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Migration of ITX (Isopropyl Thioxantone) from Tetra Pak Bricks into Food

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Abstract

At the beginning of September 2005, ITX, a photoinitiator used in UV cured ink, has been identified to have migrated from packaging to food products. Tetra Pak has identified the source of migration to be UV cured offset printing ink.
The presence of ITX in food packed in Tetra Pak bricks is the result of the contamination of the inner polyethylene layer of the box walls. ITX can either migrate through the packaging material or it can reach the food by contact, for example, as a result of the print set-off phenomenon. Most likely, the transfer of ITX was due to the physical contact between the printed outer layer with the inner layer of the packaging, whereby the ink or ink substance transfers from the print to the reverse of the adjacent sheet.
Tetra Pak has committed itself to move away from this technology immediately and to use alternative printing technologies to ensure that there is no or minimal migration of ITX or other substances from its packages.
ITX is still not on the EU's negative list of banned substances in food nor does the World Health Organization (WHO) categorize it as being detrimental to human health. After an investigation in the health risks of ITX following the incident, the European Food Safety Authority (EFSA) concluded that the levels found in foods, "while undesirable, do not give cause for health concern."

Key words:

ITX (Isopropyl Thioxanton), Tetra Pak packaging, RASFF (Rapid Alert System for Food and Feed), HAH (Croatian Food Agency), EFSA (European Food Safety Authority)

1. Introduction

ITX (IsopropylThioXanton) – a yellow powder with a chemical formula of $C_{10}H_{14}OS$ is a chemical substance used as a photoinitiator in offset printing inks, due to its property to absorb UV light. In the process of printing, the energy of absorbed UV light activates the process of polymerisation of the printing ink, whereby the ink dries and becomes fixed on the substrate *(Ambalaza Journal, 2005)*.

UV inks are printing inks which remain liquid until the moment of exposure to UV radiation of a certain wavelength, whereupon a very fast chain reaction occurs and the inks dry instantaneously. Such inks consist of prepolymer resin, solvent, photoinitiator (which is activated by UV radiation and initiates the drying reaction), various additives and a pigment which provides the colouring *(Sršen, 1999)*.

ITX (photoinitiator in UV offset ink) consists of two components – most frequently combined for the stated purposes *(Haglind, 2005a)*. These are:

2 – isopropylthioxanton (CAS 5495-84-1) and
4 – isopropylthioxanton (CAS 8346-86-0)
whose chemical structure is:

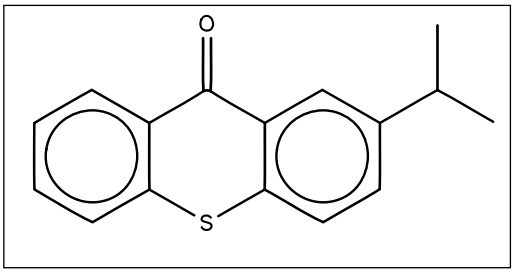

Figure 1. Structural formula of ITX.

In handling ITX, certain protective measures should be undertaken, as it can cause irritation of the skin, eyes and mucosa of the respiratory tract in exposed persons during the production process.

In recent months we have witnessed alarming news of contamination by ITX of food packaged in Tetra Pak packaging, the product of a reputable Swedish producer.

2. Tetra pak packaging

Tetra Pak packaging has been in use since the 1960s. The development of an aseptic packaging technology applicable to easily perishable liquid foodstuffs, particularly milk and milk products, enabled the keeping of foodstuffs for as long as 12 months, without the use of preservatives and/or the need of storage at low temperatures *(Tetra Pak, 2006)*.

The slogan of the producer of Tetra Pak packaging – "Protects what's good" – was compromised, to say the least, after it was made public that the health safety of foodstuffs was at risk, precisely due to certain unwanted properties of their product.

Aseptic technology of packaging implies that the foodstuff is subjected to an ultra high temperature treatment (UHT) for a couple of seconds, and then cools rapidly. In the sterilized Tetra Pak packaging, the sterile foodstuff is protected against light and contact with oxygen (oxidation). This is due to the fact that the wall of the Tetra Pak packaging consists (from the inside toward the outside) of:

- 2 layers of polyethylene
- 1 layer of aluminium foil, 0.006 mm thick
- 1 layer of polyethylene
- 1 layer of laminate paper, which gives strength to the packaging wall and on which prints are applied by means of flexographic, rotogravure or offset printing techniques;
- 1 layer of polyethylene.

