations in food commodities and whether member states report the data consistently. In 2007, the Commission made recommendations to monitor levels of acrylamide in certain food categories. (2007/331/EC), these data will be reported to EFSA by member states on a yearly basis for the next three years (EC 2007). The content of acrylamide in different food commodities will also be discussed to establish food sources which contribute most to acrylamide exposure.

DISCUSSION POINTS
1. Data reliability with regards to sensitivity of the analytical techniques and consistency of the data reported by the member states, including new analytical techniques
2. Review the occurrence data for acrylamide in food commodities available in Europe. Is there a need to revisit the exposure assessment?
3. Which food commodities contribute most to acrylamide exposure – possibility and efficacy of mitigation measures?
4. Recommendations to improve data collection and data assessment in the future.
BACKGROUND DOCUMENTS