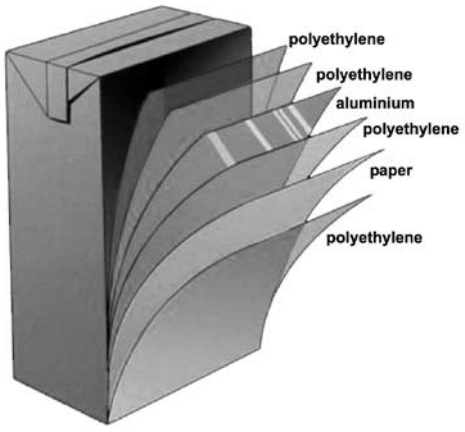

Figure 2. Wall layers of Tetra Pak aseptic packaging.

The above implies that the only layer which is in direct contact with the foodstuffs is the inner wall layer consisting of polyethylene.

We shall presume that the presence of ITX in foodstuffs packaged in Tetra Pak packaging is the result of "contamination" of the inner polyethylene layer of the packaging wall, as the product, after applying the ink on the outer layer, is reeled up in a roll. Most probably, the migration of the ITX was a result of mechanical transfer of ink or an ink substance from a printed surface to a contacting unprinted surface (set-off phenomenon). The polyethylene film that covered the print was obviously not an adequate barrier to a fat-soluble substance in the ink. Therefore, the ITX was able to easily permeate through the protective polyethylene layer and to reach the food contact side *(Aurela & Söderhjelm, 2007)*.

3. Rapid alert systems for unsafe foods

Notification of unsafe food and feed by means of the European RASFF (Rapid Alert System for Food and Feed) is used in cases of direct and indirect risk for human health emerging from food and feed. The Decision of the Council of Europe 92/59/EEC of June 20, 1992 sets out the framework of the present-day European RASFF system, but only for food, and not for feed. However, the subsequent crisis situations with harmful substances in animal feed, which penetrated into the food chain for humans, created the preconditions to expand the system to include the feed too.

Since 2003, the European Commission posts weekly reports on the web site of DG SANCO, the Directorate for Health and Protection of Consumers, containing information on unsafe food and feed found on the EU market or banned from the outer borders of the EU.

The Croatian Food Agency (HAH) has also established its own system of rapid alert, copying the renowned and affirmed European system (HAH, 2006). The activities of the Croatian Food Agency situated in Osijek include in the first place the analysis of risk with respect to food and feed safety. Similar agencies exist in most developed countries. Some of them, like the American Food and Drug Administration, also analyse risks from medical drugs. The key institution on the European level is the EFSA (European Food Safety Authority), established by the European Parliament in 2002, whose seat is in Parma, Italy.

4. Alert due to contamination by ITX of food packaged in tetra pak packaging

In early September 2005 the European RASFF (Rapid Alert System for Food and Feed) informed the European public (ref. No. 2005.631 of 12. September) that contamination by ITX was found in samples of children's milk of the Nestle Group, whereupon 30 million litres of those products were withdrawn from the Italian market. In addition to children's milk, in December 2005, ITX was found in olive oil, wine and fruit juices *(Haglind, 2005b)*.

In mid-January 2006, in the Zagreb Institute of Public Health, the only authorized Croatian laboratory for the detection of ITX in food, contamination by ITX was proven in several fruit juices packaged in Tetra Pak packaging and distributed on the Croatian market. This was the first information released to the public by the Croatian system of rapid alert, which began its work on 1. January 2006.

It is interesting that in Italy higher concentrations of ITX were found in juices which contain fruit pulp, fibres and citrus oils (dense juices), while for example, the findings in apple juices were negative. It was proven that a fatty component in the liquid is necessary for the migration and dissolution of ITX, such as found in milk and dense juices. Likewise, higher concentrations were found in smaller

packaging (200-250 ml). The Croatian Sanitary Inspection decided to follow the Italian example, and, in order to ensure the highest possible health protection of the consumers, decided to withdraw 33,000 packages of Pfanner juices from the Croatian market due to contamination with ITX, until the provision of further scientifically founded information, obtained, among other, from the Scientific Committee for Biological, Chemical and Physical Hazards of the Croatian Food Agency.

The Tetra Pak Company claimed that of the total packaging which the company produced on a world scale, ITX was used in the production of only 1 to 2 per cent. By agreement with the Directorate for Food Safety within the European Commission, Tetra Pak agreed to immediately stop using ITX for the packaging of children's food, after the first indications of contamination of these products, while for all other products a deadline for the cessation of the use of ITX was set on 31. December 2005.

5. Regulations on safety of food packaging

in the Republic of Croatia, pursuant to the Food Act *(Official Gazette 117/03 & 130/03)* subsidiary regulations have been passed – "Ordinance on the Health Safety of Objects which Come into Direct Contact with Food" *(Official Gazette 46/04)* which sets the basic safety requirements for objects which come into contact with foodstuffs

There are two basic (general) conditions which must be satisfied – for the stated objects:

1. They must not be produced from material which releases hazardous compounds, i.e. hazardous in quantities detrimental to health, or which can affect the sensory, physical or chemical properties of the foodstuff, and its preservation in a safe state.

2. They must not be produced from material which is leaky or porous and which does not protect the foodstuff from adverse outside influence.

Chapter IV of the above Ordinance covers the conditions relating to the safety of packaging used in food handling.

For paper packaging which comes into direct contact with food, the Ordinance specifies that it may be impregnated with paraffin, wax, covered with protective lacquer or polymer materials for which strictly defined standards have been prescribed. As stated by the Ordinance on General Declaration or Labelling of Food *(Official Gazette 114/04)*, packaging can in a certain sense be seen as a component of the foodstuff itself. In Article 2, Paragraph 1, this Ordinance defines packaged food as every individual product consisting of food and packaging into which the food was placed before being offered for sale, irrespective of whether the packaging encloses the food completely or only partially.

Regarding the printing and dying of the paper packaging, the Ordinance on the Safety of Objects which Come into Direct Contact with Food prescribes that the paper packaging used for direct packaging of greasy and milk products rich in fats, as well as for the packaging of chocolate, meat products and table salt must not be dyed. This also means that printed surfaces shall not come into direct contact with food. On the outer side, the packaging can have coloured labels (or prints), under the condition that the ink does not penetrate into the food (Article 100, Paragraph 2 of the Ordinance).

This legal provision (in the lack of specific regulation for individual chemical substances which could be found in foodstuffs) enables health control of foodstuffs imported into Croatia, the imposition of a ban on the import and distribution of foodstuffs contaminated by ITX originating from the packaging.

As the EU does not have specific legislation for the use of printing inks for packaging, the health authorities in the EU decided, in the case of foodstuffs contaminated by ITX, to resort to the Directive 1935/2004, which states that sub-

stances hazardous to human health or causing unacceptable changes in the composition or characteristics of food should not be traceable in the food. As ITX is not intended for food colouring, its presence in the food is seen as accidental and undesirable.

6. Assessments of the toxicity of food contaminated by ITX and analyses of risk for the consumers

Upon the request of the European Commission, the European Food Safety Authority – EFSA – carried out a risk analysis for the consumers. Studies in mice and rats excluded the possibility of genotoxic impact on mammal cells. The investigations have shown that even quantities as high as 2g/kg did not have a harmful effect. Based on the concentrations found in juices in Italy, the presumed intake was 12 mg/kg/day in children and 6 mg/kg/day in adults. On the basis of results published so far, ITX can be assumed to be non-carcinogenic and not harmful to human health. Moreover, ITX is (still) not on the World Health Organization list of substances harmful to human health nor is it on the EU's negative list of banned substances in food.

Still, EFSA refrains from taking stance on other possible harmful effects, which will be assessed by further investigations. On 7. December 2005, the Scientific Panel on Food Additives, Flavourings, Processing Aids and Materials in Contact with Food (AFC) of the European Food Safety Authority (EFSA) has adopted an opinion on the possible health risks related to 2-Isopropylthioxanthone (ITX). They concluded that the presence of ITX in foods, whilst undesirable, does not give cause for health concern at the levels reported. This confirms the previous advice published by EFSA on 24. November 2005.

At the same time, a Task Group consisting of our eminent experts has been formed in the Republic of Croatia with the purpose of providing a scientific opinion on the presence of 2-Isoprophylthioxantone in food. The scientific opinion of the Task Group was submitted to the Scientific Council of the Croatian Food Agency in April 2006.

By analysing the data from available materials and scientific literature, the Task Group concluded that the genotoxic effect of ITX should have priority in the assessment of its possible impact on human health. Genotoxic agents are substances whose noxious effect is in the first place caused by direct or indirect impact on hereditary material, i.e. the DNA. The distinctive effect of genotoxic agents also lies in the fact that genetic changes tend to cumulate and are transferred to the offspring.

The Task Group presented its findings and opinions to the Croatian Food Agency, analyzing in particular the opinion of the EFSA, published on 7. December 2005 (EFSA Journal, 2005). The summary of this opinion was sent to the media two days later. The opinion of EFSA could be summarized as follows:

a) ITX, as undesirable as it may be in foodstuffs, does not present a significant health risk and

b) due to the above, there is no need for undertaking any special measures, particularly in view of the fact that the producers (in the first place Tetra Pak) have announced a forthcoming replacement of ITX by alternative methods of package processing.

In the assessment of genotoxic effect, the investigations are conducted in a series ("battery") of tests, each of which responds to a specific question. A positive response in any of these tests means that the tested substance produces a genotoxic effect under certain circumstances and represents an important warning that it is a substance that could have a harmful effect on human health.

Tests were conducted in vitro (on a cell culture and on the bacterium Salmonella typhimurium, where the target cells (animal or bacterial) were directly exposed to ITX or its metabolite generated by metabolic activation) and in vivo,

where the experimental animals (mice and rats) were fed with food containing ITX and the genetic changes were monitored on a chosen tissue or cell types. Both in vitro tests proved positive, while the in vivo test of micronuclear induction in murine bone marrow cells and the test of DNA repair and synthesis in rat liver cells proved negative.

These results suggest that ITX can primarily act as a so-called "direct mutagen", causing errors in DNA synthesis, which later lead to mutations. Although these results do not directly imply that ITX detected in foodstuffs represents an unacceptable risk for human health due to its genotoxic effect, they do show that such a possibility exists and that additional research is necessary in order to arrive at a scientifically founded conclusion.

On the basis of the above facts, the Task Group believes that the conclusion of the investigation is surprising because "The results of the investigation of the genotoxic effect of ITX were contradictory in a limited number of in vitro studies, while clearly negative results were obtained in two appropriate in vivo studies". Hence, it can be concluded that the in vivo studies do not point to a genotoxic potential of ITX.

Finally, the opinion of the appointed Task Group on the presence of 2-Isopropylthioxantone (ITX) in food can be summarized as follows:

1. It is evident that the food which contains ITX is unfit for human consumption because it contains a substance, which has not been toxicologically evaluated, verified and proven safe for human use. Moreover, taking into account the positive results obtained in mutagenicity tests, the cumulative effect of mutagens, as well as the special exposure of the youngest population to food which contains ITX, we believe that the presence of such food on the market is unacceptable because it presents a risk for consumer health.

2. In the absence of appropriate studies for a comprehensive assessment of the genotoxic effect of ITX, we believe that the presence of ITX in food in a concentration equal to or greater than 5 μg/L is unacceptable because it presents a risk for consumer health *(Scientific Opinion on the Presence of ITX in Food, 2006).*

7. Monitoring of imported foodstuffs for contamination by ITX in Croatia

The Ministry of Health and Social Welfare of the Republic of Croatia, among other duties, monitors the import of food and objects of general use through its service of border sanitary inspection. The officials on border posts have been ordered to check the imported foodstuffs packaged in Tetra Pak packaging for possible contamination by ITX. In the first four weeks of 2006, the Zagreb Institute of Public Health detected contamination by ITX of fruit juices imported from Austria, packaged in Tetra Pak packaging.

8. Most recent information on ITX in foodstuffs

The reports posted on the web site of EU RASFF for the first 9 weeks of 2006 reveal sporadic cases of detection of ITX in various foodstuffs, such as children's milk, fruit juices, milk sauces, cream, and yoghurt. Apparently these are the remainders of old stock of incriminated packaging, which was still used to package foodstuffs. All the cases in 2006 (according to EU RASFF weekly reports on the findings of ITX in foodstuffs) were detected in Italy, where, in September 2005, the whole "episode" with ITX started. This tells us that the Italian public is highly aware of the fact that a chemical substance appears in foodstuffs as a contaminant, a substance on whose possible toxicity and implications for the health of consumers we still can only speculate (until the publication of the results of detailed toxicological investigation).

9. Conclusions

The rapid alert system which has been in place in the Republic of Croatia since 1 January 2006 functions according to its European model RASFF, on the basis of which it was structured, and reacts in cases of direct and indirect risk for coming from food.

We could conclude that the European legislation on food safety was in a way caught unprepared – after the first alarming news on the contamination of food by ITX (food packaged in highest quality packaging and, until now, impeccable guarantees of health safety). Likewise, there is a pending conclusion that amendments to the regulations on the health control of food are likely to be adopted. Undoubtedly, the experience with ITX as a "new type" of food contaminant will contribute to the increase in the number of health safety parameters, which must be analytically verified in deciding whether a certain food is safe. In brief, on the basis of the experience with Tetra Pak packaging, we can assume that monitoring of foodstuffs (packaged in this and similar packaging) for specific contamination by printing inks could soon become part of "routine control" of the health safety of foodstuffs.

References

AURELA, B., SÖDERHJELM, L. 2007, „Food packaging inks and varnishes and chemical migration into food", in K. A. Barnes et al. (ed.) Chemical migration and food contact materials, Woodhead Publishing Limited, Cambridge, England 2007, 304

AMBALAZA JOURNAL, 2005; ITX, opasnost iz ambalaže?; Professional journal for manufacturers and users of packaging and printing industry, No. 4, December 2005 (in Croatian)

EFSA JOURNAL, 2005, Opinion of the Scientific Panel on Food Additives, Flavourings, Processing Aids and Materials in Contact with Food on a request from the Commission related to 2- isopropylthioxanthone (ITX) and 2-ethylhexyl-4-dimethylaminobenzoate (EHDAB) in food contact materials, 2005, 293:1-15

HAGLIND, J., 2005a, Isopropylthioxanthone (ITX) in Food Packed in TetraPak Bricks Printed with UV-Cured Inks (Revised Preliminary Safety Evaluation, 23. 09. 2005.), 2005, 1-8

HAGLIND, J., 2005b, Migration of Isopropylthioxanthone (ITX) in fat containing food products RASFF 2005. 631, 2005, 1-3

NARODNE NOVINE RH, 117, 2003; 130, 2003 AND 48, 2004, Zakon o hrani (Food Act), (in Croatian)

NARODNE NOVINE RH, 46, 2004, Pravilnik o zdravstvenoj ispravnosti predmeta koji dolaze u neposredan dodir s hranom (Ordinance on the health safety of objects which come into direct contact with food), (in Croatian)

NARODNE NOVINE RH, 114, 2004, Pravilnik o općem deklariranju ili označavanju hrane (Ordinance on the general declaring or labelling of food), (in Croatian)

SRŠEN, A., 1999, Sušenje tiskarskih boja, Graduation thesis, Faculty of Graphic Arts of the University of Zagreb, 1999 (in Croatian)

***WWW.HAH.HR/DOC/MISLJENJE_O_ITX-U.DOC Znanstveno mišljenje o prisutnosti 2-isopropylthioxantona (ITX-a) u hrani (Scientific opinion on the presence of 2-Isoprophylthioxantone in food.), April 11th 2006, , (in Croatian)

***WWW.HAH.HR, viewed January 2006.

***WWW.TETRAPAK.COM, viewed January 2006.